the internal TCGA test cohort and 0.132 (95% CI: 0.025,0.704) on the external Stanford Hospital validation cohort.

Conclusions An artificial intelligence derived histological biomarker utilizing only routine whole-slide histopathology images can robustly predict responders and non-responders to platinum-based chemotherapy.

Conclusions Molecular profiles and TME are associated with OS. TME differs per profile, with higher immune cell densities showing a favorable OS, even within the profiles. HGSOC does not reflect one entity but comprises different entities based on molecular profile and TME which could assist with patient-tailored treatment in the future.

Poster rounds with the professors: Group 06

Objectives To investigate the role of a preoperative apparent diffusion coefficient (ADC) of magnetic resonance imaging (MRI) and machine learning for the prediction of platinum-based chemotherapy resistance in patients with epithelial ovarian cancer (EOC).

Methods The ADC of MRI was preoperatively evaluated on the largest solid portion of the ovarian mass on the axial MRI maps. All patients underwent platinum-based chemotherapy after cytoreductive surgery. Logistic regression and machine learning applications were used to investigate the role of the ADC and clinical factors for the prediction of platinum-based chemotherapy resistance in ovarian cancer.

Results Of the 168 patients, 97 had high-grade serous ovarian cancer (HGSOC) and 71 had non-HGSOC patients; 33 clear cell carcinoma, 18 mucinous carcinoma, 15 endometrioid carcinoma, 5 low-grade serous carcinoma. The patients were divided into the platinum-sensitive group (n=146) and the platinum-resistant group (n=22). The gradient boosting machine algorithm showed the highest accuracy in differentiating histologic types of ovarian cancers (accuracy: 0.91, AUC: 0.93). In the ROC curve, CA 125 and the ratio of solid to the total area were significantly associated with platinum-based chemotherapy resistance (AUC: 0.758, AUC: 0.687, respectively). The deep learning algorithm demonstrated increased accuracy (AUC: 0.814). In cox regression analysis, the area of the solid portion was significantly related to the resistance to chemotherapy (hazard ratio: 1.033, p=0.014).

Conclusions The ADC and area of the solid portion on MRI using machine learning can be helpful to predict histologic types and resistance of platinum-based chemotherapy in EOC.
Objectives Cytoreductive surgery with HIPEC has shown promising results in interval setting in advanced epithelial ovarian cancer. Its role in upfront setting has not yet been established.

Methods All eligible patients underwent CRS HIPEC as per institution protocol. Relevant data was entered prospectively in institutional HIPEC registry and analysed retrospectively for study period from February 2014 – February 2019.

Results Out of 190 patients, 80 underwent CRS HIPEC in upfront setting and 110 in interval setting. Median age was 54±7.45 years, upfront group had higher PCI (14.1±8.75 vs. 9.6±5.2, 2), and required longer duration of surgery (10.6±1.73 vs. 8.4±1.71 hrs) had more blood loss (1025±668.76 vs.680±302.23 ml). Upfront group required more diaphragmatic resections, bowel resections and multivisceral resections. The overall G3-G4 morbidity was comparable (25.4%vs. 27.3%), upfront group had more surgical morbidity (20%vs.9.1%) whereas interval group had more medical morbidity i.e. electrolyte imbalance and haematological. After a median follow up of 43 months, median DFS was 33 months in upfront vs. 30 months in interval group, p=0.75, median OS was 46 months interval group and was not yet achieved in upfront group (p=0.13). 4 year OS was 85%vs 60%. Performance status (P =0.025 C.I 1.190–12.80) was the only factor predicting morbidity on multivariate analysis.

Conclusions In patients of advanced EOC upfront CRS HIPEC showed promising outcomes and better survival with similar morbidity and mortality. Upfront group had more surgical morbidity whereas interval group had more medical morbidity. Multi-institutional randomised studies are needed to define patient selection and study morbidity patterns.

