Clinical trial results:
A randomised placebo-controlled trial of saracatinib (AZD0530) plus weekly paclitaxel in platinum-resistant ovarian, fallopian tube or primary peritoneal cancer.

Summary

EudraCT number	2009-017171-13
Trial protocol	GB
Global end of trial date	12 January 2014

Results information

Result version number	v1 (current)
This version publication date	25 May 2017
First version publication date	25 May 2017

Trial information

Trial identification

Sponsor protocol code	UCL/09/0105

Additional study identifiers

ISRCTN number	ISRCTN32163062
ClinicalTrials.gov id (NCT number)	NCT01196741
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Joint Research Office, Gower Street, London, United Kingdom, WC1E 6BT
Public contact	Mr Lee Webber, Cancer Research UK & UCL Cancer Trials Centre, 44 2076799872, ctc.sapproc@ucl.ac.uk
Scientific contact	Mr Lee Webber, Cancer Research UK & UCL Cancer Trials Centre, 44 2076799872, ctc.sapproc@ucl.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	31 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2012
Global end of trial reached?	Yes
Global end of trial date	12 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research question was to see whether adding the drug saracatinib to weekly paclitaxel chemotherapy improves 6 month progression-free survival in patients with platinum-resistant ovarian cancer.

Protection of trial subjects:

Protection included risk assessment, on-site monitoring, dose modifications and emergency unblinding procedure.

Background therapy:

Not applicable, both saracatinib (and matched placebo) and paclitaxel were classed as IMP

Evidence for comparator:

Not applicable

Actual start date of recruitment	11 April 2011
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: 107
Worldwide total number of subjects	107
EEA total number of subjects	107

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)	62

From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 107 patients were randomised from 12 UK sites between April 2011 and May 2012

Pre-assignment

Screening details:

Patients were recruited following successful screening, according to pre-specified protocol eligibility criteria and baseline assessments

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Blinding via Interactive Web-based Randomisation System (IWRS). Sites were provided with a detailed unblinding procedure

Arms

Are arms mutually exclusive?	Yes
Arm title	Weekly paclitaxel plus saracatinib

Arm description:

Weekly paclitaxel plus saracatinib

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Full dose of 80mg per metre squared, with dose reductions to 70mg and 60mg per metre squared - 8 weekly cycles whereby paclitaxel given weekly for 6 weeks followed by a 2 week rest

Investigational medicinal product name	Saracatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

175 mg daily, commencing 7 days prior to start of weekly paclitaxel - daily until disease progression

Arm title	Weekly paclitaxel plus placebo

Arm description:

Weekly paclitaxel plus placebo

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
Full dose of 80mg per metre squared, with dose reductions to 70mg and 60mg per metre squared - 8 weekly cycles whereby paclitaxel given weekly for 6 weeks followed by a 2 week rest	
Investigational medicinal product name	Matched placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Commencing 7 days prior to start of weekly paclitaxel - daily until disease progression	

Number of subjects in period 1	Weekly paclitaxel plus saracatinib	Weekly paclitaxel plus placebo
Started	71	36
Completed	69	35
Not completed	2	1
Adverse event, non-fatal	1	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Weekly paclitaxel plus saracatinib
Reporting group description: Weekly paclitaxel plus saracatinib	
Reporting group title	Weekly paclitaxel plus placebo
Reporting group description: Weekly paclitaxel plus placebo	

Reporting group values	Weekly paclitaxel plus saracatinib	Weekly paclitaxel plus placebo	Total
Number of subjects	71	36	107
Age categorical Units: Subjects			
Adults (18-64 years)	46	16	62
From 65-84 years	25	20	45
Age continuous Units: years			
median	62.8	66.9	
full range (min-max)	34.5 to 78.8	20 to 82.1	-
Gender categorical Units: Subjects			
Female	71	36	107
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Intention-to-treat weekly paclitaxel plus saracatinib
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised who took at least one dose of study medication	
Subject analysis set title	Intention-to-treat weekly paclitaxel plus placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised who took at least one dose of study medication	

Reporting group values	Intention-to-treat weekly paclitaxel plus saracatinib	Intention-to-treat weekly paclitaxel plus placebo	
Number of subjects	69	35	
Age categorical Units: Subjects			
Adults (18-64 years)	45	15	
From 65-84 years	24	20	
Age continuous Units: years			
median	62.4	67	
full range (min-max)	34.5 to 78.8	47.4 to 82.1	

Gender categorical Units: Subjects			
Female	69	35	
Male	0	0	

End points

End points reporting groups

Reporting group title	Weekly paclitaxel plus saracatinib
Reporting group description: Weekly paclitaxel plus saracatinib	
Reporting group title	Weekly paclitaxel plus placebo
Reporting group description: Weekly paclitaxel plus placebo	
Subject analysis set title	Intention-to-treat weekly paclitaxel plus saracatinib
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised who took at least one dose of study medication	
Subject analysis set title	Intention-to-treat weekly paclitaxel plus placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised who took at least one dose of study medication	

