Clinical trial results:
A phase 3, open-label study to assess the clinical utility of fluciclovine (18F) PET/CT in patients with prostate cancer with biochemical recurrence after radical treatment

Summary

EudraCT number	2015-000625-37
Trial protocol	GB
Global end of trial date	25 October 2018

Results information

Result version number	v1 (current)
This version publication date	08 November 2019
First version publication date	08 November 2019

Trial information

Trial identification

Sponsor protocol code	BED-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02578940
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Blue Earth Diagnostics Limited
Sponsor organisation address	Oxford Science Park, Magdalen Centre, Robert Robinson Avenue, Oxford, United Kingdom, OX4 4GA
Public contact	Blue Earth Diagnostics Limited, Blue Earth Diagnostics Limited, 44 1865784186, contact@blueearthDx.com
Scientific contact	Blue Earth Diagnostics Limited, Blue Earth Diagnostics Limited, 44 1865784186, contact@blueearthDx.com

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	25 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2018
Global end of trial reached?	Yes
Global end of trial date	25 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the clinical impact of fluciclovine (18F) PET/CT in affecting management decisions in patients with biochemical recurrence of prostate cancer (BCR) being considered for radical salvage treatment (with curative intent).

Protection of trial subjects:

Safety Monitoring Committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2015
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: 109
Worldwide total number of subjects	109
EEA total number of subjects	109

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)	31
From 65 to 84 years	77
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted between 27 November 2015 (first patient, screening visit) and 22 June 2018 (last patient, completed) at seven sites (one did not enrol) in the UK.

Pre-assignment

Screening details:

104 (95.4%) patients received 18F-fluciclovine injection, 103 (94.5%) patients completed the study and 6 (5.5%) patients prematurely discontinued the study. The most frequent reason for withdrawal was screening failure (5 [4.6%] patients). In addition, 1 (0.9%) patient had 'other' listed as their reason for study discontinuation.

Pre-assignment period milestones

Number of subjects started	109
Number of subjects completed	104

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen Failure: 5

Period 1

Period 1 title	Received 18F-fluciclovine (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	18F-Fluciclovine

Arm description:

Single intravenous administration of 18F-Fluciclovine for PET Scan
18F-Fluciclovine PET CT: Radioligand for PET CT scanning

Arm type	Experimental
Investigational medicinal product name	18F-Fluciclovine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Radioligand for PET CT scanning

Number of subjects in period 1[1]	18F-Fluciclovine
Started	104
Completed	103
Not completed	1
Lost to follow-up	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 109 Consented and 104 received study drug, 103 completed

Baseline characteristics

Reporting groups	
Reporting group title	18F-Fluciclovine
Reporting group description:	
Single intravenous administration of 18F-Fluciclovine for PET Scan 18F-Fluciclovine PET CT: Radioligand for PET CT scanning	

Reporting group values	18F-Fluciclovine	Total	
Number of subjects	104	104	
Age categorical 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)	31	31	
From 65-84 years	73	73	
85 years and over	0	0	
Age continuous Units: years			
median	67		
full range (min-max)	49 to 81	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	104	104	
Ethnicity (NIH/OMB) Units: Subjects			
Not Hispanic or Latino	104	104	
Region of Enrollment Units: Subjects			
United Kingdom	104	104	
Height Units: cm			
median	176.0		
full range (min-max)	157 to 197	-	
Weight Units: Kg			
median	82.80		
full range (min-max)	56.0 to 134.0	-	
Body Mass Index Units: kg/m2			
median	26.50		
full range (min-max)	19.6 to 42.3	-	

End points

End points reporting groups

Reporting group title	18F-Fluciclovine
Reporting group description: Single intravenous administration of 18F-Fluciclovine for PET Scan 18F-Fluciclovine PET CT: Radioligand for PET CT scanning	
Subject analysis set title	Overall Evaluable Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: Overall Evaluable Analysis Set	
Subject analysis set title	Positive 18F-fluciclovine Scan
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with a Positive 18F-fluciclovine Scan	
Subject analysis set title	Negative 18F-fluciclovine Scan
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with a Negative 18F-fluciclovine Scan	
Subject analysis set title	Salvage therapy
Subject analysis set type	Sub-group analysis
Subject analysis set description: Proportion of patients who had to radical salvage therapy	
Subject analysis set title	Salvage therapy guided by 18F-fluciclovine
Subject analysis set type	Sub-group analysis
Subject analysis set description: Salvage therapy guided by 18F-fluciclovine	
Subject analysis set title	Salvage therapy not guided by 18F-fluciclovine
Subject analysis set type	Sub-group analysis
Subject analysis set description: Salvage therapy not guided by 18F-fluciclovine	
Subject analysis set title	PSA Subgroup 0 to 0.2 (ng/mL)
Subject analysis set type	Sub-group analysis
Subject analysis set description: PSA Subgroup 0 to 0.2 (ng/mL)	
Subject analysis set title	PSA Subgroup >0.2 to 0.5 (ng/mL)
Subject analysis set type	Sub-group analysis
Subject analysis set description: PSA Subgroup >0.2 to 0.5 (ng/mL)	
Subject analysis set title	PSA Subgroup >0.5 to 1.0 (ng/mL)
Subject analysis set type	Sub-group analysis
Subject analysis set description: PSA Subgroup >0.5 to 1.0 (ng/mL)	
Subject analysis set title	PSA Subgroup >1.0 to 2.0 (ng/mL)
Subject analysis set type	Sub-group analysis
Subject analysis set description: PSA Subgroup >1.0 to 2.0 (ng/mL)	
Subject analysis set title	PSA Subgroup >2.0 to 5.0 (ng/mL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PSA Subgroup >2.0 to 5.0 (ng/mL)

Subject analysis set title	PSA Subgroup >5.0 to 10.0 (ng/mL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PSA Subgroup >5.0 to 10.0 (ng/mL)

Subject analysis set title	PSA Subgroup >10 (ng/mL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PSA Subgroup >10 (ng/mL)

Primary: Impact on Patient Treatment /Management

End point title	Impact on Patient Treatment /Management[1]

End point description:

The record of the revised management plan post fluciclovine (18F) PET/CT scan in comparison to the pre-scan intended management plan - descriptive statistics only.

