Introduction In ARIEL3 (NCT01968213), rucaparib maintenance for recurrent ovarian cancer (rOC) significantly improved investigator-assessed PFS and postprogression efficacy outcomes versus placebo regardless of biomarker status. PFS was also improved in patients with rOC associated with either BRCA1 or BRCA2 mutations (HR, 0.32 [95% CI, 0.19–0.53] and 0.12 [0.06–0.26], respectively). This exploratory analysis further examined the subgroup of patients with rOC associated with BRCA1 or BRCA2 mutations to assess the durability of the clinical benefit of rucaparib maintenance following disease progression.

Methods Patients were randomised 2:1 to oral rucaparib (600 mg twice daily) or placebo. Postprogression efficacy endpoints were assessed in patients with germline or somatic BRCA1 or BRCA2 mutations.

Results Investigator-assessed postprogression efficacy endpoints for patients with either BRCA1 or BRCA2 mutations are presented in the table 1.

There was a trend for better outcomes across all endpoints in patients with BRCA1 and BRCA2 mutations, with larger differences between the median values among patients with a BRCA2 mutation. The treatment-by-mutation group interaction test reached statistical significance for TFST and CFI.

Among rucaparib-treated patients, the most common treatment-emergent adverse events (any grade) in the BRCA1 and BRCA2 subgroups were nausea (81.0% and 78.0%) and asthenia/fatigue (74.7% and 80.0%).

Conclusions/Implications All postprogression efficacy endpoints were longer with rucaparib maintenance than with placebo in both BRCA-mutant subgroups. Safety data for the two subgroups were similar and were consistent with the overall safety population.

Plenary II

IGCS20_1447

4 REFINING PATHOLOGIC INTERPRETATION OF ENDOMETRIAL CARCINOMAS: LESSONS LEARNED FROM A NATIONWIDE STUDY IN A NEW ERA OF MOLECULAR CLASSIFICATION

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Abstract 4 Table 1 Univariable association of clinicopathologic characteristics by proactive molecular risk classifier for endometrial cancer (ProMisE) subtype

Variable	Total		POLE		MMR		NSMP/p53wt		p53abn		p value
Total	**862**		**55**	**(6.4%)**	**247**	**(28.7%)**	**387**	**(44.9%)**	**173**	**(20.1%)**	
Age at dx											**<0.001**
≤60	321	(37.2%)	35	(63.6%)	78	(31.6%)	181	(46.8%)	27	(15.6%)	
>60	541	(62.8%)	20	(36.4%)	169	(68.4%)	206	(53.2%)	146	(84.4%)	
BMI ≥30	396	(45.9%)	20	(36.4%)	117	(47.4%)	180	(46.5%)	79	(45.7%)	**0.004**
Histotype											**<0.001**
Endometrioid	681	(79.0%)	49	(89.1%)	231	(93.5%)	371	(95.9%)	30	(17.3%)	
LG	584	(67.7%)	38	(69.1%)	186	(75.3%)	349	(90.2%)	11	(6.4%)	
HG	97	(11.3%)	11	(20.0%)	45	(18.2%)	22	(5.7%)	19	(11.0%)	
Non endometrioid	183	(21.2%)	6	(10.9%)	16	(6.5%)	16	(4.1%)	143	(82.7%)	
FIGO stage											**<0.001**
I	635	73.7%)	44	(80.0%)	188	(76.1%)	315	(81.4%)	88	(50.9%)	
II-IV	198	(23.0%)	11	(20.0%)	52	(21.1%)	56	(14.5%)	79	(45.7%)	
LVI											**<0.001**
positive	274	(31.8%)	16	(29.1%)	101	(40.9%)	79	(20.4%)	78	(45.1%)	
negative	550	(63.8%)	38	(69.1%)	135	(54.7%)	288	(74.4%)	89	(51.4%)	
LN sampling performed											
Yes (any)	519	(60.2%)	36	(65.5%)	155	(62.8%)	179	(46.3%)	149	(86.1%)	
LN metastases											**<0.001**
yes	93	(10.8%)	5	(9.1%)	22	(8.9%)	22	(5.7%)	44	(25.4%)	
Post-surgical Treatment											**<0.001**
yes	374	(43.4%)	19	(34.5%)	122	(49.4%)	110	(28.4%)	123	(71.1%)	

Objectives Molecular classification of endometrial carcinoma (EC) enables consistent classification of tumours and provides valuable prognostic and predictive information. Herein we describe molecular subtype distribution and histomorphologic correlates in recently diagnosed (2016) ECs from across Canada.

Methods Molecular classification was performed on representative tumour specimens from participating centres. Clinicopathologic, management and outcome data were collected (REDCap).

Results 1453 ECs from 30 centres have been identified. Complete molecular (ProMisE) and outcome data is reportable for 862 patients. Histologic and clinicopathologic parameters associated with molecular subtype and are summarised in table 1. Amongst participating centres, routine testing of MMR and p53 immunohistochemistry (IHC) was performed in only 23.5% (range 3.5–80.0% per centre) and 15% (2.2–45.7%) of cases respectively. We found p53 abn ECs across a range of histotypes, including low grade endometrioid EC. Subclonal p53 staining was observed in 3.9% of cases and significantly associated with the presence of pathogenic POLE mutations (p≤0.001). Subclonal MMR IHC expression was seen in 3.5% of cases and has previously been shown to occur predominantly in the context of MLH1 hypermethylation. MMRd was significantly associated with LVI (p <0.001). ProMisE subtype was significantly associated with clinical outcomes (p<0.001) even in low stage disease [OS p=0.045, DSS p=0.009, PFS p=0.005 for stage I].

Conclusions Observation of unusual or unexpected p53 and MMR IHC staining patterns and associated clinical implications highlight the importance of routine testing of these parameters in ECs.

IGCS20_1251

5 UNDERSTANDING THE CLINICAL IMPLICATION OF MISMATCH REPAIR DEFICIENCY IN ENDOMETRIOID ENDOMETRIAL CANCER THROUGH A PROSPECTIVE STUDY

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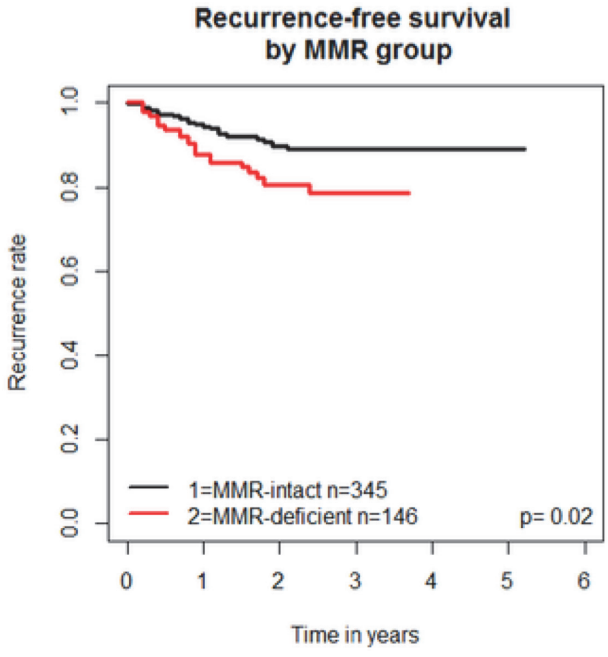
Objectives Findings on impact of mismatch repair deficiency (MMRd) on patient outcomes in endometrial cancer (EC) have been inconsistent to date. The objective of this study was to compare oncologic outcomes between MMRd and MMR-intact (MMRi) endometrioid EC (EEC).

Methods Between 2015–2018, we prospectively recruited 668 EC cases from three cancer centers in Ontario, Canada. Tumors were reflexively assessed for MMR protein expression by immunohistochemistry (IHC). Clinicopathological, treatment and survival data were compared between MMRd and MMRi cases.

Results Out of 668, there were 496 EEC (74%), with 347 MMRi (70%) and 149 MMRd (30%) cases treated with surgery and with complete follow-up information. Median follow-up was 16.8 months (6–96 months). MMRd tumors tended to be grade 2 or 3 (56% vs. 29%, p<0.001), with propensity for lymphovascular space invasion (LVSI) (29% vs. 17%, p=0.004) and received more adjuvant treatment (45% vs. 33%, p=0.03). This group also had significantly lower 3-year RFS (78% vs. 89%, p=0.02) although there was no difference in OS (p=0.91). MLH1/PMS2 deficient tumors had the lowest 3-year RFS compared to intact and other MMRd tumors (76% vs. 89% vs 87%, p=0.02). After adjusting for age, stage, grade, use of adjuvant treatment, and LVSI status, MLH1/PMS2 deficiency was still associated with the lowest RFS (p=0.05).



Abstract 5 Figure 1 Comparison of recurrence free survival between mismatch repair deficient (MMRd) and mismatch repair intact (MMRi) endometrioid endometrial cancers

Conclusions MLH1/PMS2 deficient EECs exhibit more aggressive features compared to other MMRd and MMRi cases, with worse RFS. This may indicate an inherent difference in tumor biology, suggesting the importance of individualized management based on tumor's molecular phenotype.