INTERLACE: A phase III multicentre trial of weekly induction chemotherapy followed by standard chemoradiation versus standard chemoradiation alone in patients with locally advanced cervical (INduction chemoThERapy in Locally Advanced CErvix)

ELIGIBILITY CRITERIA-summarised

~Histologically confirmed FIGO stage Ib2- IVa squamous, adeno or adenosquamous carcinoma of the cervix except for disease extending to lower third of vagina. Stage 1B1 with positive nodes also eligible
~ Suitable and fit to receive radical chemoradiation
~ Medically fit to receive carboplatin and paclitaxel
~Patients with positive nodes (either histologically/PET positive ≥ 15 mm on CT/MR) at or below the level of the aortic bifurcation may be included provided none of the exclusion criteria apply
~HIV negative (high risk countries only or patients who have moved within the past 10 years from high risk countries)
~No evidence of active TB
~ECOG performance status 0 – 1
~Aged 18 and over
~Adequate renal function as defined by GFR ≥ 60 ml/min (Wright equation) or ≥ 50 ml/min using radioisotope GFR assessment
~Adequate liver function, as defined by ALT or AST < 2.5 ULN and bilirubin < 1.25 ULN
~Adequate bone marrow function as defined by ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L
~Adequate contraception precautions if relevant
~Written or witness informed consent

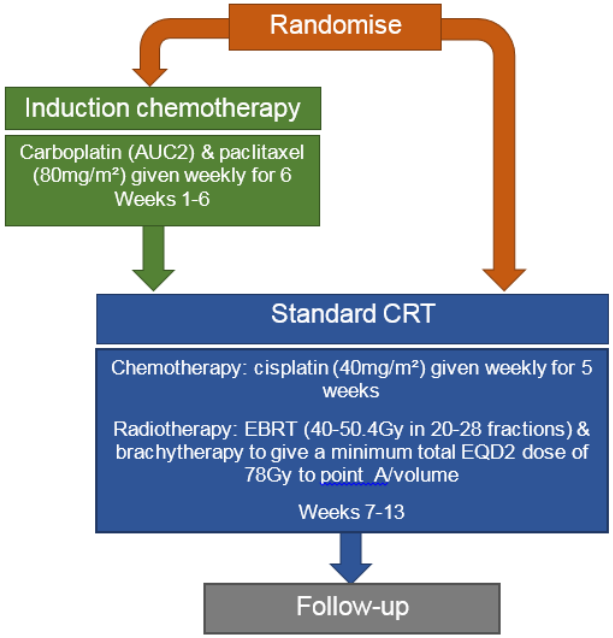
TRANSLATIONAL RESEARCH

~Paraffin embedded cervical tissue blocks will be collected from the original diagnosis at baseline to test the efficacy of various biomarkers in predicting response to treatment in patients with cervical cancer

~A sub-study investigating the use of physiological methods of imaging, as surrogate biomarkers for response to induction chemotherapy as well as chemoradiation using diffusion weighted and perfusion imaging MR

STUDY DESIGN

Induction Chemotherapy in Locally Advanced Cervical Cancer



Objectives: A phase III mulitcentre trial of weekly induction chemotherapy followed by standard chemoradiation (experimental arm) versus standard chemoradiation alone (control arm) in patients with locally advanced cervical cancer

Treatment: Patients in the investigations arm will receive weekly IV infusions of carboplatin at AUC2 and paclitaxel at 80mg/m2 weeks 1-6 inclusive and then commence standard chemoradiation in week 7 and receive five cycles of cisplatin. Patients in the control arm will receive standard chemoradiation only.

Primary endpoint: Overall survival

Secondary endpoints: Progression free survival; Adverse events (AE); Quality of Life and Patterns of relapse

EXCLUSION CRITERIA-summarised

~Previous pelvic malignancy (regardless of interval since diagnosis)
~Previous malignancy not affecting the pelvis (except for BCC skin cancer) where disease free interval is less than 10 years
~Positive lymph nodes (imaging or histological) above the aortic bifurcation
~Hydronephrosis which has not undergone ureteric stenting or nephrostomy except where the affected kidney is non-functioning
~Evidence of distant metastasis i.e. any non-nodal metastasis beyond the pelvis
~Previous pelvic radiotherapy
~Prior diagnosis of Crohn's disease or Ulcerative colitis
~HIV positive (high risk countries only or patients who have moved within the past 10 years from high risk countries)
~Active TB
~Uncontrolled cardiac disease (defined as cardiac function which would preclude hydration during cisplatin administration and any contraindication to paclitaxel)
~Pregnant or lactating

SAMPLE SIZE

500 patients

DURATION OF RECRUITMENT

9 years

DURATION OF PATIENT FOLLOW-UP

Both arms will be followed up 3 monthly for 2 years and 6 monthly for 3 years. Survival data will then be collected until trial closure, which is defined as 3 years after the last patient has completed treatment

PARTICIPATING COUNTRIES

United Kingdom, Mexico, Italy, India

UCL

CANCER RESEARCH UK