# 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<br>18F-Fluciclovine PET CT: Radioligand for PET CT scanning | |

| Reporting group values | 18F-Fluciclovine | Total | |
|---|---|---|---|
| Number of subjects | 104 | 104 | |
| Age categorical<br>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<br>Units: years | | | |
| median | 67 | | |
| full range (min-max) | 49 to 81 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 104 | 104 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Not Hispanic or Latino | 104 | 104 | |
| Region of Enrollment<br>Units: Subjects | | | |
| United Kingdom | 104 | 104 | |
| Height<br>Units: cm | | | |
| median | 176.0 | | |
| full range (min-max) | 157 to 197 | - | |
| Weight<br>Units: Kg | | | |
| median | 82.80 | | |
| full range (min-max) | 56.0 to 134.0 | - | |
| Body Mass Index<br>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:<br>Single intravenous administration of 18F-Fluciclovine for PET Scan<br>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:<br>Overall Evaluable Analysis Set | |
| Subject analysis set title | Positive 18F-fluciclovine Scan |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description:<br>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:<br>Patients with a Negative 18F-fluciclovine Scan | |
| Subject analysis set title | Salvage therapy |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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<br>Urinary tract obstruction<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 104 (0.96%)<br>1 | | |
| Musculoskeletal and connective tissue disorders<br>Groin pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Neck pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Neck mass<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1 | | |
| Infections and infestations<br>Oral herpes<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Electrocardiogram abnormal<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1<br><br>1 / 104 (0.96%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported