excluded. The number of dispensed VE prescriptions was used to categorize women into 3 groups: "4 or more," "1-3," and "0".
Results: Approximately 450,000-530,000 women in each year were included. The mean number per year of patients that dispensed "4 or more" was 11,327, "1-3" was 30,376, and "0" was 454,516. The overall average yearly disease incidence of endometrial hyperplasia/cancer in the "4 or more," "1-3," and "0" groups was 9.96, 10.25, and 9.96 (per 10,000 women), respectively.
Conclusions: The data suggests using unopposed topical vaginal estrogen is not associated with an increased risk of endometrial hyperplasia or cancer.

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Poster #45

Synchronous cervical and vulvar dysplasia – High likelihood in women who are immunocompromised

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Objectives: Dysplastic lesions of the cervix and vulva have similar risk factors. However, the incidence of cervical dysplasia is 10 times more than that of vulvar dysplasia suggesting high risk HPV induced transformation of the vulvar epithelium occurs less often than cervical epithelium. This implies there are novel factors required for the progression normal vulvar to dysplasia. The aim of this study was to evaluate the clinicopathologic characteristics that predispose patients to synchronous cervical and vulvar dysplasia/cancer.
Methods: We performed a case-control study on patients seen from January 2010 to October 2013 and diagnosed with cervical intraepithelial neoplasia (CIN) or cancer on excisional biopsy (cold knife cone or loop electrosurgical excision procedure) who also developed synchronous vulvar intraepithelial neoplasia or cancer. Clinical variables predisposing women to cervical and/or vulva dysplasia were evaluated. Number of lifetime sexual partners and age at coitarche were not readily available for statistical analysis. SPSS software was used to calculate the odds ratio (OR) for binary dependent variables.
Results: The average age was 37 year old in both subgroups of women with synchronous lesions as well as those with cervical dysplasia alone. Approximately 43% of the women who had cervical dysplasia alone had a BMI > 30kg/m2 compared with 25% in those with synchronous lesions. There was no difference in the odds ratio of smoking, alcohol use, illicit drug use, OCP use, parity, hypertension, hyperlipidemia, diabetes and depression between women with cervical dysplasia alone versus those with cervical and vulvar dysplasia/cancer. The only statistically significant findings were found in those with immunosuppression or an HIV infection with an odds ratio of 18.9 (95% CI 7.9676 to 44.7392 with P value < 0.001).
Conclusions: Immunocompromised patients have a significantly higher likelihood of developing synchronous cervical and vulvar dysplasia. Our findings underscore the necessity of a complete examination of the lower genital tract especially in those who are immunocompromised.

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Poster #46

Invasive vulvar Extramammary Paget's Disease in the United States

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Objectives: Extramammary Paget's disease (EMPD) is an intraepithelial neoplasm commonly found in the vulva. Large national databases are useful due to disease rarity, particularly for invasive forms of EMPD. We sought to assess the incidence, treatment modality, and outcomes in patients with invasive vulvar EMPD.
Methods: The National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) population-based cancer registries was searched for patients diagnosed with invasive Extramammary Paget's disease (ICD-O-3 histology code: 8542) of the vulva (ICD-O-3 topography code: C51.0-51.9) between 1992-2014. Incidence rate, demographics, survival, synchronous and secondary malignancies were analyzed.
Results: From 1992-2014, 1110 patients were diagnosed with invasive vulvar EMPD: of those, 74.0% had localized disease, 13.2% regional disease, 1.5% distant disease and 11.3% were unstaged. The overall annual incidence of invasive vulvar EMPD was 0.35 per 100,000 person years: rates have increased more than 2-fold since 1992 (1992: 0.19 per 100,000 person years to 0.50 per 100,000 person years in 2014). Surgery was the primary treatment for most (n=898, 80.9%) patients, with 24 (2.2%) having surgery and radiation. In 4 cases (0.4%) radiation alone was used: 184 (16.6%) did not undergo radiation or surgery. Five-year cancer specific survival (CSS) overall was 94.2% and was closely related to stage. Patients with localized disease or those who were unstaged had the best survival (P<0.0001). Patients who presented with distant disease had significantly worse outcomes vs. local disease (HR: 85.911 (29.8-248) p<0.0001). CSS was 95.7% in patients undergoing surgery alone, 90.0% observation, and 57.9% surgery and radiation (p<0.0001). Synchronous cancers (diagnosed within 12 months of EMPD) were observed in 30 cases (2.7%), and 161 patients (14.5%) developed a secondary malignancy (diagnosed >12 months from EMPD) malignancy. The most common synchronous and secondary cancers were gastrointestinal, breast, or genitourinary.
Conclusions: The incidence of invasive vulvar EMPD has increased over time. Cancer specific survival is excellent for localized disease, but those with metastatic disease are in need of novel therapies: radiation appears to have limited benefit. A large number of EMPD patients (14.5%) will develop a secondary malignancy and should undergo site specific preventative health screens during recurrence surveillance.

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Poster #47

Primary chemoradiation therapy for locally advanced cervical cancer: Outcomes and disparities

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Objectives: To identify disparities in timely receipt of primary chemoradiation in patients with locally invasive cervical cancer.
Methods: The National Cancer Database (NCDB) was queried to identify stage II-IVA cervical cancer patients diagnosed in the United States between 2004 to 2015 and receiving chemoradiation (CRT) as primary treatment. Patients were divided into those whose duration of CRT treatment was <=8 weeks and >8 weeks. The primary outcome was overall survival. Patients were stratified by demographic factors including age, race/ethnicity, insurance status, distance from hospital, and hospital setting, as well as clinical factors including stage and grade.
Results: We identified 21,579 women. 11,265 women (52.2%) completed chemoradiation therapy in <=8 weeks. The median OS was longer for patients who completed CRT in <=8 weeks (95.1 vs 73.7 months, p $63,000. Patients with Medicaid/Medicare insurance (OR 0.85, 95% CI 0.80-0.90) were also less likely to complete CRT in <=8 weeks compared to those with private insurance. Patients with stage III disease (OR 0.81, 95% CI 0.77-0.85) were less likely to complete CRT in <=8 weeks than those with stage II disease. Age, distance from

hospital, hospital setting, and tumor grade were not associated with any difference between groups.
Conclusions: We confirmed an improved overall survival for patients completing primary CRT within 8 weeks. However, with only 52% of patients with locally invasive cervical cancer receiving primary CRT within the recommended 8 week duration, much work remains to be done to bridge this disparity.

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Poster #48

Clinical factors associated with overall survival in patients with uterine sarcoma

