Clinical trial results:
A Single-Arm, Open-Label, Multicenter, Extended Treatment, Safety Study in Patients Treated With Talazoparib

Summary

EudraCT number	2016-001972-31
Trial protocol	GB HU PL DE
Global end of trial date	20 July 2021

Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

Trial information

Trial identification

Sponsor protocol code	MDV3800-13 (C3441010)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02921919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E42nd 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	07 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to obtain additional safety data on long-term talazoparib use.

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 Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2016
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	Canada: 23
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Moldova, Republic of: 1
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 62
Worldwide total number of subjects	118
EEA total number of subjects	17

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	68
From 65 to 84 years	47
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Eligible subjects who received talazoparib as a single agent or in combination with another agent in following qualifying studies: PRP-001(NCT01286987), MDV3800-01(NCT02997163), MDV3800-02(NCT02997176), MDV3800-03(NCT03070548), MDV3800-04(NCT03077607), MDV3800-14(NCT03042910) continued talazoparib therapy as single agent in this extension study.

Pre-assignment

Screening details:

A total of 120 subjects were enrolled in the study of which 118 subjects received the study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Initial Dose Talazoparib: < 1 mg/day

Arm description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of less than (<) 1 milligram (mg) orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

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 capsules at an initial dose (i.e. the last tolerated dose in the originating study) of < 1 mg orally once daily.

Arm title	Initial Dose Talazoparib: 1 mg/day

Arm description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of 1 mg orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

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 capsules at an initial dose (i.e. the last tolerated dose in the originating study) of 1 mg orally once daily.

Number of subjects in period 1	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day
Started	66	52
Completed	0	0
Not completed	66	52
Adverse event, serious fatal	-	1
Consent withdrawn by subject	5	1
Physician decision	3	2
Adverse event, non-fatal	6	3
Unspecified	5	6
Lost to follow-up	-	1
Disease Progression	47	38

Baseline characteristics

Reporting groups

Reporting group title	Initial Dose Talazoparib: < 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of less than (<) 1 milligram (mg) orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Reporting group title	Initial Dose Talazoparib: 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of 1 mg orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Reporting group values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day	Total
Number of subjects	66	52	118
Age Categorical Units: Subjects			
< 50 years	10	9	19
50 to <65 years	30	17	47
>= 65 years	25	25	50
Missing	1	1	2
Sex: Female, Male Units: Subjects			
Female	46	37	83
Male	20	15	35
Race Units: Subjects			
Asian	3	0	3
Black or African American	1	2	3
White	59	48	107
Unknown or Not Reported	3	2	5
Ethnicity Units: Subjects			
Hispanic or Latino	6	5	11
Not Hispanic or Latino	56	45	101
Unknown or Not Reported	4	2	6

End points

End points reporting groups

Reporting group title	Initial Dose Talazoparib: < 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of less than (<) 1 milligram (mg) orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Reporting group title	Initial Dose Talazoparib: 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of 1 mg orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Treatment Emergent Serious Adverse Events (SAEs), Treatment Emergent Treatment Related AEs and Treatment Emergent Treatment Related SAEs

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Treatment Emergent Serious Adverse Events (SAEs), Treatment Emergent Treatment Related AEs and Treatment Emergent Treatment Related SAEs[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject administered a study drug without regard to possibility of a causal relationship. SAE was any untoward medical occurrence that at any dose resulted in death; inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect or was considered as an important medical event. TEAEs were AEs that occurred on or after the administration of first dose of study drug through approximately 30 days after the last dose. AE included both SAEs and all non-SAEs. Treatment-related TEAEs were defined as any TEAE with at least a possible relationship to the study drug as assessed by the investigator or that was missing the assessment of causal relationship whose relationship to the study drug could not be ruled out. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

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: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects				
TEAE	63	47		
SAE	27	18		
Treatment-related TEAEs	45	31		
Treatment-related SAEs	6	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Grade 3 or 4 TEAEs Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4

End point title	Number of Subjects With Grade 3 or 4 TEAEs Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4[2]

End point description:

An AE was any untoward medical occurrence in a subject administered a study drug without regard to possibility of a causal relationship. TEAEs were AEs that occurred on or after the administration of first dose of study drug through approximately 30 days after the last dose. Severity was graded using NCI-CTCAE version 4 where, Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Number of subjects with Grade 3 or 4 TEAEs were reported. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects	38	32		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With TEAEs Leading to Dose Reduction, Permanent Study Drug Discontinuation and Death

End point title	Number of Subjects With TEAEs Leading to Dose Reduction, Permanent Study Drug Discontinuation and Death[3]

End point description:

An AE was any untoward medical occurrence in a subject administered a study drug without regard to possibility of a causal relationship. TEAEs were AEs that occurred on or after the administration of first dose of study drug through approximately 30 days after the last dose. Number of subjects with TEAEs leading to dose reduction, permanent study drug discontinuation and death were reported. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

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: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects				
TEAE leading to dose reduction	6	7		
TEAE leading to study drug discontinuation	5	4		
TEAE leading to death	7	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Laboratory Abnormalities: Liver Function Tests

End point title	Number of Subjects With Clinically Significant Laboratory Abnormalities: Liver Function Tests[4]

End point description:

The following liver parameters were analysed: aspartate transaminase (AST), alanine aminotransferase (ALT), total bilirubin (TBL) and alkaline phosphatase (ALP). The criteria for clinically significant abnormalities for liver parameters included AST or ALT greater than or equal to (>=) 3 times upper limit of normal (ULN); ALT or AST greater than (>) 5 times ULN; ALT or AST > 10 times ULN; ALT or AST > 20 times ULN; total TBL >2 times ULN; ALT or AST >= 3 times ULN and TBL > 2 times ULN and ALT or AST >= 3 times ULN and TBL > 2 times ULN and ALP < 2 times ULN. Safety population included all subjects who received any amount of talazoparib. Here, "number of subjects analysed" signifies number of subjects who were evaluable for this end point.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	50		
Units: Subjects				
ALT or AST >= 3*ULN	5	2		
ALT or AST > 5*ULN	0	0		
ALT or AST > 10*ULN	0	0		
ALT or AST > 20*ULN	0	0		

TBL > 2*ULN	4	0		
ALT or AST >= 3*ULN and TBL > 2*ULN	2	0		
ALT or AST >=3*ULN and TBL > 2*ULN and ALP <2*ULN	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With NCI-CTCAE Grade 3/4 Postbaseline Laboratory Toxicities: Hematology Parameters

End point title	Number of Subjects With NCI-CTCAE Grade 3/4 Postbaseline Laboratory Toxicities: Hematology Parameters[5]

End point description:

The following hematology parameters were analysed: hemoglobin, leukocytes, lymphocytes, neutrophils and platelets. Laboratory toxicities were graded using NCI-CTCAE version 4 where, grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (potentially life threatening) and grade 5 (death) for each parameter. Number of subjects with Grade 3 and 4 toxicities were reported. Low indicates values lower than the normal range. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

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: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects				
Hemoglobin (low): Grade 3	7	16		
Hemoglobin (low): Grade 4	0	0		
Leukocytes (low): Grade 3	5	2		
Leukocytes (low): Grade 4	0	0		
Lymphocytes (low): Grade 3	11	8		
Lymphocytes (low): Grade 4	1	1		
Neutrophils (low): Grade 3	9	4		
Neutrophils (low): Grade 4	1	0		
Platelets (low): Grade 3	4	4		
Platelets (low): Grade 4	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With NCI-CTCAE Grade 3/4 Postbaseline Laboratory Toxicities: Chemistry Parameters

End point title	Number of Subjects With NCI-CTCAE Grade 3/4 Postbaseline Laboratory Toxicities: Chemistry Parameters[6]

End point description:

The following chemistry parameters were analysed: alkaline phosphatase, bilirubin and creatinine. Laboratory toxicities were graded using NCI-CTCAE version 4 where, grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (potentially life threatening) and grade 5 (death) for each parameter. Number of subjects with Grade 3 or 4 toxicities were reported. High indicates values higher than the normal range. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects				
Alkaline Phosphatase (high): Grade 3	5	1		
Alkaline Phosphatase (high): Grade 4	1	0		
Bilirubin (high): Grade 3	3	0		
Bilirubin (high): Grade 4	1	0		
Creatinine (high): Grade 3	1	0		
Creatinine (high): Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Vital Signs and Weight

End point title	Number of Subjects With Clinically Significant Changes in Vital Signs and Weight[7]

End point description:

Criteria for clinically significant changes in vital signs included a) Systolic blood pressure (SBP): 1) absolute results >180 millimeter of mercury (mmHg) and increase from baseline (IFB) >=40 mmHg, 2) absolute results <90 mmHg and decrease from baseline (DFB) >30 mmHg; b) Diastolic blood pressure (DBP): 1) absolute results >110 mmHg and IFB >=30 mmHg , 2) absolute results <50 mmHg and DFB >20 mmHg , 3) IFB >=20 mmHg; c) Heart rate: 1) absolute results >120 beats per minute (bpm) and IFB >30 bpm, 2) absolute results <50 bpm and >20 bpm DFB; d) Temperature: <=34.5 or >=38 degree Celsius. Criteria for clinically significant changes in weight: >10 percent (%) DFB. Safety population included all subjects who received any amount of talazoparib.

