Clinical trial results:
A Phase 3, Open-Label, Randomized, Parallel, 2-Arm, Multi-Center Study of Talazoparib (BMN 673) Versus Physician's Choice in Germline BRCA Mutation Subjects With Locally Advanced and/or Metastatic Breast Cancer, Who Have Received Prior Chemotherapy Regimens for Metastatic Disease

Summary

EudraCT number	2013-002716-28
Trial protocol	GB BE IT IE FR ES DE PL
Global end of trial date	05 March 2021

Results information

Result version number	v2 (current)
This version publication date	11 January 2022
First version publication date	21 September 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	673-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01945775
WHO universal trial number (UTN)	U1111-1155-7579

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the progression free survival (PFS) of subjects treated with talazoparib as a monotherapy relative to those treated with protocol-specified physician's choice treatment (PCT).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	28 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Brazil: 25
Country: Number of subjects enrolled	France: 50
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Korea, Republic of: 32
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Ukraine: 1
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 156
Worldwide total number of subjects	431
EEA total number of subjects	146

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)	394
From 65 to 84 years	35
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study was conducted from 14-Oct-2013 to 05-Mar-2021 at multiple sites.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Talazoparib

Arm description:

Subjects received talazoparib 1 milligram (mg), orally, once daily, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 70.2 months). One cycle was of 21 days.

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

Dosage and administration details:

Subjects received talazoparib 1 mg, orally, once daily, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 70.2 months).

Arm title	Physician's Choice Treatment

Arm description:

Subjects received 1 of the following drugs in specified regimens, as per the physician’s choice: 1) capecitabine 1250 milligram per meter square (mg/m^2) orally twice daily on Day 1 to 14 in each cycle; 2) eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/ m^2), as 2 to 5 minute intravenous (IV) infusion on Day 1 and 8 in each cycle; 3) gemcitabine 1250 mg/m^2 as 30-minute IV infusion on Day 1 and 8 in each cycle; 4) vinorelbine 30 mg/m^2 as 6 to 10 minute IV infusion on Day 1, 8, and 15 in each cycle; until radiographic disease progression as determined by the central IRF, unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 45.3 months). One cycle was of 21 days.

Arm type	Active comparator
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received Capecitabine 1250 milligram per meter square (mg/m^2) orally twice daily on Day 1 to 14 for 21 day cycle, as per the physician’s choice, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 45.3 months).

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

Dosage and administration details:

Subjects received Eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/ m^2), as 2 to 5 minute intravenous (IV) infusion on Day 1 and 8 for 21 day cycle, as per the physician's choice, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 45.3 months).

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

Dosage and administration details:

Subjects received Gemcitabine 1250 mg/m^2 as 30-minute IV infusion on Day 1 and 8 for 21 day cycle, as per the physician's choice, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 45.3 months).

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

Dosage and administration details:

Subjects received Vinorelbine 30 mg/m^2 as 6 to 10 minute IV infusion on Day 1, 8, and 15 for 21 day cycle, as per the physician's choice, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 45.3 months).

Number of subjects in period 1	Talazoparib	Physician's Choice Treatment
Started	287	144
Treated	286	126
Completed	0	0
Not completed	287	144
Consent withdrawn by subject	11	21
Death	214	98
Unspecified	50	18
Lost to follow-up	12	7

Baseline characteristics

Reporting groups	
Reporting group title	Talazoparib
Reporting group description:	
Subjects received talazoparib 1 milligram (mg), orally, once daily, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 70.2 months). One cycle was of 21 days.	
Reporting group title	Physician's Choice Treatment
Reporting group description:	
Subjects received 1 of the following drugs in specified regimens, as per the physician's choice: 1) capecitabine 1250 milligram per meter square (mg/m^2) orally twice daily on Day 1 to 14 in each cycle; 2) eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/ m^2), as 2 to 5 minute intravenous (IV) infusion on Day 1 and 8 in each cycle; 3) gemcitabine 1250 mg/m^2 as 30-minute IV infusion on Day 1 and 8 in each cycle; 4) vinorelbine 30 mg/m^2 as 6 to 10 minute IV infusion on Day 1, 8, and 15 in each cycle; until radiographic disease progression as determined by the central IRF, unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 45.3 months). One cycle was of 21 days.	

