Introduction/Background MLH1 promoter hypermethylation is common in sporadic microsatellite unstable endometrial cancer but data on MLH1 promoter hypermethylated endometrial cancer (MLH1-PM EC) is sparse. We aimed to identify the clinical and molecular characteristics of MLH1-PM EC.

Methodology Descriptive analysis of 246 tumours from patients treated between September 2007 to June 2022.Mismatch repair proteins (MMR) were tested by immunohistochemistry (IHC). Tumour specimens were sequenced using the Royal Marsden RMH200Solid panel which includes 233 genes and evaluates microsatellite instability (MSI) and tumour mutational burden (TMB). Droplet Digital PCR (ddPCR) was used for DNA methylation analysis in each case. Patients’ characteristics were recorded from our electronic records.

Results MLH1-PM was identified in 71/246 tumours (28.9%): 61 were MMRd and 10 MMR proficient by IHC. The most common protein loss was MLH1/PMS2 in 57/61 cases (93.5%). Isolated loss of MSH6 was present in 3 cases and MSH2/MSH6 loss in 1 case. MLH1-PM tumours were MSI high in 47/71 (66.2%) of cases with a mean TMB of 30.96 mut/mb (12.21–193.93) and MSS in 24/71 (33.8%) of cases with a mean TMB of 48.65 mut/mb (0–231.91). The predominant histological subtype was endometrioid (n=64). Most tumours were stage I or II at diagnosis (n=55). Mean age at diagnosis was 65 years (32–90) and mean body mass index (BMI) was 31.64 (17.3–53.9). 14/71 (19.7%) patients presented with relapsed disease after initial diagnosis: loco-regional in 4 cases and systemic in 10 cases. Genomic analysis revealed that MLH1-PM ECs were enriched in PTEN, ARID1A, PIK3CA, KMT2D, KMT2C, PIK3R1, KRAS, FAT1, BCOR and ATM mutations. In patients who relapsed (n=14), gain of chromosome 1q was identified in 7 cases (50%).

Conclusion MLH1-PM EC is found in 30% of unselected EC patients and harbors genomic alterations that may have potential prognostic and therapeutic implications. Further studies are needed to develop appropriate treatment strategies.

Disclosures Dr. Alexandra Taylor: MSD.
Dr. Angela George: Astra Zeneca, GSK, Roche, Merck.
Extrenal beam radiotherapy (EBRT), brachytherapy (BT) or both in combination can be used in this scenario. Recent advances in EBRT and the advent of high dose rate (HDR) brachytherapy have improved tumour delineation and dose delivery. We report survival data of patients with inoperable endometrial cancer treated with definitive EBRT ± BT.

**Methodology** We conducted a retrospective review of patients with inoperable endometrial cancer who underwent definitive radiotherapy (BT ± EBRT) between 2017 and 2023 at our single center. Patient and disease characteristics, including stage, grade, and histopathological subtype, were collected, and survival data were obtained through electronic medical records.

**Results** Seven patients with inoperable endometrial cancer were included in the analysis. Six patients had stage III disease, with IIIB (57.14%) and IIIC (28.58%) sub-stages, and one had stage IA disease (14.28%). The median age of the patients was 70 (range 42–83 years). Five had endometrioid adenocarcinoma, two had carcinosarcoma. All had EBRT with lowest total dose of 45Gy (receiving a simultaneous integrated boost to positive nodes if present). Six patients had sequential brachytherapy (21–28Gy) and three of them received concurrent chemotherapy. Only one patient had evidence of progression of endometrial disease, 10 months after finishing treatment, and died five months later. One patient was lost to follow-up. Censored overall survival data is described, with a range from 8–42 months.

**Conclusion** Definitive radiotherapy treatment can be used effectively and safely in those medically inoperable or with inoperable endometrial cancer, including those with Stage III disease.

**Disclosures** None.

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Abstract #993 Figure 1

**Results** Seven patients with inoperable endometrial cancer were included in the analysis. Six patients had stage III disease, with IIIB (57.14%) and IIIC (28.58%) sub-stages, and one had stage IA disease (14.28%). The median age of the patients was 70 (range 42–83 years). Five had endometrioid adenocarcinoma, two had carcinosarcoma. All had EBRT with lowest total dose of 45Gy (receiving a simultaneous integrated boost to positive nodes if present). Six patients had sequential brachytherapy (21–28Gy) and three of them received concurrent chemotherapy. Only one patient had evidence of progression of endometrial disease, 10 months after finishing treatment, and died five months later. One patient was lost to follow-up. Censored overall survival data is described, with a range from 8–42 months.

**Conclusion** Definitive radiotherapy treatment can be used effectively and safely in those medically inoperable or with inoperable endometrial cancer, including those with Stage III disease.

**Disclosures** None.

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**Introduction/Background** Endometrial stromal sarcoma is a rare subgroup of uterin sarcomas. More than half the patients are premenopausal, young women and girls may be affected. Abnormal vaginal bleeding is the most common presenting symptom, and abdominal pain and uterine enlargement may occur. Total abdominal hysterectomy and bilateral salpingo-oophorectomy, with radical cytoreductive surgery for extraterine involvement, has been the standard recommendation for endometrial stromal sarcomas. Preservation of the ovaries is controversial. Adnexal metastases were indentified in 11 of 87 cases (%13) in the series from Memorial Sloan Kettering, and all were macroscopically apparent. This group has higher recurrence rates. It is concluded that ovarian preservation may be an option in well-informed patients. We presented a 24 years old women with low grade endometrial sarcoma.

**Methodology** In our case report, a 24 years old married women came with abnormal uterine bleeding. In Pelvic MR report, a large fibroid seen also suspected to sarcoma. The curettage result was reported as an uterin sarcoma. Patient is screened with PETCT and tumor is limited to the uterus. The patient well-informed about standard treatment and she did not accept salpingo-oophorectomy at the first line treatment. Total Abdominal Hysterectomy operation made and final pathological result reported as low grade endometrial sarcoma, tumor size 6,5 cm and more than half myometrial invasion.

**Results** The patient informed again about choices; salpingo-oophorectomy and preserving of ovaries with risks and outcomes. She selected the preserving ovaries option and being observed in often intervals.

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**Abstract #993 Figure 1**

**Introduction/Background** Isolated inguinal metastases from endometrial carcinoma are a rare occurrence and pose a challenge in the management of endometrial cancer.

**Methodology** In this study, we present the clinical outcomes and management of three cases with isolated inguinal metastases from endometrial cancer.

**Results** All three patients underwent total abdominal hysterectomy and bilateral pelvic lymphadenectomy.

**Conclusion** The appearance of extra-abdominal metastases from endometrial cancer is rare, and the presence of isolated inguinal recurrences presents a unique challenge for the management of endometrial cancer. Careful follow-up and close monitoring are essential in identifying these rare occurrences and ensuring timely intervention.

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