Introduction/Background Cervical cancer (CaCx) is one of the common malignancies in women worldwide. Autophagy is a significant hallmark of cancer wherein high mobility group box 1 (HMGB-1) plays a crucial role. Aberrant expression of HMGB-1 is associated with tumor development, progression and poor prognosis. There are no reports available studying HMGB-1, autophagy related molecule in context to clinical significance in cancer cervix. Thus, we aim to investigate the association between HMGB-1 and its associated molecules (RAGE, p53 & p62) in CaCx. We have also evaluated the clinical significance of serum HMGB-1 in CaCx diagnosis.

Methodology 50 subjects including 20 CaCx patients, 20 healthy women and 10 controls having gynecological disorder other than malignancy were recruited. Circulatory levels of HMGB-1 were measured by ELISA. mRNA and protein levels of HMGB-1 and its associated molecules were quantitated using Q-PCR and western blotting respectively in tissues of study subjects. The data obtained were then validated using Q-PCR and western blotting respectively in tissues of study subjects.

Results Circulatory levels of HMGB-1 were significantly higher in patients as compared to controls. mRNA and protein expression of HMGB-1 were significantly higher in tumor tissues. The levels of RAGE, p53 and p62 were also significantly altered than their expression in controls at mRNA and protein levels. ROC curve analysis showed better sensitivity and specificity for HMGB-1 for non-invasive diagnosis of CaCx. Furthermore, siRNA-mediated targeting of HMGB-1 significantly altered expression of associated molecules, thus, validating the patients’ data.

Conclusion HMGB-1 level could be a useful marker for evaluating disease and diagnosis in non-invasive liquid biopsy. Autophagy mediated HMGB-1/RAGE pathway might play a significant role in pathogenesis of CaCx. Validation in larger patient cohort might exploit HMGB-1 as a novel non-invasive diagnostic marker for CaCx in liquid biopsy in future.
prognosis, however markers that further risk-stratify intermediate groups are needed. Serum cancer antigen-125 (CA125) and human epididymis-4 (HE4) show promise as prognostic markers. The aim of this study was to evaluate the association between serum CA125, HE4 and endometrial cancer survival outcomes when stratified by molecular subgroup.

Methodology Pre-treatment serum CA125 and HE4 levels were measured and endometrial tumours classified according to WHO molecular classification. The relationship between biomarkers and survival was evaluated using Kaplan-Meier analysis and multivariable cox regression.

Results Overall, 327 women were included, with POLE status available for 216. Tumours were POLE-mutant (5%), p53-abnormal (11%), MMR-deficient (30%) and NSMP (54%). Median follow up was 50 months (IQR 30–60), during which 42 (13%) recurred and 71 (21%) women died. CA125 ≥35U/mL was independently associated with overall mortality [aHR=2.42 (95%CI:1.45–4.06), p=0.001], cancer specific death [aHR=2.00 (95%CI:1.04–3.87), p=0.04] and recurrence [aHR=2.69 (95%CI:1.38–5.27), p=0.004]. When stratified by molecular subgroup, CA125 ≥35U/mL and HE4 ≥150pmol/L were prognostic of overall survival in MMR-deficient [CA125: aHR=4.92 (95%CI:1.74–13.89), p=0.003 and HE4: aHR=4.03 (95%CI:1.34–12.11), p=0.01] and NSMP subgroups [CA125: aHR=3.72 (95%CI:1.30–10.67), p=0.001].

Conclusion CA125 and HE4 may risk-stratify those at intermediate risk of recurrence and death. Evaluation in a larger population is required.