#538 THE RELATIONSHIP BETWEEN MISMATCH REPAIR DEFICIENCY AND LYMPHOVASCULAR SPACE INVASION IN ENDOMETRIAL CANCER

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Introduction/Background The presence of MMR-deficiency along with LVSI positivity may indicate a more aggressive form of endometrial cancer and is an important factor to consider in patient monitoring and treatment planning.Studies evaluating the relationship between MMR-deficiency and LVSI positivity in endometrial cancer have been conducted. These studies have generally observed a higher prevalence of LVSI positivity in endometrial cancer cases with MMR-deficiency.The aim of our study is to investigate the presence of this relationship using a large dataset from a tertiary center.

Methodology The study was designed as a retrospective case-control study.The research involved the examination of data from all patients diagnosed with endometrial cancer who presented to our clinic between June 2020-May 2023.The aim of this study was to investigate the relationship between LVSI negative,focal,and substantial positivity and MMR-gene defect.The statistical method used was the Pearson Chi-Square test.

Results A total of 226 patients with endometrial cancer were included.The mean age of the patients,whose age range was between 23 and 88 years,was 60.64±10.59.The number of patients with positive lymphovascular space invasion was 81, and the number of patients with negative invasion was 145. While the number of patients with MMR-deficits was 58,the number of patients with proficiency was 168.A significant correlation was found between MMRd patients and LVSI positivity($p< 0.05$)(table 1).

Conclusion The MMR-defect suggests that tumors may have a tendency to be more invasive and spread to lymphovascular spaces.McMeekin et al.found that women with tumors with MMR-defects were more likely to have higher-grade cancers and more frequent lymphovascular space invasion.In our study, a significant association was observed between patients with MMR-deficiency and the presence of lymphovascular space invasion(LVSI),which is supported by the existing literature.In some cases,positive survival trends are detected in patients with MMR-defects,while in other cases,this relationship is not evident.Therefore,further research is required to fully understand the relationship between MMR-defect and lymphovascularspace invasion.

Abstract #538 Table 1

	MMRd (n=58)	MMRp(n=168)	p value
LVSI + (n=81)	%46,6 (n=27)	%32,1 (n=54)	0,048
LVSI- (n=145)	%53,4 (n=31)	%67,9 (n=114)	

Chi-Square Tests, Pearson Chi-Square

Disclosures There are no conflicts of interest to disclose

#540 SAFETY OF DOSTARLIMAB IN COMBINATION WITH CHEMOTHERAPY IN PATIENTS WITH PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER IN A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED TRIAL (ENGOT-EN6-NSGO/GOG-3031/RUBY)

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Introduction/Background In the phase 3 RUBY trial (NCT03981796) in patients with primary advanced or recurrent endometrial cancer (pA/rEC) dostarlimab+carboplatin/paclitaxel significantly improved PFS versus carboplatin/paclitaxel alone in the mismatch repair deficient/microsatellite instability-high (HR 0.28) and overall populations (HR 0.64) with a favourable OS trend (HR 0.64). Here, we report on safety for the RUBY trial.

Methodology Patients with pA/rEC were randomised 1:1 to dostarlimab 500 mg, or placebo, plus carboplatin AUC 5 and paclitaxel 175 mg/m2 Q3W for 6 cycles, followed by dostarlimab 1000 mg, or placebo, Q6W for up to 3 years. Adverse events (AEs) were assessed according to CTCAE v4.03.

Results The safety population included 487 patients who received ≥1 dose of treatment (241 dostarlimab+carboplatin/paclitaxel; 246 placebo+carboplatin/paclitaxel). Treatment-emergent adverse events (TEAEs) were experienced by 100% of patients; 70.5% of the dostarlimab arm and 59.8% of the placebo arm experienced grade ≥3 TEAEs (table 1). Median time to TEAE was 2.0 days in the dostarlimab+carboplatin/paclitaxel arm and 2.5 days in the placebo+carboplatin/paclitaxel arm. TEAEs led to discontinuation in 23.7% of the dostarlimab+carboplatin/paclitaxel arm and 16.7% of the placebo +carboplatin/paclitaxel arm. Higher rates of discontinuation were reported during the chemotherapy phase (cycles 1–6) versus the monotherapy phase (cycles ≥7). TEAEs led to discontinuation of dostarlimab or placebo in 17.4% and 9.3% of

patients (table 1). Discontinuation rates of carboplatin or paclitaxel were similar between arms. Immune-related AEs related to dostarlimab or placebo were reported in 38.2% of the dostarlimab arm and 15.4% of the placebo arm. Five deaths were reported in the dostarlimab arm; 2 were related to dostarlimab.

Conclusion The safety profile of dostarlimab+carboplatin/paclitaxel was consistent with that of the individual components. The addition of dostarlimab did not compromise the completion rate of chemotherapy. Dostarlimab+carboplatin/paclitaxel has a favourable benefit-risk profile that makes it a valuable treatment option for patients with pA/rEC.

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Abstract #540 Table 1

Event, n (%)	Dostarlimab+ carboplatin/paclitaxel (N=241)	Placebo+ carboplatin/paclitaxel (N=246)
TEAEs		
Any grade	241 (100.0)	246 (100.0)
Grade ≥3	170 (70.5)	147 (59.8)
SAEs	91 (37.8)	68 (27.6)
Time to TEAE, median (95% CI), days	2.0 (2.0–3.0)	2.5 (2.0–3.0)
TEAEs by treatment phase		
Cycles 1–6 (chemotherapy phase)		
All TEAEs	240 (99.6)	246 (100)
Grade ≥3	138 (57.3)	126 (51.2)
Cycles ≥7 (monotherapy)[a]		
All TEAEs	164 (88.6)	154 (83.7)
Grade ≥3	71 (38.4)	42 (22.8)
TEAEs leading to discontinuation of any study treatment	57 (23.7)	41 (16.7)
TEAEs leading to discontinuation of dostarlimab or placebo	42 (17.4)	23 (9.3)
TEAE leading to discontinuation of carboplatin	24 (10.0)	19 (7.7)
TEAE leading to discontinuation of paclitaxel	24 (10.0)	23 (9.3)
Discontinuation of any study treatment by treatment phase		
Cycles 1–6 (chemotherapy phase)	41 (17.0)	35 (14.2)
Cycles ≥7 (monotherapy)[a]	17 (9.2)	6 (3.3)
Immune-related AEs related to dostarlimab or placebo[b]	92 (38.2)	38 (15.4)
TEAEs leading to death	5 (2.1)[c]	0
TEAEs in ≥50% of either arm		
Fatigue	125 (51.9)	134 (54.5)
Alopecia	129 (53.5)	123 (50.0)
Nausea	130 (53.9)	113 (45.9)
Grade ≥3 TEAEs in ≥10% of either arm		
Anaemia	36 (14.9)	40 (16.3)
Neutrophil count decreased	20 (8.3)	34 (13.8)
TEAEs leading to discontinuation in ≥2% of either arm		
Infusion related reaction	5 (2.1)	8 (3.3)
Peripheral neuropathy	3 (1.2)	6 (2.4)
Peripheral sensory neuropathy	7 (2.9)	1 (0.4)
Thrombocytopenia	1 (0.4)	5 (2.0)
TEAEs leading to discontinuation of dostarlimab or placebo in ≥1% of either arm		
Infusion-related reaction	3 (1.2)	1 (0.4)
Thrombocytopenia	1 (0.4)	3 (1.2)
Maculopapular rash	3 (1.2)	0

[a]At cycle ≥7, dostarlimab+carboplatin/paclitaxel n=185 and placebo+carboplatin/paclitaxel n=184.
[b]Immune-related AEs are defined as grade ≥2 and above from a predefined list.
[c]Two deaths were reported by the investigators as related to dostarlimab: 1 during the first 6 cycles (myelosuppression) and 1 during the 90-day safety follow-up (hypovolemic shock). Three deaths were not related to study treatment (opiate overdose, coronavirus disease 2019, and general deterioration of physical health).

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#866 DIAGNOSTIC POTENTIAL OF DNA METHYLATION DETECTION FOR ENDOMETRIAL CANCER IN REPRODUCTIVE-AGED WOMEN PRESENTING WITH ABNORMAL UTERINE BLEEDING

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Introduction/Background With the increasing incidence and early onset of endometrial cancer, there is a need for improved diagnostic methods in reproductive-aged women presenting with abnormal uterine bleeding (AUB). This study aims to evaluate the diagnostic potential of DNA methylation detection compared to other non-invasive approaches for endometrial cancer screening.

Methodology A prospective study was conducted involving 517 reproductive-aged women with AUB, who underwent hysteroscopy at a tertiary hospital. Cervical exfoliated cells were collected for cytology, human papillomavirus (HPV) testing, and DNA methylation analysis. Clinical information and transvaginal ultrasound measurements were also obtained. Univariate logistic regression and receiver operating characteristic curve analysis were performed to assess the risk factors and diagnostic efficacy of DNA methylation detection.

Results Age, body mass index (BMI) $\geq$25 kg/m^2, endometrial thickness $\geq$11 mm, CDO1 ΔCt $\leq$ 8.4, CELF4 ΔCt $\leq$ 8.8, and combined gene methylation showed significant associations with endometrial cancer in young women ($p < 0.05$). The highest diagnostic accuracy (AUC = 0.90) for endometrial cancer was achieved with CDO1/CELF4 methylation testing. Sensitivity and specificity were 91.7% and 88.8%, respectively. Combining transvaginal ultrasound with DNA methylation testing improved sensitivity to 95.8% but decreased specificity to 68.0%.

Conclusion DNA methylation detection in cervical cells provides enhanced accuracy for endometrial cancer diagnosis in reproductive-aged women with AUB. The combination of CDO1 and CELF4 methylation testing with transvaginal ultrasound improves sensitivity, highlighting its potential as a valuable screening approach.

Disclosures No potential conflict of interest was reported by the authors.

#908 THE IMPACT OF MOLECULAR CLASSES ON ONCOLOGIC OUTCOME OF ENDOMETRIAL CANCER: A PROSPECTIVE ANALYSIS FROM A TERTIARY REFERRAL CENTER

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Introduction/Background In the past few years, the molecular classification system, which categorize endometrial cancer (EC) into four risk classes, has become a crucial tool for determining the appropriate treatment following surgical staging. The primary objective of this study was to compare recurrence-free survival among the four molecular classes.

Methodology Starting from April 2019, we prospectively performed molecular characterization of all EC patients according to the WHO-endorsed algorithm. Molecular analysis included IHC for p53 and MMR proteins, microsatellite instability assay and Next Generation Sequencing for POLE exonuclease domain and TP53. ECs were classified into 4 molecular classes (POLEmut, MMR deficiency [MMRd], p53 abnormality [p53abn], and non-specific molecular profile [NSMP]). For the current analysis patients with stage IV disease, vaginal approach, no lymph node assessment, no molecular analysis, and follow-up < 6 months were excluded.