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

[1]Luigi Antonio de Vitis, [1,2]Gabriella Schivardi, [3,4]Caterina Fumagalli, [1]Benedetta Zambetti, [5]Mariacristina Ghioni, [5]Paola Rafaniello Raviele, [5]Alessandra Rappa, [1]Maria Teresa Achilarre, [1]Alessia Aloisi, [1]Annalisa Garbi, [1]Mariateresa Lapresa, [1]Gabriella Parma, [1]Vanna Zanagnolo, [1,6]Giovanni Damiano Aletti, [2]Andrea Mariani, [1]Angelo Maggioni, [5]Massimo Barberis, [1,7]Nicoletta Colombo, [1]Francesco Multinu, [1]Ilaria Betella. *[1]Department of Gynecology, European Institute of Oncology, Milan, Italy; [2]Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN; [3]Clinical Unit of Oncogenomics, European Institute of Oncology, Milan, Italy; [4]Department of Diagnostic Services, Division of Pathology, ASST Valle Olona, Gallarate, Italy; [5]Department of Pathology, European Institute of Oncology, Milan, Italy; [6]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy; [7]Faculty of Medicine and Surgery, University of Milan Bicocca, Milan, Italy*

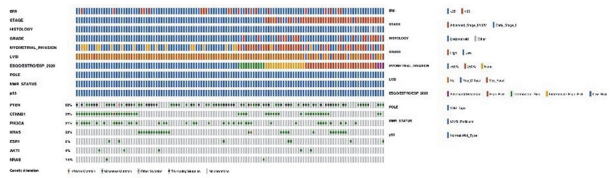
10.1136/ijgc-2022-ESGO.301

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

[1]Ana Oaknin, [2]Bhavana Pothuri, [3]Lucy Gilbert, [4]Renaud Sabatier, [5]Jubilee Brown,[6]Sharad Ghamande, [7]Cara Mathews, [8]David M O'Malley, [9]Rebecca Kristeleit, [10]Valentina Boni*, [11]Adriano Gravina, [12]Susana Banerjee, [13]Rowan E Miller, [14]Joanna Pikiel, [15]Mansoor R Miza, [16]Tao Duan, [16]Yuping Dong, [17]Eleftherios Zografos, [18]Jennifer Veneris, [19]Anna V Tinker, NEXT Oncology Hospital Universitario Quirónsalud *Affiliation at time of study. Current affiliation. *[1]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [2]Department of Obstetrics/Gynecology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY; [3]Division of Gynecologic Oncology, McGill University Health Centre, Montreal, QC, Canada; [4]Department of Medical Oncology, Institut Paoli Calmettes, Aix-Marseille University, Marseille, France; [5]Division of Gynecologic Oncology, Levine Cancer Institute, Atrium Health, Charlotte, NC; [6]Department of Obstetrics & Gynecology, Georgia Cancer Center, Augusta University, Augusta, GA; [7]Women and Infants Hospital of Rhode Island, Providence, RI; [8]Division of Gynecologic Oncology Oncology and Gynecologic Oncology Phase I Program, The Ohio State University and the James Cancer Center, Columbus, OH; [9]Guy's and St. Thomas' Hospital NHS Foundation Trust, London, United Kingdom; [10]START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Hospital Universitario HM Sanchinarro, Madrid, Spain; [11]Clinical Trial Unit, Istituto Nazionale Tumori Fondazione G. Pascale, Naples, Italy; [12]Gynaecology Unit, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, United Kingdom; [13]University College London, St. Bartholomew's Hospitals London, London, United Kingdom; [14]Department of Chemotherapy, Regional Center of Oncology, Gdansk, Poland; [15]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Denmark and Nordic Society of Gynaecologic Oncology-Clinical Trial Unit, Copenhagen, Denmark; [16]GSK, Pennington, NJ; [17]GSK, London, United Kingdom; [18]GSK, Waltham, MA; [19]Department of Medicine, British Columbia Cancer, Vancouver Centre, University of British Columbia, Vancouver, BC, Canada*

10.1136/ijgc-2022-ESGO.302

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

characteristics in patients with advanced or recurrent endometrial cancer who were treated with the anti-PD-1 dostarlimab.

Methodology GARNET is a multicentre, open-label, single-arm phase 1 study. Patients were assigned to cohort A1 (mismatch repair deficient [dMMR]/microsatellite instability-high [MSI-H EC]) or A2 (mismatch repair proficient [MMRp]/microsatellite stable [MSS] EC) based on immunohistochemistry assessment. Patients received 500 mg of dostarlimab IV every 3 weeks for 4 cycles, then 1000 mg every 6 weeks until disease progression, discontinuation, or withdrawal. Patient baseline demographics (age and BMI), histology, and prior lines of therapies were collected for enrolled patients. ORR by BICR per RECIST v1.1 for prior lines of therapy and histology were pre-specified exploratory subgroup analyses, whereas age and BMI were post hoc subgroup analyses.

Results 153 patients with dMMR/MSI-H and 161 patients with MMRp/MSS EC were enrolled and treated. The efficacy-evaluable population included 143 patients with dMMR/MSI-H EC and 156 patients with MMRp/MSS EC with measurable disease at baseline and the opportunity for at least 6 months of follow-up. ORR for each subgroup (age, BMI, prior lines of therapy, and histology) in each cohort were similar to that of the ORR for each overall cohort (see table 1). Overlapping 95% CIs are observed for all the subgroups assessed.

Abstract 2022-RA-1297-ESGO Table 1 Subgroup analysis by patients characteristics

	dMMR/MSI-H EC	MMRp/MSS EC
Overall, n/N (%; 95% CI)	65/143 (45.5%; 37.1–54.0)	24/156 (15.4%; 10.1–22.0)
Subgroups, n/N (%; 95% CI)		
Age		
<65 years	32/68 (47.1%; 34.8–59.6)	6/66 (9.1%; 3.4–18.7)
≥65 years	33/75 (44.0%; 32.5–55.9)	18/90 (20.0%; 12.3–29.8)
BMI[b,c]		
<25 kg/m²	21/46 (45.7%; 30.9–61.0)	5/42 (11.9%; 4.0–25.6)
25–29.9 kg/m²	16/30 (53.3%; 34.3–71.7)	9/45 (20.0%; 9.6–34.6)
≥30 kg/m²	27/64 (42.2%; 29.9–55.2)	9/66 (13.6%; 6.4–24.3)
Prior lines of therapy		
1	40/90 (44.4%; 34.0–55.3)	12/72 (16.7%; 8.9–27.3)
≥2	25/53 (47.2%; 33.3–61.4)	12/84 (14.3%; 7.6–23.6)
Histology		
Grade 1 or 2 endometrioid carcinoma (type I)	40/92 (43.5%; 33.2–54.2)	3/36 (8.3%; 1.8–22.5)
Endometrial carcinoma type II	24/49 (49.0%; 34.4–63.7)	21/120 (17.5%; 11.2–25.5)
Serous carcinoma	3/7 (42.9%; 9.9–81.6)	11/63 (17.5%; 9.1–29.1)
Grade 3 endometrioid	10/21 (47.6%; 25.7–70.2)	0/14 (0; 0.0–23.2)
Mixed carcinoma	5/7 (71.4%; 29.0–96.3)	4/11 (36.4%; 10.9–69.2)
Unspecified	2/4 (50.0%; 6.8–93.2)	1/9 (11.1%; 0.3–48.2)
Clear cell carcinoma	1/1 (100.0%; 2.5–100.0)	3/11 (27.3%; 6.0–61.0)
Undifferentiated carcinoma	2/4 (50.0%; 6.8–93.2)	1/3 (33.3%; 0.8–90.6)
Squamous carcinoma	1/1 (100.0%; 2.5–100.0)	0/3 (0; 0.0–70.8)
Carcinosarcoma	0/0	0/2 (0; 0.0–84.2)
Other[d]	0/4 (0; 0.0–60.2)	1/4 (25.0%; 0.6–80.6)
Unknown	1/2 (50.0%; 1.3–98.7)	0/0

