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.

doi:10.1016/j.ygyno.2019.03.237

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.

doi:10.1016/j.ygyno.2019.03.238

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.

doi:10.1016/j.ygyno.2019.03.239