A randomised phase III trial of induction chemotherapy followed by chemoradiation compared with chemoradiation alone in locally advanced cervical cancer: The GCIG INTERLACE trial


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Background
Locally advanced cervical cancer (LACC) is treated with chemoradiation (CRT). However, many patients relapse and die from metastatic disease. A feasibility study demonstrated a good response rate to short course weekly induction chemotherapy (IC) delivered before standard CRT and the INTERLACE trial investigated whether this approach improves both progression free survival (PFS) and overall survival (OS).

Methods
Women with squamous, adeno or adenosquamous carcinoma FIGO (2008) stage IB1 node positive,IB2,II,IIIB, IVA were eligible. Patients were randomised (1:1) to receive either CRT alone (5 cycles weekly cisplatin) or IC (6 weeks carboplatin AUC2 and paclitaxel 80mg/m²) followed by the same CRT in week 7. Mandated minimum total EQD2 dose 78Gy to Point A with 3D brachytherapy recommended. All centres underwent radiation quality assurance. Primary endpoints were PFS (target hazard ratio [HR] 0.65) and OS (target HR 0.65-0.70).

Results
500 patients were recruited from 32 centres in 5 countries (Nov 2012-Nov 2022). Median age 46 (range 24-78) years. Stage distribution was: IB1/2: 9%; II:77%, IIIb:11% and IVA:3%. 57% were node negative and 82% squamous subtype. Arms were balanced. 92% of IC patients had 5/6 cycles carboplatin/paclitaxel. Median interval from IC to CRT was 7 days. 84% (IC/CRT) vs. 89% (CRT alone) had 4/5 cycles cisplatin. In the CRT arm 92% and 89% completed external beam and brachytherapy respectively; corresponding figures in the IC/CRT arm were 97% and 95%. The median overall treatment time for CRT was 45 days in both arms. Grade ≥3 adverse events were seen in 59% (IC/CRT) vs. 48% (CRT alone). Median follow up 64 months. 5 year PFS rate is 73% with IC/CRT and 64% with CRT alone (HR 0.65; 95%CI:0.46-0.91, p=0.013). The corresponding 5-year OS rates are 80% and 72% (HR 0.61:95%CI:0.40-0.91, p=0.04).

Conclusions
Induction chemotherapy followed by CRT significantly improves PFS and OS in LACC and should be considered a new standard of care. INTERLACE recruited patients from diverse health care settings demonstrating that IC followed by CRT is feasible in all countries.

Clinical trial identification
EudraCT: 2011-001300-35.

Legal entity responsible for the study