2022-RA-653-ESGO THE IMPACT OF HISTOLOGY, PRIOR THERAPY, AND DMMR STATUS ON LENVATINIB + PEMBROLIZUMAB OUTCOMES IN PATIENTS WITH ADVANCED ENDOMETRIAL CANCER: A SUBGROUP ANALYSIS OF STUDY 309/KEYNOTE-775

[1]Domenica Lorusso, [2]Vicky Makker, [3]Antonio Casado Herraez, [4]Bradley J Monk, [5]Helen Mackay, [6]Alessandro D Santin, [7]David S Miller, [8]Richard Moore, [9]Sally Baron-Hay, [10]Isabelle Ray-Coquard, [11]Ronnie Shapira-Frommer, [12]Kimio Ushijima, [13]Kan Yonemori, [14]Yong Man Kim, [15]Eva M Guerra Alia, [16]Ulus A Sanli, [17]Jie Huang, [18]Jodi McKenzie, [19]Gianmaria Barresi, [20]Nicoletta Colombo. *[1]Division of Gynecologic Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [2]Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY; [3]Medical Oncology Department, Hospital Clinico Universitario San Carlos, Madrid, Spain; [4]HonorHealth Research Institute, University of Arizona, Creighton University, Phoenix, AZ; [5]Medical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [6]Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, CT; [7]Division of Gynecologic Oncology, University of Texas Southwestern Medical Center, Dallas, TX; [8]Division of Gynecologic Oncology, University of Rochester Medical Center, Rochester, NY; [9]Medical Oncology Department, Royal North Shore Hospital, St. Leonards, NSW, Australia; [10]Medical Oncology Department, Centre Léon Bérard, University Claude Bernard, GINECO Group, Lyon, France; [11]Oncology Department, Sheba Medical Center, Ramat, Israel; [12]Department of Obstetrics and Gynecology, Kurume University School of Medicine, Kurume, Japan; [13]Department of Medical Oncology, National Cancer Center Hospital, Chuo-ku, Japan; [14]Department of Obstetrics and Gynecology, Asan Medical Center, University of Ulsan, Seoul, Korea, Republic of; [15]Department of Medical Oncology, Hospital Universitario Ramon y Cajal, Madrid, Spain; [16]Individualized Medicine Application and Research Center and Department of Medical Oncology, Ege University, Izmir, Turkey; [17]Biostatistics, Eisai Inc., Nutley, NJ; [18]Oncology Business Group, Eisai Inc., Nutley, NJ; [19]MSD Austria, Vienna, Austria; [20]Gynecologic Oncology Department, University of Milan-Bicocca, European Institute of Oncology IRCCS, Milan, Italy*

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Introduction/Background In the phase 3 Study 309/KEYNOTE-775 (Makker 2022, *NEJM*), lenvatinib plus pembrolizumab (L+P) demonstrated statistically and clinically significant improvements in progression-free survival (PFS), overall survival (OS), and objective response rate (ORR) versus treatment of physician's choice (TPC) in previously treated advanced endometrial cancer (aEC; in mismatch-repair proficient [pMMR] and all-comer patients). In this updated analysis (data cutoff: March 1, 2022), we report efficacy by histology, prior therapy, and deficient (d)MMR status.

Methodology Pts with aEC and 1 prior platinum-based chemotherapy regimen (up to 2 if 1 was given in the neoadjuvant/adjuvant setting) were randomized (1:1) to L 20 mg orally once daily + P 200 mg IV every 3 weeks (Q3W) or TPC (doxorubicin at 60 mg/m^2 IV Q3W or paclitaxel at 80 mg/m^2 IV QW [3 weeks on; 1 week off]). Randomization was stratified by MMR status; pMMR patients were further stratified by Eastern Cooperative Oncology Group Performance Status, geographic region, and history of pelvic irradiation. We report PFS, OS, and ORR (by blinded independent central review per RECIST v1.1) by histology (endometrioid vs non-endometrioid), prior therapy (1, 2, ≥3 lines), and dMMR status.

Results 827 patients were randomized to L+P (n=411) or TPC (n=416). PFS and OS in all-comers favored L+P regardless of histology (PFS HR, endometrioid: 0.54/non-endometrioid: 0.55; OS HR, endometrioid: 0.63/non-endometrioid: 0.61), prior therapy (PFS HR: 1 line, 0.49/2 lines, 0.68/≥3 lines, 0.61; OS HR: 1 line, 0.63/2 lines, 0.64/≥3 lines, 0.69), or dMMR status (PFS HR, 0.39; OS HR, 0.43) (table 1). The table 1 also shows PFS, OS, and ORR in all-comers and pMMR patients.

