**Oral Abstract 27:** Differential Effects of GPX4 Inhibitor on Drug-tolerant Persister Ovarian Cancer Cells

**Presenting Author:** Katherine Jane Chua, MD, University of California Davis Health System

Topic
Translational Research

Objectives
The purpose of this study is to determine the effects of ML210, a GPX4 inhibitor, on ovarian cancer parental and drug persister cells (DTP) cells.

Methods
Parental ovarian cancer cell lines (OVSAHO, OVCAR3) and their DTP counterparts were utilized. DTP cells were created by treating parental cells with predetermined concentrations of carboplatin. After about 12 days, DTP cells were examined under the microscope and used for experiments. Separate synergy assays were performed between varying concentrations of carboplatin and ML210 for both parental and DTP cell lines. Dose response and synergy assays were analyzed 72 hours after treatment and results interpreted with respective software programs. Clonogenic assays for parental and DTP cells were performed using varying concentrations of ML210. Once the control wells had adequate colonies noted, the assays were analyzed per protocol. Standard immunofluorescence protocol was also utilized. DTP cells were treated with 0 nM, 25 nM (low), and 250 nM (high) of ML210 24 hours after seeding. Primary monoclonal antibodies included were: p21 to demonstrate cell cycle arrest and caspace-3 to reflect apoptosis. Cells were fixed 24 hours after ML210 treatment and visually analyzed with the appropriate software.

Results
Western blot confirmed that GPX4 levels were lower in DTP cells compared to parental cells. Increasing ML210 doses demonstrated a cytostatic effect on parental cells seen on dose response and clonogenic assays. DTP cells appeared to have a cytotoxic relationship with increasing ML210 doses. Similar effects were also noted on clonogenic assays. DTP cells were more sensitive to ML210 revealing lower IC50 doses compared to parental cells. OVCAR3 DTP immunofluorescence assay further demonstrated ML210 cytotoxic effects with weak p21 staining and strong caspase-3 staining. Carboplatin and ML210 has an antagonistic effect on parental cells. However, additive or synergistic effects were seen in DTP cells.

Conclusions
ML210 may be promising drug for DTP cells. ML210 has a cytotoxic effect in DTP cells compared to a cytostatic effect noted in parental cells. ML210 may be useful for eliminating DTP cells left behind after platinum-based chemotherapy. Further studies are needed to determine ML210's role in improving progression-free survival in ovarian cancer patients.

Uploaded File(s)
Abstract Table or Graph
INEXBPJK-2394814-1-ANY.pdf