Reporting group values	Talazoparib	Physician's Choice Treatment	Total
Number of subjects	287	144	431
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)	260	134	394
From 65-84 years	27	8	35
85 years and over	0	2	2
Age Continuous Units: Years			
arithmetic mean	47.5	49.4	
standard deviation	± 11.61	± 12.12	-
Sex: Female, Male Units: Subjects			
Female	283	141	424
Male	4	3	7
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	31	16	47
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	11	1	12
White	190	108	298
More than one race	0	0	0

Unknown or Not Reported	55	19	74
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	31	15	46
Not Hispanic or Latino	207	111	318
Unknown or Not Reported	49	18	67

End points

End points reporting groups

Reporting group title	Talazoparib

Reporting group description:

Subjects received talazoparib 1 milligram (mg), orally, once daily, until radiographic disease progression as determined by the central independent radiology facility (IRF), unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 70.2 months). One cycle was of 21 days.

Reporting group title	Physician's Choice Treatment

Reporting group description:

Subjects received 1 of the following drugs in specified regimens, as per the physician's choice: 1) capecitabine 1250 milligram per meter square (mg/m^2) orally twice daily on Day 1 to 14 in each cycle; 2) eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/ m^2), as 2 to 5 minute intravenous (IV) infusion on Day 1 and 8 in each cycle; 3) gemcitabine 1250 mg/m^2 as 30-minute IV infusion on Day 1 and 8 in each cycle; 4) vinorelbine 30 mg/m^2 as 6 to 10 minute IV infusion on Day 1, 8, and 15 in each cycle; until radiographic disease progression as determined by the central IRF, unacceptable toxicity, consent withdrawal, physician's decision to terminate treatment, or Sponsor's decision to terminate the trial (up to a maximum of 45.3 months). One cycle was of 21 days.

Primary: Progression-Free Survival (PFS): Independent Radiological Facility (IRF) Assessment

End point title	Progression-Free Survival (PFS): Independent Radiological Facility (IRF) Assessment

End point description:

IRF assessed PFS was defined as time (in months) from randomization until the date of first documented radiologic progressive disease per response evaluation criteria in solid tumors (RECIST) version 1.1 or death from any cause, whichever occurs first. As per RECIST v1.1, progression defined as 1) for target lesions: at least a 20% increase in the sum of target lesion measurements, compared to the smallest sum on study (including baseline), the absolute increase in the sum has to be at least 5 millimetre (mm); 2) for non-target lesions: unequivocal progression of non-target lesions, evaluated as a whole, such that it is clear that treatment has failed and disease is progressing, regardless of the status of the target lesions; 3) and/or appearance of one or more new lesions. The analysis was performed by Kaplan-Meier method. Intent-to-treat (ITT) analysis population included all randomized subjects.

End point type	Primary

End point timeframe:

Baseline until radiologic progressive disease or death due to any cause (up to maximum duration of 36.9 months)

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	144		
Units: months				
median (confidence interval 95%)	8.6 (7.2 to 9.3)	5.6 (4.2 to 6.7)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment

Statistical analysis description:

Hazard ratio was based on stratified Cox regression model with treatment as the only covariate (stratification factors: number of prior cytotoxic chemotherapy regimens, triple negative status, history of central nervous system metastasis status).

Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Logrank
Parameter estimate	Log hazard ratio
Point estimate	0.542
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.413
upper limit	0.711

Secondary: Percentage of Subjects With Objective Response: Investigator Assessment

End point title	Percentage of Subjects With Objective Response: Investigator Assessment

End point description:

Investigator assessed overall response was defined as the percentage of subjects with a partial response (PR) or complete response (CR) as defined by RECIST v1.1. For target lesions: 1) CR: disappearance of all non-nodal target lesions. Target lymph nodes must reduce to less than 10 mm in short axis. 2) PR: At least a 30% decrease in the sum of diameters of target lesions, compared to the sum at baseline. For non-target lesions, CR: disappearance of all non-target lesions. ITT analysis population included all randomized subjects. Percentage of subjects with objective response reported are based upon unconfirmed CR/PR. ITT with measurable disease analysis population included all subjects in the ITT population who had at least 1 target lesion identified at baseline.

