



## Clinical trial results:

### PHASE II TRIAL OF THE EFFECT OF GEMCITABINE WITH INTRAVENOUS OMEGA 3 FISH OIL INFUSION IN PATIENTS WITH UNRESECTABLE PANCREATIC ADENOCARCINOMA.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2009-009470-27 |
| Trial protocol           | GB             |
| Global end of trial date | 01 June 2014   |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 22 March 2020 |
| First version publication date | 22 March 2020 |

#### Trial information

##### Trial identification

|                       |                      |
|-----------------------|----------------------|
| Sponsor protocol code | Version 4 27/06/2011 |
|-----------------------|----------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01019382 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University Hospitals of Leicester NHS Trust   |
| Sponsor organisation address | Gwendolen Road, Leicester, United Kingdom, LE5 4PW  |
| Public contact               | Mrs Carolyn Maloney R&D department Leicester General Hospital Leicester LE5 4PW, University Hospitals of Leicester, +44116 2584109, carolyn.maloney@uhl-tr.nhs.uk |
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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                       | 06 August 2014 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 01 June 2014   |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 01 June 2014   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

Objective response rate (complete + partial response) of response of patients receiving gemcitabine plus parenteral omega-3. To assess the effect of intravenous (given by a drip into the blood vessels) omega-3 fish oil, in combination with standard gemcitabine chemotherapy protocol upon patients with advanced pancreatic cancer.

Protection of trial subjects:

This study provides little potential risk over and above standard clinical care. The main ethical issue anticipated is the desire of patients to continue fish oils despite careful explanation of the lack of proven benefit. Since the side effect profile of taking oral fish oils is very safe, oral preparation will be offered to these patients. Otherwise this study is felt to be very safe and of potential benefit. Rare complications of study treatments aside, little harm can be expected to come to patients, and the potential benefits should be explored.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 23 November 2009 |
| 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: 50 |
| Worldwide total number of subjects   | 50                 |
| EEA total number of subjects         | 50                 |

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)      | 15 |
| From 65 to 84 years       | 35 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

50 patients will be recruited to the study. This number has been calculated to give the study sufficient power. There will be no control group as this is a phase IIa exploratory therapeutic trial. Results will be reviewed after 21 patients have been recruited. If two or fewer patients have a response of CT scan to treatment, the trial will be stop

### Pre-assignment

Screening details:

Eligible patients (>18 years of age) had an ECOG performance status of 0 or 1, histologically proven locally advanced and or metastatic pancreatic adenocarcinoma, measurably disease on CT by RECIST 1.1 criteria and have not received prior chemotherapy. Patients could not have undergone any major surgical procedure within 4 weeks

### Period 1

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

### Arms

|  |                       |
|--|-----------------------|
| Arm title                              | Arm 1                 |
| Arm description:                       |                       |
| A single arm trial                     |                       |
| Arm type                               | Experimental          |
| Investigational medicinal product name | Lipidem               |
| Investigational medicinal product code | PR 1                  |
| Other name                             |                       |
| Pharmaceutical forms                   | Emulsion for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

10 ml of lipidem 200mg/ml per kilogram body weight per day by intravenous infusion. Total dose per day 500 ml

| Number of subjects in period 1            | Arm 1 |
|---|-------|
| Started                                   | 50    |
| Completed                                 | 35    |
| Not completed                             | 15    |
| early death and withdrawal from treatment | 15    |

## Baseline characteristics

## End points

### End points reporting groups

|                              |       |
|------------------------------|-------|
| Reporting group title        | Arm 1 |
| Reporting group description: |       |
| A single arm trial           |       |

**Primary: objective response rate which is a percentage of patients experiencing a 30% or greater reduction in the size of their target lesion at any point subsequent to commencing on treatment on CT**

|                 |  |
|-----------------|--|
| End point title | objective response rate which is a percentage of patients experiencing a 30% or greater reduction in the size of their target lesion at any point subsequent to commencing on treatment on CT <sup>[1]</sup> |
|-----------------|--|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

objective response rate which is a percentage of patients experiencing a 30% or greater reduction in the size of their target lesion at any point subsequent to commencing on treatment on CT (which is measured)

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: Statistical analysis title: simon's two stage design.

Description : This design was used so there is no formal statistical analysis for the primary outcome measure.

Type: optimal design p0 (0.10), and p1 (0.25) were parameters used for the design with rejection parameters of 2/21 patients for the first stage and 7/50 patients for the complete trial.

| End point values                 | Arm 1           |  |  |  |
|----------------------------------|-----------------|--|--|--|
| Subject group type               | Reporting group |  |  |  |
| Number of subjects analysed      | 50              |  |  |  |
| Units: number of patients (0-50) |                 |  |  |  |
| number (not applicable)          | 50              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

Timeframe for reporting adverse events:

This varies between patients. Assuming toleration of chemotherapy, the minimal amount of time each patient will be in the trial is 8 weeks. Patients will exit on disease progression and will continue until this occurs, or consent withdrawn

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 23.0   |

### Reporting groups

|                              |       |
|------------------------------|-------|
| Reporting group title        | Arm 1 |
| 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 were not recorded for this study

| Serious adverse events                               | Arm 1            |  |  |
|--|------------------|--|--|
| Total subjects affected by serious adverse events    |                  |  |  |
| subjects affected / exposed                          | 28 / 50 (56.00%) |  |  |
| number of deaths (all causes)                        | 0                |  |  |
| number of deaths resulting from adverse events       | 0                |  |  |
| Vascular disorders                                   |                  |  |  |
| Hypotension  |                  |  |  |
| subjects affected / exposed                          | 1 / 50 (2.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Surgical and medical procedures                      |                  |  |  |
| Elective ERCP & stent change                         |                  |  |  |
| subjects affected / exposed                          | 5 / 50 (10.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 5            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| surgical gastro jejunostomy                          |                  |  |  |
| subjects affected / exposed                          | 1 / 50 (2.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| General disorders and administration site conditions |                  |  |  |
| Pyrexia  |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 3 / 50 (6.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hypothermia                                     |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Elevated temperature                            |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| SOB unknown cause                               |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| raised LFTs                                     |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Tachycardia                                     |                |  |  |
| subjects affected / exposed                     | 3 / 50 (6.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| ST elevated MI                                  |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Vertigo   |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| 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                     | 2 / 50 (4.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Nausea  |                |  |  |
| subjects affected / exposed                     | 2 / 50 (4.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infective enteritis                             |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholangitis                                     |                |  |  |
| subjects affected / exposed                     | 2 / 50 (4.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Biliary colic                                   |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| obstructive jaundice                            |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Liver failure                                   |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Biliary obstruction                             |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blocked biliary stent                           |                |  |  |
| subjects affected / exposed                     | 4 / 50 (8.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| External biliary drain                          |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Cellulitis                                      |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bilateral cellulitis                            |                |  |  |
| subjects affected / exposed                     | 1 / 50 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| acute renal failure                             |                |  |  |
| subjects affected / exposed                     | 2 / 50 (4.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|  |                                  |  |  |
|--|----------------------------------|--|--|
| Deteriorating renal function<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                       | 1 / 50 (2.00%)<br>0 / 1<br>0 / 0 |  |  |
| Endocrine disorders<br>Newly diagnosed IDDM<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 1 / 50 (2.00%)<br>0 / 1<br>0 / 0 |  |  |
| Infections and infestations<br>Empirical infection<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 50 (2.00%)<br>0 / 1<br>0 / 0 |  |  |
| Biliary sepsis<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                     | 3 / 50 (6.00%)<br>0 / 3<br>0 / 0 |  |  |
| Infected biliary stent<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 1 / 50 (2.00%)<br>0 / 1<br>0 / 0 |  |  |
| Sepsis<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 50 (2.00%)<br>0 / 1<br>0 / 0 |  |  |
| Neutropenic sepsis<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | 2 / 50 (4.00%)<br>0 / 2<br>0 / 0 |  |  |
| Chest infection<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                    | 2 / 50 (4.00%)<br>0 / 2<br>0 / 0 |  |  |

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

|   |                |  |  |
|---|----------------|--|--|
| <b>Non-serious adverse events</b>                     | Arm 1          |  |  |
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 0 / 50 (0.00%) |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 01 June 2010 | Protocol Variation and Lipidem Dose Reduction The dose of IV $\omega$ -3 could be reduced in the interest of patient safety at the discretion of the investigator should any adverse events occur thought to be attributable to the infusion. The infusion would be discontinued and subsequent treatments given at a 25% or 50% dose reduction. Dose reductions below 50% were not allowed. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported