



Clinical trial results:

A randomised placebo-controlled, double blinded, phase III trial of sorafenib in combination with transarterial chemoembolisation in hepatocellular cancer.

Summary

EudraCT number	2008-005073-36
Trial protocol	GB IE
Global end of trial date	27 November 2016

Results information

Result version number	v1 (current)
This version publication date	20 July 2025
First version publication date	20 July 2025
Summary attachment (see zip file)	Lay summary (TACE-2 lay Summary v1.0 01-Mar-2022.pdf)

Trial information

Trial identification

Sponsor protocol code	07130
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Additional study identifiers

ISRCTN number	ISRCTN93375053
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	250 Euston Road, London, United Kingdom, NW1 2PG
Public contact	UCLH/UCL Joint Research Office, University College London, uclh.jro-communications@nhs.net
Scientific contact	Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, crctu-generalenquiries@trials.bham.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	25 February 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of this study is to determine whether the addition of sorafenib to TransArterial ChemoEmbolisation (TACE) performed with doxorubicin eluting beads, prolongs progression free survival in patients with unresectable Hepatocellular Carcinoma compared to TACE alone. TACE is the standard treatment for patients with liver cancer that cannot be removed by surgery. This procedure involves blocking the blood vessel that supplies the tumour with small particles and killing it by starving it of oxygen. These particles can be loaded with the chemotherapy drug doxorubicin which is delivered directly to the tumour and may increase the effectiveness of the procedure. Sorafenib is a relatively new anti-cancer treatment which is approved for use in the treatment of liver cancer. It works by slowing down the growth of cancer cells and it also slows the rate of new vessel formation on which tumour growth depends.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. Site staff received GCP and trial specific training prior to recruiting patients to the study. A Data Monitoring Committee reviewed patient safety data throughout the trial. Additional measures were taken during the course of the study to monitor subject safety: (1) Medical history prior to randomisation to identify safety-related exclusion criteria, (2) Continuous assessment of adverse events and serious adverse events, (3) ECG, Haematology and biochemistry laboratory tests at regular intervals, (4) full review of body system through physical examination and vital signs assessment

Background therapy:

A first trans-arterial chemoembolisation (TACE) will be performed between 2 and 5 weeks after randomisation using DC Bead® loaded with Doxorubicin-HCl 150mg. In the absence of complete devascularisation of the tumour(s), as assessed by follow-up contrast enhanced scan, further TACE(s) should be performed unless technical or patient factors preclude retreatment. After six procedures further TACE with DC Bead® should only be performed if the left ventricular ejection fraction is $\geq 45\%$ on repeat assessment. If the ejection fraction is $< 45\%$ bland embolisation with unloaded DC Bead® should be performed.

Evidence for comparator: -

Actual start date of recruitment	19 November 2010
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: 313
Worldwide total number of subjects	313
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)	127
From 65 to 84 years	183
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

23 UK sites and 1 Irish site took part in the study. The trial opened to recruitment on 04-Nov-2010. The first participant was recruited into the trial on 19-Nov-2010. The last subject was recruited on 27-Nov-2015. All patients were recruited in the UK.

Pre-assignment

Screening details:

Formal screening logs were requested. A total of 399 patients were considered for the trial, of these 313 were recruited and 86 subjects excluded. Reasons for exclusion: 81 patients did not meet all entry criteria; 5 declined to participate.

Period 1

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

Blinding implementation details:

Study medication was labelled with a unique number (Treatment Pack Number) which was assigned to a patient.

A 24 hour unblinding service was provided by CRCTU (office hours) and Guys and St Thomas emergency scientific & medical services (outside office hours).

Unblinding was performed for medical reasons i.e. when knowledge of the treatment was essential for the correct patient clinical care, including externally verified evidence of disease progression.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sorafenib

Arm description:

Patients who commenced Sorafenib treatment

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

Dosage and administration details:

200 mg po BD, continuous dosing until death, disease progression, unacceptable toxicities or withdrawal of patient consent.

Arm title	Placebo
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Arm description:

Patients who commenced Placebo treatment

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

Dosage and administration details:

200 mg po BD, continuous dosing until death, disease progression, unacceptable toxicities or withdrawal of patient consent.