End point type	Secondary

End point timeframe:

Baseline until radiologic progressive disease or death due to any cause (up to a maximum duration of 36.9 months)

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	114		
Units: percentage of subjects				
number (confidence interval 95%)	62.6 (55.78 to 68.99)	27.2 (19.28 to 36.33)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment

Statistical analysis description:

p-value was based on stratified Cochran-Mantel-Haenszel method. Stratification factors: number of prior cytotoxic chemotherapy regimens, triple negative status, history of central nervous system metastasis status.

Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.93
upper limit	8.83

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time (in months) from randomization to death due to any cause. If death was not observed at the time of study cut-off date or permanently lost to follow-up, OS was censored at the date the subject was last known to be alive on or before the study cut-off date, whichever was earlier. The analysis was performed by Kaplan-Meier method. ITT analysis population included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline until death due to any cause or analysis cut-off, up to a maximum duration of 61.4 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	144		
Units: months				
median (confidence interval 95%)	19.3 (16.6 to 22.5)	19.5 (17.4 to 22.4)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment

Statistical analysis description:

Hazard ratio was based on stratified Cox regression model with treatment as the only covariate (stratification factors: number of prior cytotoxic chemotherapy regimens, triple negative status, history of central nervous system metastasis status).

Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1693
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.848
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.073

Secondary: Trough Plasma Talazoparib Concentrations

End point title	Trough Plasma Talazoparib Concentrations[1]

End point description:

A predose PK sample was considered dose-compliant based on the following criteria: A subject must have received 21 consecutive days of 1 mg talazoparib without dosing interruption prior to sample collection; and the predose PK sample must have been collected 24 hours +/- 10% (2 hours and 24 minutes) after the previous day's dose and no more than 5 minutes (0.083 hours) after the administration of the dose on the day of PK sample collection. Analysis population included subjects who received at least 1 dose of talazoparib and had dose compliant pharmacokinetic (PK) predose sample. Here, "n" signifies number of subjects who were evaluable for the specified categories. This endpoint was not planned to be analysed for the reporting arm "Physician's Choice Treatment".

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycle 2, 3 and 4

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed only for reporting arm "Talazoparib".

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Picogram per milliliter (pg/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 2 Day 1: Predose (n=137)	3370 (± 76.9)			
Cycle 3 Day 1: Predose (n=120)	3570 (± 49.9)			
Cycle 4 Day 1: Predose (n=107)	3400 (± 48.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence (eg, sign, symptom, illness, disease or injury) in a subject administered study drug or other protocol-imposed intervention, regardless of attribution. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to primary analysis data cut-off date or the day before initiation of a new antineoplastic therapy or 30 days after the date of the last dose date of study drug, whichever occurred first, that were absent before treatment or that worsened relative to pretreatment state. AEs included both SAEs and all non-SAEs. Safety analysis population.

End point type	Secondary

End point timeframe:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	126		
Units: subjects				
TEAEs	282	123		
SAEs	103	39		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or 4 Post baseline Toxicities in Laboratory Parameters: Hematology

End point title	Number of Subjects With Grade 3 or 4 Post baseline Toxicities in Laboratory Parameters: Hematology

End point description:

Toxicity grades were evaluated based on as National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03 (NCI CTCAE v4.03). NCI CTCAE v4.03 defined the severity grade as: grade 1 (mild), grade 2 (moderate), grade 3 (severe) and grade 4 (potentially life threatening) and grade 5 (death related to AE) for each parameter. Key hematology parameters included hemoglobin (gram per liter [g/L]), leukocytes (10^6 cells per liter), lymphocytes (10^6 cells per liter), neutrophils (10^6 cells per liter), and platelets (10^9 cells per liter). Low value indicated lower values than the baseline values and high value indicated higher values than the baseline values. Only those categories in which at least 1 subject had data were reported. Safety analysis population included all subjects who received at least 1 dose of any study drug (talazoparib or protocol-specified PCT).

