Title

A Novel Rat Ovarian Cancer Model Developed to Examine Chemotherapy-Related Cognitive Impairments

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frequency of nodal interaction, IHC was performed to analyze protein expression within the ovarian cancer tumor samples.

RESULTS: cfDNA sequencing and pairwise analysis showed that gene composition varied amongst poor and favorable prognosis pts. 29 genes were identified to be of higher and 64 genes of lower dosages in the poor prognosis compared to favorable prognosis pts. Gene ontology analysis of higher dose genes was predominantly grouped into cytoskeletal proteins, while lower doses yielded hydrolases and receptors. When cross-referenced for cancer-relatedness in Reactome database, 15 genes were referenced. Among them, TGFB2, ZMIZ2 and NRG2 were identified. IHC analysis of the tumor microarray indicated downregulation of TGFBR2 membrane expression and upregulation of ZMIZ2 nuclear expression in poor versus favorable prognosis pts.

CONCLUSIONS: Serum cfDNA gene dosage and correlating tumor sample protein expression warrant further development in biomarker panels for determination of platinum resistance in ovarian cancer pts.

LEARNING OBJECTIVES: Learners will be able to explain the role of circulating tumor cell free DNA in determining platinum resistance in ovarian cancer patients.

Oral Abstract #7
A Novel Rat Ovarian Cancer Model Developed to Examine Chemotherapy-Related Cognitive Impairments
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OBJECTIVES: To describe a novel method of developing an ovarian cancer intraperitoneal (IP) and subcutaneous (SC) xenograft model with the purpose of extrapolating chemotherapy-related cognitive impairments (CRCI) in tumor-bearing rats.

METHODS: An SKOV3.ip1 cell line was cultured in RPMI 1640 medium with 2 mM L-glutamine supplemented with 10% FBS. Under an approved IACUC protocol, 6 female 12-week old athymic (Cr:NIH-RNU) rats were injected IP with 10 million SKOV3.ip1 cells in the lower left quadrant and 10 million SKOV3.ip1 cells SC in the right flank. Using the SC implanted tumor as a biomarker of IP tumor growth, rats were treated with chronic cisplatin chemotherapy via an IP approach. Rats received 25 mg/kg of IP cisplatin therapy split in 5 doses, mimicking the ovarian cancer platinum-based regimen given in humans. During and after chemotherapy, rats were monitored for tumor growth and neurocognitive function.

RESULTS: Thirteen days following tumor implantation, measurable SC tumors developed on 83% of rats (n=5/6). Using a well-established method to test learning and memory, the novel object recognition task was used to evaluate neurocognitive function in rats. Although able to significantly differentiate between familiar and novel objects at baseline (pre-chemotherapy), two weeks post-chemotherapy completion, rats were not able to differentiate between novel and familiar objects, suggesting cognitive impairment. While SC tumors shrunk to 0 mm on all but 33% of rats (n=2/6), IP tumors were still present in post-mortem examination in 66% of rats (n=4/6).

CONCLUSIONS: Rat xenograft models are seldom developed likely secondary to difficulty in uptake of ovarian tumors by the species and the relative ease of developing mice models of ovarian cancer. This study demonstrates that SC tumor implantation is a feasible, non-fatal method to monitor tumor growth in longer animal studies. Given the rat models increased applicability to human physiology in studying the effects of CRCI, this unique pilot model suggests a feasible approach to simulate a female ovarian cancer model to study the quality of life effects of chemotherapy in a controlled environment and

to examine therapeutic interventions for preventing CRCI. Impairment in novel object recognition, as displayed in these results, demonstrates weakening in hippocampal-dependent cognitive processes suggesting a possible area of further research in CRCI.

LEARNING OBJECTIVES: Learners will be able to appreciate the feasibility of a rat ovarian cancer tumor model with a commonly used, ovarian cancer cell line. They will also be able to determine the extent of disease during the course of therapy and follow a measurable subcutaneous biomarker to monitor tumor growth without added harm to rats or cost. Finally, they will be able to extrapolate the possible mechanism underlying CRCI.

ATTACHMENT: On next page

Novel Object Recognition (NOR)
2 weeks status post CIS 25/ mg/kg
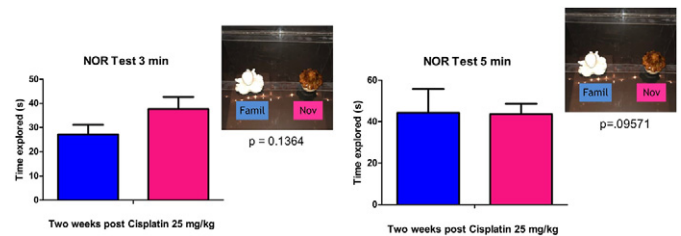
Oral Abstract #8
Safety and Efficacy Results of Retreatment With a PARP Inhibitor Monotherapy in Late-Line Recurrent Ovarian Cancer: Results From a Subset of the QUADRA Trial
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OBJECTIVES: Promising data in the front- and second-line settings are moving the use of poly(ADP-ribose) polymerase inhibitors (PARPi) earlier in the treatment of ovarian cancer (OC); thus, data on PARPi retreatment have increasing clinical relevance. It remains unknown whether patients (pts) who discontinue PARPi treatment for disease progression or other reasons (eg, planned fixed duration, adverse events [AEs], treatment fatigue) will experience different tumor response upon re-exposure. Here, we present safety and