

Combination of bortezomib with olaparib decreases ovarian cancer chemoresistance

Caglar Berkel

Tokat Gaziosmanpasa University, Turkey

Statement of the Problem: Ovarian cancer is one of the deadliest malignancies in women and chemoresistance is a challenge for management of ovarian cancer. In this study, we aimed to investigate the cytotoxic efficacy of combination treatment with bortezomib (inhibition of 26S proteasome) and olaparib (inhibition of poly (ADP- ribose) polymerases (PARP); PARPi) on chemosensitive and chemoresistant ovarian cancer cell lines. **Methodology & Theoretical Orientation:** Experiments were performed in both chemosensitive ovarian cancer cell lines (OV2008, A2780) and their chemoresistant daughter cell lines (C13, A2780-AD). Cell viability was evaluated by Sulphorhodamine B (SRB) assay following bortezomib and/or olaparib treatments with or without cisplatin.

Findings: Bortezomib and olaparib combination treatment resulted in increased cytotoxicity relative to either drug alone at certain concentrations in both chemosensitive and chemoresistant ovarian cancer cell lines. In addition, combination treatment sensitized these tumor cells to cisplatin and decreased chemoresistance at certain concentrations used.

Conclusion & Significance: This study suggests that combination of proteasome inhibition with PARP inhibition shows increased efficacy when compared to use of either drug alone in ovarian cancer cells. Based on this preclinical study, it can be assumed that administration of these agents in combination (bortezomib plus olaparib) to ovarian cancer patients may exert enhanced therapeutic effects in the clinic, improving the effect of either drug alone.

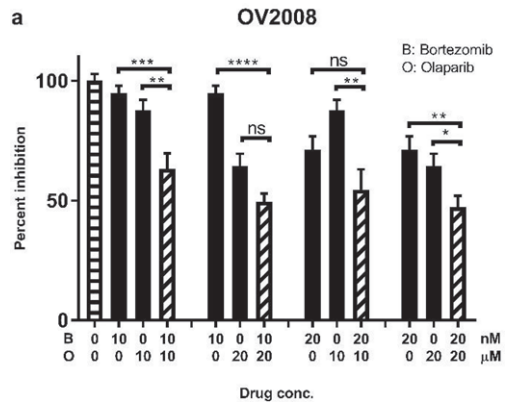


Figure 1. Representative figure of cytotoxicity of bortezomib (B) plus olaparib treatment for one of the ovarian cancer cell lines used in this study (OV2008). In this particular cell line, at B10 + O10 and B20 + O20, cell viability decreases significantly when compared to effects of either drug alone. B: bortezomib, O: olaparib.

caglar.berkel@gop.edu.tr