Clinical trial results:
GEM for Ectopic Pregnancies II: Combination gefitinib and methotrexate to treat ectopic pregnancies

Summary

EudraCT number	2011-001747-69
Trial protocol	GB
Global end of trial date	01 June 2016

Results information

Result version number	v1 (current)
This version publication date	12 June 2019
First version publication date	12 June 2019

Trial information

Trial identification

Sponsor protocol code	01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ACTRN: 12610000684022

Notes:

Sponsors

Sponsor organisation name	University of Edinburgh
Sponsor organisation address	QMRI, 51 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Ann Doust, University of Edinburgh, +44 1312429492, ann.doust@ed.ac.uk
Scientific contact	Andrew Horne, University of Edinburgh, +44 1312429492, andrew.horne@ed.ac.uk
Sponsor organisation name	NHS Lothian
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Public contact	Ann Doust, University of Edinburgh, +44 1312429492, ann.doust@ed.ac.uk
Scientific contact	Prof Andrew Horne, University of Edinburgh, +44 1312429492, andrew.horne@ed.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	18 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2016
Global end of trial reached?	Yes
Global end of trial date	01 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of a single intramuscular injection of MTX (50mg/m2) and seven days of oral gefitinib 250mg in regressing stable ectopic pregnancies with a serum human chorionic gonadotrophin level at presentation (reflects ectopic pregnancy size) of between 1000-10,000 IU/L.

It was a single arm trial that aimed to recruit 50 participants who met the inclusion criteria. It was powered to show the drug is at least 70% effective in successfully resolving ectopic pregnancies without need for surgery.

This trial also set out to further collect information on safety and tolerability of the drug.

Protection of trial subjects:

For protection of subjects

1) The trial was overseen by a Trial Steering Committee who had a member assessing safety sitting on the committee. In addition, this committee comprised of members from The University of Melbourne (2 Professors) and an independent Professor of Reproductive Biology at the University of Edinburgh.

2) The protocols had full REC approval and all participants provided written, informed consent

3) All adverse / serious adverse outcomes were formally reported to REC committees.

4) All trial subjects were aware of what to do in an event of any emergency: contact details for the hospital as well as a phone number where they could contact study investigators.

Background therapy:

All participants had the standard intramuscular methotrexate dose that is widely used to medically treat ectopic pregnancies. Thus, all were given a single intramuscular injection of methotrexate (50mg/m2), but they also then were given seven tablets of 250 mg of gefitinib (the trial medication).

Evidence for comparator:

This was a single arm trial and there was no comparator arm.

The thought when designing this small trial was that it was premature to embark of a formal randomised trial therefore the next step was this small single arm phase II study.

Actual start date of recruitment	01 March 2012
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	United Kingdom: 19
Country: Number of subjects enrolled	Australia: 11
Worldwide total number of subjects	30
EEA total number of subjects	19

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We recruited participants between March 2012 and April 2014.

Participants were recruited from 3 Australian Centres and 1 in Edinburgh. Recruitment was done in the early pregnancy units where investigators were alerted by staff of potential participants who were diagnosed with an ectopic pregnancy that may fit the criteria as per our protocol.

Pre-assignment

Screening details:

Patients we referred by their direct clinical care team to members of the research team.

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	Active arm (single arm study)
Arm description: -	
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:

250mg, once daily for 7 days

Number of subjects in period 1	Active arm (single arm study)
Started	30
Completed	28
Not completed	2
Consent withdrawn by subject	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical			
Study inclusion criterion stipulated an age range of 18-45 years.			
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)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Age	0	0	
Age continuous			
Units: years			
arithmetic mean	30.5		
inter-quartile range (Q1-Q3)	23.5 to 33.8	-	
Gender categorical			
This study investigates a treatment for women with ectopic pregnancies - all subjects are female			
Units: Subjects			
Female	30	30	
Age categorical			
Study inclusion criterion stipulated an age range of 18-45 years			
Units: Subjects			
18-45 years	30	30	
Maternal serum hCG concentration			
Units: iu/l			
median	2108		
full range (min-max)	1031 to 8575	-	

Subject analysis sets

Subject analysis set title	Analysis of ectopic pregnancy outcomes
Subject analysis set type	Full analysis

Subject analysis set description:

Outcomes analysed from 28 subjects (19 from the UK) who completed the study medication regime as per the protocol (single stat dose of 50mg/m² intramuscular methotrexate, plus 250mg oral gefitinib daily for seven days) for the treatment of tubal ectopic pregnancy.

Reporting group values	Analysis of ectopic pregnancy outcomes		
Number of subjects	28		
Age categorical			
Study inclusion criterion stipulated an age range of 18-45 years.			
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)	28		
From 65-84 years	0		
85 years and over	0		
Age	0		
Age continuous			
Units: years			
arithmetic mean	30.5		
inter-quartile range (Q1-Q3)	23.5 to 33.8		
Gender categorical			
This study investigates a treatment for women with ectopic pregnancies - all subjects are female			
Units: Subjects			
Female	28		
Age categorical			
Study inclusion criterion stipulated an age range of 18-45 years			
Units: Subjects			
18-45 years	28		
Maternal serum hCG concentration			
Units: iu/l			
median			
full range (min-max)			

End points

End points reporting groups

Reporting group title	Active arm (single arm study)
Reporting group description: -	
Subject analysis set title	Analysis of ectopic pregnancy outcomes
Subject analysis set type	Full analysis

Subject analysis set description:

Outcomes analysed from 28 subjects (19 from the UK) who completed the study medication regime as per the protocol (single stat dose of 50mg/m² intramuscular methotrexate, plus 250mg oral gefitinib daily for seven days) for the treatment of tubal ectopic pregnancy.

Primary: Resolution of ectopic pregnancy without need for surgical intervention

End point title	Resolution of ectopic pregnancy without need for surgical intervention[1]

End point description:

Resolution of ectopic pregnancy without need for surgical intervention

End point type	Primary

End point timeframe:

Serial blood tests to track serum hCG concentration levels collected and analysed pre-treatment (day 1), on days 4, 7 and 11, then weekly until either (i) surgical intervention was warranted or (ii) serum hCG concentration fell to non-pregnant levels.

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: No statistical analyses for this end point

End point values	Active arm (single arm study)			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Number of participants without surgery	28			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From time of consent to discharge following hCG <15 or surgical management of EP	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 30 (73.33%)		
Investigations			
All investigations			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Nervous system disorders			
All nervous system disorders			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
General disorders and administration site conditions			

All General disorders and administration site conditions			
subjects affected / exposed	10 / 30 (33.33%)		
occurrences (all)	12		
Gastrointestinal disorders			
All Gastrointestinal disorders			
subjects affected / exposed	17 / 30 (56.67%)		
occurrences (all)	34		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	16 / 30 (53.33%)		
occurrences (all)	23		
Respiratory, thoracic and mediastinal disorders			
All respiratory, thoracic and mediastinel disorders			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pain of skin			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	17 / 30 (56.67%)		
occurrences (all)	17		
Pruritus			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Infections and infestations			
All infections and infestations			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		

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/24812320

http://www.ncbi.nlm.nih.gov/pubmed/23872290

http://www.ncbi.nlm.nih.gov/pubmed/29941341