A RETROSPECTIVE ANALYSIS OF CLINICAL AND PATHOLOGIC CHARACTERISTICS OF ENDOMETRIAL CANCER CASES ACCORDING TO MISMATCH REPAIR PROTEIN STATUS

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Objectives Since 2016 our institution has performed reflex immunohistochemistry assessment of mismatch repair (MMR) protein expression in all newly diagnosed endometrial cancer patients. In this study we assessed the impact of MMR status on clinical and pathologic tumor characteristics

Methods We retrospectively analyzed 248 cases according to MMR deficient (MMRd) and proficient (MMRp) status for the following clinical and pathologic characteristics: Age and stage at presentation, histology, depth of invasion, lymph-vascular space invasion (LVSI), lower uterine segment involvement (LUSI) and adjuvant therapy received. A sub-analysis of endometrioid cancer cases was also undertaken

Results 72 (29%) of tumors exhibited loss of MMR protein expression. Most women were diagnosed with stage 1 disease (69.1% of MMRd and 73.8% of MMRp cases). Average age at presentation was 66 years in both groups. No statistically significant difference was seen with respect to depth of invasion, LVSI, LUSI or adjuvant treatment. Differences in the use of radiation (P=0.15) and chemotherapy (P=0.19) between the groups did not reach statistical significance. All patients with MMRd had endometrioid histology except 1 patient with serous histology. Subgroup analysis of endometrioid cancers revealed statistically significant higher stage at diagnosis (P<0.01), more LUSI (P<0.05), and consequently increased rates of adjuvant radiation (P<0.05) for patients with MMRd

Conclusions MMRd tumors are universally of endometrioid histology. MMRd in endometrioid tumors correlated with a more aggressive subtype which presented at a higher stage requiring more aggressive adjuvant treatment

ABERRANT BETA-CATENIN DISTRIBUTION AS POTENTIAL PROGNOSTIC BIOMARKER IN ENDOMETRIAL CANCER

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Objectives Based on the TCGA results for endometrial cancer, aberrant beta-catenin distribution may be a predictive biomarker for recurrence in early stage, low grade endometrioid endometrial cancer.

Methods This retrospective single institution cohort study reviewed 316 patients with endometrial cancer from 2017 to 2021. Uterine serous, carcinosarcoma, clear cell endometrial histologies were excluded. Stage, FIGO grade, beta-catenin status by immunohistochemistry (aberrant nuclear distribution vs. wild-type plasma membrane distribution), recurrence status (local vs. distant) were obtained from the medical records.

Stage was classified as early (stage I/IIA/IIIB/IIIC/IVB). X2 test, Fisher test, and logistic regressions were performed.

Results 213 patients were included. The majority had stage IA (50.0%, n=106) or FIGO grade I disease (69.8%, n=148). Recurrences were observed in 40 patients (18.9%) vs. no recurrences in 172 patients (81.3%). Recurrences did not correlate with beta catenin distribution: 20% (n=19) of aberrant beta-catenin recurred vs. 17.9% (n=21) of wild-type beta-catenin recurred (P=0.70). Local and distant recurrences did not vary significantly by beta-catenin status (P=0.36). Most recurrences occurred in the vaginal cuff (37.50%, n=15), followed by lung (17.50%, n=7). The odds ratio (OR) for beta-catenin aberrant distribution on recurrence risk was non-significant at 1.17 (0.59, 2.32). In a sensitivity analysis of early-stage, low-grade patients (n=109), recurrence also did not vary significantly by beta-catenin distribution (P=0.64).

Conclusions Aberrant beta-catenin distribution did not significantly correlate with recurrence in early stage, low grade endometrioid uterine cancer. Further research is warranted to evaluate the effect of aberrant beta-catenin distribution on endometrial cancer prognosis.

ANTI-LIPOLYSIS-STIMULATED LIPOPROTEIN RECEPTOR MONOCLONAL ANTIBODY INDUCES APOPTOSIS AND SHOWS AN ANTITUMOR ACTIVITY IN ENDOMETRIAL CANCER

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Objectives Advanced endometrial cancer (EC) has a poor prognosis. Since the efficacy of current chemotherapy is limited, new therapeutic agents are needed. We focused on lipolysis-stimulated lipoprotein receptor (LSR), a membrane protein highly expressed in EC cells, and developed a new anti-LSR monoclonal antibody (mAb). In this study, we aimed to investigate the function of LSR and the antitumor activity of anti-LSR mAb in EC.

Methods The relationship between LSR expression and clinical outcomes was investigated using immunohistochemistry in 230 clinical samples of EC. We newly developed a chimeric chicken-mouse anti-LSR mAb and investigated its antitumor activity in EC cell xenograft mouse model. To clarify the function of LSR, we conducted in vitro assays using EC cell lines (HEC1 and HEC116).

Results High-LSR expression was significantly associated with poor overall survival, deep myometrial invasion, and metastasis in EC patients (p < 0.05, respectively). LSR-knockdown suppressed the activation of the MEK/ERK signaling pathway and subsequent matrix metalloproteinases (MT1-MMP and MMP2), which downregulated cell proliferation, invasion, and migration in HEC1 and HEC116. Our anti-LSR mAb suppressed the phosphorylation of ERK1/2, increased the expression of cleaved caspase-3, and significantly inhibited the tumor growth in EC cell xenograft mouse model (tumor volume, 407.1 mm³ versus 726.3 mm³, p = 0.019). Moreover, anti-LSR mAb also suppressed the activation of the MEK/ERK signaling pathway in vitro.