Clinical trial results:
Cancer Oesophagus Gefitinib(COG) - Phase III randomised, double-blind, placebo-controlled trial of gefitinib (Iressa®) versus placebo in oesophageal cancer progressing after chemotherapy.

Summary

EudraCT number	2007-005391-13
Trial protocol	GB
Global end of trial date	18 May 2012

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	OCTO_005

Additional study identifiers

ISRCTN number	ISRCTN29580179
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	CTRG, Joint Research Office, 1st Floor, Boundary Brook House, Churchill Drive, Headington, Oxford, United Kingdom, OX3 7GB
Public contact	As Scientific contact, As Scientific contact, 0000 0000000000, CTRG@admin.ox.ac.uk
Scientific contact	Clinical Trials and Research Governance Team, University of Oxford, Sponsor office as above., 0000 0000000000, CTRG@admin.ox.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	23 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 May 2012
Global end of trial reached?	Yes
Global end of trial date	18 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether gefitinib will improve overall survival in patients with oesophageal cancer when compared to a placebo.

Protection of trial subjects:

Please see primary publication.

Background therapy:

Please see primary publication.

Evidence for comparator:

Please see primary publication.

Actual start date of recruitment	30 March 2009
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: 449
Worldwide total number of subjects	449
EEA total number of subjects	449

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)	231
From 65 to 84 years	216
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

For this phase 3 randomised trial, patients were recruited from 48 UK centres. Please refer to primary publication for more information.

Pre-assignment

Screening details:

766 patients assessed for eligibility. 316 excluded: 185 did not meet inclusion criteria 131 declined to participate. Please refer to primary publication for more information. 450 Enrolled. 1 withdrew consent. (Final total 449)

Period 1

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

Blinding implementation details:

Patients, clinicians, local site staff and trial office staff were all blinded to the treatment allocation. The trial statistician held the code break information in an off-site location. Six months after completion of recruitment the blind was broken for the patients remaining on trial medication and patients on the gefitinib arm were allowed to continue on gefitinib.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Please refer to primary publication.
Allocated to Placebo (n=225)
Received allocated intervention (n=219)
Did not start treatment (n=6)
Completed baseline PROs (n=214)

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 as two tablets taken orally per day

Arm title	Study Drug.

Arm description:

Allocated to Gefitinib (n=224)
Received allocated intervention (n=212)
Did not start treatment (n=11)
Completed baseline PROs (n=209)

Arm type	Experimental

Investigational medicinal product name	Gefitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two 250 mg tablets taken orally per day.

Number of subjects in period 1	Placebo	Study Drug.
Started	225	224
Completed	178	158
Not completed	47	66
Physician decision	11	16
Consent withdrawn by subject	13	16
see primary publication	-	2
Adverse event, non-fatal	12	21
Did not start treatment	6	11
Please see primary publication	5	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Please refer to primary publication.
Allocated to Placebo (n=225)
Received allocated intervention (n=219)
Did not start treatment (n=6)
Completed baseline PROs (n=214)

Reporting group title	Study Drug.

Reporting group description:

Allocated to Gefitinib (n=224)
Received allocated intervention (n=212)
Did not start treatment (n=11)
Completed baseline PROs (n=209)

Primary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

The primary outcome was overall survival (OS) defined as time from randomization until death from any cause with censoring for patients still alive at the end of the study.

End point type	Primary

End point timeframe:

The primary endpoint was overall survival (OS).

End point values	Placebo	Study Drug.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	224		
Units: Please see primary publication.	225	224		

Statistical analyses

Statistical analysis title	Please see primary publication

Statistical analysis description:

The sample size of 450 was estimated to detect an improvement from 10% 1-year survival, as reported by previous phase 2 trials to 18% with a power of 82·5%, two-sided 5% significance allowing for a 10% loss to follow-up (hazard ratio [HR] 0·745, 389 events). A statistical analysis plan was finalised before masking was broken and analysis undertaken. All analyses were done in the intention-to-treat population.

Comparison groups	Placebo v Study Drug.

Number of subjects included in analysis	449
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.05 [2]
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.95

Notes:

[1] - Sensitivity analyses of overall and progression-free survival were done in the per-protocol population, defined as all patients randomly assigned to treatment groups, excluding those who did not start treatment, or who had major protocol deviation (no previous treatment, treatment breaks of >14 days). An intention-to-treat analysis for survival used Kaplan-Meier survival curves and the log-rank test, with Cox proportional hazards modelling to estimate HRs and 95% CIs.
[2] - Please see primary publication for details of the statistical analysis.

Secondary: Progression free survival (PFS) etc.

End point title	Progression free survival (PFS) etc.

End point description:

Secondary outcome measures were progression free survival (PFS) defined as time from randomisation until radiological or clinical progression or death from any cause if progression was not previously reported with censoring for patients alive and progression free at the end of the study; safety measured by assessing adverse reactions and toxicities of grade 2-5 for skin toxicity and diarrhoea (known side effects of gefitinib) and grade 3-5 for all other toxicities, which were collected up to 30 days post treatment completion. The primary pre-specified PRO outcomes were global health status/quality of life (QLQ-C30), dysphagia, difficulty eating and odynophagia (all QLQ-OG25) at 4 weeks.

End point type	Secondary

End point timeframe:

progression free survival (PFS) - see below.

End point values	Placebo	Study Drug.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	224		
Units: Please see primary publication				
number (not applicable)	225	224		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Please see primary publication for details.	
Adverse event reporting additional description: Please see primary publication for details.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

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

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: Please see primary publication for details.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2008	CTA Initial Application
06 February 2009	Substantial Amendment Notification to add new PIs and sites
20 February 2009	Substantial Amendment to update protocol to v2.0_09Sep2008
10 March 2009	Substantial amendment to update protocol to v3.0_16Feb2009
15 April 2009	Substantial Amendment Notification to add new PIs and sites
20 May 2009	Substantial Amendment Notification to add new PIs and sites
22 June 2009	Substantial Amendment Notification to add new PIs and sites
27 August 2009	Substantial Amendment Notification to change PI at site
27 October 2009	Substantial Amendment Notification to change PI at site
20 November 2009	Substantial Amendment Notification to change PI at site
25 January 2010	Substantial Amendment Notification to add new PIs and sites and change PI at site
08 February 2010	Substantial Amendment Notification to change PI at site
12 February 2010	Substantial Amendment Notification to change PI at site
07 June 2010	Substantial Amendment Notification to change PI at site
05 July 2010	Substantial amendment to update protocol to v4.0_15Apr2010
13 September 2010	Substantial amendment to update protocol to v5.0_06Aug2009

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.

Please refer to the primary publication for more details.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24950987