Poster rounds with the professors: Group E3

HORMONAL BIOMARKERS REMAIN PROGNOSTIC RELEVANT WITHIN THE MOLECULAR CLASSIFICATION IN ENDOMETRIAL CANCER

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Objectives The relevance of hormonal biomarkers in endometrial cancer (EC) has been well-established. A revised cut-off for estrogen receptor/progesterone receptor (ER/PR) expression into three subgroups was shown to improve prognostication, however, this has not been related to the four molecular subgroups. Therefore, we aimed to investigate the prognostic relevance of this three-tiered ER/PR model within the molecular subgroups in EC.

Methods A retrospective multicenter study within the European Network for Individualized Treatment (ENITEC) network was performed. ER/PR expression was classified into: high-risk (0–10%), intermediate-risk (20–80%) and low-risk (90–100%). The molecular subgroups were conducted based on Next Generation Sequencing, allocating patients into polymerase epsilon (POLE)-mutant, microsatellite unstable (MSI), tumor protein (TP53)-mutated and no-specific molecular profile (NSMP).

Results A total of 387 patients were included with a median follow-up of 5.2-years. There were 8.3% (n=32) POLE-mutant, 22.5% (n=87) MSI, 13.7% (n=53) TP53-mutated and 55.6% (n=215) NSMP tumors. Among all molecular subgroups, patients with ER/PR 0–10% expression had significantly worse disease-specific survival (DSS) compared to ER/PR 20–80% or 90–100%. Interestingly within TP53-mutated, patients with ER/PR 90–100% expression showed an excellent DSS (100%) compared to ER/PR 20–80% and 0–10% (figure 1). In multivariable analyses ER/PR 0–10%, TP53-mutated, lymphovascular space invasion and FIGO stage remained independent prognostic factors for reduced DSS (respectively, HR 2.59 (95%-CI 1.32–5.03) P=0.005, HR 2.71 (95%-CI 1.35–5.43) P=0.005, HR 2.27 (95%-CI 1.15–4.45) P=0.018, HR 4.42 (95%-CI 2.16–9.01) P<0.001).

Conclusions ER/PR expression remains prognostic relevant in all molecular subgroups, strengthened by the three-tiered cut-off. We therefore recommend routine evaluation of ER/PR expression in clinical practice.

IMMUNOMETABOLIC CHANGES DURING WEIGHT LOSS INDUCE TUMOR IMMUNOGENICITY RESULTING IN TUMOR REGRESSION

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Objectives Endometrial cancer is the most common cancer of the female reproductive tract, and obesity is the greatest risk factor for endometrial cancer. We have recently found that in addition to enhancing tumor growth, obesity also impairs the anti-tumor immune response. Here, we investigated the effect of weight loss on the immune landscape of the tumor, during an interventional treatment for endometrial cancer in obesity patients.

Methods Metabolic surgery was performed on 12 patients deemed suitable (>18 years, BMI of 40 kg/m2 and diagnosis of grade 1 or 2 endometrial adenocarcinoma). Bulk-RNA sequencing of tumor biopsies was performed before and after surgery/weight loss. Formalin-fixed, paraffin-embedded endometrial tumor biopsies were processed for immunohistochemical staining of PD-L1, CD8 and CD3.

Results Of the 12 patients, all had significant weight loss 6 months post-surgery, with an average of 24% body fat loss. Complete pathological response was observed in 9 out of 12 patients, stable disease in 2 patients and progressive disease in one patient, at 6 months post-metabolic surgery. Tumor biopsy sequencing before and after weight loss shows a significant increase in HLA class I and class II genes. Immunostaining showed that weight loss increased CD8 T-cell infiltration and PD-L1 expression in endometrial tumors.

Conclusions Our results demonstrate the important role of weight loss in directing anti-tumor immunity in obese endometrial cancer patients by creating a more immunogenic tumor environment through upregulation of HLA.