transplantation and she still suffered from a progressive tumor recurrence and died 5 years later.

Conclusion The potential complexity and heterogeneity of cervical carcinosarcoma contributed to the variety of treatment modality. Such rapidly growing tumor may be responsive to radiotherapy and the role of chemotherapy may also be important, but their expected effects on the sarcomatous component may not be ideal. As a result salvage surgical intervention could be a therapeutic option for such locally advanced diseases.

IGCS20_1454

417 KRAS MUTANT UTERINE CARCINOMAS

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Background Inhibitors of KRAS mutations (KRASm) disease have shown efficacy in early clinical studies. Data informing about KRASm targeting in endometrial cancer (EC) are lacking.

Methods ECs (n=8336 with various histologies) were queried for presence of actionable mutations (592 genes) and fusions (Whole Transcriptome Sequencing) using Caris Genomic Profiling database. Comparison was done using Fisher-Exact/ChiSquare (p values) and adjusted for multiple tests by Benjamini-Hochberg (q) and Pairwise nonparametric analysis using Wilcoxon Method.

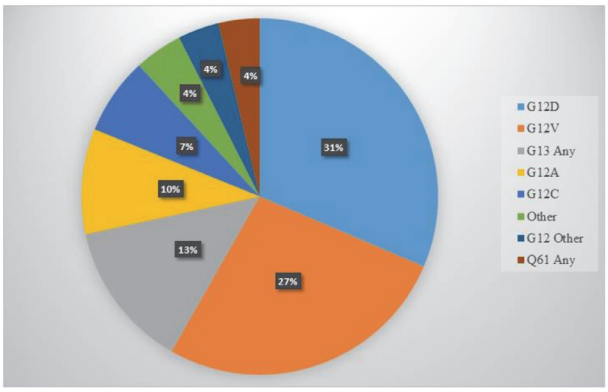
Results a. KRASm is a frequent genotype in Endometrial Cancer.

KRASm were detected in 15.2% of EC cases. Code was most frequently mutated, with G12D (31%) and G12V (27%) being the most common subtypes (figure 1).

b. Biomarkers of immunotherapy response co-occur with KRASm in EC.

MSI-H/dMMR and TMB-H (>10 mt/MB) were seen 36.4% and 42.8% in KRASm and 15.9% and 27.9% in KRASwt, respectively (p>0.05).

c. BRCA1/2 mutations were detected with equal frequency among KRASm and KRASwt. BRCA1/2 mutations were seen in 6% of KRASm vs 4.6% in KRASwt (p=0.033).



Abstract 417 Figure 1 KRAS distribution in entire endometrial cohort

d. KRASm are mutually exclusive of oncogenic fusions. No fusions in FGFR1/3, MET, ALK were detected concurrently with KRASm. Overall, incidence of fusion was extremely low, independent of KRAS status.

Conclusions KRASm EC represents a genomically distinct group of endometrial cancers. Targeted therapy using this biomarker should be explored in clinical trials. Overlap exists with predictors of immunotherapy response, suggesting a possible immunotherapy combination option. Clinical trials to evaluate these strategies are needed.

IGCS20_1455

418 CLINICAL TRANSLATION OF METHYLATED DNA MARKERS OF ENDOMETRIAL CANCER USING TAMPON-BASED DETECTION

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Objective In tampon samples from women with and without EC, we tested methylated DNA markers (MDMs) for EC originally identified through discovery and validation in tissue.

Methods From 2/2013–8/2019, women ≥45 yrs with abnormal or postmenopausal bleeding or biopsy-proven EC were

Abstract 418 Table 1 Distribution of endometrial cancer (EC) histologies and cross-validated sensitivity by methylated DNA marker panel at 95% specificity in PBS/EDTA tampon buffer (N=57 ECs)

EC histology	Endometrioid	Serous	Carcinosarcoma	Clear cell	Mixed
N	20	23	9	3	2
Sensitivity at 95% specificity % (95% CI)	85% (62-97%)	78% (56-93%)	89% (52-99%)	67% (9-99%)	50% (1-99%)

prospectively enrolled for vaginal fluid collection via tampon before endometrial sampling or hysterectomy, respectively. ECs were frequency matched by menopausal status and tampon collection date to benign endometrium (BE) controls. Tampons were placed in preservative buffer; extracted DNA from cell pellet was bisulfite-converted and underwent methylated specific PCR for 29 top performing EC and other solid tumor MDMs (MAX.chr12.52652301, CDH4, EMX2OS, c17orf64, NBPF8, SFMBT2, JSRP1, DIDO1, MAX.chr10.22624479, MPZ, ZNF506, VILL, GATA2, MAX.chr14.103021656, CYTH2, LRRC8D, LYPLAL1, MAX.chr8.145103829, SQSTM1, ZNF323, OBSCN, MAX.chr9.36739811, ZNF90, LRRC41.8188, LRRC34, GDF7, MDFI, EEF1A2, SEPT9). Random forest modeling analysis performed to generate predictive probability of underlying EC.

Results 100 EC and 92 BE were enrolled. The 29-MDM panel highly discriminated between EC and BE (96% (95% CI 89–99%) specificity; 76% (66–84%) sensitivity (AUC 0.88). In 2/2017, the PBS-based tampon buffer was modified to include 50 mmol EDTA. The 29-MDM panel demonstrated greater sensitivity in tampon samples (57 EC; 52 BE) collected into PBS/EDTA buffer (96% (95% CI 87–99%) specificity; 81% (68–90%) sensitivity (AUC 0.90). Among endometrioid and serous histologies, the panel correctly identified 85% and 78%, respectively, and the majority of other subtypes (table 1).

Conclusion Top EC plus other solid tumor MDMs performed with promisingly high sensitivity and specificity in tampon-collected vaginal fluid. PBS/EDTA buffer improves sensitivity.

IGCS20_1456

419 SURVIVAL AFTER MINIMALLY INVASIVE SURGERY IN EARLY CERVICAL CANCER: IS THE UTERINE MANIPULATOR TO BLAME?

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Objectives Minimally invasive radical hysterectomy (MIS-RH) has been associated with decreased survival in patients with early cervical cancer. The objective of this study was to determine whether the use of an intrauterine manipulator at the time of laparoscopic or robotic radical hysterectomy (RH) impacts patient outcomes.

Methods Retrospective study of all patients who underwent treatment of cervical cancer by MIS-RH at two large volume centres between 2006 and 2018.

Results A total of 224 patients were identified at the 2 centres; 115 had surgery with the use of an intrauterine manipulator, while 109 did not. Patients in whom a uterine manipulator was not used were more likely to have residual disease at hysterectomy ($p<0.0001$), positive lymphovascular space invasion (LVSI) ($p=0.02$), positive margins (0.0081), and positive lymph node metastasis (0.0029). Recurrence free survival (RFS) at 5 years was 80% in the no manipulator group and 94% in the manipulator group. After controlling for the presence of residual cancer at hysterectomy, tumor size (microscopic <7 mm or macroscopic ≥7 mm) and high-risk pathologic criteria (positive margins, parametria or lymph nodes), the use of a uterine manipulator was no longer significantly associated with RFS (HR=0.49, $p=0.12$). The only factor which was consistently associated with RFS was tumor size ≥7 mm (HR=9.5, $p=0.03$).

Conclusion The use of a uterine manipulator in patients with early cervical cancer treated with MIS-RH was not significantly associated with patients' risk of recurrence. We identified that the most significant predictor of cancer recurrence in this population was having a macroscopic tumor.

IGCS20_1457

420 TRANSCRIPTOME ANALYSIS OF GLASSY CELL CARCINOMA AND MUCINOUS ADENOCARCINOMA COMPARED WITH SQUAMOUS CELL CARCINOMA OF UTERINE CERVIX

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Objectives Cervical cancer is the fourth leading cause of cancer mortality in women worldwide. Most of cervical cancer are squamous cell carcinoma (SCC), and the standard therapy has developed in SCC. However, therapeutic strategy for minor histological types, such as glassy cell carcinoma (GCC) and mucinous adenocarcinomas intestinal type (Muc) have not yet been established. In this study, we aimed to characterize GCC and Muc compared with SCC by transcriptome analysis.

Methods Cancer tissues before treatment were kept in RNA later® immediately after resections, and frozen in -80 centidegrees until analysis. Total RNAs were extracted by TRIZOL and cDNA library was constructed by SureSelect Strand-Specific RNA library Kit (Agilent). Sequencings were performed by HiSeq2500 (Hiseq SR Rapid Cluster Kit v2, Illumina).

Results We performed RNA sequencing for 10 cervical cancers including 6 SCC, 2 adenocarcinomas usual type (Adeno), 1 Muc, and 1 GCC. Both GCC and Muc were infected by HPV 18, and FIGO stage were IB2 and IIA1, respectively. GCC patient showed poor survival but Muc patient was alive without recurrence. In comparison with SCC, the number of up-and down-regulated genes (5 Fold change) was 1456 and 3326 in GCC, while 877 and 1203 in Muc, respectively. Gene ontology analysis revealed that glycoprotein hormones in GCC and HNF3A pathway in Muc were found to be activated.

Conclusions Specific pathways may be activated in each histological type. Further analysis may provide specific markers for diagnosis and/or prognosis in minor histological type of cervical cancer.