End point type	Secondary

End point timeframe:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	126		
Units: subjects				
Hemoglobin: Low value	115	8		
Leukocytes: Low value	43	31		
Lymphocytes: Low value	54	11		
Neutrophils: Low value	65	48		
Platelets: Low value	44	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or 4 Post baseline Toxicities in Laboratory Parameters: Chemistry

End point title	Number of Subjects With Grade 3 or 4 Post baseline Toxicities in Laboratory Parameters: Chemistry

End point description:

Toxicity grades were evaluated based on as NCI CTCAE v4.03. NCI CTCAE v4.03 defined the severity grade as: grade 1 (mild), grade 2 (moderate), grade 3 (severe) and grade 4 (potentially life threatening) and grade 5 (death related to AE) for each parameter. Key chemistry parameters included alanine aminotransferase (units per liter), alkaline phosphatase (units per liter), aspartate aminotransferase (units per liter) and bilirubin (micromole per liter). High value indicated higher values than the baseline values and low value indicated lower values than the baseline values. Only those categories in which at least 1 subject had data were reported. Safety analysis population included all subjects who received at least 1 dose of any study drug (talazoparib or protocol-specified PCT).

End point type	Secondary

End point timeframe:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	126		
Units: subjects				
Alanine Aminotransferase: High Value	5	3		
Alkaline Phosphatase: High Value	6	2		
Aspartate Aminotransferase: High Value	7	4		
Bilirubin: High Value	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Significant Changes From Baseline in Vital Signs

End point title	Number of Subjects With Potentially Clinically Significant Changes From Baseline in Vital Signs

End point description:

Criteria for potentially clinically significant changes in vital signs included a) Systolic blood pressure: 1) absolute results (AB) greater than (>) 180 millimetre of mercury (mmHg) and increase from baseline (IFB) greater than or equal to (>=) 40 mmHg, 2) absolute results less than (<) 90 mmHg and decrease from baseline (DFB) >30 mmHg; b) Diastolic blood pressure: 1) absolute results >110 mmHg and >=30 mmHg increase from baseline, 2) absolute results <50 mmHg and >20 mmHg decrease from baseline 3) >=20 mmHg increase from baseline); c) Heart rate: 1) absolute results>120 beats per minute [bpm] and >30 bpm increase from baseline, 2) absolute results <50 bpm and >20 bpm decrease from baseline) and d) Weight: >10 percent [%] decrease from baseline. Safety analysis population included all subjects who received at least 1 dose of any study drug (talazoparib or protocol-specified PCT).

End point type	Secondary

End point timeframe:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	126		
Units: subjects				
SBP: AB>180 mmHg and IFB >=40 mmHg	3	2		
SBP: AB<90 mmHg and DFB >30 mmHg	8	2		
DBP: AB>110 mmHg and IFB >=30 mmHg	0	0		
DBP: AB<50 mmHg and DFB>20 mmHg	15	7		
DBP: IFB>=20 mmHg	39	13		
Heart rate: AB >120 bpm and IFB >30 bpm	6	2		
Heart rate: AB <50 bpm and DFB >20 bpm	2	0		
Weight: >10% DFB	23	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Taking At least One Concomitant Medication

End point title	Number of Subjects Taking At least One Concomitant Medication

End point description:

Any medication (other than study drug) which was administered to subjects during study after first dose of study drug were considered as concomitant medications. Safety analysis population included all subjects who received at least 1 dose of any study drug (talazoparib or protocol-specified PCT).

End point type	Secondary

End point timeframe:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	126		
Units: subjects	281	126		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Duration of Response (DOR): Investigator Assessment

End point title	Duration of Response (DOR): Investigator Assessment

End point description:

DOR = time from first radiographic documentation of OR (PR or CR) till radiographic disease progression (PD) as per RECIST v1.1 by investigator assessment or to death due to any cause, whichever was first. RECIST 1.1, a) target lesion (TL): CR= disappearance of all non-nodal TL, target lymph nodes reduce to <10 mm in short axis, PR= at least 30% decrease in sum of diameters of TL, compared to the sum at baseline, PD= at least 20% increase in sum of TL measurements, compared to smallest sum on study including baseline, absolute increase in sum has to be at least 5 mm; b) for non-TL: CR= disappearance of all non-TL. PD= unequivocal progression of non-TL, such that treatment has failed, disease is progressing, regardless of status of TL; c) PD = and/or appearance of >=1 new lesions. Kaplan-Meier method used. ITT with measurable disease analysis population: ITT population who had at least 1 target lesion identified at baseline.

