Objectives: Vitamin D deficiency confers poor outcomes in many cancers. While little data exists regarding the relationship between vitamin D deficiency and ovarian cancer (OC), the vitamin D receptor (VDR) single nucleotide polymorphism (SNP), FokI, is associated with increased OC risk. The relationship between the VDR FokI SNP and circulating serum 25 hydroxycholecalciferol (25(OH)D) is unknown. While vitamin D aids in production of inflammatory hormones such as leptin, the relationship between leptin and 25(OH)D levels in OC patients (pts) has not been studied. This study aimed to characterize 25(OH)D levels at the time of OC diagnosis and its associations with treatment-related morbidity, leptin levels, and VDR SNP status.
Methods: A retrospective review was performed of pts diagnosed with OC treated at a single institution. Pts were grouped by serum 25(OH)D status, with 25(OH)D deficiency defined as < 20 ng/mL and insufficiency 20-29 ng/mL. Demographics, clinical characteristics, treatment-related morbidity, survival, serum 25(OH)D, leptin, and VDR SNP markers were compared between groups.
Results: Of 122 pts included in the study, 82 were 25(OH)D deficient, 21 were insufficient, and 19 were normal. The median age was 67 yrs, and 70% were stage III/IV. There were no differences in demographics, stage, treatment-related morbidities or survival between groups (all p>0.05). There was no difference in serum leptin levels or SNP allele status between groups (all p>0.05). Due to differences in severity of disease and expected disease outcomes, further analysis was restricted to those with stage III/IV OC (n=85, deficient n=59, insufficient n=13, normal n=13). For this cohort, there was no difference in demographics, treatment-related morbidities, or survival (all p>0.05). When adjusted for BMI, there was no difference in serum leptin levels between groups or SNP allele status (all p>0.05, Table). There was no association between SNP allele groups and progression free (p=0.44) or overall survival regardless of 25(OH)D status (p=0.96).
Conclusions: This study did not detect an association between serum 25(OH)D levels and treatment-related morbidity, leptin levels, or VDR SNP status in women with OC in either the overall population or only those with stage III/IV disease. Interpretation is limited by small numbers and the retrospective design. Few patients receiving neoadjuvant chemotherapy were included in this study likely introducing selection bias. Prospective evaluation is ongoing.

doi:10.1016/j.ygyno.2019.03.218

Poster #29

Family history of cancer associated with improved survival in uterine serous carcinoma

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Objectives: Uterine serous carcinoma (USC), a subset of endometrial cancers, accounts for fewer than 10% of cases, but disparately accounts for 50% of uterine cancer related deaths. Prior reports indicate an association between USC and BRCA 1 germline mutations. Our objective was to compare the survival of patients with USC with and without a family history of breast, ovarian, uterine, GI, pancreatic, brain, melanoma or GU cancers (Multiple Organ Hereditary Cancers or MOHC).
Methods: We extracted all genetic alterations in the commonly tested genes during genetic panel testing, progression free survival (PFS), and overall survival (OS) from The Cancer Genome Atlas (TCGA) in all patients with USC. We performed a multi-institutional retrospective review of all patients who were diagnosed with USC from 2005 to 2014. Demographics and clinic-pathologic data were obtained. Disease progression was defined by RECIST criteria. Statistical analysis was performed using the Kaplan-Meier Survival Analysis.
Results: Genetic alterations in the following commonly tested genes were extracted from TCGA in USC patients: BRCA1, BRCA2, CHEK2, BRIP1, RAD51C, BARD1, TP53, RAD50, RAD51D, ATM, NBN, PALB2, MRE11A, MSH6, MLH1, MSH2, PMS2. In those with advanced (stage III/IV) USC (n=69), PFS and OS were worse in patients with a genetic alteration of the above genes versus those without (PFS of 47.7 versus 19 mos and OS of 50.9 versus 30.1 mos; P = 0.01). One hundred ninety patients with USC were included in the retrospective analysis. Greater than 50% of the patients had a personal and/or family history of MOHC. 30% of these patients had a personal history of MOHC. When comparing survival between those with and those without a personal and/or family history of MOHC, patients with a MOHC history had longer PFS (49 versus 20 mos, P = 0.01) and longer OS (65 versus 34 mos, P = 0.01). Although not significant, a difference in overall survival was seen among patients with advanced USC (n=104) with a personal and/or family history of MOHC versus those without (35 versus 20 mos, P = 0.16).
Conclusions: Women with USC with a personal and/or family history of MOHC have improved survival compared to those without. Identification of genetic predisposition may improve treatment options and outcomes in this subgroup of patients. Genetic testing should be considered in patients with USC.

doi:10.1016/j.ygyno.2019.03.219

Poster #30

Chromobox 2 protein identified as driver of anoikis-escape and disease progression in high grade serous ovarian cancer

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Objectives: Chromobox 2 (CBX2), a polycomb repressor complex subunit, plays an oncogenic role in a variety of cancers. In prostate cancer, CBX2 is a driver of metastatic progression. We sought to investigate the hypothesis: CBX2 upregulation promotes advanced high grade serous ovarian carcinoma (HGSOC) by promoting a stem-like transcriptional profile and inhibiting anoikis.
Methods: Gene Expression Omnibus (GEO) and The Cancer Genome Atlas (TCGA) were queried to establish CBX2's role. In vitro evaluation of CBX2 occurred in PEO1, OVCAR8, and OVCAR4 HGSOC cell lines. PolyHEMA-coated plates forced cells to grow in suspension and simulated anoikis-escape. Quantitative polymerase chain reaction and immunoblots evaluated CBX2 expression. Small hairpin RNAs (shRNAs) knocked down CBX2 for loss-of-function studies. To mimic HGSOC progression several culture conditions (2D, colony formation, and 3D, spheroid) were examined. Secreted luciferase (gLuc) activity was utilized as a proliferation indicator. Stemness was tested with the Aldefluor assay, measuring aldehyde dehydrogenase activity (ALDH). Using patient tumors from the Gynecology Tissue and Fluid Bank (GTFB) and a HGSOC tissue microarray (TMA) with matched primary, metastatic, and lymph nodes, a CBX2 expression profile was established. Student's t-test was used to define statistical significance, with a p value of < 0.05.
Results: GEO/TCGA analyses established CBX2 is upregulated in HGSOC tumors compared to benign tissues and CBX2 expression conveyed worse disease-free survival (11.7 vs 17.6 months, Log-rank test p-value < 0.005) and overall survival (34 vs. 44.8 months, Log-rank test p-value <0.005). PEO1, OVCAR8 and OVCAR4 cells upregulate CBX2 when grown in suspension compared to adherent conditions. CBX2 knockdown led to a significant inhibition of proliferation in all culture conditions. Forced suspension promoted increased ALDH