E-poster viewing: Basic/translational science

EP002/#550 PRECLINICAL SYNERGISTIC MECHANISMS OF INVESTIGATIONAL NEW DRUG, SHET2A

1Doris Benbrook*, 1Rajani Rai, 1Vishal Chandra, 2Amy Kennedy, 2Kathleen Moore.
1University of Oklahoma Health Sciences Center, Gynecologic Oncology, Stephenson Cancer Center, Oklahoma City, USA; 2Stephenson Cancer Center University of Oklahoma, Gynecologic Oncology, Oklahoma City, USA

Objectives The investigational new drug, SHetA2 (NSC 726189) is being evaluated in a Phase 1 clinical trial in advanced and recurrent ovarian, cervical and endometrial cancers (clinicaltrials.gov: NCT04928308). SHetA2 selectively kills cancer cells without harming healthy cells by disrupting complexes of heat shock protein 70 molecular chaperones (mortalin, Grp78 and hsc70) with their client oncoproteins. We sought to evaluate efficacy, toxicity and mechanisms of SHetA2 in combination with other drugs.

Methods Single and combined drug effects were compared in cell culture and murine xenograft models of human gynecologic cancer cell lines. Mechanisms were evaluated by immunohistochemistry of tumors, immunofluorescent and electron microscopic cell imaging, Seahorse assays, and co-immunoprecipitation, western blot, and mass spectrometry of protein extracts.

Results SHetA2 interacted synergistically with a p53 reactivator, paclitaxel, and cyclin dependent kinase 4 or 6 inhibitors (CDK4/6i’s) in cell culture. Synergy with paclitaxel was verified in two endometrial cancer xenograft models and additive interaction was observed for all other combinations in endometrial, cervical or ovarian xenograft models of treatment or maintenance therapy. Mechanisms of drug synergies involved SHetA2-induced mitochondrial damage, mitophagy and cell cycle arrest mediated by release of client proteins (p53, cyclin D1, CDK4/6, apoptosis inducing factor/AIF, metabolic enzymes) from HSP70 protection, and complemented by effects of the other drugs on these client proteins and their pathways.

Conclusions SHetA2 activity against gynecologic cancers can be enhanced by paclitaxel, p53 reactivators, and CDK4/6i’s, which have complementary mechanisms against HSP70 client proteins. These studies support development of SHetA2 as a synergistic complement to existing therapies in gynecologic cancers.

Objectives Multiple preclinical studies have demonstrated the benefit of augmenting immunotherapy with hyperthermia (HT) considering the proven ability of HT to enhance immune cell immunogenicity and to stimulate an antitumor immune response primarily via heat shock proteins (HSP). However, antitumor immune responses are often invalidated by immune evasion mechanisms such as the overexpression of programmed death-ligand 1 (PD-L1) and the loss of MHC class I expression. In this context, we sought to investigate the effects of HT on PD-L1 and the transcriptional activator of MHC class I genes NLRC5 and their interplay in ovarian cancer.

Methods A co-culture of ovarian cancer cell lines (IGROV1 and SKOV3) with peripheral blood mononuclear cells was set up. Culture media conditioned with IGROV1 or SKOV3 subjected to HT were tested on untreated cell cultures. Knockdown of HSPA1 and HSPB1 and inhibition of STAT3 activation were performed. Expression levels of PD-L1, NLRC5, proinflammatory cytokines and HSP were measured. The correlation between PD-L1 and NLRC5 expression in ovarian cancer was evaluated using data from The Cancer Genome Atlas (TCGA) database.

Results HT produced a significant concomitant decrease of PD-L1 and NLRC5 expression in co-culture. Notably, however the conditioned media by heat shocked cells increased their expression. Knockdown of the HSPB1 gene reversed this increase, an effect enhanced by STAT3 activation inhibition. Correlation analysis showed a positive correlation between NLRC5 and PD-L1 (r=0.54, p-value <0.001) in TCGA database.

Conclusions Our results revealed that HSP27 induces a concomitant upregulation of PD-L1 and NLRC5 expression through the activation of a common regulator ‘STAT3’.