

Scheduling nabpaclitaxel with gemcitabine (SIEGE)

Submission date 08/05/2014	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 08/05/2014	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 24/02/2023	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

<http://www.cancerresearchuk.org/cancer-help/trials/a-trial-of-nab-paclitaxel-with-gemcitabine-for-cancer-of-pancreas-that-has-spread-siege>

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

EudraCT/CTIS number

2013-001868-40

IRAS number

ClinicalTrials.gov number

NCT03529175

Secondary identifying numbers

15344

Study information

Scientific Title

Randomised phase II trial to investigate two different schedules of nab-paclitaxel (Abraxane) combined with gemcitabine as first line treatment for metastatic pancreatic ductal adenocarcinoma

Acronym

SIEGE

Study objectives

Metastatic pancreatic ductal adenocarcinoma (PDAC) carries a poor prognosis. The concomitant ABX/GEM chemotherapy regimen has been shown to improve overall survival over the standard single agent GEM. Studies in mouse models of PDAC suggest that delivery of ABX 24 hours prior to GEM might result in higher intra-tumoural GEM concentrations. SIEGE is looking at the how the scheduling of these two drugs may be critical to optimising clinical benefit.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 01/11/2013, Office for Research Ethics Committees Northern Ireland, ref: 13/NI/0143

Study design

Randomized interventional study

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 the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Topic: Cancer; Subtopic: Upper Gastro-Intestinal Cancer; Disease: Pancreas

Interventions

Eligible patients are randomly assigned via a web-based randomisation system to either the concomitant ABX/GEM arm or the sequential ABX/GEM arm in a 1:1 ratio using the stratified block randomisation method. Stratification factors are original primary site of disease (head versus body and/or tail) and presence of liver metastases (yes versus no).

Abraxane administration: On days 1, 8 and 15 of a 4 weekly cycle

Gemcitabine administration: On days 1, 8, 15 or days 2, 9 and 16 of a 4-weekly cycle dependent upon the arm; Follow Up Length: 12 month(s)

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Nabpaclitaxel, gemcitabine

Primary outcome measure

Progression-free survival is calculated from the date of randomisation to the date of clinical /radiological progression or death from any cause, whichever occurs first

Secondary outcome measures

1. Health economics (HE); Timepoint(s): 4-weekly
2. Overall survival; Timepoint(s): 3-monthly
3. Quality of life (QoL); Timepoint(s): 4-weekly
4. Response; Timepoint(s): 8-weekly
5. Safety; Timepoint(s): 4-weekly

Efficacy is measured by

1. Objective response: response will be assessed according to RECIST version 1.1
2. Disease control
3. Overall survival, calculated from date of randomisation to the date of death from any cause; surviving patients will be censored at the date last known alive.

Safety is measured via

1. Adverse Events (including Serious Adverse Events) assessed using NCI CTCAE version 4.03
2. Laboratory test results
3. Karnofsky performance status, ECOG performance status, vital signs and physical examination