Abstract 2022-RA-653-ESGO Table 1

	L+P (N=411)		TPC (N=416)		L+P vs TPC
	N	Number of events/responses[a] (%)	N	Number of events/responses[a] (%)	Hazard Ratio (95% CI)/ Difference (95% CI)[b]
Overall PFS[c]	411	320 (77.9)	416	298 (71.6)	0.56 (0.48–0.66)
PFS by Histology[c,d]					
Endometrioid	244	181 (74.2)	254	182 (71.7)	0.54 (0.44–0.67)
Non-endometrioid	167	139 (83.2)	162	116 (71.6)	0.55 (0.42–0.71)
PFS by Prior Therapy[c,d]					
1 line	295	231 (78.3)	276	210 (76.1)	0.49 (0.41–0.60)
2 lines	104	83 (79.8)	126	83 (65.9)	0.68 (0.50–0.93)
≥3 lines	11	5 (45.5)	14	5 (35.7)	0.61 (0.17–2.18)
PFS by MMR status[c]					
dMMR	65	42 (64.6)	65	49 (75.4)	0.39 (0.25–0.60)
pMMR	346	278 (80.3)	351	249 (70.9)	0.60 (0.50–0.72)
Overall OS	411	276 (67.2)	416	329 (79.1)	0.65 (0.55–0.77)
OS by Histology[d]					
Endometrioid	244	148 (60.7)	254	188 (74.0)	0.63 (0.51–0.79)
Non-endometrioid	167	128 (76.6)	162	141 (87.0)	0.61 (0.48–0.78)
OS by Prior Therapy[d]					
1 line	295	205 (69.5)	276	223 (80.8)	0.63 (0.52–0.76)
2 lines	104	64 (61.5)	126	96 (76.2)	0.64 (0.47–0.88)
≥3 lines	11	7 (63.6)	14	10 (71.4)	0.69 (0.26–1.82)
OS by MMR status					
dMMR	65	34 (52.3)	65	49 (75.4)	0.43 (0.28–0.68)
pMMR	346	242 (69.9)	351	280 (79.8)	0.70 (0.58–0.83)
Overall ORR[c]	411	139 (33.8)	416	61 (14.7)	19.2 (13.4–24.9)
ORR by Histology[c,d]					
Endometrioid	244	85 (34.8)	254	43 (16.9)	17.9 (10.3–25.4)
Non-endometrioid	167	54 (32.3)	162	18 (11.1)	21.2 (12.6–29.8)
ORR by Prior Therapy[c,d]					
1 line	295	98 (33.2)	276	37 (13.4)	19.8 (13.0–26.5)
2 lines	104	37 (35.6)	126	21 (16.7)	18.9 (7.6–30.2)
≥3 lines	11	3 (27.3)	14	3 (21.4)	5.8 (-27.9–40.7)
ORR by MMR status[c]					
dMMR	65	27 (41.5)	65	8 (12.3)	29.2 (14.4–43.3)
pMMR	346	112 (32.4)	351	53 (15.1)	17.2 (11.0–23.5)

[a]Events refer to PFS and OS measures and responses refer to ORR measures; [b]hazard ratios are reported for PFS and OS measures, and differences are reported for ORR measures; [c]based on BICR assessment per RECIST v1.1; [d]prior therapy and histology are not stratification factors; thus, results of the prior therapy and histology subgroup analyses may be subject to confounding factor imbalance.
BICR, blinded independent central review; CI, confidence interval; dMMR, mismatch-repair deficient; L, lenvatinib; MMR, mismatch-repair; ORR, objective response rate; OS, overall survival; P, pembrolizumab; PFS, progression-free survival; pMMR, mismatch-repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TPC, treatment of physician's choice.

Conclusion PFS, OS, and ORR continued to favor L+P vs TPC in all subgroups of interest, including patients with dMMR tumors. These data further support L+P as a standard therapy in previously treated aEC.

2022-RA-654-ESGO IDENTIFICATION OF CLINICOPATHOLOGIC FACTORS RELATED TO PD-1/PD-L1 EXPRESSIONAND > FORSURVIVAL ANALYSIS IN ENDOMETRIAL CANCER PATIENTS

Yeorae Kim. *Obstetrics and Gynecology, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of*

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Introduction/Background We investigated the relationship of programmed death-ligand 1(PD-L1) expression with clinicopathologic characteristics, to identify clinical significance of PD-1/PD-L1 immunotherapy in endometrial cancer.

Methodology Total 232 patients with endometrial cancer were selected who underwent medical or surgical treatment in Seoul National University Bundang Hospital from May 2003 to March 2022. Paraffin-embedded tissues were immunohistochemically stained with PD-L1 antibody, p53 antibody and antibodies against MMR proteins. We regarded PD-L1 positivity as a 1 or more of Combined Positive Score (CPS). The correlation of PD-L1 expression, clinicopathologic factors and survival outcomes were statistically analyzed with SPSS ver.25.0.