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SGI-110 with cisplatin and gemcitabine chemotherapy in patients with bladder cancer

Submission date 03/02/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/02/2016	**Overall study status** Completed	
Last Edited 04/06/2024	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-sgi-110-with-cisplatin-and-gemcitabine-for-advanced-solid-tumours-spire

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Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-004062-29

Protocol serial number
20447

Study information

Scientific Title
SGI-110 to potentiate platinum response: a phase Ib/randomised IIa open label clinical trial combining SGI-110 with cisplatin and gemcitabine chemotherapy for solid malignancies including bladder cancer

Study objectives
Phase I:
The aim of this phase is to find the optimum dose of gemcitabine (GC) for the treatment of bladder cancer to use in the phase II of the study.

Phase II:
The aim of this phase is to investigate the whether treatment with a combination of SGI-110 and GC or GC alone is most effective.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West - Haydock Research Ethics Committee, 14/01/2016, ref: 15/NW/0936

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bladder cancer

Interventions
Phase I: Dose-escalation phase
Patients will be entered into sequential dose level cohorts and (at the relevant dose level). Escalating dose level cohorts (4 cohorts are planned) of SGI-110 + standard gemcitabine /cisplatin chemotherapy for up to 6 cycles of 21 days each.

Phase II: Dose expansion phase
Patients will be randomised to one of two groups.

Group 1: Participants receive 3-4 cycles (21 days each) of standard GC chemotherapy + SGI-110 (at the RP2D established in Phase I)

Group 2: Participants receive 3-4 cycles (21 days each) of standard GC chemotherapy only.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
SGI-110, cisplatin, gemcitabine

Primary outcome(s)
To establish the Recommended Phase II Dose (RP2D) for SGI-110 when combined with GC within the first year of the study.

Key secondary outcome(s)
1. Investigation of other potential pharmacodynamic biomarkers for SGI-110 target is measured at the end of the study
2. Pharmacokinetics of SGI-110 when combined with GC are determined within the first year of the study
3. The pathological complete response rate of bladder cancer patients is measured at the end of the study
4. Toxicity profile of SGI-110 when combined with GC is measured throughout the trial

Completion date
24/04/2020

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 26/06/2019:
All patients:
1. ECOG performance status of 0 or 1
2. Glomerular filtration rate estimation of = 60 mL/min according to either the Cockcroft and Gault formula or by Cr-51EDTA or Tc-99m DTPA clearance
3. Adequate haematological parameters:
3.1. Haemoglobin >= 90 g/dL
3.2. Neutrophil count >= 1.5 x109/L
3.3. Platelets >= 100 x109/L
4. Adequate biochemical parameters
4.1. Bilirubin <= 1.5 x ULN
4.2. ALT and ALP <= 2.5 x ULN (ALP = 5 x ULN if caused by liver or bone metastases)
5. Aged 16 years or over
6. Life expectancy greater than 3 months
7. Provision of written informed consent

Patients in the dose escalation phase:
Incurable histologically or cytologically confirmed, locally advanced or metastatic, solid cancer, for which the use of gemcitabine and cisplatin is a clinically appropriate treatment in the view of the local principal investigator. Any number of previous lines of systemic chemotherapy is permitted.

Patients in the dose expansion phase:
1. Bladder cancer with a pure or a predominant component of transitional cell carcinoma
2. Clinical stage T2-4a N0 M0
3. Planned to commence GC for 3 or 4 cycles

Previous participant inclusion criteria:
All patients:
1. ECOG performance status of 0 or 1
2. Glomerular filtration rate estimation of = 60 mL/min according to either the Cockcroft and Gault formula or by Cr-51EDTA or Tc-99m DTPA clearance
3. Adequate haematological parameters:
3.1. Haemoglobin = 90 g/dL
3.2. Neutrophil count = 1.5 x109/L
3.3. Platelets = 100 x109/L
4. Adequate biochemical parameters
4.1. Bilirubin = 1.5 x ULN
4.2. ALT and ALP = 2.5 x ULN (ALP = 5 x ULN if caused by liver or bone metastases)
5. Aged 16 years or over
6. Life expectancy greater than 3 months
7. Provision of written informed consent

Patients in the dose escalation phase:
Incurable histologically or cytologically confirmed, locally advanced or metastatic, solid cancer, for which the use of gemcitabine and cisplatin is a clinically appropriate treatment in the view of the local principal investigator. Any number of previous lines of systemic chemotherapy is permitted.