Exploratory Outcome Measures via

1. Quality of life questionnaires (EORTC QLQ-C30, QLQ-PAN26)
2. Health Economics questionnaires (EQ-5D-5L)

Overall study start date

23/01/2014

Completion date

01/07/2015

Eligibility

Key inclusion criteria

1. Aged ≥ 18 years old
2. Signed informed consent and ability to comply with the protocol
3. Histologically or cytologically confirmed metastatic PDAC
4. Radiologically confirmed stage IV disease and measurable disease by RECIST version 1.1; baseline tumour assessments and measurements must be done within 28 days prior to randomisation
5. Karnofsky performance status $\geq 70\%$
6. Life expectancy >12 weeks from the date of screening assessment
- Adequate bone marrow function
 - 6.1. Absolute neutrophil count (ANC) $= 1.5 \times 10^9 /L$
 - 6.2. Haemoglobin (Hb) $= 100 \text{ g/L}$
 - 6.3. Platelets $= 100 \times 10^9 /L$
 - 6.4. White blood cell count (WBC) $= 3 \times 10^9 /L$
7. Adequate liver function
 - 7.1. Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) $= 2.5 \times$ upper limit of normal range (ULN)
 - 7.2. Total bilirubin $< 1.5 \times$ ULN
8. Adequate renal function defined as a serum creatinine $\leq 1.5 \times$ ULN or calculated creatinine clearance by CockcroftGault of $\geq 50 \text{ mL/min}$
9. Received no prior systemic therapy for metastatic disease
10. Prior adjuvant chemotherapy (with GEM or any other drug/s) is allowed if completed at least 6 months previously
11. Prior radiotherapy is allowed as long as there is measurable disease which has not been irradiated
12. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, completion of QoL and HE questionnaires and other study procedures
13. Confirmation of tumour tissue sample collected within 12 weeks prior to randomisation and blood to be taken prior to randomisation
14. Women of childbearing potential (WCBP), defined as a sexually mature woman not surgically sterilized or not postmenopausal for at least 24 consecutive months if age ≤ 55 years or 12 months if age > 55 years, must have a negative serum or urine pregnancy test within 14 days prior to randomisation
15. All WCBP, all sexually active male patients, and all partners of patients must agree to use effective contraception methods throughout the study and for 30 days after the final dose of study drug for WCBP and for up to 6 months after treatment for male patients

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 120; UK Sample Size: 120

Total final enrolment

146

Key exclusion criteria

1. Patients with operable or locally advanced PDAC
2. Other invasive malignancies diagnosed within the last 5 years, except nonmelanoma skin cancer and localized cured prostate cancer
3. Significant acute or chronic medical or psychiatric condition, disease or laboratory abnormality which in the judgment of the investigator would place the patient at undue risk or interfere with the trial. Examples include, but are not limited to:
 - 3.1. Patients who have had a venous thromboembolic event who are not appropriately anticoagulated or have had a significant bleeding episode in the 3 weeks prior to randomisation
 - 3.2. Patients with symptoms of severe chronic obstructive airways disease or significant shortness of breath at rest AND have an FEV1<1.0 L within the last 6 months
 - 3.3. Patients with a history of interstitial lung disease, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, pulmonary hypersensitivity pneumonitis, cystic fibrosis or bronchiectasis
 - 3.4. Patients with uncontrolled ischaemic heart or other cardiovascular event (myocardial infarction (MI), new angina, stroke transient ischaemic attack (TIA), or new congestive cardiac failure (CCF)) within the last 6 months
 - 3.5. Patients with stable but significant cardiovascular disease defined by heart failure (New York Heart Association Functional Classification (NYHF) III or IV) or frequent angina
 - 3.6. Presence of active infection
 - 3.7. Cirrhotic liver disease, known chronic active or acute hepatitis B, or hepatitis C
 - 3.8. Known allergy or hypersensitivity to GEM or ABX
4. Women who are pregnant, plan to become pregnant or are lactating
5. Use of oral antioxidant supplements: betacarotene, selenium, lutein, zeaxanthin, lycopene, pycnogenol, farnesol, omega3S, vitamin C, vitamin E, astaxanthin

Date of first enrolment

23/01/2014

Date of final enrolment

01/07/2015

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Cambridge Cancer Trials Centre

Cambridge

United Kingdom

CB2 0QQ

Sponsor information

Organisation

Cambridge University Hospitals NHS Foundation Trust (UK)

Sponsor details

Addenbrookes Hospital
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/04v54gj93>

Funder(s)

Funder type

Industry

Funder Name

Celgene Europe Ltd (UK)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
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Abstract results	results abstract, 2017 Gastrointestinal Cancers Symposium	01/02/2017		No	No
Results article	Results	22/02/2023	24/02/2023	Yes	No
HRA research summary			28/06/2023	No	No