

## Objective

- Given the NRG GY012 trial for uterine cancer patients randomized women to olaparib as a treatment arm, we determined whether combination therapy with AVB-S6-500 (AVB), an AXL inhibitor, could improve response in a uterine serous cancer (USC) model.

## Methods

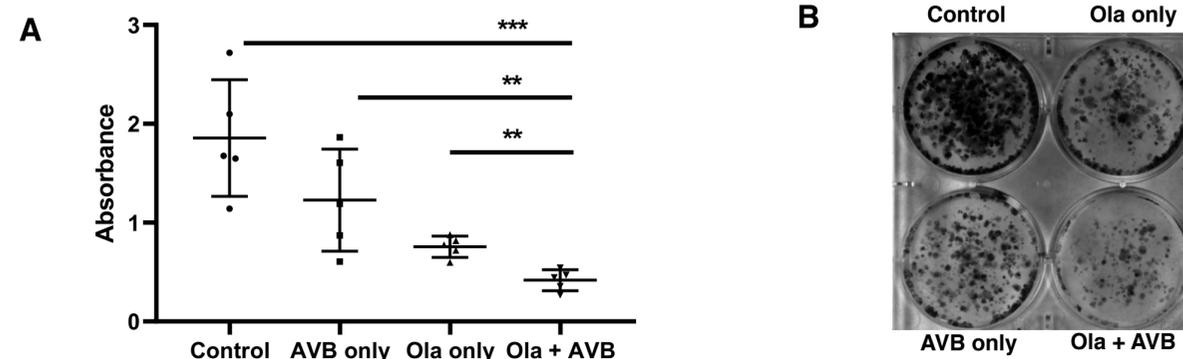
- USC (ARK1 and ARK4) cell lines were treated with AVB (Aravive Biologics, Houston, TX) in combination with a poly ADP ribose polymerase (PARP) inhibitor, olaparib.
- Colony forming assays were assessed after 4 days of treatment with either AVB alone, olaparib alone, or combination treatment (olaparib + AVB). Relative cell viability for were calculated using Graph Pad Prism.
- In-vivo studies were performed using NOD-SCID mice injected with  $1 \times 10^7$  ARK1 cells intraperitoneally followed by treatment q3 days for a 21 day treatment period.

## Results

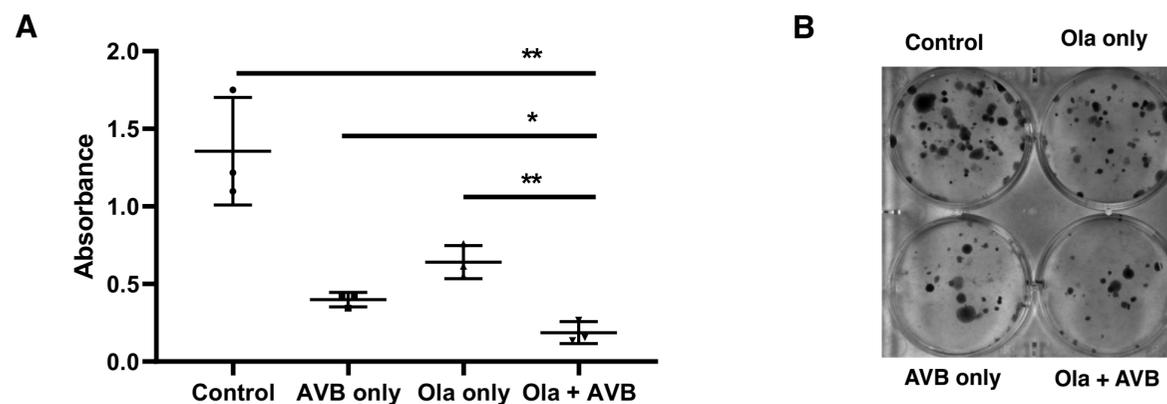
- In clonogenic assays, colonies were stained and absorbance was obtained for each experimental arm. In the ARK1 cell line, the absorbance for olaparib + AVB was significantly less than the absorbance for the olaparib only group 0.417nm vs 0.756nm,  $p=0.001$  (Figure 1A and 1B).
- In the ARK4 cell line the absorbance for olaparib + AVB was significantly less than the absorbance for the olaparib alone group 0.186nm vs 0.641nm,  $p=0.004$  (Figure 2A and 2B).
- In vivo*, mice receiving the olaparib + AVB had significantly less tumor weight than those treated with olaparib alone (0.212g vs 0.586g,  $p=0.03$ ) and AVB alone (0.212g vs 0.494g,  $p=0.005$ ).
- Similarly, mice receiving olaparib + AVB had significantly less tumor volume than those treated with olaparib alone ( $85.86\text{mm}^3$  vs  $781.3\text{mm}^3$ ,  $P=0.0007$ ) and AVB alone ( $85.86\text{mm}^3$  vs  $428.6\text{mm}^3$ ,  $p=0.0013$ ) (Figure 3A and 3B).

## Results

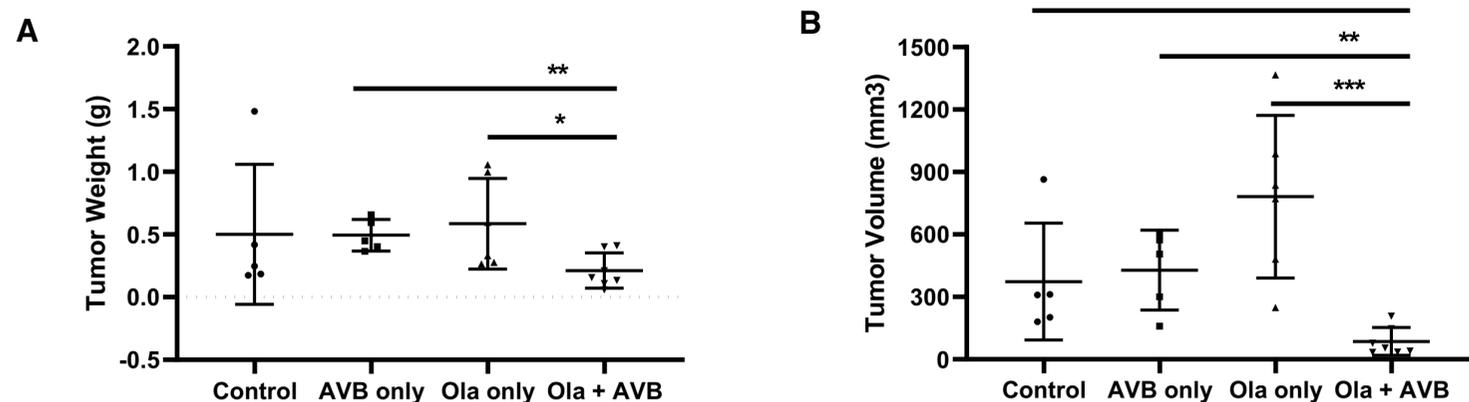
**Figure 1: Increased cell death with olaparib + AVB versus olaparib alone in clonogenic assay in ARK1 cell line (a) Dot plot graph indicating significance (b) Representative picture of clonogenic plate**



**Figure 2: Increased cell death with olaparib + AVB versus olaparib alone in clonogenic assay in ARK4 cell line (a) Scatter plot graph indicating significance (b) Representative picture of clonogenic plate**



**Figure 3: *In vivo* 21 day treatment period showed decreased (a) tumor burden and (b) decreased tumor volume in the olaparib + AVB group than olaparib alone.**



## Conclusions

- AVB500 in combination with olaparib demonstrates an improved response than olaparib alone with a greater decrease in tumor burden through increasing DNA damage.
- Additional therapeutic and mechanistic experiments with primary USC cancer cells developed from metastatic USC patients are ongoing.

## Acknowledgements