Patients in the dose expansion phase:
1. Bladder cancer with a pure or a predominant component of transitional cell carcinoma
2. Clinical stage T2-4a N0 M0
3. Planned to commence GC for 3 or 4 cycles with neoadjuvant (i.e. curative) intent prior to a planned radical cystectomy

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
39

Key exclusion criteria
Current participant exclusion criteria as of26/06/2019:
All patients:
1. Unresolved toxicities from prior therapy greater than CTCAE v4.03 grade 1 (with the exception of alopecia) at the time of registration
2. Prior radiotherapy to > 30% of bone marrow
3. Major surgery within 30 days
4. Any investigational medicinal product within 30 days

5. Allergy or other known intolerance to any of the proposed study drugs including supportive agents and inclusive of G-CSF and locally utilised anti-emetics
6. Coronary artery bypass graft, angioplasty, vascular stent, myocardial infarction, unstable angina pectoris or congestive cardiac failure (New York Heart Association = grade 2) within the last 6 months
7. Women who are pregnant or breast feeding. (Women of child-bearing potential must have a negative pregnancy test performed within 7 days prior to the start of trial treatment)
8. Patients of child-bearing potential who are not using, or who are unwilling to use, a highly effective method of contraception
9. Any patient who, in the judgment of the local investigator, is unlikely to comply with trial procedures, restrictions or requirements
10. Any patient who has received a live vaccine within 4 weeks of initiation of their treatment

Patients in the dose expansion phase:
Current separate other malignancy. Current nonmelanoma skin cancer, cervical carcinoma in situ or incidental localised prostate cancer is permissible. Other prior malignancy is acceptable if the treatment within the SPIRE trial would be given with curative intent.

Previous participant exclusion criteria:
All patients:
1. Unresolved toxicities from prior therapy greater than CTCAE v4.03 grade 1 (with the exception of alopecia) at the time of registration
2. Prior radiotherapy to > 30% of bone marrow
3. Major surgery within 30 days
4. Any investigational medicinal product within 30 days
5. Allergy or other known intolerance to any of the proposed study drugs including supportive agents and inclusive of G-CSF and locally utilised anti-emetics
6. Previously-identified central nervous system metastases unless treated and clinically stable and not requiring steroids for at least 4 weeks prior to the start of trial treatment
7. Coronary artery bypass graft, angioplasty, vascular stent, myocardial infarction, unstable angina pectoris or congestive cardiac failure (New York Heart Association = grade 2) within the last 6 months
8. Women who are pregnant or breast feeding. (Women of child-bearing potential must have a negative pregnancy test performed within 7 days prior to the start of trial treatment)
9. Patients of child-bearing potential who are not using, or who are unwilling to use, a highly effective method of contraception
10. Any patient who, in the judgment of the local investigator, is unlikely to comply with trial procedures, restrictions or requirements
11. Any patient who has received a live vaccine within 4 weeks of initiation of their treatment

Patients in the dose expansion phase:
Recent or current separate other malignancy. Current non-melanoma skin cancer, cervical carcinoma in situ or incidental localised prostate cancer is permissible. Participants with a history of a separate other malignancy having completed all active treatment 2 or more years previously may be entered.

Date of first enrolment
01/04/2016

Date of final enrolment
26/09/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Southampton
University Road
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Sponsor information

Organisation
Southampton University Hospitals NHS Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Data won't automatically be available upon request but the trialists are happy to consider data sharing approaches (based on consent and contractual obligations) through the Trial Management Group, based on scientific merit.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2021	22/01/2021	Yes	No
Protocol article	protocol	03/04/2018		Yes	No
Plain English results			07/09/2021	No	Yes