Primary: 6 month progression-free survival (PFS) rate

End point title	6 month progression-free survival (PFS) rate
End point description:	
End point type	Primary
End point timeframe: The number and proportion of patients who are alive and progression free at 6 months from randomisation	

End point values	Intention-to-treat weekly paclitaxel plus saracatinib	Intention-to-treat weekly paclitaxel plus placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	35		
Units: Number of patients	20	12		

Statistical analyses

Statistical analysis title	Primary endpoint statistical analysis
Comparison groups	Intention-to-treat weekly paclitaxel plus placebo v Intention-to-treat weekly paclitaxel plus saracatinib
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.589
Method	Regression, Cox

Secondary: Median overall survival (OS)

End point title	Median overall survival (OS)

End point description:

End point type	Secondary

End point timeframe:

The period of time between the date of randomisation to date of death

End point values	Intention-to-treat weekly paclitaxel plus saracatinib	Intention-to-treat weekly paclitaxel plus placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	35		
Units: Months				
median (full range (min-max))	10.1 (8.3 to 16.2)	12.3 (11 to 14.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median progression free survival (PFS)

End point title	Median progression free survival (PFS)

End point description:

End point type	Secondary

End point timeframe:

Defined as the date from randomisation to the date of first progression or death (whichever occurs first)

End point values	Intention-to-treat weekly paclitaxel plus saracatinib	Intention-to-treat weekly paclitaxel plus placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	35		
Units: Months				
median (full range (min-max))	4.7 (3.6 to 5.5)	5.3 (3.6 to 7.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (combined RECIST v1.1 & GCIG CA125 criteria)

End point title	Objective Response Rate (combined RECIST v1.1 & GCIG CA125 criteria)

End point description:

The number of patients with a documented complete response (CR) or partial response (PR) according to combined RECIST v1.1 & GCIG CA125 criteria

End point type	Secondary

End point timeframe:

According to protocol-specified schedule. Radiological imaging: baseline, during the rest period of each chemotherapy cycle, 3 monthly during follow up until progression. CA125: baseline, weeks 1, 3 and 6 of each chemotherapy cycle, 6 weekly follow up

End point values	Intention-to-treat weekly paclitaxel plus saracatinib	Intention-to-treat weekly paclitaxel plus placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	35		
Units: Number of patients	20	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Between informed consent and 30 days post last trial treatment administration

Adverse event reporting additional description:

The specified serious adverse events are those presented in the published paper i.e. SAEs of grade 3-5 according to CTCAE v4.0

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Weekly paclitaxel plus saracatinib

Reporting group description:

Weekly paclitaxel plus saracatinib

Reporting group title	Weekly paclitaxel plus placebo

Reporting group description:

Weekly paclitaxel plus placebo

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The published results did not specify non-serious adverse events, only serious adverse events of grade 3-5 according to CTCAE v4.0. Under each reporting group, 0 has been entered for 'Subjects affected by non-serious adverse events' to enable validation of the results data set. Please refer to the published paper.

Serious adverse events	Weekly paclitaxel plus saracatinib	Weekly paclitaxel plus placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 69 (36.23%)	11 / 35 (31.43%)	
number of deaths (all causes)	51	26	
number of deaths resulting from adverse events			
Investigations			
Neutrophil count decreased	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	2 / 69 (2.90%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine increased	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular arrhythmia	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		

subjects affected / exposed	0 / 69 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Blood and lymphatic system disorders			
Anaemia	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	3 / 69 (4.35%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	3 / 69 (4.35%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	2 / 69 (2.90%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	4 / 69 (5.80%)	3 / 35 (8.57%)	
occurrences causally related to treatment / all	1 / 4	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	4 / 69 (5.80%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	3 / 69 (4.35%)	2 / 35 (5.71%)	
occurrences causally related to treatment / all	3 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	3 / 69 (4.35%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	0 / 69 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	2 / 69 (2.90%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	0 / 69 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		

subjects affected / exposed	2 / 69 (2.90%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Catheter-related infection	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	0 / 69 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	0 / 69 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis infective	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal chest infection	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Dehydration	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	2 / 69 (2.90%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia	Additional description: SAEs of grade 3-5 according to CTCAE v4.0		
subjects affected / exposed	1 / 69 (1.45%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Weekly paclitaxel plus saracatinib	Weekly paclitaxel plus placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 69 (0.00%)	0 / 35 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2012	Updates and clarifications to protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported