



## Clinical trial results:

### A Phase 1 Trial of Verteporfin Photodynamic Therapy in Unresectable Pancreatic Carcinoma (VERTPAC-01 study)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2006-004097-28   |
| Trial protocol           | GB               |
| Global end of trial date | 06 November 2019 |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 22 June 2022   |
| First version publication date    | 22 June 2022   |
| Summary attachment (see zip file) | Published trial article_Huggett_Vertpac_JC Feb 2014 (Huggett Vertpac BJC Feb 2014.pdf) |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 06/078 |
|-----------------------|--------|

##### 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               | Joint Research Office, University College London,<br>ctimps@ucl.ac.uk |
| Scientific contact           | Joint Research Office, University College London,<br>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                       | 04 October 2019  |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 04 October 2019  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 06 November 2019 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The trial aims to investigate the safety and efficacy of verteporfin photodynamic therapy in patients with locally advanced pancreatic carcinoma. The primary endpoint is the diameter of necrosis of tumour achieved around a single fibre for a given light energy. The study endpoint will be achieved with a 12 mm zone of necrosis around the fibre in 3 patients at a particular light dose.

Protection of trial subjects:

Following treatment, patients will be monitored closely on the ward, and given intravenous fluids and antibiotics until bowel sounds are documented, after which oral intake will be resumed. Contrast-enhanced spiral CT will be performed 3–5 days (prior to discharge from hospital) and at four weeks after photodynamic therapy (PDT), at which time patients will be eligible to commence palliative chemotherapy. Subsequent CT scans will be scheduled at three-monthly intervals after PDT or as clinically indicated until disease progression is evident, with other investigations such as ERCP performed as clinically indicated.

Clinical and laboratory assessments will be repeated prior to discharge. All patients will have clinical follow-up and blood tests on day 7, day 14 and day 28, then at least three-monthly intervals. At each visit, clinical symptoms will be reviewed, and quality of life and laboratory assessments repeated. Patients will be followed-up at 3-monthly intervals until death.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 23 April 2009 |
| 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: 15 |
| Worldwide total number of subjects   | 15                 |
| EEA total number of subjects         | 0                  |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 14 |
| From 65 to 84 years       | 1  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Symptom and adverse event monitoring

Physical examination (including weight and ECOG performance status)

FBC, INR and biochemical profile including CEA/CA19-9, amylase, glucose

CXR and pancreatic protocol CT (day -28 to 0)

Copy of report of prior histological or cytological proof of pancreatic carcinoma

QOL form (EORTC QLQ30 and PAN26)

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | Single laser fibre |

Arm description:

Thirteen patients were treated with a single laser fibre. Three treatments were carried out each at 5,10 and 20 J/cm<sup>2</sup>; and 5 treatments (4 patients) at 40 J/cm<sup>2</sup>.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Verteporfin  |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solvent for concentrate for solution for infusion |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

All patients receive a dose of verteporfin 0.4 mg/kg bodyweight intravenously, followed by light activation 60 minutes (acceptable treatment window 60-90 minutes) after photosensitisation under subdued lighting conditions. Treatment is via a single fibre which is placed under CT guidance by an experienced radiologist. Patients are treated using a 690 nm red laser at increasing light doses: patients 1-3 with 5J, 4-6 with 10J, 7-9 with 20J and patients 10-12 with 40J, with the stopping rule being a zone of necrosis around the fibre of at least 12 mm diameter in three patients treated at the same dose. Patients are kept in subdued indoor lighting for 24 hours but can be exposed to normal daylight after 72 hours.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Multiple laser fibres |
|------------------|-----------------------|

Arm description:

A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm<sup>2</sup>.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Verteporfin  |
| Investigational medicinal product code |  |
| Other name                             |  |
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of necrosis around the fibre of at least 12 mm diameter in three patients treated at the same dose. Patients are kept in subdued indoor lighting for 24 hours but can be exposed to normal daylight after 72 hours.

| <b>Number of subjects in period 1</b> | Single laser fibre | Multiple laser fibres |
|---------------------------------------|--------------------|-----------------------|
| Started                               | 13                 | 2                     |
| Completed                             | 13                 | 2                     |

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 15            | 15    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 0             | 0     |  |
| From 65-84 years                                      | 0             | 0     |  |
| 85 years and over                                     | 0             | 0     |  |
| Overall trial   | 0             | 0     |  |
| 47-78 years   | 15            | 15    |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 4             | 4     |  |
| Male  | 11            | 11    |  |

