Introduction/Background Microsatellite instability plays an important role in the development of sporadic endometrial cancer. Mutations in mismatch repair proteins lead to MSI which leads most commonly to somatic hypermethylation and inactivation of MLH1-gene.

Methodology We report a case of endometrioid endometrial inactivation of MLH1-gene.

Results A 56 yo nulliparous lady presented with post-menopausal bleeding. Histology of endometrial curettings confirmed grade one EAC, estrogen receptor positive, p53 wild type and MMR deficient. CT-TAP was negative for metastasis. Patient underwent total laparoscopic hysterectomy and bilateral salpingo-oophorectomy. Sentinel lymph node mapping was unsuccessful however intra-operative assessment demonstrated myometrial-invasion <50%, and comprehensive pelvic lymph node dissection was deemed unnecessary. Post-operative histology gave a stage of FIGO 1a, pT1aNxMo, Grade 1 EAC. The was no LVSI/cervical stroma/adnexal/parametrial involvement. MMR-immunohistochemistry demonstrated loss of MSH2 and MSH6 suggestive of Lynch syndrome (LS), however germline testing failed to identify any abnormality. Further somatic testing identified two independent presumed somatic pathogenic MSH2 mutations. This reduces likelihood of LS and presented an extremely rare case of double somatic mutation of MSH2-gene.

Conclusion MMR gene alterations (hMLH1/hMSH2) play an important role in the development of MSI in sporadic EAC. Most presumed sporadic MSI-positive EACs are associated with epigenetic silencing of MLH1, via promoter hypermethylation. A smaller fraction have somatic mutations in MSH6, or loss of MSH2 protein expression. Hereditary cancers can also display mutations in MSH2-gene. LS is an autosomal dominant hereditary cancer syndrome which increases cancer risk, most notably colorectal and endometrial. It is caused by germ-line mutations in MMR genes – MSH1/MSH2/MSH6/MSR2 and EPCAM-genes. ~36% of MMR deficient EAC are caused by LS. Here we report a case of EAC demonstrating a ‘double hit’ or bi-allelic somatic inactivation of MSH2-gene highlighting the importance of complete clinical algorithms in these cases.

Introduction/Background Endometrial carcinoma (EC) is the most common cancer of the female genital tract in developed countries. Lymphovascular space invasion (L VSI), an histological characteristic, is also included in the molecular classification. We aimed to compare the clinical profile but also overall survival (OS) and progression-free survival (PFS) in patients with and without L VSI.

Methodology Between January 2019 and December 2021, we conducted a monocentric retrospective study of 166 patients treated for EC (all stages) at the CHU of Liège. Thirty-nine patients were excluded. Data of the 127 remaining patients were analyzed for quantification of L VSI: absence, rare (< 5), substantial (≥ 5) or lymphangitis. The statistical correlation between the L VSI status and various clinical (FIGO stage, lymph node invasion, histological type and grade) and molecular factors was assessed using chi-square and Fisher’s exact tests. Kaplan-Meier methods were used to determine OS and PFS.

Results 33.6% (n = 37/127) of absence, rare (n = 45/127) - 21.8% (n = 24/127) and 3.6% (n = 4/127) have absence, rare, substantial L VSI and lymphangitis, respectively. There is a significant correlation between the presence of L VSI (L VSI+) and higher grade (p=0.0001) but also with lymph node invasion (12.2% vs 0%, p=0.046). OS at 24 months was 96% and 82% in L VSI - and L VSI + cohorts, respectively (HR = 2.59, p=0.37).

Regarding molecular analyses, more patients with L VSI+ have microsatellite instability (42.7% vs 16.2%, p=0.0045). No significant correlation was found between the L VSI quantification and p53 mutation, POLE status or histological subtype.

Conclusion The presence of L VSI is a negative prognostic factor, with aggressive features, but without statistically reduction in OS. However, concerning absolute values, the presence of L VSI demonstrates worse prognosis. A significant association with microsatellite instability is demonstrated. The L VSI status should systematically be determined to optimally define the patient prognosis.