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, ctimps@ucl.ac.uk
Scientific contact	Joint Research Office, University College London, 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
Arm title	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/cm2; and 5 treatments (4 patients) at 40 J/cm2.

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.

Arm title	Multiple laser fibres

Arm description:

A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm2.

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:

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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.

Number of subjects in period 1	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 (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)	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:	
Thirteen patients were treated with a single laser fibre. Three treatments were carried out each at 5,10 and 20 J/cm2; and 5 treatments (4 patients) at 40 J/cm2.	
Reporting group title	Multiple laser fibres
Reporting group description:	
A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm2.	

Primary: Area of pancreatic necrosis

End point title	Area of pancreatic necrosis[1]
End point description:	
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/cm2; and 5 treatments (4 patients) at 40 J/cm2. A further 2 patients were treated with 2 or 3 laser fibres at 40 J/cm2. 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:	
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/cm2. 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[1]

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 %

Non-serious adverse events	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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported