1 PROTOCOL SUMMARY

1.1 Summary of Trial Design

Title:	A phase III multicentre trial of weekly induction chemotherapy followed by standard chemoradiation versus standard chemoradiation alone in patients with locally advanced cervical cancer
Short Title/acronym:	INTERLACE
EUDRACT no:	2011-001300-35
Sponsor name & reference:	University College London -11/0034
Funder name & reference:	Cancer Research UK – C37815/A12832
Clinicaltrials.gov no:	NCT01566240
Design:	Randomised, controlled, phase III, multicentre trial
Overall aim:	To investigate in a randomised trial whether additional short-course chemotherapy given on a weekly schedule immediately before standard chemoradiation leads to an improvement in overall survival
Primary endpoint:	Overall survival
Secondary endpoints:	Progression free survival Adverse events Quality of life Patterns of relapse
Target accrual:	500 patients
Inclusion & exclusion criteria:	Inclusion criteria • Histologically confirmed FIGO stage Ib2- IVa squamous, adeno or adenosquamous carcinoma of the cervix (except those with disease extending to lower third of vagina). Patients with FIGO stage IB1 and positive lymph nodes are also eligible • Deemed suitable and fit for radical chemoradiation • Medically fit to receive carboplatin and paclitaxel • ECOG performance status 0 – 1 • No evidence of active TB • Aged 18 and over • Adequate renal function, defined as a GFR ≥ 60 ml/min calculated using the Wright equation (or ≥ 50 ml/min for 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 • Using adequate contraception precautions if relevant • A documented negative HIV test (patients recruited from high risk countries or who have moved within the past 10 years from high risk countries) • A documented negative pregnancy test (if applicable) • Capable of providing written or witnessed informed consent Exclusion criteria • Previous pelvic malignancy (regardless of interval since diagnosis) • Previous malignancy not affecting the pelvis (except basal cell carcinoma of the skin) 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 • Uncontrolled cardiac disease (defined as cardiac function which would preclude hydration during cisplatin administration and any contraindication to paclitaxel) • Pregnant or lactating
Planned number of sites:	40-50
Target countries:	United Kingdom, Mexico, Italy, India, Brazil
Treatment summary:	Patients with locally advanced cervical cancer will be randomised to receive either induction chemotherapy with weekly carboplatin AUC2 and paclitaxel 80mg/m2 for six weeks, followed by standard chemoradiation (investigational arm) or chemoradiation alone (standard arm). The radiation in both arms will comprise external beam 40–50.4Gy in 20–28 fractions plus intracavity brachytherapy to achieve a minimum total EQD2 dose of 78-86Gy with weekly cisplatin 40mg/m2 for 5 weeks

Anticipated duration of recruitment:	8 years
Duration of patient follow up:	3 monthly for 2 years and 6 monthly until the end of the trial from the end of treatment.
Definition of end of trial:	30 days after the last patient has completed 3 years of follow up visits at which point the 'declaration of end of trial' form will be submitted
Translational component (optional):	Paraffin embedded cervical tissue block from original diagnosis for future translational studies
Other related research:	Economic evaluation – Various costs associated with trial treatment and patient care will be recorded in the Case Report Forms, allowing for a formal economic evaluation comparing the two arms of the study to be conducted

1.2 Trial Schema