

A clinical study comparing Acelarin with gemcitabine in patients with metastatic pancreatic carcinoma

Submission date 22/07/2015	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 23/07/2015	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 19/07/2022	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-acelarin-and-gemcitabine-for-pancreatic-cancer-that-has-spread-acelarate>

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

2014-004653-14

IRAS number

ClinicalTrials.gov number

NCT03610100

Secondary identifying numbers

19200

Study information

Scientific Title

A phase III, open label, multicentre randomised clinical study comparing Acelarin (NUC1031) with gemcitabine in patient with metastatic pancreatic carcinoma (ACELARATE)

Acronym

ACELARATE

Study objectives

To evaluate the efficacy and safety of Acelarin compared with gemcitabine in patients with metastatic pancreatic carcinoma. Exploratory objectives are to discover possible biomarkers to predict additional benefit of Acelarin over gemcitabine for subsequent validation.

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee East Midlands - Nottingham 2, 07/04/2015, ref: 15/EM/0095

Study design

Randomised; Interventional; Design type: Treatment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Metastatic pancreatic carcinoma

Interventions

Arm 1: Acelarin: 825 mg/m² administered intravenously on days 1, 8 and 15 of a 28 day cycle.
Arm 2: Gemcitabine 1000mg/m² administered intravenously on days 1, 8 and 15 of a 28 day cycle.

Randomisation will be stratified by ECOG performance status (PS) (0/1 vs 2). The planned treatment duration per patient will be until progression of disease, unacceptable toxicity or withdrawal of consent. Participation in the study will be until withdrawal of consent or death. Patients who stop treatment before having developed progressive disease (PD) will be assessed every 12 weeks for response until PD occurs. Patients will receive screening CT scan and ECG. CT scan every 12 weeks after screening until PD as per RECIST 1.1. Optional additional biopsy for translational biomarker analysis. Optional translational blood sample taken at baseline, day 1 of each cycle and end of treatment.

Added 20/07/2018:

Sub-study

Eight of the existing sites are running the peripheral infusion sub-study. This is open to 30 patients who have been randomised onto Arm A: Acelarin first.

The purpose of the sub-study is to explore whether a peripheral infusion of Acelarin (NUC-1031) through a vein in the back of the hand or arm is well-tolerated. The bag of Acelarin has 500ml of saline, rather than 250ml for the main study.

The sub-study's purpose is to explore if any sub-study patients encounter any injection site reactions.

In the sub-study CTCAE grade 2 pain is split into two levels:

Grade 2A for pain only, with no associated phlebitis, lipdostrophy or oedema

Grade 2B for pain with associated phlebitis, lipdostrophy or oedema

Patients are reviewed for any injection site reactions during the infusion and again one hour after the infusion has completed.

Patients who are participating in the sub-study will sign the supplemental appendix to the Patient Information Sheet as well after signing the main study consent form.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Acelarin, gemcitabine

Primary outcome measure

Overall survival; Timepoint(s): Date of randomisation to date of death.

Secondary outcome measures

1. Discover possible biomarkers to predict additional benefit of Acelarin over gemcitabine alone; Timepoint(s): For subsequent validation in larger scale studies
2. Progression Free Survival; Timepoint(s): Date of randomisation to the earlier of date of progressive disease, date of death or censoring date

3. Quality of life; Timepoint(s): Assessed using the EORTC QLQ-C30 v3 and EORTC QLQ-PAN26 throughout the study and 3 monthly follow up
4. Radiological response and disease control rate; Timepoint(s): Objective radiological response is defined as occurrence of complete (CR) or partial responders (PR)
5. Safety; Timepoint(s): Occurrence of SAE or grade 3+ toxicity measured until 30 days after last study treatment

Overall study start date

09/09/2014

Completion date

31/12/2020

Eligibility

Key inclusion criteria

1. Aged at least 18 years
2. Histologically or cytologically proven pancreatic ductal adenocarcinoma or undifferentiated carcinoma of the pancreas*
3. Metastatic disease precluding curative surgical resection or definitive locally directed therapies such as chemo radiation. Patients who have relapsed following previously resected pancreatic cancer can be included
4. Contrast enhanced computerised tomography (CT) scan of the thorax, abdomen and pelvis within 28 days prior to commencing treatment
5. Unidimensionally measurable disease
6. ECOG performance status 0, 1 or 2 where treatment with combination chemotherapy is not deemed appropriate or is declined by the patient
7. Platelets = $100 \times 10^9/l$; neutrophils = $1.5 \times 10^9/l$ at entry
8. Documented life expectancy > 3 months
9. Informed written consent

*Patients will be approached for consenting to provide either an additional core of tissue material for biomarker discovery at the same time as a diagnostic biopsy or in those patients that have already had a diagnostic biopsy to undergo a second biopsy after randomisation into the trial. Neither of these biopsies is compulsory. Patients who don't wish to have extra tissue taken for Biomarker discovery will be approached for consent to released surplus tissue from the original diagnostic specimen if this exists

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 328; UK Sample Size: 328; Description: From our own data for recruitment to advanced pancreatic cancer trials (VIP and Telovac), we can estimate that this would require 328 patients in total yielding 270 deaths - assuming that 4 sites opened/month to a total of 40 sites with mean recruitment rate 0.39 pts/site/month, and 36 month study duration inclusive of 10 month minimum follow-up (excluding time for set-up and closedown).

Key exclusion criteria

1. Laboratory results:

- 1.1. Serum bilirubin = 1.5x the upper limit of reference range (ULRR)
- 1.2. Haemoglobin < 10G/dl
- 1.3. Creatinine clearance < 30 mL/minute (calculated by Cockcroft-Gault formula)
- 1.4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) or alkaline phosphatase (ALP) >2.5 x ULN or > 5x ULN if judged by the investigator to be related to liver metastases.
2. Medical or psychiatric conditions compromising informed consent.
3. Intracerebral metastases or meningeal carcinomatosis.
4. Evidence of severe or uncontrolled systemic disease or any concurrent condition which in the Investigator's opinion makes it undesirable for the patient to participate in the trial or which would jeopardize compliance with the protocol.
5. Pregnancy or breast feeding.
6. Previous chemotherapy for locally advanced and metastatic disease. Adjuvant chemotherapy for resected pancreatic cancer will be permitted provided that chemotherapy was completed > 12 months previously.
7. Radiotherapy within the last 4 weeks prior to start of study treatment.
8. Concurrent malignancies or invasive cancers diagnosed within past 5 years except for adequately treated basal cell carcinoma of the skin, in situ carcinoma of the uterine cervix or resected pancreatic cancer.
9. Hypersensitivity to gemcitabine or any of the excipients of gemcitabine or Acelarin (NUC-1031).
10. All men or women of reproductive potential, unless using at least two contraceptive precautions, one of which must be from the list below, the other must be a condom (1) or abstaining from sexual intercourse, until six months after treatment has ended:
 - 10.1. Combined (oestrogen and progesterone containing) hormonal contraception associated with inhibition of ovulation: either oral, intravaginal or transdermal.
 - 10.2. Progesterone-only hormonal contraception associated with inhibition of ovulation: either oral, injectable or implantable.
 - 10.3. Intra-uterine device (IUD)
 - 10.4. Intra-uterine hormone-releasing system (IUS)
 - 10.5. Bilateral tubal occlusion
 - 10.6. Vasectomised partner (2)
 - 10.7. Sexual abstinence (3)

(1) Male or female condom with or without spermicide is not an acceptable method of contraception alone.

(2) Vasectomised partner is a highly effective birth control method provided that partner is the sole sexual partner of the woman of childbearing potential trial participant and that the vasectomised partner has received medical assessment of the surgical success.

(3) In the context of this guidance sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject.

Date of first enrolment

17/08/2015

Date of final enrolment

31/12/2019

Locations

Countries of recruitment

England

United Kingdom

Study participating centre**Liverpool Cancer Trials Unit**

Cancer Research UK

University of Liverpool

1st floor Block C, Waterhouse Building

3 Brownlow Street

Liverpool

United Kingdom

L69 3GL

Sponsor information

Organisation

Clatterbridge Centre for Oncology NHS Trust

Sponsor details

Clatterbridge Hospital

Clatterbridge Road

Wirral

England

United Kingdom

CH63 4JY

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/05gcq4j10>

Funder(s)

Funder type

Industry

Funder Name

NuCana BioMed Ltd

Results and Publications

Publication and dissemination plan

The trialists intend to publish the study results with regard to the primary and secondary endpoints upon completion of the study. The abstract will be discussed at meetings and will be in peer reviewed papers.

Intention to publish date

31/10/2022

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the Trial Statistician Dr Richard Jackson (richj23@liverpool.ac.uk).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No