

## POSTER 34

## Combining Paclitaxel with repurposing drugs improve ovarian cancer management

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## Resumo

**Introduction:** The main challenge in ovarian cancer is to unveil therapeutic approaches to overcome chemoresistance and recurrence. Drug combinations and repurposing of non-oncological agents to treat neoplasms are two attractive strategies which allow higher efficacy, decreased toxicity, and overcoming chemoresistance [1-3]. The goal of combining drugs is improve therapeutic responses using lower doses of two more drugs comparing with single treatment [4]. Several non-oncological drugs, e.g., antihypertensives, antidiabetics, anthelmintics, antifungal, antibiotics and antivirals display an effective anti-cancer activity and have been studied to be repurposed in multi-drug resistant cancers [5]. **Objectives:** The purpose of this study was to explore whether combining Paclitaxel with repurposed drugs (i.e., Pitavastatin, Metformin, Ivermectin, Itraconazole and Alendronate) led to therapeutic benefits, comparing to isolated drugs. **Material and Methods:** Herein, we achieve cell viability by Presto Blue assay to evaluate the efficacy of combining Paclitaxel with repurposed drugs (mentioned above) in two chemoresistant ovarian cancer models, i.e., OVCAR8 (Carboplatin-resistant) and OVCAR8 PTX RP (Carboplatin and Paclitaxel-resistant) cell lines [2]. Significant differences ( $p < 0.05$ ) between

drug combination and respective individual drugs were evaluated by two-way ANOVA test. **Results:** Pitavastatin, Ivermectin, Itraconazole and Alendronate demonstrate a significant anti-cancer activity at low doses with IC50 values ranging between 1 and 150  $\mu$ M for both OVCAR8 and OVCAR8 PTX RP cells. In combination experiments, almost all repurposed drugs demonstrate higher ability than Paclitaxel alone to decrease cell viability for both cell lines. Indeed, we observed a significant cellular viability reduction in OVCAR8 cells when combining Paclitaxel to Pitavastatin ( $40,262 \pm 4,541\%$ ), Ivermectin ( $44,514 \pm 2,497\%$ ), Itraconazole ( $32,573 \pm 6,001\%$ ) and Alendronate ( $36,12 \pm 5,434\%$ ) comparing to Paclitaxel alone. Accordingly, in OVCAR8 PTX RP cells the concomitant treatment using Paclitaxel and Pitavastatin ( $62,805 \pm 8,845\%$ ), Ivermectin ( $76,491 \pm 8,351\%$ ), Itraconazole ( $68,073 \pm 4,981\%$ ) or Alendronate ( $66,977 \pm 5,566\%$ ) resulted in a significant cellular viability reduction comparing to single treatment with Paclitaxel. **Conclusion:** Overall, our results shown that almost all the repurposed drugs have the capacity to reduce cell viability at low IC50 values as single agents and in combination can improve anti-cancer activity of Paclitaxel.

**Keywords:** Chemoresistance; Combination Therapy; Drug Repurposing; Ovarian Cancer; Paclitaxel.

## Keypoints:

- Pitavastatin, Metformin, Ivermectin, Itraconazole and Alendronate exhibit anti-cancer activity at low IC50 values.
- Combining Paclitaxel with all the repurposed drugs studied led to therapeutic benefits, comparing with single drugs.
- Antineoplastic agents combined with repurposing drugs are a promising strategy to overcome chemoresistance.

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