RRSO. Further study of cancer risks associated with gHRD/non-BRCA mutations is necessary to guide recommendations for risk-reducing surgery.

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Abstract #34

Exploratory analysis of somatic BRCA mutations in endometrial cancer and its clinical implications

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Objectives: Germline BRCA mutations in ovarian cancer patients are associated with improved response to chemotherapy and survival. With the increased use of molecular profiling, many women with endometrial cancer (EC) have been found to harbor somatic BRCA mutations, the significance of which is unknown. The goal of this study is to evaluate the prognostic and predictive features of somatic BRCA mutations (sBRCA+) in EC.

Methods: An IRB-approved, retrospective review of patients with molecularly profiled, EC from 3 academic institutions between 2010 – 2017 was performed. Summary statistics were used to describe demographic and clinical characteristics. Analysis included a comparison of response and survival following treatment with platinum-based chemotherapy among sBRCA+ and somatic BRCA wild-type (sBRCAwt) patients.

Results: Of the 109 patients included, 12.8% were sBRCA+ (Table). Of these, the median age was 47.5 yrs and 62% were endometrioid. This was not statistically different from the 95 sBRCAwt patients, of which the median age was 50 yrs and 66% were endometrioid (all $p>0.05$). sBRCA+ pts were more likely to have microsatellite instability-high (MSI-H) tumors than sBRCAwt (50% vs 17%, $p=0.01$). Of the 45 patients with complete chemotherapy data available, the median progression-free survival (PFS) was 26 mo. There was no difference in the distribution of sBRCA+ patients above and below the median PFS (23% vs 18%, $p=0.69$). The median overall survival (OS) for the 108 pts with evaluable data was 30.4 mo. There was no statistical difference in the distribution of sBRCA+ patients above and below the median PFS (19% vs 8%, $p=0.11$). Of the 14 sBRCA+ patients, 4 had germline mutation testing and all 4 were negative.

Conclusions: Among EC patients, somatic BRCA mutations are relatively uncommon. sBRCA+ patients are more likely to have MSI-H tumors, but no other clinical factors were associated with these mutations. While there appears to be a trend towards improved OS among sBRCA+ patients, this was not statistically significant, likely due to the small numbers in our cohort. Data collection continues with recruitment of additional sites to improve the power of this study.

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Abstract #35

Pilot early detection trial of longitudinal combined biomarker assessment for ovarian cancer risk among BRCA affected women

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Objectives: Screening for ovarian cancer with CA-125 using a set cut off for normal values has inadequate sensitivity for clinical use. A risk of ovarian cancer algorithm which systematically interprets longitudinal changes in CA-125 values to detect the first significant rise above a woman's baseline has shown promise. The objective of this pilot early detection study was to assess personalized risk using an expanded longitudinal algorithm that detects the first significant rise above a woman's baseline in either CA-125 or HE4.

Methods: BRCA1/2 affected women who had chosen to defer prophylactic oophorectomy were recruited to participate in a prospective early detection trial. Patients self-allocated into two groups: 1. standard of care surveillance according to NCCN recommendations and 2. combined biomarker surveillance using CA-125 and HE4 assayed every 4 months. Biomarkers were evaluated using the Risk of Ovarian Cancer Algorithm (ROCA) which calculates the probability of having a change-point in the biomarker, used as a surrogate for having undetected ovarian or fallopian tube cancer. ROCA risk scores were calculated for the individual markers as well as for the combination. Risk estimates were categorized as normal, intermediate, and elevated. Post-test follow up for elevations in any individual risk score (CA-125, HE4 or combination) was trans-vaginal sonography (TVS) for intermediate risk, and TVS and review by gynecologic oncologist for elevated risk.

Results: 149 BRCA 1 and 2 affected women enrolled in the ROCA biomarker arm of the screening study and 409 blood draws over 1.4 years provided 409 time points for analysis. Abnormal individual risk scores were identified in 95 (23%) of 409 time points; 68 (16.7%) were intermediate and 27 had elevated risk scores (6.7%). Retrospective analyses of the combination CA125/HE4 ROCA score showed that 50 time points (12.2%) had a rise over time in one or both markers with an elevated combined risk score. One stage IIA fallopian tube cancer with serous tubal intra-epithelial cancer (STIC) was identified from the study group at patient-initiated risk reducing salpingo-oophorectomy (RRSO). Nonetheless, in that case the combined ROCA and the individual HE4 ROCA reported elevated risks.

Conclusions: Combination biomarker risk scoring is feasible, and this preliminary evaluation appears to show improved specificity compared with individual risk scoring, reducing the number of false positives by about one-half. Further evaluation, particularly to clarify potential confounders, is needed before firm judgments can be made about mitigating the clinical imprecision of CA 125 testing when using this novel testing method.

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Poster Presentations

Poster #1

Predictive factors of genetic referral for advanced, epithelial ovarian cancer patients at a Single-Institution Cancer Center

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Objectives: Given 15-20% of invasive epithelial ovarian cancer (EOC) cases are attributed to genetic mutations, the Society for Gynecologic Oncology (SGO), National Comprehensive Cancer Network (NCCN)