End point type	Primary

End point timeframe:

1 month

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: Descriptive analysis only

End point values	Overall Evaluable Analysis Set	Positive 18F-fluciclovine Scan	Negative 18F-fluciclovine Scan	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	58	46	
Units: Participants				
Patients with Revised Management Plan	66	53	13	
No Revision to Management Plan	38	5	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Response Rate to Radical Salvage Therapy

End point title	Response Rate to Radical Salvage Therapy

End point description:

To establish the proportion of patients who have a sustained response to radical salvage therapy - Descriptive analysis only

End point type	Secondary

End point timeframe:

7 months

End point values	Salvage therapy	Salvage therapy guided by 18F-fluciclovine	Salvage therapy not guided by 18F-fluciclovine	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	17	39	
Units: Participants				
Treatment response	43	15	28	
Stable disease	5	0	5	
Disease progression	8	2	6	

Statistical analyses

No statistical analyses for this end point

Secondary: PSA Threshold for Positive Lesion Detection by 18F Fluciclovine PET/CT in BCR

End point title	PSA Threshold for Positive Lesion Detection by 18F Fluciclovine PET/CT in BCR

End point description:

PSA levels in relation to scan positivity were analysed to determine the optimal PSA threshold for detecting recurrent prostate cancer by 18F fluciclovine PET/CT - Descriptive analysis only

End point type	Secondary

End point timeframe:

1 month

End point values	PSA Subgroup 0 to 0.2 (ng/mL)	PSA Subgroup >0.2 to 0.5 (ng/mL)	PSA Subgroup >0.5 to 1.0 (ng/mL)	PSA Subgroup >1.0 to 2.0 (ng/mL)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	27	11	5
Units: Percentage of Detection Rate				
number (confidence interval 95%)	33.3 (13.3 to 59.0)	25.9 (11.1 to 46.3)	36.4 (10.9 to 69.2)	20 (0.5 to 71.6)

End point values	PSA Subgroup >2.0 to 5.0 (ng/mL)	PSA Subgroup >5.0 to 10.0 (ng/mL)	PSA Subgroup >10 (ng/mL)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	11	8	
Units: Percentage of Detection Rate				
number (confidence interval 95%)	91.7 (73.0 to 99.0)	90.9 (58.7 to 99.8)	100 (63.1 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Safety of 18F Fluciclovine Injection in Patients Undergoing PET/CT.

End point title	Safety of 18F Fluciclovine Injection in Patients Undergoing PET/CT.

End point description:

Safety was assessed from data on the occurrence of adverse events (AEs) and changes in clinical laboratory tests, vital signs, injection-site status and physical examination findings from the time of administration of 18F fluciclovine injection throughout the study period - Descriptive analysis only.

End point type	Secondary

End point timeframe:

1 Month

End point values	18F-Fluciclovine			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Participants				
TEAEs Unrelated	18			
TEAEs Possibly	8			
TEAEs Probably	0			
TEAEs Definitely	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

As specified in the Statistical Analysis Plan, results are presented as only those treatment-emergent adverse events which occurred up to 42 days after the 18F fluciclovine administration

Adverse event reporting additional description:

3 additional pre-treatment (None Treatment treatment-emergent) Adverse Events also reported during the study are not listed below.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	18F-Fluciclovine PET CT

Reporting group description:

Single intravenous administration of 18F-Fluciclovine for PET Scan
18F-Fluciclovine PET CT: Radioligand for PET CT scanning

Serious adverse events	18F-Fluciclovine PET CT		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 104 (0.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Renal and urinary disorders			
Urinary tract obstruction	Additional description: One serious TEAE was reported for one (1.0%) patient. This Grade 1 event of urinary tract obstruction occurred on Day 2 of the study, but was judged as unrelated to 18F-fluciclovine administration.		
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	18F-Fluciclovine PET CT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 104 (25.96%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	3		

Biopsy prostate			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanoma recurrent			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Post procedural contusion			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences (all)	4		
Dizziness			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Dysgeusia			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Parosmia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Restless legs syndrome			

subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
General disorders and administration site conditions			
Application site reaction			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	3		
Application site erythema			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Catheter site bruise			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary mass			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		

Renal and urinary disorders Urinary tract obstruction subjects affected / exposed occurrences (all)	 1 / 104 (0.96%) 1		
Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Neck mass subjects affected / exposed occurrences (all)	 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1		
Infections and infestations Oral herpes subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all) Electrocardiogram abnormal subjects affected / exposed occurrences (all)	 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2015	Changes include: • Principal Investigator list updated • Planned study period was corrected in the synopsis • Clarification on patients undergoing scan in the presence of an abnormal urinalysis. • Schedule of Assessments updated • Timings of follow-up telephone consultations updated
05 April 2016	Changes Include: • Updates to the site and Principal Investigator list. • Inclusion of a description of the site specific sub study. • Duration of 18F-fluciclovine injection was reduced. • Timing of the first blood pressure measurement post-injection and Vital signs measurements adjusted. • Timing of the post-scan telephone call to the patient to report AEs post-injection was increased
02 March 2017	Changes include: • Reporting of how suspected non-prostate cancer related cancer findings clarified. • Change of medical monitor. • Inclusion of reference to the SAP.
04 June 2018	Changes include: • Removal of two secondary endpoints:

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported