POLEmut-MMRd-p53abn. Clinicopathological and molecular characteristics of 'multiple-classifiers' are shown in table 1.

'Multiple-classifiers' were more frequently high-grade (56% vs 28%,p=0.003), non-endometrioid (24% vs 10%,p=0.04) ECs when compared to 'single-classifier'(table 2).

Conclusion Multiple-classifier ECs represent 9% of the entire study population. Compared to previous studies, the higher proportion of 'multiple-classifiers' could be related to the extensive molecular analysis, comprising the evaluation of both p53 expression and TP53 mutations. More studies addressing the clinical implications on prognosis of 'multiple-classifiers' are needed.

2022-RA-449-ESGO CLINICAL-MOLECULAR CORRELATIONS OF ENDOMETRIAL CANCER. RETROSPECTIVE STUDY

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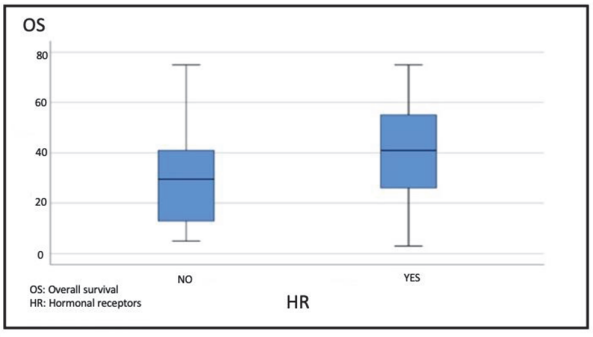
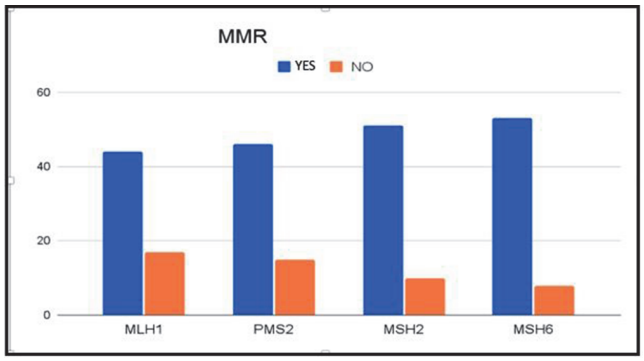
Introduction/Background Endometrial cancer (EC) is the most common gynecological tumor in developed countries, with more than 75% diagnosed at early stages. It is associated in 20–30% with microsatellite instability (MSI) due to mutations in the MMR genes, which can be sporadic (80–90%) or hereditary (10–20%) such as Lynch syndrome (LS).Objective: To establish the clinical-molecular profile of endometrial carcinoma and its implication for treatment.

Methodology Retrospective cross-sectional observational study. 162 patients diagnosed with EC during the period 2010–2020 and treated in Medical Oncology Service at the HUNSC were studied.Study variables: age, histology grade and type, stage, hormone receptors (HR), MSI, LS, overall survival. SPSS 25 was used for statistical analysis.



Abstract 2022-RA-449-ESGO Figure 1

Results The median age was 64,51 years. The most frequent stages at diagnosis were IA (25.3%) and IB (24.7%). Histologically, endometrioid adenocarcinoma accounted for 51.2% and grade 3 for 41.4% of cases. Patients with LS were mainly diagnosed at stage III, being endometrioid or serous adenocarcinomas, and mainly grade 3 (60%). Overall survival was longer in the HR+ group (40.5 months). MSI-H was observed in 36.1% of the sample and the dMMR distribution: MLH1 (27.9%) and PMS2 (24.6%), MSH2 (16.4%), MSH6 (13.1%). Ten patients were diagnosed with LS.



Abstract 2022-RA-449-ESGO Figure 2

Conclusion Our EC and LS results are comparable to those published for other settings. There is a significant association between HR+ and longer overall survival. The percentage of dMMR/MSI-H is higher than reported in other studies. Further studies with a larger sample would be needed.