End point type	Other pre-specified

End point timeframe:

From first documentation of CR or PR until disease progression or death due to any cause, whichever occurred first (up to 36.9 months)

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	114		
Units: months				
median (inter-quartile range (Q1-Q3))	5.4 (2.8 to 11.2)	3.1 (2.4 to 6.7)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Global Health Status/Quality of Life (QoL) Measured by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) at Average Duration Over Week 4 up to Week 160

End point title	Change From Baseline in Global Health Status/Quality of Life (QoL) Measured by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) at Average Duration Over Week 4 up to Week 160

End point description:

EORTC QLQ-C30: 30 questions to assess subject QoL. First 28 questions:5 functional scales(physical, role,cognitive,emotional,social),3 symptom scales(fatigue,nausea and vomiting,pain) and other single items(dyspnea,appetite loss,insomnia,constipation,diarrhea and financial difficulties).Each question assessed on 4-point scale(1=not at all, 2=a little, 3=quite a bit, 4=very much);functional scale:higher score=better level of functioning; symptom scale: higher score=more severe symptoms. Last 2 questions: GHS/QoL. Each question assessed on 7-point scale 1(very poor)-7(excellent). Score averaged, transformed to 0-100 scale; higher score=better QoL. Patient-reported outcomes (PRO) evaluable population: all subjects who completed PRO questionnaire at baseline and atleast 1 visit postbaseline.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 4 up to Week 160

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	114		
Units: units on a scale				
arithmetic mean (confidence interval 95%)	3.0 (1.2 to 4.8)	-5.4 (-8.8 to -2.0)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment

Statistical analysis description:

Analysis was based on repeated measures mixed-effect model with an intercept term, treatment, time, treatment-by-time, and baseline as covariate. Analysis was based on restricted maximum likelihood using unstructured covariance matrix.

Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	8.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	12.3

Other pre-specified: Time to Deterioration (TTD) in Global Health Status (GHS)/Quality of Life (QOL)

End point title	Time to Deterioration (TTD) in Global Health Status (GHS)/Quality of Life (QOL)

End point description:

TTD in global health status (GHS)/QoL=time (in months) from randomization to the first observation with >=10 point decrease and no subsequent observations with<10 point decrease from baseline in GHS/QoL score based on EORTC-QLQ-C30. EORTC QLQ-C30 is a cancer-specific instrument with 30 questions to assess subject quality of life. Question 29 and 30 were used to evaluate GHS/QoL. Each question was assessed on a 7-point scale (1=very poor to 7=excellent). Scores averaged, transformed to 0-100 scale; higher score=better quality of life/better level of functioning. Here, 99999 = upper 95% CI was not estimable, since only few subjects had event. PRO-evaluable population included all subject who completed the PRO questionnaire at baseline and at least 1 visit postbaseline.

End point type	Other pre-specified

End point timeframe:

Baseline up to a maximum duration of 36.9 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	114		
Units: months				
median (confidence interval 95%)	24.3 (13.8 to 99999)	6.3 (4.9 to 12.2)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment

Statistical analysis description:

Hazard ratio is based on stratified Cox regression model with treatment as the only covariate (stratification factors: number of prior cytotoxic chemotherapy regimens, triple negative status, history of central nervous system).

Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.376

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.257
upper limit	0.549

Other pre-specified: Time to Deterioration (TTD) in Breast Symptoms Scale as Assessed by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Breast Cancer Module (EORTC-QLQ-BR23)

End point title	Time to Deterioration (TTD) in Breast Symptoms Scale as Assessed by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Breast Cancer Module (EORTC-QLQ-BR23)

End point description:

TTD was defined as the time from randomization to the first observation with a>=10 point increase and no subsequent observations with a <10 point increase from baseline in breast symptom score based on the EORTC-QLQ-BR23. EORTC-QLQ-BR23 is a disease-specific module for breast cancer developed as a supplement for the EORTC-QLQ-C30 to assess the quality of life of subjects with breast cancer. EORTC-QLQ-BR23 symptoms subscale includes 4 items: systemic therapy side effects, breast symptoms, arm symptoms, upset by hair loss. Each item is rated by choosing 1 of 4 possible responses that record the level of intensity (1= not at all, 2= a little, 3= quite a bit, and 4= very much) within each scale. PRO-evaluable population included all subjects who completed the PRO questionnaire at baseline and at least 1 visit postbaseline. Here, 99999 = median and 95% CI was not estimable due to the low number of subjects with event.

End point type	Other pre-specified

End point timeframe:

Baseline up to a maximum duration of 36.9 months

End point values	Talazoparib	Physician's Choice Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	114		
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (10.3 to 99999)		

Statistical analyses

Statistical analysis title	Talazoparib versus Physician's Choice Treatment
Comparison groups	Talazoparib v Physician's Choice Treatment
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0053
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.392

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.198
upper limit	0.775

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Talazoparib: Baseline up to a maximum duration of 71.3 months; Physician’s Choice Treatment: Baseline up to maximum duration of 46.1 months

Adverse event reporting additional description:

Same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study. AEs and SAEs were collected for safety population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v20.0

Reporting groups

Reporting group title	Physician's Choice Treatment

Reporting group description:

Subjects received 1 of the following drugs in specified regimens, as per the physician’s choice: 1) capecitabine 1250 mg/m^2 orally twice daily on Day 1 to 14 in each cycle; 2) eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/ m^2), as 2 to 5 minute IV infusion on Day 1 and 8 in each cycle; 3) gemcitabine 1250 mg/m^2 as 30-minute IV infusion on Day 1 and 8 in each cycle; 4) vinorelbine 30 mg/m^2 as 6 to 10 minute IV infusion on Day 1, 8, and 15 in each cycle; until radiographic disease progression as determined by the central IRF, unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 45.3 months). One cycle was of 21 days.

Reporting group title	Talazoparib

Reporting group description:

Subjects received talazoparib 1 mg, orally, once daily, until radiographic disease progression as determined by the central IRF, unacceptable toxicity, consent withdrawal, physician’s decision to terminate treatment, or Sponsor’s decision to terminate the trial (up to a maximum of 70.2 months). One cycle was of 21 days.

Serious adverse events	Physician's Choice Treatment	Talazoparib	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 126 (30.95%)	103 / 286 (36.01%)	
number of deaths (all causes)	100	220	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 126 (0.00%)	4 / 286 (1.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			

subjects affected / exposed	1 / 126 (0.79%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to pancreas			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute promyelocytic leukaemia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Second primary malignancy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis malignant			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 126 (1.59%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Breast reconstruction			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingo-oophorectomy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenectomy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 126 (1.59%)	8 / 286 (2.80%)	
occurrences causally related to treatment / all	1 / 2	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 126 (1.59%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Non-cardiac chest pain			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Discomfort			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	7 / 126 (5.56%)	4 / 286 (1.40%)	
occurrences causally related to treatment / all	0 / 8	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	0 / 126 (0.00%)	4 / 286 (1.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 126 (0.00%)	6 / 286 (2.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumopathy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed mood			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 126 (0.00%)	4 / 286 (1.40%)	
occurrences causally related to treatment / all	0 / 0	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 126 (1.59%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	6 / 6	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scar			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 126 (0.00%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 126 (0.00%)	5 / 286 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 126 (0.79%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neurological symptom			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	2 / 126 (1.59%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 126 (0.00%)	18 / 286 (6.29%)	
occurrences causally related to treatment / all	0 / 0	20 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 126 (3.17%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	4 / 4	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 126 (0.79%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	2 / 126 (1.59%)	5 / 286 (1.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 126 (1.59%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 126 (0.79%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 126 (2.38%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	2 / 126 (1.59%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Venoocclusive liver disease			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cholecystitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Scar pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary retention			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
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			
Back pain			
subjects affected / exposed	1 / 126 (0.79%)	5 / 286 (1.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 126 (0.79%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 126 (0.79%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal chest pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 126 (1.59%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 126 (0.79%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 126 (1.59%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Physician's Choice Treatment	Talazoparib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	123 / 126 (97.62%)	282 / 286 (98.60%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	9 / 126 (7.14%)	23 / 286 (8.04%)	
occurrences (all)	9	30	

