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 ($p \leq 0.001$). 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.

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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.