ISRCTN98873899 https://doi.org/10.1186/ISRCTN98873899

Weekly neoadjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer

Submission date 29/04/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 29/04/2010	**Overall study status** Completed	
Last Edited 10/09/2019	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-at-chemotherapy-followed-by-chemotherapy-and-radiotherapy-together-for-locally-advanced-cervical-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00462397

Clinical Trials Information System (CTIS)
2005-000134-20

Protocol serial number
1517

Study information

Scientific Title
Phase II non-randomised interventional treatment study of weekly neoadjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer

Acronym
CxII

Study objectives
For the past 10 years cisplatin-based chemoradiation (CRT) has been the treatment of choice for all patients with locally advanced cervical cancer. The key CRT trials showed a reduction in the risk of death by 30 - 50% with an absolute improvement in 5 year survival of 12%. However, a large proportion of patients in these trials had early stage disease (stage I, II) so the results may not be broadly applicable to women with more advanced disease/large tumours, or positive nodes. The outlook for such patients remains poor and new approaches are needed.

To date, trials addressing the role of neoadjuvant chemotherapy (NACT) have generated conflicting data. Although a meta-analysis of 21 randomised trials failed to show any overall improvement in survival with NACT, an association between outcome and cycle length has been observed. Trials with a cycle length of 14 days or less were associated with an improvement in survival of approximately 7% at 5 years, while longer cycle lengths had a detrimental effect on outcome.

Therefore, it is postulated that a short course of dose dense NACT with weekly cycles of treatment prior to definitive CRT might downstage the tumours, lengthen the exposure to systemic treatment and improve outcome. Several cytotoxic agents have shown activity in cervical cancer, however very few of these agents have been tested in the weekly setting. This phase II study will assess the use of neoadjuvant weekly paclitaxel and carboplatin chemotherapy followed by concomitant chemoradiation in 50 patients with locally advanced cervical cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridgeshire 1 Research Ethics Committee approved on the 17/05/2005 (ref: 04/Q0104/163)

Study design
Non-randomised interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Neoadjuvant chemotherapy:
Weekly treatment for six weeks: paclitaxel (80 mg/m^2 IV) followed by carboplatin AUC2 IV on days 1, 8, 15, 22, 29 and 36.

Chemoradiation:
Cisplatin: 40 mg/m^2 (maximum 70 mg) weekly for 6 weeks maximum, commencing in week 7 of treatment regimen (or as soon as blood counts have recovered).
Pelvic radiotherapy: 50.4 Gy in 28# over 5.5 weeks
High dose rate brachytherapy: 14 Gy in 2# (1 or 2 intracavitary insertions)
Pelvic sidewall boost (unilateral or bilateral) for all patients FIGO stage IIb and above with parametrial/pelvic sidewall disease extension, 5.4 Gy in 3# over 3 days.

Patient follow-up after treatment: 3 monthly for 2 years
Study entry: registration only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cisplatin

Primary outcome(s)
Overall response to both the neoadjuvant combination chemotherapy and the concomitant chemoradiotherapy. 6 week assessment after neoadjuvant chemotherapy by clinical examination and MRI pelvis according to RECIST; 12 week assessment after concomitant chemoradiotherapy by clinical examination, MRI pelvis and CT abdomen by RECIST.

Key secondary outcome(s))
1. Response rate to neoadjuvant chemotherapy
2. The toxicity of neoadjuvant weekly paclitaxel and carboplatin chemotherapy, as defined by Common Toxicity Criteria (CTC)
3. Overall survival
4. Progression free survival

Patients will be followed 3 monthly for two years, patients will be evaluated clinically and toxicity assessed.

Completion date
28/11/2008

Eligibility

Key inclusion criteria
1. Histologically confirmed and reviewed at the cancer centre International Federation of Gynaecology and Obstetrics (FIGO) stage Ib2 - IVa squamous, adeno-, or adenosquamous carcinoma of the cervix suitable for radical chemoradiation

2. EUA, cystoscopy and sigmoidoscopy performed by Gynaecological Oncologist +/- Clinical Oncologist to confirm FIGO stage with biopsy of any suspicious lesions in bladder, vagina or rectum
3. Eastern Cooperative Oncology Group (ECOG) performance status 0 - 1
4. Age over 18, no upper limit, providing patient deemed fit by supervising oncologist to receive chemoradiation
5. Adequate renal function, as defined by glomerular filtration rate (GFR) estimated by EDTA or creatinine clearance (24 hour urine) greater than or equal to 60 ml/min
6. Adequate liver function, as defined by alanine aminotransferase (ALT) or aspartate aminotransferase (AST) less than 2.5 upper limit of normal (ULN), and bilirubin less than 1.25 ULN
7. Adequate bone marrow function, as defined by white cell count (WCC) greater than 3.0 x 10^9 /litre, neutrophils greater than 1.5 x 10^9/litre, and platelets greater than 100 x 10^9/litre
8. Placement of ureteric stents in all patients with hydronephrosis regardless of renal function
9. Normal electrocardiogram (ECG)
10. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Pregnant or breast feeding patients
2. Previous diagnosis of cancer, except basal cell carcinoma (BCC) skin
3. Active cardiac disease

Date of first enrolment
14/06/2005

Date of final enrolment
28/11/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cancer Research UK and UCL Cancer Trials Centre
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Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
University College London Hospitals NHS Foundation Trust (UK)

Results and Publications

Individual participant data (IPD) sharing plan

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	25/06/2013		Yes	No
Plain English results				No	Yes