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 126 (9.52%)	45 / 286 (15.73%)	
occurrences (all)	17	103	
Fatigue			
subjects affected / exposed	54 / 126 (42.86%)	147 / 286 (51.40%)	
occurrences (all)	97	260	
Pyrexia			
subjects affected / exposed	21 / 126 (16.67%)	31 / 286 (10.84%)	
occurrences (all)	34	45	
Oedema peripheral			
subjects affected / exposed	8 / 126 (6.35%)	23 / 286 (8.04%)	
occurrences (all)	14	28	
Mucosal inflammation			
subjects affected / exposed	9 / 126 (7.14%)	16 / 286 (5.59%)	
occurrences (all)	11	19	
Influenza like illness			
subjects affected / exposed	2 / 126 (1.59%)	20 / 286 (6.99%)	
occurrences (all)	2	33	
Non-cardiac chest pain			
subjects affected / exposed	5 / 126 (3.97%)	17 / 286 (5.94%)	
occurrences (all)	6	18	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 126 (15.08%)	54 / 286 (18.88%)	
occurrences (all)	25	88	
Cough			
subjects affected / exposed	20 / 126 (15.87%)	65 / 286 (22.73%)	
occurrences (all)	24	102	
Oropharyngeal pain			
subjects affected / exposed	10 / 126 (7.94%)	28 / 286 (9.79%)	
occurrences (all)	16	34	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 126 (7.94%)	38 / 286 (13.29%)	
occurrences (all)	10	47	

Depression			
subjects affected / exposed	4 / 126 (3.17%)	24 / 286 (8.39%)	
occurrences (all)	4	28	
Anxiety			
subjects affected / exposed	9 / 126 (7.14%)	24 / 286 (8.39%)	
occurrences (all)	10	29	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	18 / 126 (14.29%)	30 / 286 (10.49%)	
occurrences (all)	42	98	
Weight decreased			
subjects affected / exposed	15 / 126 (11.90%)	23 / 286 (8.04%)	
occurrences (all)	19	33	
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 126 (11.90%)	15 / 286 (5.24%)	
occurrences (all)	29	21	
White blood cell count decreased			
subjects affected / exposed	5 / 126 (3.97%)	32 / 286 (11.19%)	
occurrences (all)	7	86	
Platelet count decreased			
subjects affected / exposed	4 / 126 (3.17%)	36 / 286 (12.59%)	
occurrences (all)	7	128	
Alanine aminotransferase increased			
subjects affected / exposed	15 / 126 (11.90%)	11 / 286 (3.85%)	
occurrences (all)	26	14	
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 126 (10.32%)	51 / 286 (17.83%)	
occurrences (all)	17	69	
Headache			
subjects affected / exposed	29 / 126 (23.02%)	96 / 286 (33.57%)	
occurrences (all)	39	146	
Dysgeusia			
subjects affected / exposed	11 / 126 (8.73%)	30 / 286 (10.49%)	
occurrences (all)	12	39	
Paraesthesia			

subjects affected / exposed	15 / 126 (11.90%)	13 / 286 (4.55%)	
occurrences (all)	20	16	
Peripheral sensory neuropathy			
subjects affected / exposed	7 / 126 (5.56%)	2 / 286 (0.70%)	
occurrences (all)	8	3	
Neuropathy peripheral			
subjects affected / exposed	9 / 126 (7.14%)	19 / 286 (6.64%)	
occurrences (all)	10	23	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	24 / 126 (19.05%)	153 / 286 (53.50%)	
occurrences (all)	57	746	
Thrombocytopenia			
subjects affected / exposed	7 / 126 (5.56%)	50 / 286 (17.48%)	
occurrences (all)	10	140	
Neutropenia			
subjects affected / exposed	36 / 126 (28.57%)	77 / 286 (26.92%)	
occurrences (all)	113	279	
Leukopenia			
subjects affected / exposed	12 / 126 (9.52%)	24 / 286 (8.39%)	
occurrences (all)	43	70	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	9 / 126 (7.14%)	10 / 286 (3.50%)	
occurrences (all)	10	11	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	60 / 126 (47.62%)	142 / 286 (49.65%)	
occurrences (all)	100	228	
Diarrhoea			
subjects affected / exposed	32 / 126 (25.40%)	68 / 286 (23.78%)	
occurrences (all)	77	139	
Vomiting			
subjects affected / exposed	28 / 126 (22.22%)	74 / 286 (25.87%)	
occurrences (all)	47	126	
Abdominal pain			

