

Poster 25: An immune gene signature identifies an immune-responsive subset within copy number high endometrial cancer

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Topic

Endometrial

Objectives

In advanced-stage endometrial cancer (EC), immune checkpoint inhibition (ICI) provides clinical benefit in a subset of patients, yet robust biomarkers of response remain limited. The copy number high (CNH; p53 abnormal) molecular subclass is associated with poor prognosis and heightened immune suppression. We previously developed and validated STRATsig, a gene expression signature that stratifies high-grade serous ovarian cancer (HGSC) tumors by intrinsic immunoregulatory state, distinguishing immune-suppressed STRATsig tertile 1 (S-T1) from immunologically active (S-T3) tumors. In HGSC, S-T3 tumors exhibit a survival advantage associated with increased immune cytolytic activity (CYTscore; PRF1 and GZMA). Here, we evaluated the performance of STRATsig and CYTscore in EC, with a focus on the CNH subclass.

Methods

Clinical and normalized transcriptomic data from the TCGA uterine corpus endometrial carcinoma (UCEC; n=543) were analyzed. Tumors were stratified into STRATsig tertiles and CYTscore tertiles. Kaplan-Meier survival analyses of CYTscore tertiles were performed with comparisons by log-rank test. Analyses were conducted in all patients and stratified by stage and molecular subclass.

Results

Among advanced-stage patients (stage III-IV; n=153), a CYTscore-associated survival benefit was observed exclusively in S-T3 (n=51; p=0.021), with no significant association observed in S-T1 or S-T2. Within the CNH subclass (n=78), this relationship was preserved in S-T3 tumors (n=20; p=0.036, median OS 37 months for CYTtert 1, not reached for CYTtert 3), whereas no association was observed in other molecular subclasses (n=275; p=0.980). STRATsig and CYTscore values did not differ significantly between early and advanced-stage disease, although both trended higher in early-stage tumors (p=0.136 and p=0.06, respectively). Consistent with this, no CYTscore-associated survival benefit was observed in early-stage disease, including within S-T3 tumors.

Conclusions

STRATsig identifies an immune-competent subset within advanced-stage EC, including within the otherwise immunosuppressed CNH subclass, in which cytolytic activity is associated with improved survival. Despite the modest cohort size, these findings support STRATsig as a candidate biomarker for immunotherapy stratification in EC and warrant validation in larger clinically annotated cohorts.