Objectives: Research has shown that some cancers have a unique intra-tumoral environment which allows the cancer to regulate its own growth through production of estrogen as well as expression and activation of ER-a nd ER-B. ER-a activation has been shown to be proliferative. The effect of ER-B activation is less clear but thought to be antiproliferative. Our objective is to define the intratumoral environment in a cohort of premenopausal endometrial cancers and to study the effect of specific ER-B activation on cell growth.
Methods: Tissue microarrays were constructed. Immunohistochemistry was used to evaluate the expression of ER-a, ER-B, aromatase, TNF-α, and IL-6. Scores were assigned for proportion and intensity of staining and a total score was calculated. ER-B function was studied using the commercially available endometrial cancer cell lines Ishikawa, RL952, and HEC1A. Cells were treated with serial concentrations of the commercially available ER-B agonists, S-Equol and Liquiritigenin, for 24, 48, 72, and 96 hours. The MTT assay was used to test for cell growth. Western blot analysis was performed in the standard fashion on Ishikawa cells for expression of ER-a and ER-B proteins. Statistical analysis for immunohistochemistry was carried out using Kendall rank correlation coefficient and Kruskal-Wallis test as appropriate. Cell culture statistical analysis utilized paired t-tests. Differences were considered statistically significant at $p < 0.05$.
Results: Endometrial cancers in this premenopausal cohort had high intratumoral expression of ER-a, ER-B, aromatase, and TNF-a and IL-6. TNF-α had increased expression in the cancers as compared to controls, $p = 0.001$. TNF-α expression was positively correlated with the expression of aromatase, $p = 0.02$. Western blot showed that Ishikawa cells expressed both ER-a and ER- B protein. All three cell lines exhibited an antiproliferative response to the ER- B agonists in a dose dependent fashion. Optimal effects were seen at 72 and 96 hour of incubation. The EC50 was 75uM -100uM for all cell lines.
Conclusions: High expression of intra-tumoral TNF-a may be a driver of carcinogenesis through induction of aromatase and a subsequent increase in local estrogen production. ER- B was highly expressed in this patient cohort. Specific activation of ER- B with either of the ER- B agonists resulted in a robust antiproliferative effect. Targeted therapy with the ER- B agonists is an area that deserves further investigation.

doi:10.1016/j.ygyno.2019.03.199

Poster #10

Long term survival in advanced stage low grade serous ovarian cancer

C. Bisson, J. Maxwell, K.N. Moore, L.L. Holman. *Department of Gynecologic Oncology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma*

Objectives: Low grade serous ovarian cancer (LGOC) represents approximately 6% of all ovarian cancers, with a median overall survival (OS) of approximately 6-8 years. A subgroup of LGOC patients (pts) appear to have more aggressive disease, but little is understood about what differentiates pts with short-term survival (STS) from those with long-term survival (LTS). The objective of this study was to determine clinical factors associated with STS and LTS in pts with stage III and IV LGOC.
Methods: A retrospective review of pts with newly diagnosed LGOC between 2005-2018 was conducted. Summary statistics were used to describe demographics and clinical characteristics. STS was defined as OS ≤ 25%ile for the cohort. LTS was defined as OS ≥ 75%ile for the cohort. Data were compared between the two groups using ANOVA and chi-square analyses.
Results: Of the 70 pts included, 94.3% were Caucasian, median age was 54.7 yrs, and 90% had stage III or IV disease. In pts with stage III or IV disease, median OS was 49.5 mo. Of the 16 pts in the LTS group, 100% were Caucasian, median age was 52.8 yrs, and 87.5% were stage III. This was not significantly different from the 16 pts in the STS group, of which 87.5% were Caucasian, median age was 61.9 yrs, and 62.5% were stage III (all $p>0.05$, Table). As expected, RFS and OS were significantly longer in the LTS group (49 vs 3.5 mo and 101 vs 17.5 mo, all $p<0.001$). STS pts had a higher CA-125 at diagnosis ($p=0.03$) and were less likely to have a complete response after primary therapy ($p<0.001$) than LTS pts. While there was no difference in recurrence rates between groups ($p=0.37$), STS pts were more likely to be platinum resistant at the time of their first recurrence (8.3% vs 50%, $p=0.03$).
Conclusions: STS in advanced LGOC pts is associated with higher CA-125 levels at diagnosis, lack of CR to primary therapy, and platinum resistance at the time of the first recurrence. While other factors, such as age, appear to be clinically significant, there was likely a lack of statistical significance secondary to small numbers in each cohort. The recruitment of additional sites to improve the power of this study is ongoing. Additional research on the genetics and molecular characteristics of STS compared to LTS is an area of future focus.

doi:10.1016/j.ygyno.2019.03.200

Poster #11

Factors that influence survival in high-grade serous ovarian cancer: A complex relationship between molecular subtype, disease dissemination, and operability

D. Torres, C. Wang, A. Kumar, J. Bakkum-Gamez, A. Weaver, M. McGree, G. Konecny, E. Goode, W. Cliby. *Mayo Clinic, Rochester, MN*

Objectives: To investigate the relationship between molecular subtype, intraperitoneal (IP) disease dissemination patterns, resectability, and overall survival (OS) in advanced high-grade serous ovarian cancer (HGSOC).
Methods: Patients undergoing primary surgery for stage III-IV HGSOC at a single institution from 1994-2011 were categorized into three IP disease dissemination patterns: upper abdominal or miliary; lower abdominal; and pelvic. Residual disease was defined as 0 (RD0), 0.1-0.5, 0.6-1.0, or >1 cm. Molecular subtypes were derived from Agilent 4x44k tumor mRNA expression profiles and categorized as mesenchymal (MES) or non-mesenchymal (non-MES).
Results: Operative and molecular data was available for 334 patients. Median OS was shorter in patients with MES compared to non-MES subtypes (34.2 vs 44.6 months; $P=0.009$). Patients with MES subtype were more likely to have upper abdominal/miliary disease compared to non-MES subtype (90% vs. 72%, $P<0.001$). For patients with upper abdominal/miliary disease, complete resection (RD0) was less common in MES compared to non-MES subtypes (11% vs. 27%, $P=0.004$). On multivariable analysis, RD was the only factor associated with OS ($P<0.001$). In patients with upper abdominal/miliary disease, though less commonly achieved, RD0 improved survival irrespective of molecular subtype (median OS of 69.2 and 57.9 months for MES and non-MES subtype).
Conclusions: Our results support a paradigm in which molecular subtype is an important driver of dissemination pattern; this in turn impacts resectability and ultimately survival. Consequently mesenchymal subtype is associated with much lower rates of complete resection, though RD0 remains the most important independent predictor of survival.

doi:10.1016/j.ygyno.2019.03.201