Conclusions: This study sought to 1) determine the feasibility of implementing a brief genetic risk screening tool and 2) assess the unmet need for referral to genetic counseling/testing in a community clinic serving predominantly non-white, low SES patients without health insurance. The preliminary data is promising that a patient administered survey can aid clinicians in identifying patients for referral. It also demonstrates the unmet need in this population, with 32% of these patients meeting criteria for referral. This tool identified an important area of health inequity in cancer prevention in this population.

doi:10.1016/j.ygyno.2019.03.176

Abstract #22

Bridging the actionability gap: Virtual molecular tumor board impact on integrating comprehensive genomic profiling in management of gynecologic malignancies

C. Griffiths[a], R. Valant[a], J. Elvin[b], L. Gay[b], M. Murray[b], N. Almog[b], E. Jimenez[a], E. Chalas[a]. [a]*Division of Gynecologic Oncology, NYU Winthrop Hospital, Mineola, NY.* [b]*Foundation Medicine, Inc., Cambridge, MA*

Objectives: Individualizing care by identifying molecular changes within each patient's tumor is being considered more commonly in gynecologic oncology. While economic and logistic barriers in accessing comprehensive genomic profiling (CGP) testing have diminished, considerable hurdles in interpreting the results and integrating them with clinical information to impact subsequent treatment options for an individual patient still prevail.
Methods: CGP of formalin fixed paraffin embedded (FFPE) tumor samples from 138 patients with predominantly advanced, treatment resistant/refractory gynecologic malignancies (78 ovarian; 42 endometrial; 6 cervical; 13 other rare histologies) by hybridization-capture of up to 315 cancer-related genes (FoundationOne) identified genomic alterations (GA), tumor mutational burden (TMB; mutations/Mb; Low < 6; Intermed 6-19.9; High >20), microsatellite instability status (MS-Stable vs MSI-High) and Clinically relevant (CRGA) defined as GA associated with on-label targeted therapies and targeted therapies in mechanism-driven clinical trials.
Results: 110/139 GM (79.1%) had > 1 CRGA/biomarker. Overall BRCA1/2 mutations were identified in 17/78 (21.7 %) OC. Of 65 OC with LOH scores (51 serous, 8 nonserous, 6 NOS), 34 (52%) were LOH-H; 14/15 (93.3%) mutBRCA and 20/50(40%) wtBRCA OC were LOH-H. All OC were MSS and 1 endometrioid OC was TMB-H (273 muts/Mb). 9/41 (22%) EC were MSI-H and/or TMB-H. Of the remaining cases using TP53 to assign EC molecular classifier, 15/41 (36.6%) had TP53 GA consistent with copy number high/"serous-like" and 17 (42.4%) copy number-low. 5 of 6 cervical adenocarcinomas had CRGA (2 in ERBB2 [HER2], 2 in KRAS, 1 in PIK3CA). In 5/25 (20%) of VTMB cases and 19/108 (17.6%) of cases CGP-matched therapy has been initiated/considered/offered to the patient, most commonly PARPi (54%).
Conclusions: CGP yielded potential molecularly matched therapy options for almost 4 out of 5 GM patients profiled. Approximately 60% of our late stage ovarian cancer population had either a BRCA1/2 mutation or high LOH score, suggesting a population with increased benefit from PARPi therapy. 22% of EC were MSI-H/TMB-H, reflecting a subset which may respond best to immunotherapy. This suggests that the impact information gained in VTMBs may be generalize across the entire group of patients receiving CGP analysis. Lastly, 17% of patients had a plan or discussion of entering matched therapy and/or consideration for a clinical trial.

doi:10.1016/j.ygyno.2019.03.177

Abstract #23

An integrated prediction model for recurrence in endometrioid endometrial cancer

M.D. Miller[a], E.A. Salinas[b], D. Sharma[c], E.J. Devor[a], J. Gonzalez-Bosquet[a]. [a]*University of Iowa Hospitals and Clinics, Iowa City, IA.* [b]*Compass Oncology: The Northwest Cancer Specialists, Portland, OR.* [c]*University of Kentucky College of Medicine, Lexington, KY*

Objectives: Endometrial cancer is the most common gynecologic malignancy in developed countries. Moreover, both incidence and mortality are rising in the United States. A major contributor to mortality is disease recurrence. Prior studies have suggested that certain clinical, immunologic, and radiologic features of tumors are associated with disease recurrence. However, a comprehensive method to assess a patient's risk of recurrence has yet to be developed. Here, we have constructed an integrated prediction model composed of clinical information as well as molecular characteristics of endometrioid endometrial cancer (EEC) in order to predict the risk of recurrence.
Methods: A cohort of 125 patients diagnosed with EEC at our institution was assembled under IRB# 201607815. Clinical data were extracted from patient charts. Primary tumor tissue was available for 62 of these patients. Total tissue RNA was extracted from these tumors. After assessing for concentration and purity, extracted RNAs were submitted for RNA sequencing. Cox proportional hazard regression was utilized to determine an association between the clinical and molecular data with recurrence. Prediction models were then constructed utilizing only variables significantly associated with recurrence, and analyzed utilizing lasso regression method, measured with an area under the curve (AUC).
Results: Of the 125 patients in our cohort, 22 (17.6%) recurred while 103 (82.4%) did not. Average follow up time was 75.6 months. A recurrence prediction model utilizing only clinical data predicted recurrence with an AUC of 0.85 (95% CI: 0.81, 0.89). The addition of mRNA and miRNA expression, somatic mutations, and copy number variation to the clinical data improved the model's predictive power with AUCs varying between 0.89 and 1.
Conclusions: A prediction model of recurrence in EEC based solely on clinical data predicts recurrence with high accuracy. The addition of tumor molecular data to the clinical prediction model further improves the predictive power with AUCs approaching 1. This high accuracy is promising for the eventual clinical application of these prediction models. Additionally, the vast molecular information available from RNA sequencing will permit assessment of the molecular pathways responsible for EEC recurrence, a phenomenon for which reliable mechanistic data are currently unavailable.

doi:10.1016/j.ygyno.2019.03.178

Abstract #24

Molecular markers in recurrent stage I, grade 1 endometrioid endometrial cancers

Marisa R. Moroney[a], Kurtis D. Davies[b], Adam C. Wilberger[b], Jeanelle Sheeder[a], Miriam D. Post[c], Amber Berning[c], Christine Fisher[d], Carolyn Lefkowits[a], Saketh R. Guntupalli[a], Kian Behbakht[a], Bradley R. Corr[a]. [a]*University of Colorado Denver, Department of Obstetrics and Gynecology.* [b]*University of Colorado Medical School, CMOCO Laboratory.* [c]*University of Colorado Denver, Department of Pathology.* [d]*University of Colorado Denver, Department of Radiation Oncology*

Objectives: Stage I, grade 1 endometrioid endometrial cancers have low recurrence rates and often do not receive adjuvant therapy. We compared recurrent cases to matched non-recurrent controls to evaluate for molecular markers associated with higher risk of recurrence in a low risk population.

Methods: A case-control study was performed including all cases of recurrent stage I, grade 1 endometrioid endometrial cancer at a single institution in a ten-year period. Cases were matched to controls in a 1:2 ratio. Controls were matched by age, BMI, weight and stage. Controls had clinical surveillance lasting at least 6 months beyond the longest time to recurrence of the cases. Molecular testing was performed on archival tumor specimens: microsatellite instability testing with Promega MSI Analysis, POLE mutational status with Sanger sequencing, and mutational status of 67 genes with next-generation sequencing using the ArcherDx VariantPlex Solid Tumor kit. Patient and tumor characteristics and molecular results were compared using chi-square and Fisher's exact tests.
Results: 311 stage I, grade 1 endometrioid endometrial cancers were identified; 15 cases had recurrent disease and available tumor specimens. Cases and controls were similar in median age (57 vs. 59, p=0.53), BMI (33.1 vs. 34.2, p=1.00), weight (83.5 vs. 87.1kg, p=1.00) and stage (IA 86.7% vs. 93.1%, IB 13.3% vs. 6.9%, p=0.60). Recurrence location was vaginal in 60% of cases, pelvic in 20% and abdominal in 20%. Mutations identified at high frequency among cases included PTEN (80%), PIK3CA (67%), CTNNB1 (60%). Both CTNNB1 and MSI-H were present at significantly higher rates in cases than in controls (CTNNB1 60% vs. 27.6%, p=0.04, MSI-H 46.7% vs. 13.8%, p=0.03), while PTEN, PIK3CA, KRAS and TP53 all had equivalent distribution (p values 0.68, 0.34, 0.74 and 0.65 respectively). POLE mutations were found in 0.0% of cases vs. 6.9% of controls (p=0.54). Among specimens demonstrating microsatellite stability (MSS), 87.5% of cases vs. 24.0% of controls had CTNNB1 mutations (p=0.003). CTNNB1 wild type tumors were MSI-H in 83.3% of cases vs. 9.5% of controls (p<0.001).
Conclusions: Compared to controls, CTNNB1 mutation is present at significantly higher rates in recurrent stage I, grade 1 endometrioid endometrial cancers and is found most commonly in MSS tumors. This marker may be useful for prognostic risk stratification and adjuvant therapy decision-making in this otherwise low risk population.

doi:10.1016/j.ygyno.2019.03.179

Abstract #25

Combining methylation markers, genomic instability, and next generation sequencing as a panel for endometrial cancer detection via intravaginal tampon collection

A. Sangtani, J. Bakkum-Gamez, B. Kipp, S. Kerr, A. Abyzov, J. Voss, C. Wang

Objectives: We aimed to develop and evaluate a molecular panel for the early detection of endometrial cancer (EC) from intravaginal tampons by methylation markers, genomic instability, and next generation sequencing (NGS).
Methods: Tampons were collected from women undergoing hysterectomy for EC and women undergoing hysterectomy for benign indications. Extracted tampon DNA underwent the following: 1) low-coverage whole genome sequencing (LC-WGS) using the Illumina HiSeq 2500 according to 51 base-pair single-end sequencing protocol and evaluated for copy number gains and losses (genomic instability) using an in-house bioinformatics pipeline (http://bioinformaticstools.mayo.edu/research/wandy/); 2) pyrosequencing to measure promotor methylation of HOXA9, RASSF1, and CDH13; and 3) NGS using PCR amplification primers followed by Ion Torrent and orthogonal Illumina covering 19 genes commonly found in EC. Sensitivity and specificity for each test and combinations of tests were calculated.
Results: Data from all 3 molecular approaches is presented in Table 1. Sensitivity and specificity for EC via methylation was as follows: 25 benign and 36 EC tampon samples had HOXA9 methylation (42% sensitivity; 100% specificity); 22 benign and 35 EC tampon samples had RASSF1 methylation (40% sensitivity; 100% specificity); 20 benign and 36 EC tampon samples had CDH13 methylation (39% sensitivity;100% specificity). Genomic instability was identified in tampons from 9 (64%) of 14 ECs and 1 (11%) of 9 benign endometrial controls. 18 benign samples and 21 EC samples underwent NGS with mutations detected in 11 (52%) EC samples and 3 (17%) benign samples. When combining the three tests, 11/12 (92%) ECs and 1/7 (14%) controls were positive for either genomic instability, methylation or NGS, resulting in a sensitivity of 92% and specificity of 86%. Interestingly, the benign endometrial control that was positive for genomic instability had an underlying leiomyosarcoma uncovered at hysterectomy.
Conclusions: When combined, genomic instability, methylation, and NGS have a high sensitivity and specificity in detecting EC; however, the combination of genomic instability and methylation provides comparably high sensitivity. Validation of the molecular biomarker combinations and further methylation marker discovery, especially among the rarer EC histologies, are needed to further develop a tampon-based EC detection test.

doi:10.1016/j.ygyno.2019.03.180

Abstract #26

MLH-1 hypermethylation is associated with lower recurrence free survival in patients with endometrial cancer

C. Carr[a], J. Marquard[b], M. Radeva[c], A. Priyadarshini[a], M. AlHilli[a]. *[a]Cleveland Clinic Foundation, Department of Gynecologic Oncology, Cleveland, OH. [b]Cleveland Clinic Foundation, Department of Quantitative Health Sciences, Cleveland, OH. [c]Cleveland Clinic Foundation, Genomic Medicine Institute, Cleveland, OH*

Objectives: Approximately 25% of endometrial cancers (EC) are characterized by microsatellite instability due to MLH1 promotor hypermethylation.This study evaluates the prognostic importance of MLH1 hypermethylation among EC patients undergoing universal screening for Lynch Syndrome (LS).
Methods: From August 2012- August 2016, all patients with EC underwent screening for LS using immunohistochemistry (IHC) for mismatch repair (MMR) proteins. Tumors with lack of expression of PMS2 or MLH1 were assessed for MLH1 promotor methylation. Tumors were classified as MMR-I (intact expression of MMR proteins) and MMR- DM (MMR deficient due to MLH1 methylation) Clinical and pathologic factors associated with MMR-DM evaluated using univariate and multivariate analysis. Overall survival (OS) and recurrence free survival (RFS) assessed using cox proportional hazards for patients with at least 2 years of follow up.
Results: Among 720 EC samples evaluated for MMR, 516 (71.6%) were MMR- I, 172 (23.8%) MMR-DM and 32 (4.4%) MMR-DU. Patients with MMR-DM tumors were older (p<0.001) and had a lower BMI (p=0.03) vs. MMR-I patients. MMR-DM tumors were higher grade (grade 2/3,p=<0.001), had positive LVSI (p<0.01), and myometrial invasion >50%(p=0.002). There was no significant difference in stage, adnexal involvement, or cervical stromal invasion between groups. Lymphadenectomy was performed in 316 patients (43.9%), specifically 44.2% of MMR-DM and 41.8% of MMR-I groups. On multivariable analysis, older age (OR 1.03, CI (1.01-1.05), p=0.001), endometrioid histology (OR 5.60, CI (1.71-17.88), p=0.004), and tumor size < 2 cm (OR 0.50 CI (0.31-0.80), p=0.004) were independently associated MMR-DM. Recurrences were observed in 11.2%(19/169) MMR-DM and 5.9% (30/509) of MMR-I patients (p=0.02). Evaluating by FIGO stage, recurrences at early stage (I/II) were seen in 6.6% of MMR-DM (9/137) vs. 2.9% of MMR-I (12/421)