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Phase I/II feasibility study of cetuximab with 5-fluorouracil (5FU) and mitomycin C or cisplatin with concurrent radiotherapy in muscle invasive bladder cancer

Submission date 17/08/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/08/2011	**Overall study status** Completed	
Last Edited 11/01/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-cetuximab-with-chemotherapy-and-radiotherapy-for-muscle-invasive-bladder-cancer-tuxedo

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-014805-15

Protocol serial number

7949

Study information

Scientific Title
Phase I/II feasibility study of cetuximab with 5-fluorouracil (5FU) and mitomycin C or cisplatin with concurrent radiotherapy in muscle invasive bladder cancer

Acronym
TUXEDO

Study objectives
This is a Phase I combination study, followed by an early phase II, single-arm, multicentre, open-label study.

The primary objective of the phase I study is to determine the feasibility and toxicity profile of cetuximab with 5FU and mitomycin C, and in addition to determine the optimal dose of cisplatin in combination with cetuximab. Feasibility will be based on assessment of using the proposed drugs in combination with radical radiotherapy.

The primary objective of the phase II study is to assess preliminary evidence of the efficacy of the treatment selected from phase I, by determining whether a combination of radiotherapy with cetuximab, and chemotherapy, improves cystoscopic local control of advanced bladder cancer at three months after treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
11/LO/1313

Primary study design
Interventional

Study design
Non-randomised; Interventional; Design type: Treatment

Study type(s)
Screening

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Bladder Cancer; Disease: Bladder (advanced)

Interventions
1. FU: In cohort I, patients receive 5FU in weeks 1 and 4 as a continuous infusion for 5 days (total of 10 days) concurrently with radiotherapy 2. Cetuximab, Loading dose given in week before start of RT, then given on day 1 of each week of RT (weeks 1 - 7)
3. Cisplatin: Patients in cohorts II and III of phase I receive cisplatin on the first day of each week of radiotherapy (weeks 1 - 7)
4. Mitomycin C: In cohort I, patients receive mitomycin C on day 1 only of week 1 of radiotherapy

5. Radical Radiotherapy: All patients in the study receive 64Gy in 32 fractions (given over 5 days in weeks 1 - 7)
Follow Up Length: 18 month(s); Study Entry : Registration only

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Mitomycin C, 5FU, cetuximab, cisplatin

Primary outcome(s)
Feasibility and toxicity; Timepoint(s): Phase I outcome

Key secondary outcome(s)
Cystoscopic local control at three months post-treatment; Timepoint(s): Primary outcome in Phase II

Completion date
29/11/2013

Eligibility

Key inclusion criteria
1. Aged 18 or over
2. Histologically proven invasive bladder carcinoma [adenocarcinoma, transitional cell carcinoma (TCC) or squamous cell carcinoma (SCC)]
3. Localised muscle invasive carcinoma either surgically or by imaging (T2-T4a N0 M0)
4. World Health Organisation (WHO) performance status grade 0 to 1
5. Adequate haematological function (haemoglobin > 10g/dl; white blood cells (WBC) > 3.0x109 /L; absolute neutrophils count (ANC) > 1.5x109/L; platelet count > 100,000/mm3)
6. Adequate hepatic function {billirubin < 1.5 upper limit fo normal (ULN), Alkaline phosphatase (ALP) < 2xULN, [aspartate aminotransferase (AST)/alanine aminotransferase (ALT)] < 3.0xULN}
7. Glomerular filtration rate (GFR) > 40 ml/min [by ethylenediamine tetraacetic acid (EDTA) clearance, 24h urine collection, or Cockcroft-Gault]
8. Available for long-term follow-up
9. Able to receive a radical course of radiotherapy
10. Patients written informed consent
11. Have received 3-4 cycles of neo-adjuvant chemotherapy (preferably Gemcitabine/Cisplatin) with a positive response (confirmed by cystoscopy & radiological response) with pre neo-adjuvant imaging computerised tomography (CT) scan or magnetic resonance imaging (MRI) of abdomen and pelvis.; Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
33

Key exclusion criteria
1. Uncontrolled systemic disease which would preclude the patient from participating in the study including severe or uncontrolled cardiovascular disease (congestive heart failure New York Heart Association (NYHA) III or IV, unstable angina pectoris, history of myocardial infarction within the last twelve months, significant arrhythmias
2. Pregnant or breast feeding
3. Concomitant or previous malignancy which is likely to interfere with protocol treatment
4. Inflammatory bowel disease
5. Previous pelvic radiotherapy
6. Bilateral hip replacements compromising accurate radiotherapy planning
7. Evidence of significant clinical disorder, or laboratory finding which, in the opinion of the investigator, makes it undesirable for the patient to participate in the trial
8. Male and female patients (of childbearing age) not using adequate contraception
9. Significant decrease in GFR during previous chemotherapy treatments
10. Widespread carcinoma in situ (CIS), or CIS remote from the muscle invasive tumour
11. Simultaneous upper tract, urethral or prostatic transitional cell carcinoma
12. Untreated hydronephrosis
13. Participation in another trial within the previous 30 days [except for observational studies, e. g. Bladder Cancer Prognosis Programme (BCPP)]

Date of first enrolment
07/11/2011

Date of final enrolment
29/11/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Cancer Research UK Clinical Trials Unit
Birmingham
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Clinical Trials Awards and Advisory Committee (CTAAC) (UK) Grant Codes: C547/A10900

Results and Publications

Individual participant data (IPD) sharing plan
Not added 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		31/07/2022	02/08/2022	Yes	No
Abstract results		20/05/2017	14/04/2022	No	No
Abstract results		20/02/2020	14/04/2022	No	No
HRA research summary			28/06/2023	No	No
Other publications	Results of sub-study investigating whether urinary DNA analysis can be used to investigate whether treatment response is associated with tumor mutations	07/09/2021	14/04/2022	Yes	No