Clinical trial results:
Phase-II study of olaparib as maintenance therapy after response to trabectedinpegylated liposomal doxorubicin in recurrent ovarian carcinoma.

Summary

EudraCT number	2017-003183-13
Trial protocol	ES
Global end of trial date	28 December 2022

Results information

Result version number	v1 (current)
This version publication date	05 May 2023
First version publication date	05 May 2023

Trial information

Trial identification

Sponsor protocol code	OLATRA

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GEICO - Grupo Español de Investigación en Cáncer de Ovario
Sponsor organisation address	Santa Engracia 151, 5º-2 28003 Madrid, Madrid, Spain,
Public contact	Ana María Moreno, APICES, 0034 918166804, ana.moreno@apices.es
Scientific contact	Ana María Moreno, APICES, 0034 918166804, ana.moreno@apices.es

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	23 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 August 2022
Global end of trial reached?	Yes
Global end of trial date	28 December 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Effect of maintenance treatment with olaparib on progression free survival (PFS) in patients with recurrent ovarian carcinoma, treatment-free interval of platinum (TFIp) higher than 6 months, and BRCA1/2 germline or somatic deleterious mutation, who have received treatment with trabectedin + pegylated liposomal doxorubicin (PLD) and reached a partial or complete response, assessed by RECIST 1.1 criteria.

Protection of trial subjects:

The patient signed the informed consent before carrying out any procedure related to the study. Physical examination, hematology, biochemistry, ECG and evaluation of the tumor were made before the inclusion of the patient in the study.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	16 July 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	7
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were included in the study between 23th July 2018 and 27th June 2019.
On October 09, 2019, notification is given of the premature closure of the study due to the new treatments available and the impossibility of recruiting the necessary patients within a reasonable time frame.

Pre-assignment

Screening details:

If the patient meets eligibility and screening requirements she will be included and will return to the site for the Cycle 1 Day 1 visit and dosing.

Period 1

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

Arms

Arm title	Olaparib arm

Arm description:

2 tablets of 150 mg of olaparib every 12 hours.

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

Dosage and administration details:

2 tablets of 150 mg of olaparib every 12 hours.

Number of subjects in period 1	Olaparib arm
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib arm
Reporting group description:	
2 tablets of 150 mg of olaparib every 12 hours.	

Reporting group values	Olaparib arm	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	53		
full range (min-max)	46 to 84	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	0	0	
Ethnicity Units: Subjects			
Caucasian	9	9	
ECOG-PS Units: Subjects			
Zero	8	8	
One	1	1	
ECG result Units: Subjects			
Normal	8	8	
Abnormal, not clinically significant	1	1	
Mutation Units: Subjects			
Germinal	6	6	
Somatic	3	3	
Weight Units: Kg			
median	70.2		
full range (min-max)	57.0 to 81.0	-	

Body Surface Area Units: m2			
median	1.7		
full range (min-max)	1.5 to 1.8	-	

End points

End points reporting groups

Reporting group title	Olaparib arm
Reporting group description:	
2 tablets of 150 mg of olaparib every 12 hours.	

Primary: Progression free survival (PFS)

End point title	Progression free survival (PFS)[1]
End point description:	
Progression-free survival (PFS) has been defined as the time from the first dose of olaparib to the date of first radiological disease progression or death for any reason.	
End point type	Primary
End point timeframe:	
Every 12 weeks	

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: Not statistical analysis have been performed.

End point values	Olaparib arm			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Months				
median (confidence interval 95%)	15.8 (0.0 to 37.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events will be collected from time of signature of informed consent throughout the treatment period up to and including the 30-day follow-up period.

Adverse event reporting additional description:

All patients included have at least one adverse event.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Olaparib arm

Reporting group description: -

Serious adverse events	Olaparib arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hypertransaminasaemia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Olaparib arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	7 / 9 (77.78%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Aphonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cold			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Investigations			
Blood uric acid			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed occurrences (all) Haemoglobin decreased subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all) Neutrophil count decreased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) leukocytes count decreased subjects affected / exposed occurrences (all) linfocytes count decreased subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 2 / 9 (22.22%) 2		
Injury, poisoning and procedural complications Femur fracture subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Anaemia			
subjects affected / exposed	6 / 9 (66.67%)		
occurrences (all)	6		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Aerophagia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Colitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Haemorrhoids			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Epigastric discomfort			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tooth loss			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Lower abdominal pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Upper abdominal pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Erythema			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pain limb			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hepatitis E			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Epstein-Barr virus infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Influenza subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Pneumonia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Folate deficiency subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Fluid retention subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2018	Study amendment 2: Protocol version 3.0

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.

Low sample size and lack of control group. On October 09, 2019, notification is given of the early study closure due to the new treatments available and the impossibility of recruiting the necessary patients within a reasonable time frame.

Notes: