2022-RA-1289-ESGO UNDERSTANDING CLINICAL AND PATHOLOGICAL HETEROGENEITY OF ENDOMETRIAL CANCER WITH NO SPECIFIC MOLECULAR PROFILE (NSMP)

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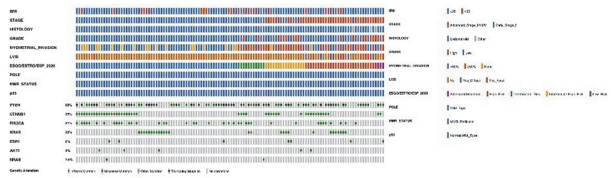
Introduction/Background No-specific molecular profile (NSMP) endometrial cancers (ECs) lack a unique molecular feature and show considerable molecular heterogeneity. However, CTNNB1 hotspot mutations have been associated with adverse outcomes. The aim of the study is to explore molecular features of NSMP-ECs and to investigate the role of CTNNB1.

Methodology Among all ECs undergoing molecular analysis at the European Institute of Oncology, Milan, between April 2019 and December 2021, NSMP-ECs were identified. The molecular profiling included MMR-proteins and p53 immunohistochemistry, microsatellite instability evaluation and Next Generation Sequencing of 26 cancer-related genes, including POLE, TP53 and CTNNB1. NSMP-ECs were classified according to CTNNB1 status. Clinicopathological characteristics between CTNNB1-mutated and CTNNB1-wild-type ECs were compared. To compare continuous and categorical variables Mann-Whitney test and chi-square test were used, respectively.

Results Overall, 124 (44.6%) NSMP-ECs were identified among the 278 ECs that underwent complete molecular analysis. Clinicopathological and molecular characteristics of NSMP-ECs are shown in figure 1.

The majority of NSMP-ECs were endometrioid (n=121, 97.6%), low-grade (n=107, 86.3%), FIGO stage I (n=82, 66.1%), with no/focal lymphovascular space invasion (n=119, 96.0%) and with <50% myometrial invasion (n=85, 68.5%). According to the ESGO/ESTRO/ESP guidelines, 52.4% (n=65) were low-risk ECs.The most commonly mutated genes were PTEN (n=82, 66%), CTNNB1 (n=48, 39%), PIK3CA (n=39, 31%) and KRAS (n=27, 22%). CTNNB1 and KRAS mutations were mutually exclusive (p<0.001). CTNNB1-mutated were younger (55.3±12.9 vs 63.2±12.3, p=0.002) than CTNNB1 wild-type. Histotype, myometrial invasion, lymphovascular space invasion, grade, stage, and ESGO/ESTRO/ESP risk class did not differ between the two groups (table 1).



Abstract 2022-RA-1289-ESGO Figure 1

Abstract 2022-RA-1289-ESGO Table 1 Clinicopathological characteristics comparison between CTNNB1 wild type and mutated NSMP endometrial cancers

	NSMP N = 124	CTNNB1-mutated N = 48	CTNNB1-wild type N = 76	P-value
Age mean (years) ± SD	60.1 ± 13.1	55.3 ± 12.9	63.2 ± 12.3	**0.002**
BMI mean (kg/m²) ± SD	28.1 ± 7.7	27.4 ± 8.3	28.6 ± 7.3	0.137
Histotype				
Endometrioid	121 (98%; 93.7-99.3%)	48 (100%; 92.6-100%)	73 (96.1%; 89.8-98.9%)	0.163
Other	3 (2%; 0.7-6.3%)	0 (0%; 0.0-7.4%)	3 (3.9%; 1.1-10.2%)	
Myometrial invasion				
<50 %	85 (69%; 60.0-76.2%)	35 (72.9%; 59.3-83.9%)	50 (65.8%; 54.7-75.7%)	0.405
≥50%	39 (32%; 23.8-40.0%)	13 (27.1%; 16.1-40.7%)	26 (34.2%; 24.3-45.3%)	
LVSI				
None or focal	119 (96%; 91.4-98.4%)	46 (95.8%; 87.3-99.1%)	73 (96.1%; 89.8-98.9%)	0.952
Diffuse	5 (4%; 1.6-8.6%)	2 (4.2%; 0.9-12.7%)	3 (3.9%; 1.1-10.2%)	
Grade				
Low grade (G1-2)	107 (86%; 79.4-91.5%)	45 (93.8%; 84.3-98.2%)	62 (81.6%; 71.8-89.0%)	0.055
High grade	17 (14%; 8.5-20.6%)	3 (6.3%; 1.8-15.7%)	14 (18.4%; 11.0-28.2%)	
FIGO stage				
I	82 (66%; 57.5-74.0%)	30 (65.2%; 48.4-75.1%)	52 (68.4%; 57.4-78.0%)	0.497
II - IV	42 (34%; 26.0-42.5%)	18 (37.5%; 24.9-51.6%)	24 (31.6%; 22.0-42.6%)	
ESGO/ESTRO/ESP (2020) risk classes				
Low	65 (52%; 43.7-61.1%)	25 (52.1%; 38.2-65.7%)	40 (52.6%; 41.5-63.6%)	0.843
Intermediate	11 (9%; 4.8-14.8%)	4 (8.3%; 2.9-18.6%)	7 (9.2%; 4.2-17.2%)	
High-Intermediate	16 (13%; 7.9-19.6%)	7 (14.6%; 6.8-26.5%)	9 (11.8%; 6.0-20.5%)	
High	29 (23%; 16.6-31.4%)	10 (20.8%; 11.2-33.8%)	19 (25.0%; 16.3-35.5%)	
Advanced/metastatic	3 (2%; 0.7-6.3%)	2 (4.2%; 0.9-12.7%)	1 (1.3%; 0.1-6.0%)	

NOTE: Data reported as Count (Column%; 95% Confidence interval) unless otherwise indicated
Abbreviations: BMI, body mass index; NSMP, no-specific molecular profile; SD, standard deviation; LVSI, lymph-vascular space invasion.

Conclusion Our study confirms the high prevalence of PI3K/AKT/mTOR and Wnt pathways alterations in NSMP-ECs and the mutually exclusive pattern between CTNNB1 and KRAS. Mutations in CTNNB1 occur in younger patients, but do not imply different clinicopathological characteristics.

2022-RA-1297-ESGO A SUBGROUP ANALYSIS OF RESPONSE RATE BY PATIENT CHARACTERISTICS IN PATIENTS WITH ENDOMETRIAL CANCER RECEIVING MONOTHERAPY DOSTARLIMAB IN THE GARNET TRIAL

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Introduction/Background Clinical characteristics of patients have demonstrated that there may be independent predictors of response to cancer drug therapies. In this analysis, we evaluated objective response rate (ORR) by subgroups of clinical