Clinical trial results:
A proof of concept, multi-centre, clinical trial of the combination cediranib-olaparib at the time of disease progression on PARP inhibitor in ovarian cancer.

Summary

EudraCT number	2017-001192-23
Trial protocol	ES
Global end of trial date	21 June 2021

Results information

Result version number	v2 (current)
This version publication date	03 July 2022
First version publication date	20 May 2022
Version creation reason	• New data added to full data set Addition of the global end date
Summary attachment (see zip file)	SMS-0388_CSR_22May2020 (1078-0432.CCR-19-4121.full.pdf)

Trial information

Trial identification

Sponsor protocol code	OZM-060

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02681237
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Health Network, Toronto
Sponsor organisation address	610 University Avenue, Toronoto, Canada, ON M5G2M9
Public contact	Amit Oza, Unversity Health Network, Toronto, 1 4169462818, amit.oza@uhn.ca
Scientific contact	Amit Oza, Unversity Health Network, Toronto, 1 4169462818, amit.oza@uhn.ca

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	Interim
Date of interim/final analysis	22 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2020
Global end of trial reached?	Yes
Global end of trial date	21 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine efficacy of the combination of cediranib and olaparib in women previously receiving PARP inhibitor for ovarian cancer, with co-primary endpoints of
• objective response rate by RECIST 1.1 at 8 weeks
• progression-free-survival (PFS) at 16 weeks

Protection of trial subjects:

Patient data is kept confidential throughout the whole study and physicians strive to protect the health and rights of each trial subject throughout the whole study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 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: 27
Country: Number of subjects enrolled	Spain: 7
Worldwide total number of subjects	34
EEA total number of subjects	7

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)	24
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between June 2016 and October 2018, 34 women were enrolled in two centers in Canada and Spain.

Pre-assignment

Screening details:

Women with a histologically confirmed diagnosis of recurrent ovarian, fallopian tube, or primary peritoneal cancer with high-grade serous or high-grade endometrioid histology and radiographically documented disease progression on any PARPi. Patients were required to have disease evaluable by RECIST v1.1 and amenable to a baseline biopsy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Platinum sensitive

Arm description:

platinum sensitive patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression

Arm type	Experimental
Investigational medicinal product name	Cediranib
Investigational medicinal product code	288383-20-0
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cediranib to be taken orally and should be taken at the same time each day approximately. All doses should be taken with approximately 240 mL of water. The study treatment should be swallowed whole and not chewed, crushed, dissolved or divided. Tablets should be administered on an empty stomach at least 1 hour before or 2 hours after eating.

Investigational medicinal product name	Olaparib
Investigational medicinal product code	L01XX46
Other name	Lynparza
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Olaparib to be taken orally and should be taken at the same times each day approximately 12 hours apart. All doses should be taken with approximately 240 mL of water. The study treatment should be swallowed whole and not chewed, crushed, dissolved or divided. Tablets can be taken with a light meal/snack (e.g., two pieces of toast or a couple of biscuits).

Arm title	Platinum resistant

Arm description:

platinum resistant patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression

Arm type	Experimental

Investigational medicinal product name	Cediranib
Investigational medicinal product code	288383-20-0
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cediranib to be taken orally and should be taken at the same time each day approximately. All doses should be taken with approximately 240 mL of water. The study treatment should be swallowed whole and not chewed, crushed, dissolved or divided. Tablets should be administered on an empty stomach at least 1 hour before or 2 hours after eating.

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Investigational medicinal product code	L01XX46
Other name	Lynparza
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Olaparib to be taken orally and should be taken at the same times each day approximately 12 hours apart. All doses should be taken with approximately 240 mL of water. The study treatment should be swallowed whole and not chewed, crushed, dissolved or divided. Tablets can be taken with a light meal/snack (e.g., two pieces of toast or a couple of biscuits).

Arm title	Exploratory cohort

Arm description:

patients whose disease had progressed on a PARPi and progressed again on subsequent standard chemotherapy, regardless of platinum sensitivity

Arm type	Experimental
Investigational medicinal product name	Cediranib
Investigational medicinal product code	288383-20-0
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cediranib to be taken orally and should be taken at the same time each day approximately. All doses should be taken with approximately 240 mL of water. The study treatment should be swallowed whole and not chewed, crushed, dissolved or divided. Tablets should be administered on an empty stomach at least 1 hour before or 2 hours after eating.

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Number of subjects in period 1	Platinum sensitive	Platinum resistant	Exploratory cohort
Started	11	10	13
Discontinued treatment	11	9 [1]	11 [2]
Still on treatment	0 [3]	1 [4]	2 [5]
Completed	11	10	13

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The discontinuation of treatment in this study does not make the patient not evaluable for efficacy

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The discontinuation of treatment in this study does not make the patient not evaluable for efficacy

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The discontinuation of treatment in this study does not make the patient not evaluable for efficacy

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The discontinuation of treatment in this study does not make the patient not evaluable for efficacy

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The discontinuation of treatment in this study does not make the patient not evaluable for efficacy

Baseline characteristics

Reporting groups	
Reporting group title	Platinum sensitive
Reporting group description:	
platinum sensitive patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression	
Reporting group title	Platinum resistant
Reporting group description:	
platinum resistant patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression	
Reporting group title	Exploratory cohort
Reporting group description:	
patients whose disease had progressed on a PARPi and progressed again on subsequent standard chemotherapy, regardless of platinum sensitivity	

Reporting group values	Platinum sensitive	Platinum resistant	Exploratory cohort
Number of subjects	11	10	13
Age categorical Units: Subjects			
Adults (18-64 years)	3	2	5
From 65-84 years	8	8	8
Gender categorical Units: Subjects			
Female	11	10	13
Male	0	0	0

Reporting group values	Total		
Number of subjects	34		
Age categorical Units: Subjects			
Adults (18-64 years)	10		
From 65-84 years	24		
Gender categorical Units: Subjects			
Female	34		
Male	0		

End points

End points reporting groups

Reporting group title	Platinum sensitive
Reporting group description:	
platinum sensitive patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression	
Reporting group title	Platinum resistant
Reporting group description:	
platinum resistant patients who had progressed on PARP and then underwent standard chemotherapy with further disease progression	
Reporting group title	Exploratory cohort
Reporting group description:	
patients whose disease had progressed on a PARPi and progressed again on subsequent standard chemotherapy, regardless of platinum sensitivity	

Primary: Objective response rate by RECIST 1.1

End point title	Objective response rate by RECIST 1.1[1]
End point description:	
ORR as assessed by RECIST 1.1	
End point type	Primary
End point timeframe:	
at 8 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: This is a proof of concept study that aims to detect initial signal of efficacy with the combination cediranib/olaparib after failure on PARP inhibitor, such as olaparib. Therefore no statistical analyses are specified

End point values	Platinum sensitive	Platinum resistant	Exploratory cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	13	
Units: number	0	2	1	

Statistical analyses

No statistical analyses for this end point

Primary: Progression Free Survival

End point title	Progression Free Survival[2]
End point description:	
End point type	Primary
End point timeframe:	
at 16 weeks	

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: This is a proof of concept study that aims to detect initial signal of efficacy with the combination cediranib/olaparib after failure on PARP inhibitor, such as olaparib. Therefore no statistical analyses are specified

End point values	Platinum sensitive	Platinum resistant	Exploratory cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	13	
Units: percentage	55	50	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of response rate according to CA125-GCIG criteria

End point title	Evaluation of response rate according to CA125-GCIG criteria

End point description:

End point type	Secondary

End point timeframe:

post-progression on PARP inhibitor to progression on cediranib and olaparib

End point values	Platinum sensitive	Platinum resistant	Exploratory cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	13	
Units: number	2	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate

End point title	Disease control rate

End point description:

Disease control rate
o OS will be defined by the time between randomization and the occurrence of death whatever the cause.
o Response assessed by RECIST 1.1

End point type	Secondary

End point timeframe:

post-progression on PARP inhibitor to progression on cediranib and olaparib

End point values	Platinum sensitive	Platinum resistant	Exploratory cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	13	
Units: number	9	6	8	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the safety of the combination olaparib and cediranib

End point title	To evaluate the safety of the combination olaparib and cediranib

End point description:

The toxicity profile will be evaluated according to the NCI CTC AE v.4.03, AEs from grade 3/4 are added

End point type	Secondary

End point timeframe:

from cycle 1 day 1 till the date of scheduled 4 weeks (+ 1 week) follow-up visit or 28 days after discontinuation of the study drug, whichever is later.

End point values	Platinum sensitive	Platinum resistant	Exploratory cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	13	
Units: number	23	11	17	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The eCRF should capture all AEs occurring from cycle 1 day 1 till the date of scheduled 4 weeks (+ 1 week) follow-up visit or 28 days after discontinuation of the study drug, whichever is later.

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 34 (32.35%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colonic obstruction			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Ileus			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 34 (100.00%)		
Vascular disorders			
Hypertension			

subjects affected / exposed	10 / 34 (29.41%)		
occurrences (all)	15		
General disorders and administration site conditions			
difficulty finding words			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Early satiety			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	5		
Chills			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
oedema limbs			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	17 / 34 (50.00%)		
occurrences (all)	31		
fever			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	6		
left lower quadrant pain			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
shoulder pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
hoarseness			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	6 / 34 (17.65%) 9		
Dyspnoea subjects affected / exposed occurrences (all)	5 / 34 (14.71%) 7		
Epistaxis subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 4		
Nasal congestion subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 5		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	4 / 34 (11.76%) 8		
Alkaline phosphatase increased subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 3		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 7		
Blood bilirubin increased subjects affected / exposed occurrences (all)	4 / 34 (11.76%) 7		
Creatine urine increased subjects affected / exposed occurrences (all)	6 / 34 (17.65%) 12		
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	6 / 34 (17.65%) 13		
ggt increased			

subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 3		
Neutrophil count decreased subjects affected / exposed occurrences (all)	8 / 34 (23.53%) 13		
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 13		
Weight decreased subjects affected / exposed occurrences (all)	5 / 34 (14.71%) 5		
White blood cell count decreased subjects affected / exposed occurrences (all)	5 / 34 (14.71%) 12		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	5 / 34 (14.71%) 7		
Dysgeusia subjects affected / exposed occurrences (all)	4 / 34 (11.76%) 4		
Headache subjects affected / exposed occurrences (all)	8 / 34 (23.53%) 8		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 4		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	6 / 34 (17.65%) 23		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	14 / 34 (41.18%) 25		
bloating			

subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	7		
colonic obstruction			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	24 / 34 (70.59%)		
occurrences (all)	40		
Dry mouth			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Gingival pain			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	3		
mucositis oral			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	22 / 34 (64.71%)		
occurrences (all)	27		
Rectal haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	20 / 34 (58.82%)		
occurrences (all)	35		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	9		

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Generalized muscle weakness			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	14		
Myalgia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	5		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
Anorexia nervosa			
subjects affected / exposed	10 / 34 (29.41%)		
occurrences (all)	12		
Dehydration			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	6		
Hypomagnesaemia			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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/32444417