Abstract #19

Positron emission tomography as an imaging biomarker after chemoradiation and immunotherapy for cervical cancer patients treated on GOG 9929

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Objectives: We investigated the role of the post immunotherapy positron emission tomography (PET) on survival for cervical cancer patients treated with standard chemoradiation (CRT) followed by ipilimumab on GOG 9929 to better understand its potential role as an imaging biomarker for future clinical trial directions and therapy response feedback.

Methods: Locally advanced cervical cancer pateints with positive nodes were prospectively erolled and treated with 6 weekly doses of cisplatin (40 mg/m2) and extended field radiation therapy. A diagnostic PET scan was required as a pretreatment screening imaging tool. After 2-6 weeks, patients were screened radiographically, and if there was no progression of disease, sequential ipilimumab was given at the following dose levels: dose level 1: 3mg/kg, dose level 2: 10mg/kg, and an expansion cohort of 10mg/kg. After the sequential ipilimumab, patients had a post therapy PET scan at 4-12 weeks. Further investigation of the cervix pre and post therapy PET scan used two metrics: (a) standardized uptake value (SUV), and (b) ratio of post-therapy SUVmax: pre-therapy SUVmax. We then correlated the PET response with 1-year disease free and overall survival data.

Results: Thirty-two of 34 enrolled patients initiated study treatment, of whom 15 pts have complete pre and post therapy PET data, with at least 1 cycle of ipilimumab. Of the remaining 17 patients without a post-IPI PET scan, 4 patients completed a full course of treatment and 13 patients went off study (3 for disease progression, 5 patient refusal, 3 for toxicity, and 2 for other reasons). Of the 15 patients with post-ipilimumab PET scan data, 93% were squamous histology; all had pelvic lymph nodes, with 47% additional PAN. All 15 pts completed CRT, with ipilimumab completion rates of 73% with 4 cycles, 13% with 3 cycles, 7% with 2 cycles and 7% with 1 cycle. There were no minor or major RT quality deviations. 11 had a metabolic CR, 2 had stable disease, and 2 had a PR. With a median follow up of 12 months for these 15 pts, 1 patient with CR on PET had a recurrence. Overall, the DFS at 12 months is 93% and OS at 12 months is 100%.

Conclusions: PET has been shown to be predictive of tumor response and survival in cervical cancer treated with standard chemoradiation (CRT). There is a lack of data on using PET as an early surrogate to response or survival after immunotherapy across disease sites. This study is the first to describe the use of PET imaging as a predictive imaging biomarker for cervical cancer after immunotherapy. Our data suggests that the post therapy PET could be used as an early predictor of response and a potential biomarker tool after immunotherapy for clinical trials and practice.

doi:10.1016/j.ygyno.2019.03.174

Abstract #20

Predictive utility of qualitative feature clusters of pretreatment CT imaging compared to traditional PET/CT to predict treatment outcomes in locoregionally advanced cervix cancer

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Objectives: To compare the predictive ability of computer aided detection (CAD) of quantitative radiographic features against the predictive value of traditional pre-treatment PET/CT in primary treatment of locally advanced cervical cancer (LACC).

Methods: A dataset of 97 patients with LACC (IB2, IIA2 to IVA) was assembled. RECIST 1.1 criteria was used to classify post-therapy imaging as either a "favorable response" (complete or partial response) or "poor response" (stable disease, progressive disease, or partial response with recurrent disease within 12 months of treatment). A CAD scheme was applied to segmented tumors labeled by radiologists on pretreatment CT; the most discriminative features were calculated by a computer learning technique to construct a predictive model of treatment response. This model was assessed by computing the area under the receiver operating characteristic (ROC) curve method (AUC). A patient subset (n=49) with both pretreatment PET/CT and surgically sampled lymph nodes was identified. Predicted response to chemoradiation by CAD modeling was calculated and compared to the both the predictive value of PET/CT and surgical lymph node status by comparing the respective AUCs.

Results: Descriptive analysis of demographics including age, stage, histology, and treatment was performed between responders (n=31) and non-responders (n=18); no significant differences were found between groups. When compared to surgical pathology, PET/CT has 88% sensitivity and 29% specificity in predicting pelvic lymph node status. In predicting para-aortic lymph node status, PET/CT has 75% sensitivity and 88% specificity. When PET/CT reported either positive pelvic or para-aortic lymph nodes, the AUC using CAD programming is 0.60 (95% CI: 0.43 – 0.77) for treatment response. Likewise, positive surgical lymph nodes has an AUC of 0.60 (95% CI: 0.43 – 0.77). The AUC is 0.64 (95% CI: 0.46 – 0.81) for the new imaging method in predicting treatment response. While the new CAD model performs slightly better than both PET/CT and surgical nodal status, the difference in AUC (Δ0.036, 95% CI -0.167 – 0.238) is not statistically significant (p=0.73).

Conclusions: Predictive capability of CAD quantitative feature modeling performs as well as traditional pre-treatment PET/CT to predict response to chemoradiation for LACC. Incorporating use of CAD quantitative feature analysis into a pre-treatment algorithm warrants further development to enhance the performance of pre-treatment PET/CT and treatment response.

doi:10.1016/j.ygyno.2019.03.175

Abstract #21

Implementing genetic risk assessment in a community free clinic

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Objectives: The purpose of this study was to implement a brief screening tool to identify patients with an increased risk of a hereditary cancer syndrome who might benefit from referral for genetic counseling/testing.

Methods: We adapted a bilingual screening tool developed at the UCSF Cancer Risk Program that is compliant with NCCN and ACOG guidelines. It relies on fact recall that patients can complete independently assuming low health literacy. Clinic providers were briefed on the project and distribution commenced in April of 2017. The questionnaires were scored and entered into a secured database.

Results: Between April 2017-January 2018, a total of 98 questionnaires were collected. Ages ranged from 19-67. Thirty-two percent (32%) of the patients identified as Hispanic. Of those who identified as non-Hispanic, only 3 of these identified as White, the others identified as Asian or Black. Twenty-one percent (21%) of the forms were completed in Spanish. First degree relative with ovarian cancer and/or multigeneration presence of breast cancer accounted for 11% of the patients who screened "positive" for referral to further genetic counseling.

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

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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.

doi:10.1016/j.ygyno.2019.03.177

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.

doi:10.1016/j.ygyno.2019.03.178

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.