2022-RA-450-ESGO BENEFIT OF ADJUVANT RADIOTHERAPY DEPENDS ON MOLECULAR CLASS OF EARLY-STAGE ENDOMETRIAL CANCER

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Introduction/Background The endometrial cancer (EC) molecular class is predictive for response to chemotherapy. Little is known about its' predictive value for response to radiotherapy. We investigated benefit of adjuvant vaginal brachytherapy (VBT) and external beam radiotherapy (EBRT) across the four molecular classes.

Methodology Participants of the randomized PORTEC-1 (n=714) and PORTEC-2 (n=427) trials were eligible if their EC were molecularly profiled according to the WHO 2020 classification. PORTEC-1 included intermediate risk EC and compared EBRT to no adjuvant treatment. PORTEC-2 included high-intermediate risk EC and compared VBT to EBRT. Locoregional recurrence-free survival (LRFS) was estimated and compared using Kaplan-Meier's methodology and log-rank tests. Correction for confounding by predefined clinicopathological factors was done using Cox proportional hazards models.

Abstract 2022-RA-450-ESGO Table 1 Multivariable analysis of predictors of locoreginal recurrence-free survival

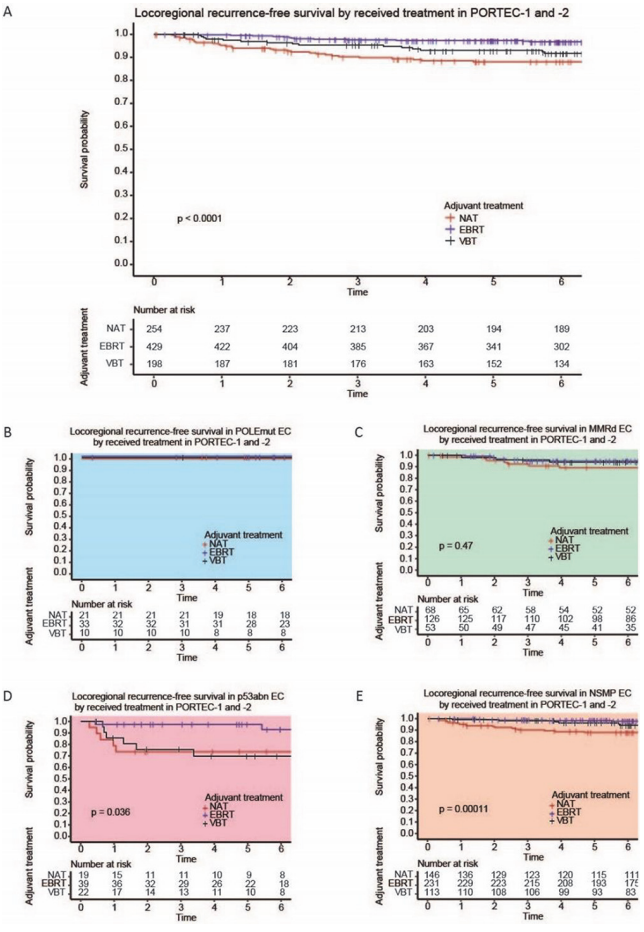
Predictor	N (%)	HR (95%CI)	p-value
Molecular class			
POLE mut	64 (7.3)	No events	
MMRd	247 (28.0)	Reference	
p53abn	80 (9.1)	3.48 (1.63-7.47)	0.001
NSMP	490 (55.6)	0.91 (0.48-1.70)	0.76
Adjuvant therapy			
None	249 (28.3)	Reference	
EBRT	435 (49.4)	0.22 (0.10-0.47)	<0.0001
VBT	197 (22.4)	0.42 (0.12-1.43)	0.17
Stage (FIGO 2009)			
IA	269 (30.5)	Reference	
≥IB*	612 (69.4)	1.90 (1.01-3.58)	0.046
Lymphovascular space invasion**			
None or focal	786 (95.3)	Reference	
Substantial	39 (4.7)	3.67 (1.63-8.28)	0.002
Grade			
1-2	746 (84.7)	Reference	
	3 135 (15.3)	1.50 (1.10-2.07)	0.012

Multivariable analysis using a Cox proportional hazard's model with stratification by trial.