Number of subjects in period 1	Sorafenib	Placebo
Started	157	156
Completed	113	134
Not completed	44	22
Ineligible	4	3
Insufficient Treatment	40	19

Baseline characteristics

Reporting groups

Reporting group title	Sorafenib
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Reporting group description:

Patients who commenced Sorafenib treatment

Reporting group title	Placebo
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Reporting group description:

Patients who commenced Placebo treatment

Reporting group values	Sorafenib	Placebo	Total
Number of subjects	157	156	313
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	65	68	
inter-quartile range (Q1-Q3)	57 to 71	63 to 74	-
Gender categorical			
Units: Subjects			
Female	18	18	36
Male	139	138	277
ECOG Performance Status			
Units: Subjects			
PS 0	98	97	195
PS 1	58	58	116
Not known	1	1	2
Disease focality			
Number of nodules			
Units: Subjects			
= 1	59	40	99
= 2	33	41	74
= 3	16	17	33
> 3	42	49	91
Not known	7	9	16
Disease Extent			
Units: Subjects			
Unilobar	94	76	170

Bilobar	59	74	133
Unknown	4	6	10
Cirrhosis Units: Subjects			
Present	129	122	251
Absent	28	33	61
Unknown	0	1	1
Previous liver resection or ablative therapy Units: Subjects			
Yes	11	20	31
No	146	135	281
Unknown	0	1	1
Child-Pugh score Units: Subjects			
= 5	106	114	220
= 6	39	34	73
= 7	4	2	6
= 8	1	1	2
Not known	7	5	12
Hepatoma arterial-embolisation prognostic score Units: Subjects			
HAP A	44	43	87
HAP B	52	61	113
HAP C	41	34	75
HAP D	14	10	24
Not known	6	8	14
Cause of cirrhosis Units: Subjects			
Alcohol	44	40	84
Hepatitis C	15	9	24
Hepatitis C and alcohol	10	12	22
Hepatitis B	7	7	14
Hepatitis B and C	3	3	6
Hepatitis B and C and alcohol	3	2	5
Hepatitis B and alcohol	2	2	4
Other	45	47	92
N/A - No cirrhosis present	28	34	62
Hepatocellular carcinoma diagnosis method Units: Subjects			
Histology	35	47	82
Radiology	122	106	228
Not known	0	3	3
Baseline blood pressure Units: Subjects			
Normal	80	77	157
Grade 1 hypertension (mild)	7	9	16
Grade 1 isolated systolic hypertension	48	41	89
Grade 2 hypertension (moderate)	2	1	3

Grade 2 isolated systolic hypertension	8	14	22
Unknown	12	14	26
serum α-fetoprotein (AFP) concentration Units: KU/L median inter-quartile range (Q1-Q3)	23 5 to 241	25 5 to 280	-
Serum Creatinine Units: micromole(s)/litre median inter-quartile range (Q1-Q3)	75 64 to 89	75 65 to 92	-
Serum bilirubin Units: micromole(s)/litre median inter-quartile range (Q1-Q3)	14 9 to 21	13 10 to 20	-
Dominant tumour diameter Units: centimetre median inter-quartile range (Q1-Q3)	6 4 to 8	5 4 to 8	-
Weight Units: kilogram(s) median inter-quartile range (Q1-Q3)	83.1 70.6 to 95.4	81.6 71.2 to 95.0	-
Height Units: metre median inter-quartile range (Q1-Q3)	1.7 1.7 to 1.8	1.7 1.7 to 1.8	-

End points

End points reporting groups

Reporting group title	Sorafenib
Reporting group description: Patients who commenced Sorafenib treatment	
Reporting group title	Placebo
Reporting group description: Patients who commenced Placebo treatment	

Primary: Progression free survival time

End point title	Progression free survival time
End point description: Time interval between randomisation and progression according to Response Evaluation Criteria In Solid Tumours version 1.1 (RECIST v1.1) or death due to any cause, analysed by intention-to-treat.	
End point type	Primary
End point timeframe: Interval between the date of randomisation and the date of progression or death from any cause	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: day				
median (confidence interval 95%)	238.0 (221.0 to 281.0)	235.0 (195.0 to 322.0)		