End point type	Primary

End point timeframe:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

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: Only descriptive analysis was planned for this endpoint.

End point values	Initial Dose Talazoparib: < 1 mg/day	Initial Dose Talazoparib: 1 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	52		
Units: Subjects				
SBP: absolute results >180 mmHg and IFB >=40 mmHg	1	0		
SBP: absolute results <90 mmHg and DFB >30 mmHg	1	0		
DBP: absolute results >110 mmHg and IFB >=30 mmHg	0	0		
DBP: absolute results <50 mmHg and DFB >20 mmHg	0	0		
DBP: IFB >=20 mmHg	6	5		
Heart rate: absolute results>120 bpm & IFB>30 bpm	2	0		
Heart rate: absolute results<50 bpm & DFB>20 bpm	0	0		
Temperature: <=34.5 or >=38 degree Celsius	0	0		
Weight: >10% DFB	7	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment up to 30 days after last dose of study treatment or before initiation of a new antineoplastic therapy, whichever occurred first (approximately maximum for 4.6 years)

Adverse event reporting additional description:

An AE term may be reported as both a serious and non-serious AE, but are distinct events. An AE may be serious for 1 subject and non-serious for another subject, or a subject may have experienced both a serious and non-serious episode of the same event. Safety population included all subjects who received any amount of talazoparib.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Initial Dose Talazoparib: 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of 1 mg orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Reporting group title	Initial Dose Talazoparib: < 1 mg/day

Reporting group description:

Subjects were administered talazoparib capsules at an initial dose (i.e. the last tolerated dose in the originating study) of < 1 mg orally once daily. Subjects received talazoparib till the investigator considered treatment to be providing clinical benefit or until other study discontinuation criteria were met. Subjects were followed-up for safety until 30 days after the last dose of talazoparib (i.e., permanent discontinuation) or before initiation of a new antineoplastic therapy, whichever occurred first.

Serious adverse events	Initial Dose Talazoparib: 1 mg/day	Initial Dose Talazoparib: < 1 mg/day	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 52 (34.62%)	27 / 66 (40.91%)	
number of deaths (all causes)	8	7	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal Proliferative Breast Lesion			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			

subjects affected / exposed	2 / 52 (3.85%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Leukaemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Pleural Effusion			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Cancer			
subjects affected / exposed	3 / 52 (5.77%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pericardial Effusion Malignant			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (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			
Disease Progression			
subjects affected / exposed	0 / 52 (0.00%)	4 / 66 (6.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 4	
Death			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gait Disturbance			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General Physical Health Deterioration			

subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (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			
Dyspnoea			
subjects affected / exposed	1 / 52 (1.92%)	3 / 66 (4.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Platelet Count Decreased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
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 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			

subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cauda Equina Syndrome			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	1 / 52 (1.92%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
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			
Thrombocytopenia			
subjects affected / exposed	0 / 52 (0.00%)	2 / 66 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anaemia			
subjects affected / exposed	2 / 52 (3.85%)	2 / 66 (3.03%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 52 (0.00%)	2 / 66 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
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 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 52 (1.92%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestinal Obstruction			

subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
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	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain In Extremity			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Endocarditis Bacterial			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 52 (0.00%)	2 / 66 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Abscess			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)	2 / 66 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal Sepsis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary Tract Infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure To Thrive			
subjects affected / exposed	1 / 52 (1.92%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gout			
subjects affected / exposed	0 / 52 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Initial Dose Talazoparib: 1 mg/day	Initial Dose Talazoparib: < 1 mg/day	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 52 (88.46%)	54 / 66 (81.82%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Ascites			
subjects affected / exposed	3 / 52 (5.77%)	0 / 66 (0.00%)	
occurrences (all)	5	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 52 (3.85%)	4 / 66 (6.06%)	
occurrences (all)	2	5	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	6 / 52 (11.54%)	6 / 66 (9.09%)	
occurrences (all)	7	8	
Fatigue			
subjects affected / exposed	11 / 52 (21.15%)	17 / 66 (25.76%)	
occurrences (all)	15	20	
Oedema Peripheral			
subjects affected / exposed	4 / 52 (7.69%)	7 / 66 (10.61%)	
occurrences (all)	4	7	
Pain			
subjects affected / exposed	3 / 52 (5.77%)	0 / 66 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 52 (7.69%)	7 / 66 (10.61%)	
occurrences (all)	5	8	
Dyspnoea			
subjects affected / exposed	6 / 52 (11.54%)	8 / 66 (12.12%)	
occurrences (all)	7	8	
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	3 / 52 (5.77%)	3 / 66 (4.55%)	
occurrences (all)	4	6	
Neutrophil Count Decreased			
subjects affected / exposed	4 / 52 (7.69%)	4 / 66 (6.06%)	
occurrences (all)	7	7	
Platelet Count Decreased			
subjects affected / exposed	9 / 52 (17.31%)	2 / 66 (3.03%)	
occurrences (all)	27	12	
Weight Decreased			
subjects affected / exposed	3 / 52 (5.77%)	3 / 66 (4.55%)	
occurrences (all)	3	3	
White Blood Cell Count Decreased			
subjects affected / exposed	3 / 52 (5.77%)	6 / 66 (9.09%)	
occurrences (all)	9	19	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 52 (1.92%)	6 / 66 (9.09%)	
occurrences (all)	1	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 52 (0.00%)	5 / 66 (7.58%)	
occurrences (all)	0	6	
Headache			
subjects affected / exposed	0 / 52 (0.00%)	7 / 66 (10.61%)	
occurrences (all)	0	8	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 52 (34.62%)	19 / 66 (28.79%)	
occurrences (all)	64	41	
Iron Deficiency Anaemia			
subjects affected / exposed	3 / 52 (5.77%)	0 / 66 (0.00%)	
occurrences (all)	4	0	
Neutropenia			
subjects affected / exposed	4 / 52 (7.69%)	10 / 66 (15.15%)	
occurrences (all)	8	19	
Thrombocytopenia			
subjects affected / exposed	5 / 52 (9.62%)	10 / 66 (15.15%)	
occurrences (all)	13	15	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 52 (1.92%)	4 / 66 (6.06%)	
occurrences (all)	1	5	
Abdominal Pain Upper			
subjects affected / exposed	2 / 52 (3.85%)	5 / 66 (7.58%)	
occurrences (all)	2	8	
Abdominal Pain			
subjects affected / exposed	5 / 52 (9.62%)	9 / 66 (13.64%)	
occurrences (all)	6	12	
Constipation			
subjects affected / exposed	2 / 52 (3.85%)	8 / 66 (12.12%)	
occurrences (all)	2	8	
Diarrhoea			

subjects affected / exposed	3 / 52 (5.77%)	8 / 66 (12.12%)	
occurrences (all)	3	8	
Nausea			
subjects affected / exposed	10 / 52 (19.23%)	18 / 66 (27.27%)	
occurrences (all)	11	21	
Vomiting			
subjects affected / exposed	4 / 52 (7.69%)	12 / 66 (18.18%)	
occurrences (all)	5	17	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 52 (9.62%)	6 / 66 (9.09%)	
occurrences (all)	5	7	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 52 (7.69%)	6 / 66 (9.09%)	
occurrences (all)	5	7	
Back Pain			
subjects affected / exposed	2 / 52 (3.85%)	10 / 66 (15.15%)	
occurrences (all)	2	11	
Myalgia			
subjects affected / exposed	1 / 52 (1.92%)	4 / 66 (6.06%)	
occurrences (all)	1	5	
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	2 / 52 (3.85%)	6 / 66 (9.09%)	
occurrences (all)	2	9	
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 52 (5.77%)	8 / 66 (12.12%)	
occurrences (all)	3	9	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	7 / 52 (13.46%)	7 / 66 (10.61%)	
occurrences (all)	9	10	
Hypokalaemia			
subjects affected / exposed	1 / 52 (1.92%)	5 / 66 (7.58%)	
occurrences (all)	1	5	

Hypomagnesaemia subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 4	1 / 66 (1.52%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2018	The exclusion criteria of the study was updated to ensure the values of hemoglobin and platelet count were in line with the inclusion criteria of the originating Study MDV3800-02/C3441002 from version 4.0 onward for subjects with moderate/severe hepatic impairment to allow extended treatment with talazoparib after completion of the originating study. Talazoparib Dose Modifications guidelines had also been updated to reflect the changes of the exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In age group breakdown, data included 2 untreated subjects and excluded 2 subjects with missing data as presented in the age categorical field of baseline section. This is done due to database limitation as there is no option to report missing data.

Notes: