Clinical trial results:
A randomised control trial to study the side effect profile and to establish measures of efficacy using Photofrin or 5 aminolaevulinic acid (ALA) photodynamic therapy in the eradication of dysplasia in Barrett's columnar lined oesophagus

Summary

EudraCT number	2005-005528-15
Trial protocol	GB
Global end of trial date	30 April 2015

Results information

Result version number	v1 (current)
This version publication date	18 October 2019
First version publication date	18 October 2019

Trial information

Trial identification

Sponsor protocol code	05/059

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom,
Public contact	Gower Street, London , United Kingdom, WC1E 6BT, Joint Research Office, ctimps@ucl.ac.uk
Scientific contact	Gower Street, London , United Kingdom, WC1E 6BT, Joint Research Office, ctimps@ucl.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 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether PDT using ALA is more efficacious for the complete ablation of high grade dysplasia in Barrett's oesophagus than Photofrin.
To establish which drug has a better side effect profile.

Protection of trial subjects:

A routine chest X ray will be taken before and 24-48 hours after PDT. Pleural effusion have been noted post-PDT with the licensed and study medications.
Dysphagia is a recognised complication of photodynamic therapy sometimes resulting in admission to hospital for rehydration and possible oesophageal dilation.
Nausea and vomiting are relatively common post photodynamic therapy. This normal settles promptly and and does not prolong the patient's length of stay.
Aspiration pneumonia has been noted after photodynamic therapy. The occurrence of pneumonias is expected in a small number patients and rarely results in prolonged length of stay.
Pigmented urine has been noted on the day following ALA administration. This is thought to be related to the metabolism of the medication via the haem-biosynthesis pathway and has not resulted in any long term problems. If this occurs these patients will be work-up in the usual way in consultation with the urologists.
Liver function tests will be taken 1-2 days after treatment. If more than twice the upper limit of normal, they will continue to be taken every 1-2 days until bilirubin and ALT return to within twice the upper limit of normal or until discharge, whichever is earlier. Transient abnormalities in liver function tests have been reported with ALA photodynamic therapy. All have resolved spontaneously without long-term sequelae.
Hypotension has been noted with the oral administration of ALA. All patients are now rehydated prior to drug administration and excluded from the study if taking depot psychotropic medications.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	01 February 2006
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: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	2
From 65 to 84 years	57
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 128 patients that were screened for eligibility from 2006–2009, 79 patients were recruited to the study and from these, 64 underwent randomisation

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Study Arm

Arm description:

PDT with oral ALA administration (study arm)

Arm type	Experimental
Investigational medicinal product name	Aminolaevulinic Acid (ALA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral ALA PDT:
• Normal saline infusion 12 hours prior to administration of ALA only.
• Anti-emetic: Granisetron (30 minutes prior to ALA administration).
• Following ingestion of ALA, patients must minimise exposure to sunlight and avoid strong indoor lighting for 36 hours.
• Patients receive ALA (60 mg/kg body weight) in 50 ml of distilled water in 3 divided doses at 5 hours, 4 hours and 3 hours before therapy. Patients receive light treatment ideally at 5 hours (but in any case not more than 7 hours) after initial oral ALA ingestion via a diffuser fibre at 1132J/cm (or 200J/cm2 in an 18mm diameter balloon or bolster).

Arm title	Standard Treatment Control

Arm description:

PDT with IV Photofrin administration (standard treatment control)

Arm type	Active comparator
Investigational medicinal product name	Photofrin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

IV Photofrin PDT (Standard treatment parameters):
• Drug is administered intravenously (2mg/kg) by a cannula placed in a large bore vein in the antecubital fossa 3 days before light treatment.

Number of subjects in period 1	Study Arm	Standard Treatment Control
Started	34	30
Completed	34	30

Baseline characteristics

End points

End points reporting groups

Reporting group title	Study Arm
Reporting group description: PDT with oral ALA administration (study arm)	
Reporting group title	Standard Treatment Control
Reporting group description: PDT with IV Photofrin administration (standard treatment control)	

Primary: Complete reversal of high-grade dysplasia (CR-HGD) at 1 year post-PDT

End point title	Complete reversal of high-grade dysplasia (CR-HGD) at 1 year post-PDT[1]
End point description:	
End point type	Primary
End point timeframe: 1 year follow-up	

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: Of the 64 patients randomised, 34 were photosensitised with ALA and 30 with Photofrin. CR-HGD was 16/34 (47 %) in the ALA group and 12/30 (40 %) in the Photofrin group (Fisher's exact test00.62). A Kaplan– Meier analysis of probability of the remaining without dysplasia demonstrated no significant difference in dysplasia-free interval between the two groups (χ20
0.91, p00.34)

End point values	Study Arm	Standard Treatment Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: percent				
number (not applicable)	47	40		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From randomisation to end of follow-up period

Assessment type	Systematic

Dictionary used

Dictionary name	ctcae
Dictionary version	4.0

Reporting groups

Reporting group title	Randomised patients

Reporting group description: -

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: Non-serious adverse events are not available to be added to this dataset.

Serious adverse events	Randomised patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 64 (20.31%)		
number of deaths (all causes)	11		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal cancer metastatic			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Pleural effusion			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Coronary artery disease			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Chest pain			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Sunburn			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Abscess neck			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Randomised patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)		

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