Statistical analyses

Statistical analysis title	Progression Free Survival
Statistical analysis description: PFS (Intention to Treat analysis)	
Comparison groups	Sorafenib v Placebo
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.23

Secondary: Overall survival time

End point title	Overall survival time
End point description:	
Time interval between randomisation and death due to any cause, analysed by intention-to-treat.	
End point type	Secondary
End point timeframe:	
Time interval between randomisation and death due to any cause	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: day				
median (confidence interval 95%)	631.0 (437.0 to 879.0)	598.0 (500.0 to 707)		

Statistical analyses

Statistical analysis title	Overall Survival
Statistical analysis description:	
OS (Intention to Treat) Analysis	
Comparison groups	Sorafenib v Placebo
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.77
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.32

Secondary: Number of TACE Procedures

End point title	Number of TACE Procedures
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: TACE Procedures	268	326		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Progression

End point title	Time To Progression
End point description:	
End point type	Secondary
End point timeframe:	
Date of randomisation to date of progression	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: day				
median (confidence interval 95%)	326.0 (240.0 to 410.0)	320.0 (232.0 to 398)		

Statistical analyses

Statistical analysis title	Time To Progression
Statistical analysis description:	
TTP (Intention to Treat analysis)	
Comparison groups	Sorafenib v Placebo

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.12

Secondary: Disease Control (RECIST)

End point title	Disease Control (RECIST)
End point description:	
Disease Control = Response as defined by RECIST v1.1 - categorised as either Complete Response, Partial Response or Stable Disease. Assessed locally.	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: patients	117	121		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Physical functioning (6 months)

End point title	EORTC C30 - Physical functioning (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	78.3 (± 21.2)	77.5 (± 22.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Role functioning (6 months)

End point title	EORTC C30 - Role functioning (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	78.9 (± 27.7)	78.9 (± 28.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Emotional functioning (6 months)

End point title	EORTC C30 - Emotional functioning (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	78.5 (± 22.6)	76.2 (± 24.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Cognitive functioning (6 months)

End point title	EORTC C30 - Cognitive functioning (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	81.8 (± 24.1)	83.8 (± 21.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Social functioning (6 months)

End point title	EORTC C30 - Social functioning (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	82.0 (± 24.1)	82.3 (± 26.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Overall QOL

End point title	EORTC C30 - Overall QOL
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	70.4 (± 22.2)	70.6 (± 24.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Fatigue (6 months)

End point title	EORTC C30 - Fatigue (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	32.2 ($\pm$ 26.6)	29.9 ($\pm$ 26.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Nausea and Vomiting (6 months)

End point title	EORTC C30 - Nausea and Vomiting (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	7.6 ($\pm$ 17.8)	5.8 ($\pm$ 14.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Pain (6 months)

End point title	EORTC C30 - Pain (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	22.0 (± 28.0)	21.5 (± 27.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Dyspnoea (6 months)

End point title	EORTC C30 - Dyspnoea (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	20.8 (± 27.7)	17.5 (± 26.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Insomnia (6 months)

End point title	EORTC C30 - Insomnia (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	34.6 (± 32.0)	28.8 (± 34.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Appetite Loss (6 months)

End point title	EORTC C30 - Appetite Loss (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	20.4 (± 28.2)	18.1 (± 28.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Constipation (6 months)

End point title	EORTC C30 - Constipation (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	12.0 (± 22.6)	18.1 (± 28.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Diarrhoea (6 months)

End point title	EORTC C30 - Diarrhoea (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	12.1 (± 24.1)	8.2 (± 19.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC C30 - Financial Difficulties (6 months)

End point title	EORTC C30 - Financial Difficulties (6 months)
End point description:	
End point type	Secondary
End point timeframe:	
6 months after randomisation	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: score (1-100)				
arithmetic mean (standard deviation)	23.2 (± 34.4)	15.2 (± 28.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control (mRECIST)

End point title	Disease Control (mRECIST)
End point description: Disease Control = Response as defined by modified RECIST v1.1 - categorised as either Complete Response, Partial Response or Stable Disease. Assessed locally.	
End point type	Secondary
End point timeframe: 12 months	

End point values	Sorafenib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	156		
Units: patients	117	120		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Details of all AEs were recorded and reported from the start of study treatment up to 30 days after last administration of study treatment or until end of study.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.0
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Reporting groups

Reporting group title	Sorafenib
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Reporting group description:

Patients who commenced Sorafenib treatment

Reporting group title	Placebo
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Reporting group description:

Patients who commenced Placebo treatment

Serious adverse events	Sorafenib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 157 (41.40%)	50 / 156 (32.05%)	
number of deaths (all causes)	76	88	
number of deaths resulting from adverse events	14	14	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Treatment related secondary malignancy			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Primary lung lesion			

subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	2 / 157 (1.27%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Surgical treatment for indurated area of buttock			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sudden death NOS			
subjects affected / exposed	0 / 157 (0.00%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Fatigue			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fever			
subjects affected / exposed	6 / 157 (3.82%)	5 / 156 (3.21%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 157 (1.27%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Localised oedema			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Night sweats			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Social circumstances			
Social circumstances			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest infection			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 157 (0.00%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	2 / 157 (1.27%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			

subjects affected / exposed	2 / 157 (1.27%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental embolisation of gallbladder			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative haemorrhage			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post embolisation syndrome			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain - cardiac			

subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	5 / 157 (3.18%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	3 / 5	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 0	
Lethargy			
subjects affected / exposed	2 / 157 (1.27%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphasia			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haemorrhage			

subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 157 (1.91%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Platelet count decreased			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eyelid function disorder			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	9 / 157 (5.73%)	3 / 156 (1.92%)	
occurrences causally related to treatment / all	4 / 9	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Constipation			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticular perforation			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Melaena			
subjects affected / exposed	2 / 157 (1.27%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis oral			
subjects affected / exposed	2 / 157 (1.27%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 157 (1.27%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			

subjects affected / exposed	3 / 157 (1.91%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ascites			
subjects affected / exposed	1 / 157 (0.64%)	4 / 156 (2.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Duodenal ulcer			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Nausea			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Blocked biliary stent			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	3 / 157 (1.91%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic pain			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholecystitis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic sepsis			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary retention			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary frequency			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anorectal infection			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic infection			
subjects affected / exposed	1 / 157 (0.64%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower respiratory tract infection subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis subjects affected / exposed	4 / 157 (2.55%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	3 / 5	1 / 2	
deaths causally related to treatment / all	1 / 2	0 / 0	
Urinary sepsis subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial infection subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection subjects affected / exposed	0 / 157 (0.00%)	1 / 156 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Infection			

subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (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			
subjects affected / exposed	0 / 157 (0.00%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyponatraemia			
subjects affected / exposed	1 / 157 (0.64%)	2 / 156 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 157 (0.64%)	0 / 156 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Sorafenib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 157 (88.54%)	147 / 156 (94.23%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 157 (12.10%)	8 / 156 (5.13%)	
occurrences (all)	36	8	
General disorders and administration site conditions			
Dyspepsia			
subjects affected / exposed	9 / 157 (5.73%)	5 / 156 (3.21%)	
occurrences (all)	19	11	
Fatigue			

subjects affected / exposed	127 / 157 (80.89%)	125 / 156 (80.13%)	
occurrences (all)	556	510	
Fever			
subjects affected / exposed	14 / 157 (8.92%)	19 / 156 (12.18%)	
occurrences (all)	15	22	
Flu like symptoms			
subjects affected / exposed	9 / 157 (5.73%)	9 / 156 (5.77%)	
occurrences (all)	11	9	
Pain			
subjects affected / exposed	24 / 157 (15.29%)	22 / 156 (14.10%)	
occurrences (all)	34	34	
Oedema limbs			
subjects affected / exposed	3 / 157 (1.91%)	18 / 156 (11.54%)	
occurrences (all)	3	32	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 157 (6.37%)	17 / 156 (10.90%)	
occurrences (all)	11	22	
Dyspnea			
subjects affected / exposed	11 / 157 (7.01%)	18 / 156 (11.54%)	
occurrences (all)	13	37	
Hoarseness			
subjects affected / exposed	17 / 157 (10.83%)	8 / 156 (5.13%)	
occurrences (all)	56	9	
Psychiatric disorders			
Depression			
subjects affected / exposed	10 / 157 (6.37%)	5 / 156 (3.21%)	
occurrences (all)	14	11	
Insomnia			
subjects affected / exposed	15 / 157 (9.55%)	8 / 156 (5.13%)	
occurrences (all)	27	13	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 157 (5.73%)	9 / 156 (5.77%)	
occurrences (all)	10	11	
Alkaline Phosphatase Increased			

subjects affected / exposed	13 / 157 (8.28%)	9 / 156 (5.77%)	
occurrences (all)	17	15	
Blood bilirubin increased			
subjects affected / exposed	16 / 157 (10.19%)	12 / 156 (7.69%)	
occurrences (all)	20	12	
Gamma-glutamyltransferase increased			
subjects affected / exposed	13 / 157 (8.28%)	11 / 156 (7.05%)	
occurrences (all)	33	15	
Platelet count decreased			
subjects affected / exposed	14 / 157 (8.92%)	9 / 156 (5.77%)	
occurrences (all)	35	14	
Weight Loss			
subjects affected / exposed	21 / 157 (13.38%)	13 / 156 (8.33%)	
occurrences (all)	27	15	
Injury, poisoning and procedural complications			
Haemorrhage			
subjects affected / exposed	34 / 157 (21.66%)	17 / 156 (10.90%)	
occurrences (all)	65	26	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 157 (5.10%)	4 / 156 (2.56%)	
occurrences (all)	12	7	
Headache			
subjects affected / exposed	10 / 157 (6.37%)	14 / 156 (8.97%)	
occurrences (all)	15	29	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 157 (12.10%)	11 / 156 (7.05%)	
occurrences (all)	34	18	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	14 / 157 (8.92%)	10 / 156 (6.41%)	
occurrences (all)	21	15	
Abdominal pain			
subjects affected / exposed	94 / 157 (59.87%)	93 / 156 (59.62%)	
occurrences (all)	243	225	

Diarrhoea			
subjects affected / exposed	88 / 157 (56.05%)	52 / 156 (33.33%)	
occurrences (all)	319	95	
Mouth pain			
subjects affected / exposed	41 / 157 (26.11%)	22 / 156 (14.10%)	
occurrences (all)	94	39	
Dry mouth			
subjects affected / exposed	8 / 157 (5.10%)	4 / 156 (2.56%)	
occurrences (all)	10	5	
Constipation			
subjects affected / exposed	24 / 157 (15.29%)	47 / 156 (30.13%)	
occurrences (all)	35	85	
Mucositis			
subjects affected / exposed	11 / 157 (7.01%)	4 / 156 (2.56%)	
occurrences (all)	15	4	
Nausea			
subjects affected / exposed	73 / 157 (46.50%)	68 / 156 (43.59%)	
occurrences (all)	133	138	
Oral Dysesthesia			
subjects affected / exposed	10 / 157 (6.37%)	5 / 156 (3.21%)	
occurrences (all)	20	8	
Vomiting			
subjects affected / exposed	24 / 157 (15.29%)	17 / 156 (10.90%)	
occurrences (all)	34	24	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	10 / 157 (6.37%)	7 / 156 (4.49%)	
occurrences (all)	10	7	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	22 / 157 (14.01%)	14 / 156 (8.97%)	
occurrences (all)	61	17	
Dry skin			
subjects affected / exposed	23 / 157 (14.65%)	19 / 156 (12.18%)	
occurrences (all)	37	32	
Palmar-plantar erythrodysesthesia syndrome			

