Clinical trial results:
A multicentre, open-label, three-arm randomised Phase II trial assessing the safety and efficacy of the HSP90 inhibitor Ganetespib in combination with Carboplatin followed by maintenance treatment with Niraparib versus Ganetespib plus Carboplatin followed by Ganetespib and Niraparib versus Carboplatin in combination with standard chemotherapy followed by Niraparib maintenance treatment in platinum-sensitive ovarian cancer patients

Summary

EudraCT number	2017-004058-40
Trial protocol	BE DE FR AT IT
Global end of trial date	01 September 2023

Results information

Result version number	v1 (current)
This version publication date	22 June 2024
First version publication date	22 June 2024

Trial information

Trial identification

Sponsor protocol code	EUDARIO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03783949
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BGOG-KULeuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Joke De Roover, Katholieke Universiteit Leuven, 32 16347419, bgog@engot.eu
Scientific contact	Joke De Roover, Katholieke Universiteit Leuven, 32 16347419, bgog@engot.eu
Sponsor organisation name	BGOG-KULeuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Ellen Reynders, BGOG-KULeuven, 32 16342996, ellen.reynders@uzleuven.be
Scientific contact	Prof. Nicole Concin, IMU Innsbruck, 43 51250481433, nicole.concin@i-med.ac.at

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	25 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2023
Global end of trial reached?	Yes
Global end of trial date	01 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the progression-free survival (PFS) by RECIST 1.1

Protection of trial subjects:

Approval for the trial was obtained from the EC and CA. Trial was performed according to the ICH-GCP guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 33
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 51
Worldwide total number of subjects	122
EEA total number of subjects	122

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)	68
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with platinum-sensitive measurable or evaluable ovarian cancer were included. Borderline tumors, increased risk for gastrointestinal perforation or history of myelodysplastic syndome or acute myeloid leukemia were excluded

Pre-assignment

Screening details:

Patients underwent the screening examinations as per protocol. No pre-screening assessments were performed in the scope of the trial

Period 1

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

Blinding implementation details:

study was not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Carboplatin + Paclitaxel or Gemcitabin followed by Niraparib maintenance treatment

Arm type	Active comparator
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

AUC5 d1 q3w IV (6 doses)

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

Dosage and administration details:

175mg/m² D1 q3w IV for 6 cycles

Investigational medicinal product name	Niraparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Oral use

Dosage and administration details:

200-300mg QD PO

Arm title	Arm B

Arm description:

Carboplatin + Ganetspib followed by Niraparib maintenance

Arm type	Experimental

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: AUC5 d1 q3w for 6 cycles	
Investigational medicinal product name	Ganetespib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 150mg/m² D1 q3w for 6 cycles	
Investigational medicinal product name	Niraparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 200/300 mg daily	
Arm title	Arm C
Arm description: Carboplatin + Ganetespib followed by Ganetespib + Niraparib maintenance	
Arm type	Experimental
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details: AUC5 d1 q3w IV (6 doses)	
Investigational medicinal product name	Ganetespib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 150mg/m² D1 q3w for 6 cycles	
Investigational medicinal product name	Ganetespib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100mg/m² D1 qw (during maintenance treatment)	
Investigational medicinal product name	Niraparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
200mg daily

Number of subjects in period 1	Arm A	Arm B	Arm C
Started	41	42	39
Start of maintenance treatment	32	27	17
Completed	2	0	2
Not completed	39	42	37
Adverse event, serious fatal	1	1	-
Consent withdrawn by subject	1	1	5
Adverse event, non-fatal	1	5	5
Lack of efficacy	36	35	27

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Carboplatin + Paclitaxel or Gemcitabin followed by Niraparib maintenance treatment	
Reporting group title	Arm B
Reporting group description:	
Carboplatin + Ganetspib followed by Niraparib maintenance	
Reporting group title	Arm C
Reporting group description:	
Carboplatin + Ganetespib followed by Ganetespib + Niraparib maintenance	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	41	42	39
Age categorical Units: Subjects			
Adults (18-64 years)	21	25	22
From 65-84 years	20	17	17
Gender categorical Units: Subjects			
Female	41	42	39
Male	0	0	0

Reporting group values	Total		
Number of subjects	122		
Age categorical Units: Subjects			
Adults (18-64 years)	68		
From 65-84 years	54		
Gender categorical Units: Subjects			
Female	122		
Male	0		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description: Carboplatin + Paclitaxel or Gemcitabin followed by Niraparib maintenance treatment	
Reporting group title	Arm B
Reporting group description: Carboplatin + Ganetspib followed by Niraparib maintenance	
Reporting group title	Arm C
Reporting group description: Carboplatin + Ganetespib followed by Ganetespib + Niraparib maintenance	

Primary: Progression free survival

End point title	Progression free survival
End point description: Progression-free survival (PFS) by RECIST 1.1	
End point type	Primary
End point timeframe: 3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	41	39	
Units: month				
median (confidence interval 95%)	8.85 (7.73 to 11.5)	8.32 (6.88 to 9.70)	8.32 (6.88 to 9.70)	

Statistical analyses

Statistical analysis title	Log-rank test
Statistical analysis description: the median time to progression was estimated using the Kaplan-Meier method and the 95% confidence interval of the median was reported. The restricted mean as a measure for PFS was calculated using the area under the survival curve (AUC) at the end of the study. In addition, Cox proportional hazards regression analysis adjusting for the stratification factors was applied. The same procedure was applied to exploratively compare the different treatment arm	
Comparison groups	Arm A v Arm B v Arm C

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5417
Method	Logrank
Parameter estimate	Median difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.88
upper limit	11.55
Variability estimate	Standard deviation

Secondary: Progression-free Survival in BRCA Mutated Patients

End point title	Progression-free Survival in BRCA Mutated Patients
End point description:	
Progression-free survival analysis in BRCA mutated patients	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	12	
Units: month				
median (confidence interval 95%)	11.78 (7.30 to 17.37)	7.98 (6.09 to 11.05)	7.98 (6.09 to 11.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Post-progression PFS (PFS2)

End point title	Post-progression PFS (PFS2)
End point description:	
Post-progression PFS (PFS2) analysis	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	40	39	
Units: month				
median (confidence interval 95%)	21.71 (17.73 to 25.30)	21.38 (15.53 to 26.18)	21.38 (15.53 to 26.18)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Subsequent Therapy (TFST)

End point title	Time to First Subsequent Therapy (TFST)
End point description:	
Time to First Subsequent Therapy (TFST) analysis	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	41	39	
Units: month				
median (confidence interval 95%)	9.38 (8.09 to 12.47)	8.75 (7.40 to 10.07)	8.75 (7.40 to 10.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Second Subsequent Therapy (TSST)

End point title	Time to Second Subsequent Therapy (TSST)
End point description:	
Time to Second Subsequent Therapy (TSST) analysis	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	41	39	
Units: month				
median (confidence interval 95%)	17.73 (14.28 to 21.61)	14.54 (13.26 to 16.94)	14.54 (13.26 to 16.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival in Patients Without BRCA Mutation or With Unkown BRCA Status

End point title	Progression-free Survival in Patients Without BRCA Mutation or With Unkown BRCA Status

End point description:

Progression-free Survival analysis in Patients without BRCA mutation or with unkown BRCA status

End point type	Secondary

End point timeframe:

3 years 10 months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	28	28	
Units: month				
median (confidence interval 95%)	7.83 (6.58 to 11.38)	8.49 (6.71 to 10.49)	8.49 (6.71 to 10.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Objective response rate (ORR) analysis

End point type	Secondary

End point timeframe:

3 years 10 months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	40	39	
Units: patients				
no response (SD/PD)	21	26	26	
response (CR/PR)	17	13	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall survival (OS) analysis	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	42	39	
Units: month				
median (confidence interval 95%)	22.14 (17.73 to 29.97)	22.27 (17.07 to 29.21)	22.27 (17.07 to 29.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival in Patients With Prior PARPi Treatment

End point title	Progression-free Survival in Patients With Prior PARPi Treatment
End point description:	
Progression-free Survival analysis in Patients with prior PARPi treatment	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	12	
Units: month				
median (confidence interval 95%)	7.40 (5.63 to 8.85)	6.09 (2.76 to 7.76)	6.09 (2.76 to 7.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival in Patients With One Prior Line of Therapy

End point title	Progression-free Survival in Patients With One Prior Line of Therapy
End point description:	
Progression-free Survival analysis in Patients with one prior line of therapy	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	23	23	
Units: month				
median (confidence interval 95%)	10.59 (5.92 to 11.94)	9.70 (7.14 to 11.35)	9.70 (7.14 to 11.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival in Patients With More Then One Prior Line of Therapy

End point title	Progression-free Survival in Patients With More Then One Prior Line of Therapy
End point description:	
Progression-free Survival analysis in Patients with more then one prior line of therapy	
End point type	Secondary
End point timeframe:	
3 years 10 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	17	17	
Units: month				
median (confidence interval 95%)	7.63 (7.30 to 12.89)	7.43 (4.11 to 8.32)	7.43 (4.11 to 8.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival in Patients Without Prior PARPi Treatment

End point title	Progression-free Survival in Patients Without Prior PARPi Treatment

End point description:

Progression-free Survival analysis in Patients without prior PARPi treatment

End point type	Secondary

End point timeframe:

3 years 10 months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	22	23	
Units: month				
median (confidence interval 95%)	11.55 (7.43 to 13.55)	9.77 (7.83 to 11.12)	9.77 (7.83 to 11.12)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 3 years 10 months	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1
Reporting groups	
Reporting group title	Arm A
Reporting group description: Carboplatin + Paclitaxel or Gemcitabin followed by Niraparib maintenance	
Reporting group title	Arm B
Reporting group description: Carboplatin + Ganetespib followed by Niraparib maintenance	
Reporting group title	Arm C
Reporting group description: Carboplatin + Ganetespib followed by Ganetspib + Niraparib maintenance	

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 41 (56.10%)	19 / 42 (45.24%)	16 / 39 (41.03%)
number of deaths (all causes)	23	24	23
number of deaths resulting from adverse events	1	2	1
Investigations			
Bilirubin increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	10 / 41 (24.39%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	8 / 10	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	5 / 41 (12.20%)	1 / 42 (2.38%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	5 / 5	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumor biopsy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transaminases increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
abdominal pain			
subjects affected / exposed	1 / 41 (2.44%)	4 / 42 (9.52%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	1 / 1	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

dehydration			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fever			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fistula			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general malaise			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
headache			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Word finding disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general deterioration			

subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			
Allergic reaction to Carboplatin			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	3 / 39 (7.69%)
occurrences causally related to treatment / all	1 / 1	3 / 3	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
allergic reaction NOS			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	21 / 41 (51.22%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastro-entiritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal perforation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal subobstruction			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal bleeding			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
stomach pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subileus			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Maligne pleuritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Pleural effusion			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Kidney insufficiency			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
hyperglycemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Anaphylactic shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 infection			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CRP increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1

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

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 41 (97.56%)	42 / 42 (100.00%)	39 / 39 (100.00%)
Investigations			
Alkaline phosphatase increased			
subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	0 / 39 (0.00%)
occurrences (all)	2	1	0
Anemia			
subjects affected / exposed	32 / 41 (78.05%)	26 / 42 (61.90%)	25 / 39 (64.10%)
occurrences (all)	50	38	32
Creatinine increased			

subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	1 / 39 (2.56%)
occurrences (all)	1	2	1
Leucocytopenia			
subjects affected / exposed	38 / 41 (92.68%)	14 / 42 (33.33%)	12 / 39 (30.77%)
occurrences (all)	38	14	12
Neutropenia			
subjects affected / exposed	35 / 41 (85.37%)	29 / 42 (69.05%)	34 / 39 (87.18%)
occurrences (all)	46	43	34
Thrombocytopenia			
subjects affected / exposed	35 / 41 (85.37%)	29 / 42 (69.05%)	29 / 39 (74.36%)
occurrences (all)	35	29	29
Transaminases increased			
subjects affected / exposed	14 / 41 (34.15%)	7 / 42 (16.67%)	7 / 39 (17.95%)
occurrences (all)	14	7	7
Cardiac disorders			
Hypertension			
subjects affected / exposed	3 / 41 (7.32%)	3 / 42 (7.14%)	0 / 39 (0.00%)
occurrences (all)	3	3	0
QTc prolongation			
subjects affected / exposed	0 / 41 (0.00%)	3 / 42 (7.14%)	2 / 39 (5.13%)
occurrences (all)	0	3	2
Tachycardia			
subjects affected / exposed	4 / 41 (9.76%)	2 / 42 (4.76%)	1 / 39 (2.56%)
occurrences (all)	4	2	1
Nervous system disorders			
Peripheral neuropathy			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	1 / 39 (2.56%)
occurrences (all)	1	3	1
General disorders and administration site conditions			
Abdominal bloating			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	2 / 41 (4.88%)	4 / 42 (9.52%)	3 / 39 (7.69%)
occurrences (all)	2	4	3
Alopecia			

subjects affected / exposed	6 / 41 (14.63%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences (all)	6	0	1
Anorexia			
subjects affected / exposed	2 / 41 (4.88%)	6 / 42 (14.29%)	6 / 39 (15.38%)
occurrences (all)	2	6	6
Asthenia			
subjects affected / exposed	15 / 41 (36.59%)	20 / 42 (47.62%)	16 / 39 (41.03%)
occurrences (all)	15	20	16
Dizziness			
subjects affected / exposed	2 / 41 (4.88%)	3 / 42 (7.14%)	2 / 39 (5.13%)
occurrences (all)	2	3	2
Dysgeusia			
subjects affected / exposed	2 / 41 (4.88%)	2 / 42 (4.76%)	4 / 39 (10.26%)
occurrences (all)	2	2	4
Epistaxis			
subjects affected / exposed	3 / 41 (7.32%)	0 / 42 (0.00%)	0 / 39 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	14 / 41 (34.15%)	9 / 42 (21.43%)	11 / 39 (28.21%)
occurrences (all)	14	9	11
General malaise			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	0 / 39 (0.00%)
occurrences (all)	1	3	0
Headache			
subjects affected / exposed	2 / 41 (4.88%)	9 / 42 (21.43%)	4 / 39 (10.26%)
occurrences (all)	2	9	4
Insomnia			
subjects affected / exposed	2 / 41 (4.88%)	2 / 42 (4.76%)	3 / 39 (7.69%)
occurrences (all)	2	2	3
Syncope			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	2 / 39 (5.13%)
occurrences (all)	0	2	2
Weight decreased			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
abdominal cramping			

subjects affected / exposed	3 / 41 (7.32%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences (all)	3	0	1
Immune system disorders			
Allergic reaction to Carboplatin			
subjects affected / exposed	6 / 41 (14.63%)	10 / 42 (23.81%)	15 / 39 (38.46%)
occurrences (all)	6	10	15
Eye disorders			
blurry vision			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	18 / 41 (43.90%)	12 / 42 (28.57%)	13 / 39 (33.33%)
occurrences (all)	18	12	13
Diarrhoea			
subjects affected / exposed	9 / 41 (21.95%)	22 / 42 (52.38%)	32 / 39 (82.05%)
occurrences (all)	9	22	32
Epigastric pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	2 / 39 (5.13%)
occurrences (all)	1	1	2
Nausea			
subjects affected / exposed	32 / 41 (78.05%)	32 / 42 (76.19%)	29 / 39 (74.36%)
occurrences (all)	32	32	29
Pyrosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	2 / 39 (5.13%)
occurrences (all)	0	1	2
Stomach pain			
subjects affected / exposed	5 / 41 (12.20%)	3 / 42 (7.14%)	2 / 39 (5.13%)
occurrences (all)	5	3	2
Vomiting			
subjects affected / exposed	9 / 41 (21.95%)	15 / 42 (35.71%)	16 / 39 (41.03%)
occurrences (all)	9	15	16
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	3 / 41 (7.32%)	6 / 42 (14.29%)	0 / 39 (0.00%)
occurrences (all)	3	6	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 41 (7.32%)	0 / 42 (0.00%)	2 / 39 (5.13%)
occurrences (all)	3	0	2
itching			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	4 / 39 (10.26%)
occurrences (all)	2	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 41 (9.76%)	2 / 42 (4.76%)	2 / 39 (5.13%)
occurrences (all)	4	2	2
Myalgia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 42 (9.52%)	0 / 39 (0.00%)
occurrences (all)	2	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2018	Addition of an extra biopsy 24h after the first dose of chemotherapy in 10 patients of UZLeuven. This was added in the scope of companion diagnostics.
07 January 2020	- Additional clarification of some in- & exclusion criteria - Addition of an exclusion criterion regarding the use of drugs prolonging the QTc interval or with a known risk to cause Torsade de Points - Addition of an exclusion criterion regarding the administration of live attenuated vaccines within 30 days prior to the start of the trial. - Addition of some recently updated information regarding the clinical experience with combining Ganetespib and Carboplatin - Addition of a section regarding the Ganetespib safety profile - Updates in the section 'diarrhoea' in the 'events of special interest with respect to Ganetespib treatment' - Addition of information regarding the potential overlapping toxicities of Ganetespib and Niraparib - Addition of information regarding the potential overlapping toxicities of Ganetespib and Carboplatin - The information regarding Gemcitabin and Paclitaxel was moved from the section 'information on the non-investigational products (non-IMPs)' to the section 'information on the comparator products (non-IMPs)' - Addition of a statement that TESARO and Aldeyra Therapeutics agree to provide the study treatment(s) to patients in case of a premature termination of the trial. - Updates to the 'statistical analysis' section based on requests received from the CAs and ECs of the participating countries during the trial approval phase. - Clarification of the guidelines on G-CSF use
12 November 2020	Addition of guidelines on Niraparib dose reductions for patients with hepatotoxicity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported