

**Clinical trial results:****A PHASE II DOUBLE BLIND, RANDOMISED CONTROLLED TRIAL OF VEGF INHIBITOR AXITINIB MONOTHERAPY WITH EARLY DYNAMIC CONTRAST ENHANCED ULTRASOUND MONITORING IN CHEMOREFRACTORY THIRD LINE METASTATIC COLORECTAL CANCER- AxMUS-C****Summary**

EudraCT number	2011-002598-49
Trial protocol	GB
Global end of trial date	15 September 2018

**Results information**

Result version number	v1 (current)
This version publication date	08 September 2022
First version publication date	08 September 2022
Summary attachment (see zip file)	Final report (EudraCT_Results_reporting_template AXMUS-C.xlsx)

**Trial information****Trial identification**

Sponsor protocol code	CRO1885
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Imperial College
Sponsor organisation address	Du Cane Road, London, United Kingdom, W12 0HS
Public contact	Becky Ward, Imperial College Joint Research Office, +44 203 312 2242, becky.ward@imperial.ac.uk
Scientific contact	Becky Ward, Imperial College Joint Research Office, +44 203 312 2242, becky.ward@imperial.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	29 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 September 2018
Global end of trial reached?	Yes
Global end of trial date	15 September 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to assess whether an absence of vascular (blood-supply) shutdown in the tumour, in metastatic colorectal cancer, using contrast enhanced ultrasound, in patients taking Axitinib will quickly select out patients who are not going to obtain benefit from this drug. This group of non-responsive patients should have a similar overall survival as the placebo group, whereas the patients on Axitinib who do have vascular tumour shutdown on contrast enhanced ultrasound should obtain significant benefit.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2012
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: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	38
From 65 to 84 years	14
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited in Hammersmith Hospital between 17/09/2012 and 25/07/2016

### Pre-assignment

Screening details:

A total of 60 participants were screened with colorectal cancer and liver metastases were screened for eligibility, of which 52 were randomised, but one of these patients was actually a screen fail and a further 8 were considered screen failures and not randomised at all

### Period 1

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

Blinding implementation details:

Randomised to axitinib or placebo in a 2:1 ratio

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Axitinib

Arm description: -

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

Dosage and administration details:

5mg BD increased fortnightly by a dose level up to 10mg or as tolerated - taken with food 12 hours apart

<b>Arm title</b>	Placebo
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Arm description: -

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:

Tablet taken twice daily

<b>Arm title</b>	Screenfails
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Arm description: -

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 1</b>	Axitinib	Placebo	Screenfails
Started	34	17	1
Completed	34	17	1

## Baseline characteristics

### Reporting groups

Reporting group title	Axitinib
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Screenfails
Reporting group description: -	

Reporting group values	Axitinib	Placebo	Screenfails
Number of subjects	34	17	1
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)	24	14	1
From 65-84 years	10	3	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	10	8	1
Male	24	9	0

Reporting group values	Total		
Number of subjects	52		
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)	39		
From 65-84 years	13		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	19		
Male	33		



## End points

### End points reporting groups

Reporting group title	Axitinib
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Screenfails
Reporting group description: -	
Subject analysis set title	CEHPI responders
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients on axitinib who were found to have CEHPI >20% reduction at 2 weeks compared with baseline	
Subject analysis set title	CEHPI non-responders
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients who received axitinib treatment who were not found to have CEHPI >20% reduction at 2 weeks compared with baseline	

### Primary: Progression-free survival

End point title	Progression-free survival <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	
05/09/2012 - 15/09/2018	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Screen fails (arm) were not assessed for any end point

End point values	Axitinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	16		
Units: Days				
median (full range (min-max))	111.5 (20 to 717)	61.00 (23 to 225)		

<b>Attachments (see zip file)</b>	PFS: Drug vs Placebo/Chart 1.docx
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### Statistical analyses

<b>Statistical analysis title</b>	Comparison of progression-free survival curves
Comparison groups	Placebo v Axitinib

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0021 [2]
Method	Logrank

Notes:

[2] - Survival curves are significantly different

### Primary: Progression-free survival of patients who were considered CEHPI responders at 2 weeks of treatment

End point title	Progression-free survival of patients who were considered CEHPI responders at 2 weeks of treatment <sup>[3]</sup>
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End point description:

CEHPI is defined as the Contrast Enhanced Hepatic Perfusion Index and is a means of measuring the ratios of arterial to portal venous flow. It is assessed using ultrasound imaging. This is able to analyse differential blood flow in liver metastases that are responding and also detect differences in the distributable flow from the portal vein and hepatic artery.

End point type	Primary
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End point timeframe:

05/09/2012 - 15/09/2018

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only one arm was assessed for this endpoint

End point values	Axitinib	CEHPI responders	CEHPI non-responders	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	14	19	
Units: Days				
median (full range (min-max))	123.0 (30 to 400)	123.0 (90 to 400)	69.0 (30 to 300)	

<b>Attachments (see zip file)</b>	Axitinib Patients (CEHPI>20% Reduction at 2 weeks)/PFS in
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### Statistical analyses

<b>Statistical analysis title</b>	Comparison of PFS for CEPHI Responders Vs CEPHI No
Comparison groups	CEHPI responders v CEHPI non-responders
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0558 [4]
Method	Logrank

Notes:

[4] - Survival curves are not statistically different

### Secondary: Overall survival between treatment and placebo arms

End point title	Overall survival between treatment and placebo arms <sup>[5]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

05/09/2012 - 15/09/2018

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Screen fails (arm) were not assessed for any end point

<b>End point values</b>	Axitinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	17		
Units: Days				
median (full range (min-max))	175.0 (20 to 893)	169.0 (36 to 875)		

<b>Attachments (see zip file)</b>	Overall Survival: Drug vs Placebo/OS.docx
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### Statistical analyses

<b>Statistical analysis title</b>	Comparison of OS of Drug Vs Placebo
Comparison groups	Axitinib v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3173 [6]
Method	Logrank

Notes:

[6] - Survival curves are not statistically different

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

Up to 30 days following end of treatment

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Assessment type	Systematic
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### Dictionary used

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Dictionary name	MedDRA
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Dictionary version	1.1
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Frequency threshold for reporting non-serious adverse events: 0 %

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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: There were no non-serious adverse events

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2016	At this time, Pfizer is making a switch from providing commercial image debossed tablets and matching debossed placebo to non-debossed tablets and matching non-debossed placebo with the intent to secure the commercial supply chain. It is therefore necessary to change from the cross-reference currently in place that references Study A4061032: Axitinib (Ag-013736) as Second Line Therapy For Metastatic Renal Cell Cancer: Axis Trial, EudraCT 2008-001451-21 to a new Investigational Medicinal Product Dossier - Quality (IMPD-Q).

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported