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

Submission date 22/07/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 23/07/2015	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 19/07/2022	**Condition category** Cancer	[_] Individual participant data [_] 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

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-004653-14

ClinicalTrials.gov (NCT)
NCT03610100

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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

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 x 109/l; neutrophils = 1.5 x 109/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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

England

Study participating centre
Liverpool Cancer Trials Unit
Cancer Research UK
University of Liverpool

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Sponsor information

Organisation
Clatterbridge Centre for Oncology NHS Trust

ROR
https://ror.org/05gcq4j10

Funder(s)

Funder type
Industry

Funder Name
NuCana BioMed Ltd

Results and Publications

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