Clinical trial results:
COUGAR-02: A randomised phase III study of docetaxel vs active symptom control in patients with relapsed oesophago-gastric adenocarcinoma

Summary

EudraCT number	2006-005046-37
Trial protocol	GB
Global end of trial date	28 November 2013

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	COUGAR-02

Additional study identifiers

ISRCTN number	ISRCTN13366390
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cambridge University Hospitals NHS Foundation Trust
Sponsor organisation address	Hills Road, Cambridge University Hospitals NHS Foundation Trus, United Kingdom, CB2 0QQ
Public contact	Prasanna Kapilan , Cambridge clinical trials unit (CCTU), +44 1223 596 474 , Prasanna.kapilan@addenbrookes.nhs.uk
Scientific contact	Hugo Ford , Cambridge University Hospitals NHS Foundation Trust, hugo.ford@addenbrookes.nhs.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	30 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2012
Global end of trial reached?	Yes
Global end of trial date	28 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether chemotherapy with docetaxel improves survival in patients with advanced gastric cancer previously treated with platinum/fluoropyrimidine or raltitrexed therapy.

Protection of trial subjects:

The study was approved by a Research Ethics Committee and received authorisation from the Medicines and Healthcare Products Regulatory Authority. Patients received verbal and written information prior to consenting to the trial and had the time to consider their participation and opportunity to ask questions. Patient data and samples were anonymised so that their information was kept confidential.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	01 April 2008
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: 168
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	82

From 65 to 84 years	86
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between April 2008 to April 2012 a total of 168 patients were randomised from 30 sites across the UK.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	356[1]
Number of subjects completed	168

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 71
Reason: Number of subjects	Not meeting inclusion criteria: 77
Reason: Number of subjects	Other reasons: 40

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 356 patients screened and 168 patients enrolled to receive protocol treatment.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Docetaxel + active symptom control

Arm description:

Docetaxel 75mg/m2 IV every 3 weeks for up to 6 cycles + active symptom control

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	N/A
Other name	TAXOTERE
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

"Docetaxel was administered as an intravenous infusion over 1 hour at a dose of 75mg/m2 in 250ml sodium chloride 0.9% solution or 5 % glucose solution every 3 weeks for a maximum of 6 cycles."

Arm title	active symptom control

Arm description:

active symptom control - may include radiotherapy, analgesia, anti-emetics, steroids.

Arm type	Active symptom control

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Docetaxel + active symptom control	active symptom control
Started	84	84
Received Allocated Intervention	77	78
Did not receive Allocated Intervention	7 [2]	6 [3]
Completed	19	30
Not completed	65	54
Unacceptable Toxicity / Died	27	32
Consent withdrawn by subject	2	5
died	3	-
entered phase I	-	7
progressive disease	-	1
patient decision (wanted CT)	-	4
delay >21 days	5	-
Lost to follow-up	-	2
Poor Performance Status / Declined Further Assessm	1	2
patient admitted	1	-
Lack of efficacy	26	1

Notes:

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 356 patients screened and 168 patients enrolled to receive protocol treatment.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 356 patients screened and 168 patients enrolled to receive protocol treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Docetaxel + active symptom control
Reporting group description:	
Docetaxel 75mg/m2 IV every 3 weeks for up to 6 cycles + active symptom control	
Reporting group title	active symptom control
Reporting group description:	
active symptom control - may include radiotherapy, analgesia, anti-emetics, steroids.	

Reporting group values	Docetaxel + active symptom control	active symptom control	Total
Number of subjects	84	84	168
Age categorical 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)	41	41	82
From 65-84 years	43	43	86
85 years and over	0	0	0
Age continuous Units: years			
median	65	66	
full range (min-max)	28 to 84	36 to 84	-
Gender categorical			
Docetaxel 75mg/m2 IV every 3 weeks for up to 6 cycles + active symptom control			
Units: Subjects			
Female	15	17	32
Male	69	67	136
ECOG PS			
ECOG Performance Status			
Units: Subjects			
T0	24	22	46
T1	46	50	96
T2	14	12	26
Disease status			
Disease status			
Units: Subjects			
Local advanced	11	10	21
metastatic disease	73	74	147
Site of primary disease			
Site of primary disease			
Units: Subjects			
Oesophagus	18	15	33

OG junction	27	32	59
Stomach	39	37	76
Time between end of previous chemotherapy and documented disease progression			
Time between end of previous chemotherapy and documented disease progression			
Units: Subjects			
During treatment	36	36	72
Within 3 months from end of treatment	27	22	49
Within 3-6 months from end of treatment	21	26	47

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised 168 patients are included in the analysis

Reporting group values	ITT		
Number of subjects	168		
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)	82		
From 65-84 years	86		
85 years and over	0		
Age continuous Units: years median full range (min-max)			
Gender categorical			
Docetaxel 75mg/m2 IV every 3 weeks for up to 6 cycles + active symptom control			
Units: Subjects			
Female	32		
Male	136		
ECOG PS			
ECOG Performance Status			
Units: Subjects			
T0	46		
T1	96		
T2	26		
Disease status			
Disease status			
Units: Subjects			

Local advanced	21		
metastatic disease	147		
Site of primary disease			
Site of primary disease			
Units: Subjects			
Oesophagus	33		
OG junction	59		
Stomach	76		
Time between end of previous chemotherapy and documented disease progression			
Time between end of previous chemotherapy and documented disease progression			
Units: Subjects			
During treatment	72		
Within 3 months from end of treatment	49		
Within 3-6 months from end of treatment	47		

End points

End points reporting groups

Reporting group title	Docetaxel + active symptom control
Reporting group description:	
Docetaxel 75mg/m2 IV every 3 weeks for up to 6 cycles + active symptom control	
Reporting group title	active symptom control
Reporting group description:	
active symptom control - may include radiotherapy, analgesia, anti-emetics, steroids.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised 168 patients are included in the analysis	

Primary: Primary

End point title	Primary
End point description:	
End point type	Primary
End point timeframe:	
Patients were assessed every 3 weeks for first 18 weeks and every 6 weeks thereafter for up to 1 year. After 1 year, patients were reviewed every 3 months until death.	

End point values	Docetaxel + active symptom control	active symptom control	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	84	84	0[1]	
Units: Months				
median (confidence interval 95%)				
Overall survival	5.2 (4.1 to 5.9)	3.6 (3.3 to 4.4)	(to)	

Notes:

[1] - this is not applicable for combining both groups.

Statistical analyses

Statistical analysis title	Overall survival
Statistical analysis description:	
Overall survival	

Comparison groups	Docetaxel + active symptom control v active symptom control
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.92

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

For patients on the Docetaxel + Active symptom control arm of the study (Arm A)
AEs will be monitored and recorded from randomisation until 21 days after the last administration of study drug.
For patients on the Active symptom control arm of the stud

Assessment type	Systematic

Dictionary used

Dictionary name	National Cancer Inst
Dictionary version	3

Reporting groups

Reporting group title	active symptom control

Reporting group description:

active symptom control - may include radiotherapy, analgesia, anti-emetics, steroids.

Serious adverse events	active symptom control		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 84 (0.00%)		
number of deaths (all causes)	81		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	active symptom control		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 84 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Adverse events reported are given in the publication attached.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24332238