## End points

### End points reporting groups

|   |                       |
|---|-----------------------|
| Reporting group title   | Single laser fibre    |
| Reporting group description:<br>Thirteen patients were treated with a single laser fibre. Three treatments were carried out each at 5,10 and 20 J/cm <sup>2</sup> ; and 5 treatments (4 patients) at 40 J/cm <sup>2</sup> . |                       |
| Reporting group title   | Multiple laser fibres |
| Reporting group description:<br>A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm <sup>2</sup> .  |                       |

### Primary: Area of pancreatic necrosis

|  |  |
|--|--|
| End point title  | Area of pancreatic necrosis <sup>[1]</sup> |
| End point description:<br>Needle placement and laser delivery were technically successful in all patients. Thirteen patients were treated with a single laser fibre. Three treatments were carried out each at 5,10 and 20 J/cm <sup>2</sup> ; and 5 treatments (4 patients) at 40 J/cm <sup>2</sup> . A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm <sup>2</sup> . Tumour necrosis was measured on CT by two radiologists 5 days after treatment. Axial and sagittal CT with segmentation of the necrotic zone was used for volume rendering. Plasma and lip fluorescence were measured for pharmacokinetics. |  |
| End point type   | Primary                                    |
| End point timeframe:<br>Tumour necrosis was measured on CT by two radiologists 5 days after treatment.   |  |

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: End point value description:

Tumour necrosis was measured on CT by two radiologists 5 days after treatment. Axial and sagittal CT with segmentation of the necrotic zone was used for volume rendering. Plasma and lip fluorescence were measured for pharmacokinetics. There was a clear dose dependent increase in necrosis, with a median area of 20 x 16 mm (range 18 x 16 to 35 x 30 mm) at 40 J/cm<sup>2</sup>. In the 2 patients treated with multiple fibres, necrosis was 40 x 36 mm and 30 x 28 mm, respectively.

| End point values            | Single laser fibre | Multiple laser fibres |  |  |
|-----------------------------|--------------------|-----------------------|--|--|
| Subject group type          | Reporting group    | Reporting group       |  |  |
| Number of subjects analysed | 13                 | 2                     |  |  |
| Units: millimetre(s)        |                    |                       |  |  |
| number (not applicable)     | 20                 | 40                    |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

Timeframe for reporting adverse events:

During and up to 1 month post-treatment

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

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 Event information was not available to sponsor at the time of reporting results.

| Serious adverse events                            | Overall trial    |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 12 / 15 (80.00%) |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |
| Investigations                                    |                  |  |  |
| Biopsy  |                  |  |  |
| subjects affected / exposed                       | 2 / 15 (13.33%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 2            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Surgical and medical procedures                   |                  |  |  |
| Pancreaticoduodenectomy                           |                  |  |  |
| subjects affected / exposed                       | 1 / 15 (6.67%)   |  |  |
| occurrences causally related to treatment / all   | 1 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Nervous system disorders                          |                  |  |  |
| Mobility decreased                                |                  |  |  |
| subjects affected / exposed                       | 1 / 15 (6.67%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Blood and lymphatic system disorders              |                  |  |  |
| Anaemia   |                  |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Fatigue  |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Fever  |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Disease progression                                  |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Gastrointestinal disorders                           |                 |  |  |
| Gastric outlet obstruction                           |                 |  |  |
| subjects affected / exposed                          | 2 / 15 (13.33%) |  |  |
| occurrences causally related to treatment / all      | 0 / 2           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Ascites  |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 2           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Vomiting   |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Abdominal pain upper                                 |                 |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Intestinal obstruction                          |                 |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal perforation                    |                 |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Bile duct obstruction                           |                 |  |  |
| subjects affected / exposed                     | 2 / 15 (13.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Biliary sepsis                                  |                 |  |  |
| subjects affected / exposed                     | 3 / 15 (20.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Jaundice  |                 |  |  |
| subjects affected / exposed                     | 2 / 15 (13.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Jaundice cholestatic                            |                 |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Acute kidney injury                             |                 |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Dehydration                                     |                 |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

|   |                |  |  |
|---|----------------|--|--|
| <b>Non-serious adverse events</b>                     | Overall trial  |  |  |
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 0 / 15 (0.00%) |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported