

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.

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Abstract #22

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

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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.

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Abstract #23

An integrated prediction model for recurrence in endometrioid endometrial cancer

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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.

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Abstract #24

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

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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.