histologies were distributed equally among the patients (92% HS vs 91% NH, p=0.82), as was the proportion of high-grade serous carcinoma (70.3% HS vs 76.5% NH, p=0.98). Twenty-one (56.8%) HS and 23 (67.6%) NH received germline testing (p=0.34); 3 (8.1%) HS and 6 (17.6%) NH had a germline mutation associated with a homologous recombination deficiency (HRD) (p=0.48). The most common somatic mutations for both groups involved TP53 (67.5% HS vs 70.6% NH, p=0.90). There were no statistically significant differences between HS and NH with respect to individual somatic gene mutations, though the genes expressed were dissimilar (Figure 1). Three (8.1%) HS and 8 (23.5%) NH had somatic BRCA2 amplifications or mutations, though this difference was not statistically significant (p=0.12). The proportion of somatic BRCA1 mutations was similar in both groups (13% HS vs. 12% NH, p=0.99). EGFR mutations were only noted in HS, while Her2/Neu mutations were only noted in NH. Twelve (32.4%) HS and 8 (16.2%) NH has positive staining for either PD-1 or PD-L1 (p=0.27).

Conclusions: HS and NH women with ovarian cancer had similar tumor characteristics and similar frequencies of germline testing and somatic mutations in this limited sample. Trends towards more frequent PD-1/PD-L1 staining in HS along with ethnic differences in somatic mutations between these two groups warrant additional study.

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Abstract #17

Is there a role for for minnelide in uterine serous cancers?

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Objectives: Most women with uterine serous carcinoma (USC) have a high risk of advanced stage disease and/or recurrence, and in these settings, there are few effective therapies. There is a need for effective therapy in the recurrent USC. Minnelide is bioavailable prodrug of Triptolide, which was isolated in the Chinese herb, Thunder god vine (Tripterygium wilfordii). Minnelide is currently in phase II clinical trials for pancreatic and GI cancers. The purpose of this study was to explore the effect of Minnelide on USC in preclinical models.

Methods: The active form of Minnelide, was tested in vitro using two USC cell lines, Ark1 & Ark2. Tumor cells were treated for 48h. Cytotoxicity was assessed with Cell Counting Kit-8 (Dojindo) and real-time growth inhibition by electrical impedance measurements (xCelligence, Roche). A mouse model using Ark2 was used to determine the efficacy of Minnelide either alone or in combination with Carboplatin on tumor growth inhibition in vivo. Western blotting was used to determine mechanism of action by induced changes in programmed cell death pathways.

Results: Cytotoxicity assays demonstrated that Minnelide's active form, Triptolide, was effective in inhibiting cell viability at nanomolar concentrations. The half maximal inhibitory concentration was 11nM for Ark1 and 17nM for Ark2. Real-time growth inhibition assays were consistent. In a mouse model using Ark2 cell line, Minnelide at high (0.4mg/kg) and low (0.2mg/kg) doses significantly inhibited growth compared to carboplatin (P<0.0005). High dose (0.4mg/kg) was more effective than low dose Minnelide (0.2mg/kg). Addition of Caboplatin to the low dose Minnelide treatment regimen did not change the efficacy of monotherapy with Minnelide alone. No gross toxicity was noted in treated animals. Western blotting showed activation of apoptotic pathway induced by p53 upregulation and downregulation of anti-apoptotic protein Bcl-2.

Conclusions: Minnelide, was very effective in inhibiting the USC cell lines at nM levels. In mouse models, Minnelide treatment showed dose-dependent inhibition of tumor growth. Caboplatin treatment showed no significant tumor growth inhibition. Efficacy of Minnelide did not improve in combination with Carboplatin. This suggest that Minnelide alone was highly effective against Carboplatin resistant USC. Mechanistic studies showed activation of intrinsic apoptotic pathway. Given the minimal toxicity profile reported in clinical trials, Minnelide is an attractive drug for further exploration.

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Abstract #18

Quantitative computed tomography image feature analysis predicts response to immune checkpoint inhibitors in gynecologic cancers

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Objectives: To investigate the role of applying quantitative image (QI) feature analysis computed from computed tomography (CT) images for early prediction of tumor response to immune checkpoint inhibitors (ICPI) amongst patients with recurrent gynecologic cancer.

Methods: We conducted a retrospective review of 39 patients with gynecologic cancer at a single institution who received an ICPI for management of recurrent disease. Each patient had CT images prior to and after the initiation of therapy. A computer-aided detection scheme was applied to segment metastatic tumors previously tracked by radiologists on CT images and computed image features. A QI feature pool was built using image features computed from the image feature difference between pre- and post-therapy images. A features selection method was applied to select optimal features, and an equal-weighted fusion method was used to generate a new quantitative imaging marker for each pool to predict 6-month progression-free survival (6PFS). The prediction accuracy between quantitative imaging markers and the response evaluation criteria in solid tumors (RECIST) criteria were also compared. Complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) were assessed by RECIST criteria.

Results: Of the 39 patients identified, 21 patients (54%) had ovarian cancer, 11 patients (28%) had cervical cancer, and 7 patients (18%) had uterine cancer. 27 patients (69.2%) received a programmed death 1 (PD-1) inhibitor, 8 patients (20.5%) received a programmed death-ligand 1 (PD-L1) inhibitor, 3 patients (7.7%) received a combination of PD-1 inhibitor and cytotoxic lymphocyte antigen-4 (CTLA-4) inhibitor, and 1 patient (2.6%) received anti-cell immunoglobulin and ITIM domain protein (TIGIT) resulting in 1 CR, 9 PR, 9 SD, and 20 PD. The area under the receiver operating characteristic curve (AUC) is 0.94 (95% CI 0.87-1.00) when using QI feature analysis to predict 6PFS and 0.76 (95% CI 0.67-0.85) when using RECIST criteria. The difference in AUC between the two methods was significant, (QI feature analysis vs RECIST 0.19, 95% CI 0.083-0.288, p=0.0004). QI feature analysis resulted in a prediction accuracy level of 92.3% versus 61.5% when using RECIST criteria.

Conclusions: Quantitative CT image feature analysis accurately predicts response to ICPI in patients with recurrent gynecologic cancer. This technology is a promising tool to predict the clinical benefit of ICPIs early in the course of treatment of gynecologic cancers.

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