subjects affected / exposed	18 / 126 (14.29%)	36 / 286 (12.59%)	
occurrences (all)	24	50	
Constipation			
subjects affected / exposed	28 / 126 (22.22%)	66 / 286 (23.08%)	
occurrences (all)	47	89	
Dyspepsia			
subjects affected / exposed	10 / 126 (7.94%)	33 / 286 (11.54%)	
occurrences (all)	14	41	
Stomatitis			
subjects affected / exposed	7 / 126 (5.56%)	24 / 286 (8.39%)	
occurrences (all)	11	36	
Dry mouth			
subjects affected / exposed	8 / 126 (6.35%)	19 / 286 (6.64%)	
occurrences (all)	9	25	
Abdominal pain upper			
subjects affected / exposed	5 / 126 (3.97%)	28 / 286 (9.79%)	
occurrences (all)	6	33	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	35 / 126 (27.78%)	78 / 286 (27.27%)	
occurrences (all)	37	87	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	28 / 126 (22.22%)	4 / 286 (1.40%)	
occurrences (all)	71	5	
Dry skin			
subjects affected / exposed	9 / 126 (7.14%)	14 / 286 (4.90%)	
occurrences (all)	10	20	
Rash			
subjects affected / exposed	12 / 126 (9.52%)	29 / 286 (10.14%)	
occurrences (all)	18	37	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	14 / 126 (11.11%)	45 / 286 (15.73%)	
occurrences (all)	20	62	
Back pain			

subjects affected / exposed	19 / 126 (15.08%)	67 / 286 (23.43%)	
occurrences (all)	28	104	
Arthralgia			
subjects affected / exposed	15 / 126 (11.90%)	55 / 286 (19.23%)	
occurrences (all)	18	95	
Musculoskeletal chest pain			
subjects affected / exposed	9 / 126 (7.14%)	28 / 286 (9.79%)	
occurrences (all)	9	33	
Musculoskeletal pain			
subjects affected / exposed	9 / 126 (7.14%)	29 / 286 (10.14%)	
occurrences (all)	9	36	
Myalgia			
subjects affected / exposed	14 / 126 (11.11%)	25 / 286 (8.74%)	
occurrences (all)	22	33	
Bone pain			
subjects affected / exposed	7 / 126 (5.56%)	15 / 286 (5.24%)	
occurrences (all)	11	18	
Neck pain			
subjects affected / exposed	6 / 126 (4.76%)	17 / 286 (5.94%)	
occurrences (all)	6	24	
Muscle spasms			
subjects affected / exposed	3 / 126 (2.38%)	18 / 286 (6.29%)	
occurrences (all)	5	25	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	13 / 126 (10.32%)	41 / 286 (14.34%)	
occurrences (all)	14	61	
Viral upper respiratory tract infection			
subjects affected / exposed	8 / 126 (6.35%)	35 / 286 (12.24%)	
occurrences (all)	8	56	
Urinary tract infection			
subjects affected / exposed	3 / 126 (2.38%)	30 / 286 (10.49%)	
occurrences (all)	5	42	
Sinusitis			
subjects affected / exposed	4 / 126 (3.17%)	21 / 286 (7.34%)	
occurrences (all)	6	25	

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	28 / 126 (22.22%) 32	62 / 286 (21.68%) 93	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 June 2019	1. Change in study visit frequency and study procedures as final OS analysis was achieved.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported