Clinical trial results:
SarCaBon: A randomised phase II trial of Saracatinib versus placebo for cancer-induced bone pain

Summary

EudraCT number	2013-002505-62
Trial protocol	GB
Global end of trial date	24 January 2018

Results information

Result version number	v1 (current)
This version publication date	02 December 2019
First version publication date	02 December 2019
Summary attachment (see zip file)	Published study (Published manuscript.pdf)

Trial information

Trial identification

Sponsor protocol code	STH16404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02085603
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	8 Beech Hill Road, Trust Headquarters, Sheffield, United Kingdom, S10 2SB
Public contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.researchadministration@nhs.net
Scientific contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.researchadministration@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	24 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2018
Global end of trial reached?	Yes
Global end of trial date	24 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Is Saracatinib effective at reducing bone pain in cancer patients that have painful bone metastases by comparing patient's self-reported pain ratings (0 – 10 point scale) after 4 weeks on treatment with pain scores from patients who receive placebo.

Protection of trial subjects:

Patients were verbally re-consented at every clinic visit to make sure they still wanted to remain within the trial.
Experimental tests that were research-specific were chosen so that any discomfort produced was minimal.
If pain control during the study deteriorated radiotherapy was offered.

Background therapy:

Usual care

Evidence for comparator:

None were used

Actual start date of recruitment	11 March 2014
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: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	6

From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial opened to recruitment: 11/3/14
Trial closed to recruitment: 31/7/17
Territories: United Kingdom (Sheffield and Leeds)

Pre-assignment

Screening details:

Cytologically or histologically confirmed solid tumours or multiple myeloma with painful bone metastases and poor control of bone pain in spite of pain medication.

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:

Pharmacokinetic measurement of study drug concentrations were not performed until the study had closed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active drug

Arm description:

Patients in the active drug arm received the study medication

Arm type	Experimental
Investigational medicinal product name	Saracatinib
Investigational medicinal product code	AZD0530
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

125mg tablet
Once per day for 4 weeks

Arm title	Placebo

Arm description:

Placebo arm

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

Dosage and administration details:

Matched placebo tablet
Once per day for 4 weeks

Number of subjects in period 1	Active drug	Placebo
Started	7	6
Completed	6	6
Not completed	1	0
participant had SAE prior to commencing any treatm	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Active drug
Reporting group description:	
Patients in the active drug arm received the study medication	
Reporting group title	Placebo
Reporting group description:	
Placebo arm	

Reporting group values	Active drug	Placebo	Total
Number of subjects	7	6	13
Age categorical			
Patients aged 16yrs or older Baseline average pain ≥ 2 and ≤ 9 on a 0-10 numerical scale recorded on at least two separate days using the Brief Pain Inventory-Short Form WHO performance status ≤ 2 Ability to take and absorb oral medications Able to give written informed consent and willing to follow the study protocol Adequate baseline haematological, hepatic and renal function			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	2	6
From 65-84 years	3	4	7
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	61	65	
full range (min-max)	50 to 74	62 to 71	-
Gender categorical			
Patients were recruited at random			
Units: Subjects			
Female	3	2	5
Male	4	4	8
Tumour type			
Histology of the primary cancer			
Units: Subjects			
Adenocarcinoma of prostate	3	3	6
Chordoma	1	0	1
Lung cancer	0	2	2
Adenocarcinoma of breast	3	1	4

End points

End points reporting groups

Reporting group title	Active drug
Reporting group description:	
Patients in the active drug arm received the study medication	
Reporting group title	Placebo
Reporting group description:	
Placebo arm	

Primary: Worst pain in last 24h after 4 weeks on treatment

End point title	Worst pain in last 24h after 4 weeks on treatment[1]
End point description:	
Worst pain in last 24h, Brief Pain Inventory-Short form Q3	
End point type	Primary
End point timeframe:	
After 4 weeks on treatment	

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: There is no statistical analysis provided for this endpoint as the trial did not reach the recruitment target and therefore performing formal statistics is not justified; the calculations lack sufficient power.

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-10				
arithmetic mean (standard deviation)	6.0 (± 2.4)	6.6 (± 2.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Least pain in last 24h after 4 weeks on treatment

End point title	Least pain in last 24h after 4 weeks on treatment[2]
End point description:	
Least pain in last 24h Brief Pain Inventory-Short form Q4	
End point type	Primary
End point timeframe:	
After 4 weeks on treatment	

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: There is no statistical analysis provided for this endpoint as the trial did not reach the recruitment target and therefore performing formal statistics is not justified; the calculations lack sufficient power.

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-10				
arithmetic mean (standard deviation)	3.2 (± 2.0)	3.0 (± 3.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Average pain in last 24h after 4 weeks on treatment

End point title	Average pain in last 24h after 4 weeks on treatment[3]

End point description:

Average pain in last 24h Brief Pain Inventory-Short form Q5

End point type	Primary

End point timeframe:

After 4 weeks on treatment

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: There is no statistical analysis provided for this endpoint as the trial did not reach the recruitment target and therefore performing formal statistics is not justified; the calculations lack sufficient power.

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-10				
arithmetic mean (standard deviation)	4.3 (± 1.9)	4.7 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Pain right now after 4 weeks on treatment

End point title	Pain right now after 4 weeks on treatment[4]

End point description:

Pain right now Brief Pain Inventory-Short form Q6

End point type	Primary

End point timeframe:

After 4 weeks on treatment

Notes:

[4] - 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: There is no statistical analysis provided for this endpoint as the trial did not reach the recruitment target and therefore performing formal statistics is not justified; the calculations lack sufficient power.

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-10				
arithmetic mean (standard deviation)	4.5 (± 2.7)	4.9 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: OME at end of 4 weeks treatment

End point title	OME at end of 4 weeks treatment

End point description:

Secondary objective: To determine if analgesic drug use deacreased when participants took saracatinib. This is measured by analgesic usage data for previous 24hours prior to baseline and each clinic visit. The dose of all opioids is coverted in to Oral Morphine Equivalent (OME).

End point type	Secondary

End point timeframe:

After 4 weeks on treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: µg/day				
arithmetic mean (standard deviation)	207 (± 327)	138 (± 167)		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-BM22 painful site score after 4 weeks of treatment

End point title	QLQ-BM22 painful site score after 4 weeks of treatment

End point description:

Secondary objective: To determine if pain thresholds at symptomatic sites increased after treatment with saracatinib. This was measured using the QLQ-BM22 painful site scores.

End point type	Secondary

End point timeframe:

After 4 weeks on treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-100				
arithmetic mean (standard deviation)	36.0 (± 18.6)	28.3 (± 12.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30 global health related quality of life score after 4 weeks treatment

End point title	QLQ-C30 global health related quality of life score after 4 weeks treatment

End point description:

Secondary objective: To determine if pain-related symptoms and quality of life are improved by saracatinib . This is measured using the QLQ-C30 global health related quality of life score after 4 weeks treatment.

End point type	Secondary

End point timeframe:

After 4 weeks of treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-100				
arithmetic mean (standard deviation)	66.6 (± 10.0)	69.1 (± 9.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30 pain score after 4 weeks treatment

End point title	QLQ-C30 pain score after 4 weeks treatment

End point description:

Secondary objective: To determine if pain-related symptoms and quality of life are improved by saracatinib . This is measured using the QLQ-C30 pain score after 4 weeks treatment.

End point type	Secondary

End point timeframe:

After 4 weeks on treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-100				
arithmetic mean (standard deviation)	58.3 (± 17.5)	61.1 (± 9.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ BM22 painful characteristics score after 4 weeks treatment

End point title	QLQ BM22 painful characteristics score after 4 weeks treatment

End point description:

Secondary objective: To determine if pain-related symptoms and quality of life are improved by saracatinib . This is measured using the QLQ BM22 painful characteristics score after 4 weeks treatment.

End point type	Secondary

End point timeframe:

After 4 weeks on treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: 0-100				
arithmetic mean (standard deviation)	44.4 (± 0)	38.9 (± 14.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: sCTX after 4 weeks treatment

End point title	sCTX after 4 weeks treatment

End point description:

Secondary endpoint: To determine whether bone turnover is further reduced by saracatinib in patients already taking bisphosphonates or denosumab. This is measured studying sCTX, a biomarker of bone resorption, after 4 weeks on treatment.

End point type	Secondary

End point timeframe:

After 4 weeks on treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: % change from baseline				
arithmetic mean (standard deviation)	-34.6 (± 12.9)	8.4 (± 12.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: uNTX/Cr after 4 weeks treatment

End point title	uNTX/Cr after 4 weeks treatment

End point description:

Secondary endpoint: To determine whether bone turnover is further reduced by saracatinib in patients already taking bisphosphonates or denosumab. This is measured studying uNTX/Cr, a biomarker of bone resorption, after 4 weeks on treatment.

End point type	Secondary

End point timeframe:

After 4 weeks treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: % change from baseline				
arithmetic mean (standard deviation)	-16.0 (± 41.9)	-3.2 (± 4.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: P1NP after 4 weeks treatment

End point title	P1NP after 4 weeks treatment

End point description:

Secondary endpoint: To determine whether bone turnover is further reduced by saracatinib in patients already taking bisphosphonates or denosumab. This is measured studying P1NP, a biomarker of bone deposition, after 4 weeks on treatment.

End point type	Secondary

End point timeframe:

After 4 weeks treatment

End point values	Active drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: % change from baseline				
arithmetic mean (standard deviation)	-12.2 (± 15.4)	7.0 (± 7.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be collected for all participants from the time of written informed consent until 30 days post cessation of trial therapy (including any IMP received during extended use).

Adverse event reporting additional description:

All AEs were monitored until resolution, or if the AE was determined to be chronic, until a cause is identified. If an AE remained unresolved at the conclusion of the study, the investigator made a clinical assessment about whether continued follow-up of the AE was warranted.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Active drug

Reporting group description:

Patients in the active drug arm received the study medication

Reporting group title	Placebo

Reporting group description:

Placebo arm

Serious adverse events	Active drug	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain Metastases			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active drug	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Foot oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Neuropathic Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Drowsiness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Tiredness			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal bloating			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Abdominal Cramp			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	3 / 6 (50.00%)	
occurrences (all)	2	3	
Loose stools			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Oral Thrush			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Persistent non-productive cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Wheeze			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Runny nose			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Hair loss			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pruritus of both hands			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Renal function test abnormal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Pain in leg			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Sacral pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Fingers stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2013	Substantial Amendment 01: Submission of Manufacturer's Authorisation.
12 May 2015	Substantial Amendment 07: Update to Reference Safety Information.
06 August 2015	Substantial Amendment 08: Addition of extended use of the IMP to the protocol, this allowed participants to take the IMP for an additional 6 months if there was significant improvement in their pain scores. Participants signed an additional consent form if they entered the 'extended use' phase and AEs continued to be collected.
22 February 2016	Substantial Amendment 10: Update to Reference Safety Information and Marketing Authorisation updated to include manufacturers from Sweden.
21 October 2016	Substantial Amendment 11: Reduction in sample size and update to trial stopping rules. Addition of new site/PI.
30 March 2017	Substantial Amendment 13: SAE clarification for inpatient hospitalisation due to progression of disease. Clarification of definition of End of Trial.

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.

Sample size of 12 participants.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31667062