* Central pathology review reclassified two patients as stage II, two patients as stage IIIA and one patient as stage IIIB.

** In 56 patients LSVI status was unknown

Definition of abbreviations: HR = hazard ratio; 95%CI = 95% confidence interval; POLEmut EC = endometrial cancer with a pathogenic mutation of DNA polymerase-ε; MMRd EC = endometrial cancer with mismatch repair deficiency (POLE wild type); p53abn EC = endometrial cancer with a p53 abnormality (POLE wildtype and MMR proficient); NSMP EC = EC with no specific molecular profile (POLE wild type, MMR proficient and p53 wildtype).



Abstract 2022-RA-450-ESGO Figure 1

Results 881 patients with a median follow-up of 11.3 years were included. Patient and tumour characteristics are presented in table 1. EC were classified as *POLE*-mutant (*POLE*mut, 7.3%) mismatch-repair deficient (MMRd, 28.0%), p53-abnormal (p53abn, 9.1%) and non-specific molecular profile (NSMP, 55.6%). Overall, adjuvant radiotherapy significantly improved LRFS (figure 1A). In *POLE*mut EC no LR were observed (figure 1B). In MMRd EC, VBT and EBRT did not significantly improve LRFS (figure 1C). In p53abn EC, EBRT but not VBT significantly improved LRFS (figure 1D). In NSMP EC, both EBRT and VBT significantly improved LRFS. Adjuvant radiotherapy and molecular class retained significant impact on LRFS after correction for clinicopathological risk factors (table 1).

Conclusion Benefit of adjuvant radiotherapy in early-stage endometrioid EC differs between EC molecular classes. Omitting radiotherapy seems safe in early-stage *POLE*mut EC. Benefit of radiotherapy in MMRd EC is uncertain as only a small, non-significant reduction in LR was observed. In p53abn EC, EBRT significantly improved LRFS, in contrast to brachytherapy and no adjuvant treatment. NSMP EC seem to have a clear benefit of radiotherapy; VBT seems sufficient for locoregional tumour control.

2022-RA-460-ESGO ENDOMETRIAL POLYPS ARE NON-NEOPLASTIC BUT HARBOR EPITHELIAL MUTATIONS IN ENDOMETRIAL CANCER DRIVERS AT LOW ALLELIC FREQUENCIES

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Introduction/Background Endometrial polyps (EMPs) are common exophytic masses associated with abnormal uterine bleeding and infertility. Unlike normal endometrium, which is cyclically shed, EMPs persist over ovulatory cycles and after the menopause. Despite their usual classification as benign entities, EMPs are paradoxically associated with endometrial carcinomas of diverse histologic subtypes, which frequently arise within EMPs. The etiology and potential origins of EMPs as clonally-derived neoplasms are uncertain, but previous investigations suggested that EMPs are neoplasms of stromal origin driven by recurring chromosomal rearrangements.

Methodology To better define benign EMPs at the molecular genetic level, we analyzed individual EMPs from 31 women who underwent hysterectomy for benign indications. The 31 EMPs were subjected to comprehensive genomic profiling by exome sequencing of a large panel of 1516 tumor-related genes including oncogenes, tumor suppressors, and chromosomal translocation partners.

Results There were no recurring chromosomal rearrangements, and copy-number analyses did not reveal evidence of significant chromosome-level events. Surprisingly, there was a high incidence of single nucleotide variants (46 among the 31 EMPs) corresponding to classic oncogenic drivers (i.e., definitive cancer drivers). The spectrum of known oncogenic driver events matched that of endometrial cancers more closely than any other common cancer. Further analyses including laser-capture microdissection showed that these mutations were