subjects affected / exposed occurrences (all)	66 / 157 (42.04%) 266	16 / 156 (10.26%) 30	
Pruritus subjects affected / exposed occurrences (all)	14 / 157 (8.92%) 17	25 / 156 (16.03%) 45	
Rash subjects affected / exposed occurrences (all)	64 / 157 (40.76%) 137	35 / 156 (22.44%) 75	
Skin ulcer subjects affected / exposed occurrences (all)	10 / 157 (6.37%) 14	2 / 156 (1.28%) 4	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	13 / 157 (8.28%) 19	16 / 156 (10.26%) 29	
Back pain subjects affected / exposed occurrences (all)	11 / 157 (7.01%) 25	17 / 156 (10.90%) 31	
Chest wall pain subjects affected / exposed occurrences (all)	8 / 157 (5.10%) 11	7 / 156 (4.49%) 8	
Muscle Cramps subjects affected / exposed occurrences (all)	9 / 157 (5.73%) 20	2 / 156 (1.28%) 2	
Myalgia subjects affected / exposed occurrences (all)	7 / 157 (4.46%) 11	17 / 156 (10.90%) 32	
Infections and infestations			
Lung infection subjects affected / exposed occurrences (all)	12 / 157 (7.64%) 17	10 / 156 (6.41%) 15	
Bronchial Infection subjects affected / exposed occurrences (all)	6 / 157 (3.82%) 7	9 / 156 (5.77%) 20	
Metabolism and nutrition disorders			

Anorexia			
subjects affected / exposed	54 / 157 (34.39%)	53 / 156 (33.97%)	
occurrences (all)	94	88	
Hypoalbuminemia			
subjects affected / exposed	10 / 157 (6.37%)	7 / 156 (4.49%)	
occurrences (all)	15	8	
Hypocalcemia			
subjects affected / exposed	11 / 157 (7.01%)	1 / 156 (0.64%)	
occurrences (all)	12	1	
Hypophosphatemia			
subjects affected / exposed	12 / 157 (7.64%)	5 / 156 (3.21%)	
occurrences (all)	16	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2010	Update to unblinding procedures Clarification of randomisation procedures Clarification of drug delivery arrangements Update to the schedule of assessments Update to the case report form completion schedule Clarification of exclusion criteria
11 June 2010	Update to the Trial Management Group Clarification of additional embolisation procedures permitted Update to contraception requirements Update to DC Bead loading instructions
11 March 2011	Removal of lipase from the eligibility criteria. Addition of Ireland as a participating country (subject to local regulatory and ethical approvals). The units for AFP have changed from ng/ml to kU/L. Therefore, stratification is now (<331, ≥ 331kU/L). Dual Phase CTs are now permitted If a trial participant or partner of a trial participant becomes pregnant, a pregnancy notification form needs to be completed instead of an SAE Form. The first 60 patients are no longer required to complete the debriefing questionnaire to validate the EORTC QLQ-HCC18 questionnaire as validation of this module has now been completed. The insurance section has been modified to comply with UCL's insurance SOP and updated policy. The primary difference is that patients may be able to claim compensation without the need to prove negligence. Removal of typographical errors.
02 October 2012	Changes to the Trial Management Group Exclusion criteria updated to cover patients with prolonged QT/QTc of greater than 450ms Increased ECG monitoring – ECG will now be monitored at each follow up visit, as well as at 72 hours pre-TACE and 7 days post-TACE time points Dose Modifications updated to include discontinuation of sorafenib for patients with QT over 500ms, or 60ms above their baseline reading Appendix 11: Expected Adverse Events updated to reflect additional expected events in line with the current version of the Sorafenib SmPC Appendix 12: Flowchart of Assessments has been revised to include the additional ECGs as earlier indicated
28 January 2013	Revised procedure for unblinding patients who have been confirmed locally as having progressive disease

12 February 2014	Update to the trial recruitment end date and recruiting centres. Change to end of trial definition and final analysis timelines following futility analysis and trial's closure to recruitment. Sites allowed to use standard practice of TACE and CT/MRI scans following the trial's closure to recruitment. End of translational sub-study sample collection. Changes to the process following progression after the trial's closure to recruitment. Patients will no longer be formally unblinded following progression as all patients have been unblinded following the trial's closure to recruitment. Details of maintaining the blind and codebreaking removed as no longer necessary. Change to scan schedule to local standard of care and removal of provision of scans to IXICO following the trial's closure to recruitment. Change to radiological assessments to local standard of care from week 16 onwards Change to the follow up period following the trial's closure to recruitment. Change to the sorafenib supply and reallocations process. Packs will no longer be allocated and sites will be provided with a supply of unblinded sorafenib. Clarification of the definition of progression in the trial. Changes to DC Bead loading times following advice from manufacturer Biocompatibles. Changes to expected adverse events following review of Sorafenib SpC.
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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.

None reported

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28648803>