controlled medical or psychiatric conditions precluding weight loss intervention, or a second active malignancy. Women with BMI ≥30kg/m2 were offered referral for medical management and women with obesity-related comorbidities or BMI ≥40kg/m2 were also offered surgical consultation. A historic control group was identified during the enrollment period. All patients were followed for a maximum of 2 years. Descriptive statistics and univariate analyses were performed using statistical software.

Results: One hundred and fifty-three women were enrolled in the intervention group and compared to a control group of 104 women. Mean initial age was 55 years (SD 8), mean initial BMI was 42 kg/m2 (SD 9), with no significant differences between groups. Median follow-up time was 18 months (IQR 12-24). One hundred forty-five women (95%) were offered referral for medical management and 63 (43%) accepted, of which 23 (37%) attended the appointment and 18 (29%) initiated a weight loss plan. One hundred and two women (67%) met criteria for surgical management and 45 (44%) accepted, of which 6 (13%) attended the appointment and 4 (9%) underwent bariatric surgery. Initial BMI was higher for women accepting versus declining referral (44.4 vs. 41.4 kg/m2, P=0.048). Of all 257 women, 74 demonstrated BMI loss >1kg/m2 (29%), 107 (42%) remained stable within 1kg/m2, and 76 (30%) demonstrated BMI gain >1kg/m2. Both women who accepted or declined the referral in the intervention cohort demonstrated BMI loss compared to the control group which demonstrated BMI gain (-0.82 vs. -0.50 vs. +0.50 kg/m2, P=0.041). Women in the intervention group were more likely to lose weight (54 vs. 39%, P=0.016). Women in the control group were more likely to experience weight gain (59 vs. 41%, P=0.005), and were almost twice as likely to gain >1kg/m2 (40 vs. 22%, P=0.001).

Conclusions: Obese endometrial cancer survivors should be referred for medical and surgical obesity management programs, as referral is associated with better long-term weight control.

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Abstract #30

Drug efficacy testing of targeted therapies in endometrial cancer organoids is partially predicted by cancer gene mutation data (Correct)

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Objectives: To determine the efficacy of targeted therapies based on genomic profiling of endometrial cancer patient derived organoids (PDO).

Methods: Genomic analysis was performed on previously derived endometrial cancer PDO lines. The panel consisted of 761 genes selected for their known or suspected associations with cancer. Drugs targeting the mutated genes were identified through an online search using clinicaltrials.gov. If no FDA-approved drugs were identified, agents were chosen using preclinical data. The following drugs were utilized in this study: Palbociclib, Everolimus, LY3039478, Mocetinostat, Trametinib, Deltarasin, LY294002, AZD5363, MK-1775, Sorafenib, PRI-724, Olaparib, Ceritinib, Critozinib, GSK126, Oxaliplatin, Paclitaxel, and VS-5584. A single concentration of each drug was selected to reflect plasma concentrations achieved in therapeutic trials. Cryopreserved, accutase-treated organoids were thawed, suspended in serum-free media, and plated on Day 0. On Day 1, targeted drugs and control media were added to each well. On Day 6, viability assays were performed using CellTiter Glo reagent and read using a Promega luminometer. The average percent inhibition for each drug was calculated and considered clinically meaningful if it was greater than 50%. Statistical analysis was performed using Student's t-test. A two-tailed p-value less than 0.05 was considered significant.

Results: Eleven previously derived endometrial cancer PDO cultures underwent genomic testing. Genomic analysis revealed an average of 43 non-synonymous mutations per PDO culture, ranging from 13 to 320 mutations. Three of these cultures (EN-734, -768, and -793) were serially passaged and underwent targeted therapy assays based on their genomic profile. For all three organoid lines, expected inhibition based on specific target mutations was 50% (15/30). Cases where the presence of mutations perfectly predicted expected inhibition were noted with LY294002, AZD5363, PRI-724, and Olaparib. There were also cases where there was unexpected resistance despite the presence of gene mutations, such as for Everolimus and VS-5584. Additionally, 44% (8/18) of agents in the drug panel produced inhibition despite the absence of mutations (Table 1).

Conclusions: These results suggest that the mutational landscape may successfully predict sensitivity to certain targeted agents but cases of unanticipated resistance or sensitivity are not uncommon. A pre-treatment empirical ex vivo assessment of a drug's anti-tumor activity using a PDO model could be helpful in the selection of the most active agents for each patient. Further research reflecting current treatment standards such as combination chemotherapy will be needed to more accurately reflect what occurs in the clinical setting.

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Abstract #31

Comparison of effectiveness of two strategies to identify Lynch Syndrome in women with endometrial cancer

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Objectives: The purpose of this study is to estimate the differences in Lynch Syndrome (LS) case identification between two strategies of IHC testing, universal immunohistochemistry (IHC) testing for all endometrial cancers (EC) and referral -based testing for EC patients under age 60.

Methods: This is a retrospective study of all EC cases from two regions of a large California healthcare system with differing LS screening protocols. There were 1,399 cases from Northern California (NC) over 19 months, where IHC testing is physician ordered (non-automated) for all cases of EC under age 60 and for those age 60 and older with family or tumor features suggestive of LS. There were 646 cases from Southern California (SC) region over 14 months, where IHC is universal and automated for all cases of EC. The following variables were compared between the two institutions for all EC cases: demographics, tumor characteristics, IHC results, and personal and family history of LS cancers. Among all abnormal IHC cases, data was collected for referral to genetics and genetic testing.

Results: Of the NC cases, 544 women (39%) were less than age 60 and 281 (52%) of them had IHC testing. The IHC results were abnormal in 52 cases (10%) and 18 (3%) had no methylation of MLH1 promoter, suggestive of Lynch Syndrome. In SC, 279 of the 646 women (43%) were under age 60 and 242 (87%) had IHC testing with 54 (19%) abnormal results and 15 (5%) abnormal after methylation testing. There were 855 cases in women older than age 60 in NC and 95(11%) had IHC testing, 23 (3%) were abnormal and 3 (<1%) abnormal after methylation testing. There were 367 cases in women older than age 60 in SC, and 300 (82%) had IHC testing with 96 (26%) abnormal results and 8(2%) abnormal after methylation testing. A genetics referral was placed for 118 (22%) women in NC and 45 (16%) women in SC underage 60, and 88 (10%) women in NC and 40 (10%) in SC over age 60. As a result of abnormal IHC testing, Lynch syndrome was diagnosed in 15(1%) women in NC and 10(1.5%) in SC. There were 6 (1%) cases in NC and 4 (1%) cases in SC for women under age 60, and no cases in NC and 2(<1%) cases in SC for women over age 60. For women referred to genetics for reasons other than abnormal IHC, LS was detected in women under 60 in 5 (1%) and 3 (1%) of cases and for women over 60 LS was detected in 4(<1%) and 1(<1%) of cases in NC and SC, respectively. When comparing detection of LSin the two regions., there were no significant differences in rates of overall detection (p=0.36) nor were there differences in detection in women less than 60 (p=0.65) or over 60 (p=0.44).
Conclusions: Although universal IHC screening of EC would be expected to identify more cases of LS than age based IHC screening, there was not a difference in the detection of lynch syndrome in EC in two regions of a large California health care system with these different policies.

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Abstract #32

Universal immunohistochemistry testing in endometrial cancer tumors maximizes Lynch Syndrome identification among affected individuals

