Clinical trial results:
Phase II single agent sorafenib in the treatment of relapsed oesophageal/gastric adenocarcinoma in platinum pre-treated patients.

Summary

EudraCT number	2008-005062-31
Trial protocol	IE
Global end of trial date	08 May 2013

Results information

Result version number	v1 (current)
This version publication date	19 April 2018
First version publication date	19 April 2018

Trial information

Trial identification

Sponsor protocol code	ICORG 06-41

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01158287
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	Innovation House, Old Finglas Road, Dublin, Ireland, D11 KXN4
Public contact	Anna Shevlin, Cancer Trials Ireland, anna.shevlin@cancertrials.ie
Scientific contact	Anna Shevlin, Cancer Trials Ireland, anna.shevlin@cancertrials.ie

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	14 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 May 2013
Global end of trial reached?	Yes
Global end of trial date	08 May 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the Disease Control rate after 4 months of treatment for each patient (complete response + partial response + stable disease) rate

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations SI 190 of 2004 as amend and European Directive 2001/20/EC. The study was approved by the HPRA and SJH/AMNCH Research Ethics Committee.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	18 March 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	27
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled in Mar 2010, 43 patients were recruited. The last patient was recruited Nov 2012 after which the trial was terminated early.

Pre-assignment

Screening details:

Relapsed platinum pre-treated patients with oesophageal/gastric adenocarcinoma.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall Trial

Arm description:

Relapsed platinum pre-treated patients with oesophageal/gastric adenocarcinoma.

Arm type	Experimental
Investigational medicinal product name	Sorafenib
Investigational medicinal product code	
Other name	Nexavar
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sorafenib will be administered orally as a twice daily dosage at 400mg bd as long as the study participant continues to gain clinical benefit and no intolerable toxicity occurs. Patients are to return to the site approximately every 28 days for re-supply of sorafenib therapy.

Number of subjects in period 1	Overall Trial
Started	43
Completed	42
Not completed	1
Disease Progession	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
Relapsed platinum pre-treated patients with oesophageal/gastric adenocarcinoma.	

Reporting group values	Overall Trial	Total	
Number of subjects	43	43	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	27	27	
From 65-84 years	16	16	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.3		
standard deviation	± 10.2	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	36	36	
Ethnic origin Units: Subjects			
Caucasian	42	42	
Asian	1	1	
Tumor Stage Units: Subjects			
Locally Advanced/Unresectable	6	6	
Distal Metastatic	36	36	
Data Missing (patient did not start treatment)	1	1	
Time from initial diagnosis to relapse Units: Days			
arithmetic mean	449.9		
standard deviation	± 363.1	-	

End points

End points reporting groups

Reporting group title	Overall Trial

Reporting group description:

Relapsed platinum pre-treated patients with oesophageal/gastric adenocarcinoma.

Primary: Disease control status

End point title	Disease control status[1]

End point description:

It is measured according to RECIST criteria every 8 weeks during the study. The primary objective was to assess the disease control rate (CR, PR or SD) after 4 months of treatment.

End point type	Primary

End point timeframe:

After all patients either received 120 days of treatment or progressed or died before receiving 120 days of 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: Study terminated early (43/54 patients recruited) after an interim report showed 33 patients had progressed before completing 4 months of treatment. At that point, the primary endpoint, number of patients achieving Disease Control, could not reach 22. Due to limited number of patients completing 4 months of treatment, it was not possible to conduct statistical analysis. Main analysis shows lack of efficacy with only 3/36 patients having stable disease before completing 4 months of treatment.

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Number of Patients				
Complete Response	0			
Progression of Disease	3			
Stable Disease	3			
Did not complete 120 days of treatment	36			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: April 2010 - February 2015 (4 years and 10 months)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Overall Trial
Reporting group description: Relapsed platinum pre-treated patients with oesophageal/gastric adenocarcinoma.	

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 42 (69.05%)		
number of deaths (all causes)	41		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain mets			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dermatology squamous cell			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Postural hypotension			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	7 / 42 (16.67%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	6 / 42 (14.29%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Ankle oedema				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Shortness of breath				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breathlessness			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusion			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			

Weight loss				
subjects affected / exposed	4 / 42 (9.52%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Raised bp				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Collapse/fainting				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial haemorrhage				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Nausea				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Constipation				

subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	6 / 42 (14.29%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Crampy abdominal pain				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Difficulty swallowing				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdo. distension				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal distension				

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dilatation of osephagus				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Esophagitis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin breakdown				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower back pain				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Shoulder pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Backpain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left leg pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in hip			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bilateral pneumonia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Loss of appetite			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4.76 %

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Investigations			
Weight loss			
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	10		
Decreased haemoglobin			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Elevated ggt			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	11		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	24 / 42 (57.14%)		
occurrences (all)	28		
Pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Mucositis			

subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Bilateral ankle oedema			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	16		
Constipation			
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	14		
Abdominal pain			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	11		
Diarrhoea			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	8		
Dysphagia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Diarrhea			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Diarrohea			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Dry mouth			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Epigastric pain			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Sore mouth			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Sore tongue			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Shortness of breath			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hoarsness			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hand-foot syndrome			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Skin rash			

subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 3		
Infections and infestations Chest infection subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 2		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Annorexia subjects affected / exposed occurrences (all) Loss of appetite subjects affected / exposed occurrences (all) Reduced appetite subjects affected / exposed occurrences (all) Hypoalbuminemia subjects affected / exposed occurrences (all) Hypocalcemia subjects affected / exposed occurrences (all) Poor appetite subjects affected / exposed occurrences (all)	 3 / 42 (7.14%) 3 3 / 42 (7.14%) 3 2 / 42 (4.76%) 3 3 / 42 (7.14%) 4 2 / 42 (4.76%) 2 2 / 42 (4.76%) 3 2 / 42 (4.76%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2008	Protocol Version 2: Regulatory authority requested changes. Changes include revised statements of patient protection, updated Patient Information Leaflet and minor administrative changes.
12 April 2010	Protocol Version 3: study synopsis added. Details of a transnational sub-study and updates to prohibited medications added, following a Sorafenib IB update. Dose modification and management of treatment-emergent hypertension section amended. Amendments to patient inclusion criteria, clinical and laboratory evaluations, and table of schedule of study procedures. Additional appendices included. Various administrative changes throughout the protocol.
06 October 2011	Protocol Version 4: administrative changes and safety updates corresponding to the revised Sorafenib SPC dated 13-Sep-2011.

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.

Study terminated early after 23-Nov-2012 interim report showed 33 patients had progressed before completing 4 months of treatment. At that point the primary endpoint, number of patients achieving Disease Control could not reach 22 so study closed.

Notes: