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Scheduling nabpaclItaxel with gemcitabine (SIEGE)

Submission date	Recruitment status	[_] Prospectively registered
08/05/2014	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/05/2014	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
24/02/2023	Cancer	

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

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03529175

Clinical Trials Information System (CTIS)
2013-001868-40

Protocol serial number
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

Study type(s)
Treatment

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(s)
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

Key secondary outcome(s)
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)

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 =70%
6. Life expectancy >12 weeks from the date of screening assessment
Adequate bone marrow function
6.1. Absolute neutrophil count (ANC) =1.5 x 10^9 /L
6.2. Haemoglobin (Hb) = 100 g/L
6.3. Platelets =100 x 10^9 /L
6.4. White blood cell count (WBC) = 3 x 10^9 /L
7. Adequate liver function

7.1. Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) =2.5 x upper limit of normal range (ULN)
7.2. Total bilirubin <1.5 x ULN
8. Adequate renal function defined as a serum creatinine =1.5 x ULN or calculated creatinine clearance by CockcroftGaultv of =50 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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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, fernblock, omega3S, vitamin C, vitamin E, astaxanthin

Date of first enrolment
23/01/2014

Date of final enrolment
01/07/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge Cancer Trials Centre
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type

Industry

Funder Name
Celgene Europe Ltd (UK)

Results and Publications

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?
Results article	Results	22/02/2023	24/02/2023	Yes	No
Abstract results	results abstract, 2017 Gastrointestinal Cancers Symposium	01/02/2017		No	No
HRA research summary			28/06/2023	No	No