



Clinical trial results:

Single arm feasibility of multi-maintenance olaparib after disease recurrence in participants with platinum sensitive BRCAm high grade serous ovarian cancer

Summary

EudraCT number	2015-003883-36
Trial protocol	GB
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	26 July 2023
First version publication date	26 July 2023

Trial information

Trial identification

Sponsor protocol code	CFTSp104
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02855697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Christie NHS Foundation Trust
Sponsor organisation address	550 Wilmslow Road, Manchester, United Kingdom, M20 4BX
Public contact	Clare Griffin, The Christie NHS Foundation Trust, +44 01614468280, the-christie.sponsoredresearch@nhs.net
Scientific contact	Clare Griffin, The Christie NHS Foundation Trust, +44 01614468280, the-christie.sponsoredresearch@nhs.net

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	17 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine the feasibility of administering a second course of maintenance olaparib for more than 6 months (26 weeks) to participants with recurrent platinum-sensitive HGS/EOC who have been previously treated with olaparib.

Protection of trial subjects:

The trial will be conducted in accordance with the principles of good clinical practice (GCP) and the Declaration of Helsinki. The sponsor and MCTU will ensure that the study protocol, participant information sheet, participant consent form, GP letter and submitted supporting documents have been approved by the research ethics committee(s) prior to any subject recruitment. The Principal Investigator will update participants whenever new information becomes available that might affect the participant's willingness to continue in the trial.

Participants will be assigned a unique ID at registration that will be used throughout the trial and any personal data recorded will be regarded as confidential and will not be released into the public domain. Investigator and site staff must not provide any participant-identifying data to the MCTU during the course of the trial, and any identifying data received by the MCTU will be redacted or destroyed. All investigators and site staff involved with the trial must comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2016
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	United Kingdom: 27
Worldwide total number of subjects	27
EEA total number of subjects	0

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)	22
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

27 participants with a known pathogenic/likely pathogenic germline BRCA1/2 mutation were recruited. All patients were recruited prior to rechallenge platinum chemotherapy. Patients recruited at EP1 had never been treated with a PARPi. Patients recruited at EP2 had received a first maintenance course of olaparib immediately prior to trial enrolment

Pre-assignment

Screening details:

Screening assessments included a CT scan of the abdomen and pelvis, ECOG performance status, ECG, safety laboratory assessments (including haematology, clinical chemistry, CA125, renal function test and coagulation parameters), pregnancy testing and a standard examination of height, weight, pulse rate, blood pressure and temperature.

Period 1

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

Arms

Arm title	Second maintenance olaparib
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Arm description:

Subjects who were intended to receive a second maintenance dose of olaparib whilst on trial.

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:

Olaparib will be provided as tablets, marked with 100mg or 150mg. The recommended dose is 300 mg taken twice daily (bd), equivalent to a total daily dose of 600 mg.

Number of subjects in period 1	Second maintenance olaparib
Started	27
Completed	27

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (trial period)
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Reporting group description: -

Reporting group values	Overall trial (trial period)	Total	
Number of subjects	27	27	
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)	22	22	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	27	27	
Male	0	0	
ECOG performance status Units: Subjects			
00	21	21	
01	6	6	
Germline BRCA1/2 mutation Units: Subjects			
BRCA1	22	22	
BRCA2	5	5	
Histology Units: Subjects			
Serous	27	27	
Endometrioid	0	0	
FIGO (2014) stage Units: Subjects			
I-II	4	4	
III	18	18	
IV	5	5	
Prior lines of platinum chemotherapy before trial entry Units: Subjects			
01	6	6	
02	9	9	
More than or equal to 3	12	12	
Prior bevacizumab therapy			

Units: Subjects			
None	16	16	
First line	6	6	
Second line/recurrent disease	5	5	
Progression-free interval prior to platinum 1			
Units: Subjects			
6–12 months	17	17	
>12 months	10	10	

End points

End points reporting groups

Reporting group title	Second maintenance olaparib
Reporting group description: Subjects who were intended to receive a second maintenance dose of olaparib whilst on trial.	
Subject analysis set title	Olaparib 1
Subject analysis set type	Sub-group analysis
Subject analysis set description: All patients who received a first maintenance course of olaparib used for post hoc analysis	
Subject analysis set title	Olaparib 2
Subject analysis set type	Sub-group analysis
Subject analysis set description: All patients who received a second maintenance course of olaparib used for post hoc analysis	

Primary: The proportion of patients who received a second maintenance course of olaparib

End point title	The proportion of patients who received a second maintenance course of olaparib ^[1]
End point description:	
End point type	Primary
End point timeframe: For Entry Point 1, the timeframe was from screening until the second instance of progressive disease. For patients at Entry Point 2 the timeframe was from screening until the first instance of disease progression.	

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: No statistical analyses were performed for this end-point due to the results being a count i. e number of patients

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[2]			
Units: Number of patients	12			

Notes:

[2] - 19 patients received at least one dose of platinum 2 and were evaluable for the co-primary outcomes

Statistical analyses

No statistical analyses for this end point

Primary: The proportion of patients who received a second course of olaparib for ≥6 months

End point title	The proportion of patients who received a second course of olaparib for ≥6 months ^[3]
End point description:	
End point type	Primary

End point timeframe:

From starting point of olaparib second course until their 6th month of treatment or greater.

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: No statistical analyses were performed for this end-point due to the results being a count i. e number of patients

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[4]			
Units: Number of patients	4			

Notes:

[4] - Patients who received a second course of olaparib

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival
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End point description:

End point type	Secondary
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End point timeframe:

The time interval between cycle 1 day 1 of the first maintenance course of olaparib to the date of clinical or RECIST defined progression or death, whichever occurred first

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[5]			
Units: month				
median (confidence interval 95%)	8.7 (4.7 to 12.2)			

Notes:

[5] - Patients eligible for platinum 2

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first subsequent therapy

End point title	Time to first subsequent therapy
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End point description:

End point type	Secondary
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End point timeframe:

The time interval between cycle 1 day 1 of the first maintenance course of olaparib to cycle 1 day 1 of platinum 2 or death, whichever occurred first.

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[6]			
Units: month				
median (confidence interval 95%)	11.8 (6.9 to 18.5)			

Notes:

[6] - Patients eligible for platinum 2

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival 2

End point title	Progression free survival 2
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End point description:

End point type	Secondary
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End point timeframe:

The time interval between cycle 1 day 1 of the first maintenance course of olaparib to the date of clinical or RECIST-defined progression or death following platinum 2, whichever occurred first.

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[7]			
Units: month				
median (confidence interval 95%)	17.4 (13.6 to 24.7)			

Notes:

[7] - Patients eligible for platinum 2 following progression on their first course of olaparib

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
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End point description:

End point type	Secondary
End point timeframe:	
The time interval from cycle 1 day 1 of the first maintenance course of olaparib to the date of death.	

End point values	Second maintenance olaparib			
Subject group type	Reporting group			
Number of subjects analysed	14 ^[8]			
Units: month				
median (confidence interval 95%)	30.5 (17.5 to 43.6)			

Notes:

[8] - Patients whose follow up data could be obtained

Statistical analyses

No statistical analyses for this end point

Post-hoc: Duration of each maintenance course of olaparib

End point title	Duration of each maintenance course of olaparib
End point description:	
End point type	Post-hoc
End point timeframe:	
The timeframe was the duration of each maintenance course of olaparib.	

End point values	Olaparib 1	Olaparib 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23 ^[9]	12 ^[10]		
Units: month				
arithmetic mean (standard deviation)	12.1 (± 9.8)	4.4 (± 2.7)		

Notes:

[9] - All patients who received a first maintenance course of olaparib whilst on the trial

[10] - All patients who received a second maintenance course of olaparib

Statistical analyses

Statistical analysis title	Olaparib 1 vs olaparib 2 duration
Statistical analysis description:	
To ascertain if there was a significant difference in the mean duration of olaparib 1 and olaparib 2 treatment	
Comparison groups	Olaparib 1 v Olaparib 2

Number of subjects included in analysis	35
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	< 0.001
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the patient's screening until disease progression on the second course of olaparib or until the patient drops out of the trial.

Adverse event reporting additional description:

Adverse events were reported for the first and second course of olaparib in addition to any serious adverse events recorded over the duration of the trial.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Single arm
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Reporting group description: -

Serious adverse events	Single arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 27 (55.56%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	2		
Investigations			
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Fever	Additional description: Fever		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Anemia	Additional description: Anemia		
	subjects affected / exposed	6 / 27 (22.22%)	
	occurrences causally related to treatment / all	7 / 8	
	deaths causally related to treatment / all	0 / 0	
Febrile Neutropenia	Additional description: Febrile Neutropenia		
	subjects affected / exposed	2 / 27 (7.41%)	
	occurrences causally related to treatment / all	0 / 2	
	deaths causally related to treatment / all	0 / 0	
Eye disorders			
	Eye Infection	Additional description: Eye Infection	
	subjects affected / exposed	1 / 27 (3.70%)	
	occurrences causally related to treatment / all	0 / 1	
Gastrointestinal disorders			
	Abdominal Pain	Additional description: Abdominal Pain	
	subjects affected / exposed	3 / 27 (11.11%)	
	occurrences causally related to treatment / all	0 / 4	
Constipation	Additional description: Constipation		
	subjects affected / exposed	1 / 27 (3.70%)	
	occurrences causally related to treatment / all	0 / 1	
	deaths causally related to treatment / all	0 / 0	
Small Intestinal Obstruction	Additional description: Small Intestinal Obstruction		
	subjects affected / exposed	1 / 27 (3.70%)	
	occurrences causally related to treatment / all	0 / 1	
	deaths causally related to treatment / all	0 / 0	
Vomiting	Additional description: Vomiting		
	subjects affected / exposed	1 / 27 (3.70%)	
	occurrences causally related to treatment / all	0 / 1	
	deaths causally related to treatment / all	0 / 0	
Respiratory, thoracic and mediastinal disorders			
	Pleural Effusion	Additional description: Pleural Effusion	

subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury	Additional description: Acute Kidney Injury		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back Pain	Additional description: Back Pain		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung Infection	Additional description: Lung Infection		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Single arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 27 (62.96%)		
Investigations			
Platelet Count Decreased	Additional description: Platelet Count Decreased		
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Neutrophil Count Decreased	Additional description: Neutrophil Count Decreased		
subjects affected / exposed	8 / 27 (29.63%)		
occurrences (all)	18		
Lymphocyte Count Decreased	Additional description: Lymphocyte Count Decreased		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Weight Loss	Additional description: Weight Loss		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Vascular disorders			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	18		
General disorders and administration site conditions			
Fatigue	Additional description: Fatigue		
subjects affected / exposed	10 / 27 (37.04%)		
occurrences (all)	13		
Eye disorders			
Eye Infection	Additional description: Eye Infection		
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal Pain	Additional description: Abdominal Pain		
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Constipation	Additional description: Constipation		

subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
Nausea	Additional description: Nausea		
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
Renal and urinary disorders			
Acute Kidney Injury	Additional description: Acute Kidney Injury		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia	Additional description: Insomnia		
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back Pain	Additional description: Back Pain		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Infections and infestations			
Urinary Tract Infection	Additional description: Urinary Tract Infection		
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
Lung Infection	Additional description: Lung Infection		
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia	Additional description: Anorexia		
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Hypomagnesemia	Additional description: Hypomagnesemia		

subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2016	Study documents updated following MHRA comments after initial submission.
08 September 2017	1. Addition of ctDNA analysis (blood samples) performed by prof Caroline Dive's team 2. archival tumour biopsies can be requested for patients entering at Entry Point 2
07 June 2018	Protocol was updated to include QP declaration, IB update, PIS/ICF change linked to translational blood collection, clarification of SAE wording, addition of a blood sample collection window (to allow use of bloods taken up to 14 days prior to visit) & addition of archival tumour block collection at entry point 2
08 October 2018	Change of PI
18 June 2020	Updated IBs for Olaparib and Cediranib with RSI changes for Olaparib
07 January 2021	Updated Cediranib IB from edition 22 to 23 and changes to the protocol to incorporate new secondary end point questions
22 June 2021	Updated Olaparib IB ed 20 with changes added to the protocol and PIS. Updated IRAS form inline with SA#7

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36799931>