Clinical trial results:
A prospective, multi-centre, open label, non-randomised two stage phase II clinical trial evaluating the efficacy of abiraterone in patients with epithelial ovarian (including fallopian tube and primary peritoneal) cancer.

Summary

EudraCT number	2013-000293-29
Trial protocol	GB
Global end of trial date	28 January 2021

Results information

Result version number	v1 (current)
This version publication date	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	ICR-CTSU/2012/10038

Additional study identifiers

ISRCTN number	ISRCTN63407050
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Identification Number:: CCR3948, ICR-CTSU Protocol Number: ICR-CTSU/2021/10038, CRUK Reference Number:: A16037, Main REC Reference:: 13/LO/1599, MHRA CTA Reference Number:: 15983/0242/001-0001

Notes:

Sponsors

Sponsor organisation name	The Institute of Cancer Research
Sponsor organisation address	5 Cotswold Road, Sutton, United Kingdom, SM2 5NG
Public contact	Christy Toms, Clinical Trials Programme Manager, The Institute of Cancer Research, +44 0208 722 4266, coral-icrctsu@icr.ac.uk
Scientific contact	Christy Toms, Clinical Trials Programme Manager, The Institute of Cancer Research, +44 0208 722 4266, coral-icrctsu@icr.ac.uk
Sponsor organisation name	The Royal Marsden NHS Foundation Trust
Sponsor organisation address	Downs Road, Sutton, United Kingdom,
Public contact	Christy Toms, Clinical Trials Programme Manager, The Royal Marsden NHS Foundation Trust, +44 0208 722 4266, coral-icrctsu@icr.ac.uk
Scientific contact	Christy Toms, Clinical Trials Programme Manager, The Royal Marsden NHS Foundation Trust, +44 0208 722 4266, coral-icrctsu@icr.ac.uk

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	22 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2021
Global end of trial reached?	Yes
Global end of trial date	28 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine whether abiraterone has clinical activity (objective response rate assessed by imaging and/or CA125 tumour marker changes in the blood) in patients with epithelial ovarian cancer (EOC) that has relapsed within 12 months of last treatment.

26 patients 'unselected' for androgen receptor (AR) status will be treated in stage one and, if successful, a further 21 patients in stage two bringing the total number of patients required to 47.

Protection of trial subjects:

Patients were provided with full verbal and written informed consent regarding the purpose and procedures of the trial and the possible risks involved. A patient information sheet and consent form were provided and patients were given sufficient time to consider their participation. The Principal Investigator at each site was responsible for ensuring written informed consent was obtained for each patient.

Full details of the trial medication and its safety profile were provided in the patient information sheet. Patients had the opportunity to discuss any concerns they had in relation to this with their study team at site.

Background therapy:

All patients received prednisone or prednisolone (at clinician's discretion) at 5mg orally once daily to prevent secondary mineralocorticoid excess.

Evidence for comparator:

This was a two-stage phase II, non-randomised clinical trial with all patients receiving abiraterone once a day on a continuous 28-day cycle until disease progression.

Actual start date of recruitment	09 December 2013
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: 42
Worldwide total number of subjects	42
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)	20
From 65 to 84 years	21
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Forty-two patients were recruited from four UK centres between21 March 2014 and 3 November 2015

Pre-assignment

Screening details:

Post-menopausal women with histologically or cytologically confirmed epithelial ovarian, fallopian tube (FT) or primary peritoneal (PP) cancer were eligible if they had progressed (radiological or CA125 criteria) within 12 months of last systemic anti-cancer therapy. 50 patients were registered, 42 proceeded to trial entry.

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	Abiraterone

Arm description:

All patients receive an oral dose of abiraterone 100mg (4 x 250mg tablets) once a day on a continuous 28 day cycle

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

Dosage and administration details:

Oral dose of 1000mg (4 x 250mg) once a day on a continuous 28 day cycle

Number of subjects in period 1	Abiraterone
Started	42
Stage 1	42
Completed	37
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	42	42	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	21	21	
85 years and over	1	1	
Age continuous Units: years			
median	65.4		
inter-quartile range (Q1-Q3)	55.7 to 72.7	-	
Gender categorical Units: Subjects			
Female	42	42	
Histological subtype (central assessment) Units: Subjects			
High grade serous	37	37	
Low grade serous	3	3	
Endometrioid	2	2	
AR status Units: Subjects			
AR positive (>10%)	29	29	
AR negative (<10%)	11	11	
Missing	2	2	

End points

End points reporting groups

Reporting group title	Abiraterone
Reporting group description:	
All patients receive an oral dose of abiraterone 100mg (4 x 250mg tablets) once a day on a continuous 28 day cycle	
Subject analysis set title	Stage 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Stage 1 includes the first 26 patients recruited to the CORAL trial regardless of evaluability of the patient.	
Subject analysis set title	Evaluable
Subject analysis set type	Per protocol
Subject analysis set description:	
Any patient who had a scan at 12 weeks and/or progressed/died prior to 12 weeks is considered evaluable and will be included in the analysis of the evaluable population. Any patient discontinuing the trial for other reasons prior to 12 weeks would not be considered evaluable.	

Primary: Objective response

End point title	Objective response[1]
End point description:	
Primary endpoint is objective response rate at 12 weeks after registration. Objective response is defined as a complete or partial response according to joint RECIST/GCIG criteria.	
End point type	Primary
End point timeframe:	
Up to 12 weeks from trial entry.	

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 single arm study and no comparative analysis was performed, however the system expects at least 2 groups to be identified. All methods and options specified in the analysis section apply to statistical methods and summary measures to report and compare at least 2

End point type	Secondary

End point timeframe:

Up to 12 weeks after trial entry.

End point values	Abiraterone	Stage 1	Evaluable	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	42	26	34[2]	
Units: Patients				
Responder	0	0	0	
Non-responder	39	25	34	
Not evaluable	3	1	0	

Notes:

[2] - 3 patients were considered evaluable for CA125 but non evaluable for RECIST.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response according to GCIG (CA125)

End point title	Objective response according to GCIG (CA125)

End point description:

The proportion of patients with objective response according to CA125 criteria as recommended by the Gynaecologic Cancer InterGroup (GCIG) guidelines issued November 2005.

End point type	Secondary

End point timeframe:

Up to 12 weeks post trial entry.

End point values	Abiraterone	Stage 1	Evaluable	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	42	26	32[3]	
Units: Patients				
Responder	1	1	1	
Non-responder	36	22	31	
Non-evaluable	5	3	0	

Notes:

[3] - 5 patients were evaluable for RECIST but not CA125 so are excluded from this analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit rate

End point title	Clinical benefit rate

End point description:

Clinical benefit rate according to RECIST/GCIG criteria at 12 weeks.

End point type	Secondary

End point timeframe:

Up to 12 weeks post trial entry.

End point values	Abiraterone	Stage 1	Evaluable	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	42	26	37	
Units: Patients				
Clinical benefit	11	7	11	
No clinical benefit	31	19	26	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

Progression free survival will be measured from date of registration until date of confirmed progressive disease or death. Subjects who have not progressed or died at time of analysis will be censored at the date of last follow up.

End point type	Secondary

End point timeframe:

From trial entry until patient progression.

End point values	Abiraterone			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Months				
median (confidence interval 95%)	2.5 (1.8 to 3.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression

End point title	Time to progression

End point description:

Time to progression is measured from date of registration until date of confirmed progressive disease. Subjects who have died without prior confirmation of progression or are alive and have not progressed will be considered censored at date of death/latest follow up.

End point type	Secondary

End point timeframe:
From trial entry until progression.

End point values	Abiraterone			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Months				
median (confidence interval 95%)	2.2 (1.8 to 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:
Overall survival is measured from the date of registration until date of death of any cause.

End point type	Secondary

End point timeframe:
From trial entry until death.

End point values	Abiraterone			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Months				
median (confidence interval 95%)	9.8 (7.3 to 17.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From trial entry until 28 days post treatment discontinuation.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14

Reporting groups	
Reporting group title	Abiraterone
Reporting group description: All patients receive an oral dose of abiraterone 100mg (4 x 250mg tablets) once a day on a continuous 28 day cycle	

Serious adverse events	Abiraterone		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 42 (35.71%)		
number of deaths (all causes)	40		
number of deaths resulting from adverse events	0		
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood potassium decreased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Migraine with aura			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Constipation			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Wheezing			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Flank pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Arthritis infective			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Abiraterone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 42 (95.24%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	8		
Hypertension			
subjects affected / exposed	28 / 42 (66.67%)		
occurrences (all)	32		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	26 / 42 (61.90%)		
occurrences (all)	35		
Oedema peripheral			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	7		
Dyspnoea			
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	16		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Hepatic enzyme increased			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Neuropathy peripheral			
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	24		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	9		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	8		
Abdominal distension			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Abdominal pain			

subjects affected / exposed	27 / 42 (64.29%)		
occurrences (all)	36		
Constipation			
subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	31		
Diarrhoea			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	17		
Dyspepsia			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	8		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	19 / 42 (45.24%)		
occurrences (all)	23		
Stomatitis			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Vomiting			
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	16		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	12		
Musculoskeletal pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	8		
Sinusitis			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	18 / 42 (42.86%)		
occurrences (all)	18		
Hypokalaemia			
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	15		
Hypomagnesaemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Hyponatraemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 September 2015	1. Update to Investigator Brochure v11 (22/09/2015) and associated protocol/patient information sheet changes 2. Change of principal analysis population to 'Intention to Treat' from the 'evaluable' population 3. Update to exclusion criterion 'unresolved bowel obstruction' to include 'or symptoms of sub-acute bowel obstruction' 4. Addition of exclusion criterion 'Ascites on clinical examination or significant ascites present on baseline imaging' 5. Addition of radiological confirmation of response (CT scan/MRI) at 28 days following initial assessment of response 6. Addition of a liver function test at the mid-point in cycle 1 to monitor serum transaminase levels following the first 2 weeks of abiraterone treatment. 7. Change in timing of optional progression sample collection from 'within 7 days after last treatment' to 'after last dose of abiraterone and before commencement of any new systemic therapy' 8. Change of AR positivity cut-off from 1% to 10%
07 October 2015	1. Temporary halt to recruitment
20 February 2017	1. Update to Investigator Brochure v12 (August 2015)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 November 2015	Recruitment to the CORAL trial was paused until the formal interim analysis following stage 1 of the trial was complete. This protocol-specified interim analysis indicated that in respect of the study's primary endpoint the pre-planned	