[a]Two-sided exact 95% confidence intervals based on the Clopper-Pearson method were provided to summarise the binomial proportion of the ORR for RECIST v1.1 assessments; [b]Three patients from the dMMR/MSI-H cohort and 3 patients from the MMRp/MSS cohort had missing BMI information; [c]One responder from each cohort had missing BMI information; [d]Other includes dedifferentiated, endometrial adenocarcinoma, endometrial adenocarcinoma NOS, endometrial neuroendocrine carcinoma, high grade uterine carcinoma, and undifferentiated clear cell carcinoma.
BMI, body mass index; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; ORR, objective response rate; NOS, not otherwise specified; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Conclusion The treatment benefit of dostarlimab was consistent across clinical characteristic subgroups on a per-cohort basis (dMMR/MSI-H response rates were consistently ≥40%, whereas MMRp/MSS response rates were between 8% and 20%). No correlation could be made between response rate and individual clinical characteristics. Given the small sample size of the subgroups, caution should be used when interpreting the results.

2022-RA-1304-ESGO MOLECULAR TESTING OF ENDOMETRIAL CARCINOMA BRINGS GROWING OPPORTUNITY TO IDENTIFY PATIENTS WITH INHERITED RISK OF CANCER

[1]Marketa Bednarikova, [2]Jitka Hausnerova, [3]Lubos Minar, [4]Jakub Trizuljak, [5]Ivona Blahakova, [1]Lucie Ehrlichova, [3]Petra Vinklerova, [3]Michal Felsinger, [2]Kvetoslava Matulova, [6]Petra Ovesna, [3]Vit Weinberger. *[1]Department of Internal Medicine, Hematology and Oncology, University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; [2]Department of Pathology, University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; [3]Department of Obstetrics and Gynecology, University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; [4]Institute of Medical Genetics and Genomics, University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; [5]Central European Institute of Technology, Masaryk University, Brno, Czech Republic; [6]Faculty of Medicine, Institute of Biostatistics and Analyses, Masaryk University, Brno, Czech Republic*

10.1136/ijgc-2022-ESGO.303

Introduction/Background Routine examination of mismatch repair (MMR) status as a part of recently introduced molecular testing in patients with newly diagnosed endometrial carcinoma (EC) enables to identify those with MMR-d (deficient) tumors, the feature known to be associated with Lynch syndrome (LS). We aimed to evaluate the outcomes of genetic testing recommended to EC patients based on results of both tumor molecular testing and clinical examination.

Methodology According to the local guidelines, all newly diagnosed EC are tested for MMR-status from January 2021 in University Hospital Brno. Those EC patients with MMR-d tumors or high-risk family or personal history of cancer are referred to genetic counseling. All consecutive primary EC patients diagnosed between January 2021 and April 2022 with known MMR status were identified from the clinical database and checked for results of genetic consulting.

Results So far, a total of 109 patients have been involved with median age 64.5 years (30–85), of which 80 (73.4%) with MMR-proficient and 29 (26.6%) MMR-d tumors. Genetic counselling was recommended to 33 (30.2%) patients and performed in 27 (81.8%) patients. At the time of analysis, the results were available in 21 (78%) cases with following outcomes: 2 (9.5%) patients with pathogenic mutations in genes associated with LS, 1 (4.8%) patient with mutation in other gene associated with increased risk of cancer, 1 (4.8%) patient with mutation in gene not related to cancer, 5 (23.8%) patients with variant of unknown significance (VUS) in genes associated with LS, 2 (9.5%) patients with VUS in other genes and 10 (47.6%) patients with negative findings.

Conclusion The genetic testing recommended to all newly diagnosed EC patients with MMR-d tumors and/or high-risk family or personal history of cancer resulted in identification of 14.3% patients with hereditary form of cancer in this pilot study.