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Objectives: Universal colorectal cancer (CC) screening for Lynch syndrome (LS) via mismatch repair proteins (MRP) immunohistochemistry (IHC) testing has become commonplace. Although endometrial cancer (EC) has been proven to be the sentinel malignancy in many women diagnosed with LS, universal screening of EC has not been widely adopted. We report our experience with the detection of Lynch syndrome comparing universal screening for both EC and CC in a large non-profit health plan.
Methods: We instituted universal CC screening in April 2014, and added universal EC screening in November 2015. All tumors are screened via IHC for presence of the four MRP, reflex methylation testing of MLH1 is employed where indicated. We tabulated all abnormal IHC and subsequent somatic and germline testing results to assess the frequency of detected LS cases amongst females with EC or CC, and males with CC based on age at diagnosis. Statistical analysis was performed using Pearson's Chi-square, and relative-risk.
Results: We performed IHC on 6164 tumors in 5804 patients (EC=1421, female CC= 2157, male CC= 2406). Abnormal IHC results were found in 982 (15.9%) tumors (347 EC, 383 female CC, 251 male CC), occurring more frequently in the EC cohort (24.4% vs 17.8% vs 10.4%, p<0.001). Mismatch repair (MMR) pathogenic/likely pathogenic gene mutations were identified in 114 patients (2%). Of the germline mutations, 35/114 (30.7%) were in patients >60 (EC 21%, female CC 27%, male CC 36%). We observed a slightly higher but not statistically significant detection of LS among women with EC than CC (2.9% vs. 2.5% vs. 2.6%, p=.80). In women ≤60 at the time of cancer diagnosis the relative risk of LS in those with EC (4.56, 95% CI 2.54-8.42) was equivalent to those with CC (7.17, 95% CI 4.49-11.44). The relative risk of LS among women with either EC or CC was higher than among male CC patients (2.90, 95% CI 1.97-4.50).
Conclusions: Our universal IHC testing results show that a larger proportion of EC tumors yield abnormal results than CC tumors. In our experience MMR gene mutations were more frequently detected among women screened via EC than CC. Routine screening in all age groups improves detection in patients who might otherwise be excluded from guideline-based approaches. Adding EC to the universal screening program identified Lynch in 25% of patients that might have otherwise been missed. Our experience confirms that universal EC screening for MRP offers the optimal management approach to identify patients with Lynch syndrome and inform future screening, detection and prevention efforts for themselves and their at-risk relatives.

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Abstract #33

Patterns of risk reducing surgery in germline homologous recombination deficiency/non-BRCA mutation carriers

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Objectives: To describe clinicopathologic characteristics of women with germline HRD/non-BRCA (gHRD/non-BRCA) mutations to those with BRCA mutations who choose to have risk reducing surgery (RRSO).
Methods: Women with pathogenic germline mutations associated with ovarian cancer who had risk reducing surgery were identified in a women's cancer program at a single institution from 1/2000- 6/2017 in a IRB approved study. All patients were asymptomatic with normal physical exams, CA 125 values and imaging prior to RRSO. Demographics and clinico-pathologic characteristics were extracted from the medical records. Continuous variables were analyzed using Mann-Whitney U tests and categorical variables were analyzed with Student's T-tests.
Results: 14 gHRD/non-BRCA (APC, ATM, BARD1, BRIP1, CHEK2, MUTYH, PALB2, PMS2, and RAD51C) and 259 BRCA1/2 mutation carriers were identified. There was no difference between gHRD/non-BRCA versus BRCA mutation carriers in age at genetic testing (47 v. 45 years, p=.27) and age at RRSO (48 v. 46 years, p=.50). Time between diagnosis and RRSO between the two groups was statistically significant (343 v. 169 days, p=.05). A family history of breast or ovarian cancer, and a personal history of breast cancer, was common in both cohorts. GHRD/non-BRCA mutation carriers more frequently had documented official genetic counseling (64% v. 31%, p=.03). Occult carcinoma, STIC, or dysplasia were only seen among BRCA mutation carriers (5%). Two gHRD/non-BRCA patients had interval salpingectomies compared to 11 BRCA mutation carriers. GHRD/non-BRCA mutation carrier were less likely to have prophylactic mastectomies (21% v. 65%, p=.01) but just as likely to have concomitant hysterectomy as BRCA mutation carriers.
Conclusions: Germline HRD/non-BRCA mutation carriers have more genetic counseling compared to women with germline BRCA mutations. Despite similar family and personal history of breast cancer, they are less likely to have prophylactic mastectomies than BRCA mutation carriers. No gHRD/non-BRCA mutation carriers had occult cancer at RRSO despite longer interval between testing and