Results Ten patients with OCCC were selected: Five had SM and 5 patients had OCCC only. We did not uncover any pathogenic or likely-pathogenic germline variants in this cohort, as annotated by ClinVar. Consistent with previous reports in OCCC, we uncovered recurrent, oncogenic mutations in PIK3CA and loss-of-function mutations in ARID1A in 8 OCCCs. One of the two OCCCs without these mutations had somatic mutations of RRAS2 (encoding downstream target of PIK3CA pathway) and loss-of-function mutation in ARID4B, consistent with the more frequent oncogenic mechanisms in OCCC. In the SM, none of the somatic mutations were shared with the primary OCCCs.

Conclusions In this pilot study, SM did not share somatic mutation with OCCC. Larger cohort and deeper molecular analysis can be used to further understand potential common pathway contributing to development of SM in patients with OCCC.

Abstract EP009/#709 Figure 1

Abstract EP009/#709 Figure 2

LIPOLYSIS-STIMULATED LIPOPROTEIN RECEPTOR – ANTIBODY-DRUG CONJUGATES (LSR-ADC) DEMONSTRATES POTENT ANTITUMOR ACTIVITY TO EPITHELIAL OVARIAN CANCER

EP009/#709

LIPOLYSIS-STIMULATED LIPOPROTEIN RECEPTOR – ANTIBODY-DRUG CONJUGATES (LSR-ADC) DEMONSTRATES POTENT ANTITUMOR ACTIVITY TO EPITHELIAL OVARIAN CANCER

Objectives Epithelial ovarian cancer (EOC) is the leading cause of cancer-related deaths among women, thus new treatment option is urgently required. Lipolysis-stimulated lipoprotein receptor (LSR) is widely expressed in EOC and associated with poor prognosis. In this study, we developed antibody-drug conjugate (ADC) targeting LSR as a new therapy for EOC.

Methods We developed novel anti-LSR monoclonal antibodies (mAbs) and LSR-ADC by conjugating monomethyl auristatin E (MMAE) as a payload. Then, we evaluated the expression of LSR in EOC cell lines and antitumor effect of LSR-ADC in vitro and in vivo xenograft models.

Results We evaluated the strong expression of LSR in EOC cell lines (NOVC7C and OVCAR3) and the strong binding affinity of LSR-ADC to theses LSR positive cell lines. Moreover, we demonstrated the rapid internalization of LSR-ADC into tumor cells and trafficked to lysosome. In vitro, LSR-ADC showed a potent antitumor effect against NOVC7C and OVCAR3. Moreover, in the OVCAR3 xenograft model (figure 1A), and patient-derived xenograft (PDX) models of LSR -positive EOC (figure 1B), LSR-ADC significantly inhibited tumor growth.

LSR-ADC also suppresses omental/bowel metastasis in OVCAR3-Luc xenografts (figure 2) and improved median survival.

Conclusions LSR-ADC showed significant antitumor activity against LSR-positive EOC cell lines and LSR-positive EOC tissues. Our preclinical data demonstrated that LSR-ADC is a novel therapy for patients with LSR-positive EOC.

TRANSCRIPTOMIC ANALYSIS OF PROGESTERONE RESISTANCE IN ENDOMETRIAL CANCER CELLS

EP010/#645

OBJECTIVES

To identify differentially expressed genes (DEGs) and signaling pathways in progesterone-resistant endometrial cancer (EC) cells.

METHODS

We conducted a genome-wide transcriptional analysis using RNA sequencing (RNA-seq) to identify DEGs in EC cell lines resistant to progesterone. We also performed functional enrichment analysis to identify gene sets that are enriched in the DEGs.

RESULTS

We identified 151 DEGs in the progesterone-resistant EC cell lines compared to the sensitive cell lines. Gene set enrichment analysis revealed that several pathways, including the MAPK signaling pathway and the PTEN pathway, were significantly enriched in the DEGs.

CONCLUSIONS

Our findings suggest that the MAPK signaling pathway and the PTEN pathway are potential targets for developing new therapeutic strategies for progesterone-resistant EC.