

# Scheduling nabpaclitaxel with gemcitabine (SIEGE)

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

### Clinical Trials Information System (CTIS)

2013-001868-40

### ClinicalTrials.gov (NCT)

NCT03529175

### 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  $\geq 18$  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 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?
<a href="#">Results article</a>	Results	22/02/2023	24/02/2023	Yes	No
<a href="#">Abstract results</a>	results abstract, 2017 Gastrointestinal Cancers Symposium	01/02/2017		No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No