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Objectives: Uterine sarcomas (US) comprise a rare, yet diverse group of clinically aggressive tumors with a high incidence of pelvic and distant recurrence. Our objective was to identify factors important in overall survival (OS) in patients with US.
Methods: We performed a retrospective chart review for all patients with a diagnosis of US seen and treated at our single institution between 1990-2008. Demographic, clinicopathologic, treatment, and survival data were extracted from the medical record and analyzed. Cox proportional hazards models were used for OS analyses. Multivariable analysis was used for association analyses. All statistical testing was two-sided and significance was determined at the 5% level using standard software.
Results: Our study included 245 patients with US treated from 1990-2009, including malignant mixed mullerian tumors (MMMT)(54.3%), leiomyosarcomas (LMS)(18.4%), endometrial stromal sarcomas (EES) (13.9%), undifferentiated stromal sarcomas (USS)(6.1%), and a mix of other cell types (other)(7.3%). Most patients underwent surgery (95.5%). Most were stage I (40.8%) with 28.2% un-staged. The percentage of patients who underwent chemotherapy and radiation were similar at 33.5% and 34.3%, respectively. At the time of analysis, 44.1% of patients had recurred and 69% are dead. The median OS was 38 months. Univariate analysis for OS demonstrated age (HR=1.04), stage (HR=1.58-7.77), elevated CA125 (HR=1.59), elevated WBC (HR=2.09), elevated platelets (HR=2.40), cell type (MMMT-HR=referent, ESS-HR=0.33, LEIO-HR=0.80, USS-HR=1.33) and not receiving a hysterectomy (HR=2.99) to be associated with worse outcomes ($p<0.01$). Multivariate analysis confirmed age, stage, elevated WBC, elevated platelets, and not undergoing hysterectomy to be associated with worse OS ($p<0.01$).
Conclusions: OS for patients with US is poor with a median survival of just over 3 years. Stage 4 US were associated with a 7 times increased risk of death compared to stage 1. Every year in age at the time of diagnosis increased the risk of death by about 5%. Patients that were treated with hysterectomy had improved OS compared with those that had non-hysterectomy surgeries or no surgical intervention, suggesting hysterectomy is critical is patients with US. Patients treated with adjuvant treatments (radiation or chemotherapy) had no improvement in OS. Elevated WBC count or elevated platelet count at the time of diagnosis doubled a patient's risk of death which could have clinical prognostic or therapeutic implications.

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Poster #49

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas9-mediated truncating mutations in BRCA1 and BRCA2 genes lead to increased baseline genetic instability and diminished growth in fallopian tube epithelial cell line

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Objectives: Different BRCA1/2 truncating mutations show varying risks for ovarian or breast cancer (Ovarian Cancer Cluster Regions, OCCR, versus Breast Cancer Cluster Regions, BCCR). To better understand progression from BRCA mutation to cancer, we sought to develop a cell line model of BRCA1 and BRCA2 variants in p53 mutated fallopian tube secretory epithelial cells (FT282) to evaluate their contribution to early steps of oncogenic transformation.
Methods: We overexpressed mutant p53 and Cas9 in FT282 cell lines to enable CRISPR/Cas9 mediated genomic alterations. Western blot was used to validate high levels of mutant p53 and ectopic Cas9 expression. FT282+p53mut+Cas9 cell line was clonally derived. Selected clone was used to introduce truncating mutations in BCCR and OCCR regions of BRCA1 and BRCA2 genes using CRISPR/Cas9 system. OR10A4 (olfactory) gene knockout was used as a control. T7 endonuclease I assay was used to confirm the occurrence of truncating mutation at the targeted CRISPR/Cas9-associated PAM sites. Cell proliferation assay assessed the growth rate of BRCA1/2 mutant cells. Soft agar assay was used to determine anchorage independent growth capabilities. Immunofluorescence and flow cytometry-based analysis of γH2AX levels were used to determine the baseline level of DNA damage. In addition, we introduced RB1 and PTEN mutation into BRCA1/2 mutant cell lines to evaluate the synergistic effects of additional oncogenic events.
Results: Clonally derived precursor cell line demonstrated high levels of mutant p53 and Cas9 proteins and resembled epithelial characteristics of naïve FT282 cells (high E-cadherin and low vimentin). T7 assay demonstrated mutated genomic DNA at the appropriate mutation sites. All OCCR and BCCR mutants in BRCA1 and BRCA2 demonstrated diminished proliferation compared to OR10A4 control. Mutations were not sufficient to confer anchorage independent growth. BRCA1/2 mutants showed increased baseline DNA damage. The addition of RB and PTEN mutations did not lead to gain in anchorage-independent growth.
Conclusions: We created fallopian tube epithelial cells with mutations in BCCR and OCCR regions in BRCA1 and BRCA2, as well as additional RB and PTEN mutations. BRCA1 and BRCA2 mutations have a higher baseline genetic instability, slower proliferation, but no increase in anchorage-independent growth. The anchorage-independent growth capabilities do not change with additional RB and PTEN mutations.

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