Combination therapy may potentially improve ovarian cancer patient outcomes

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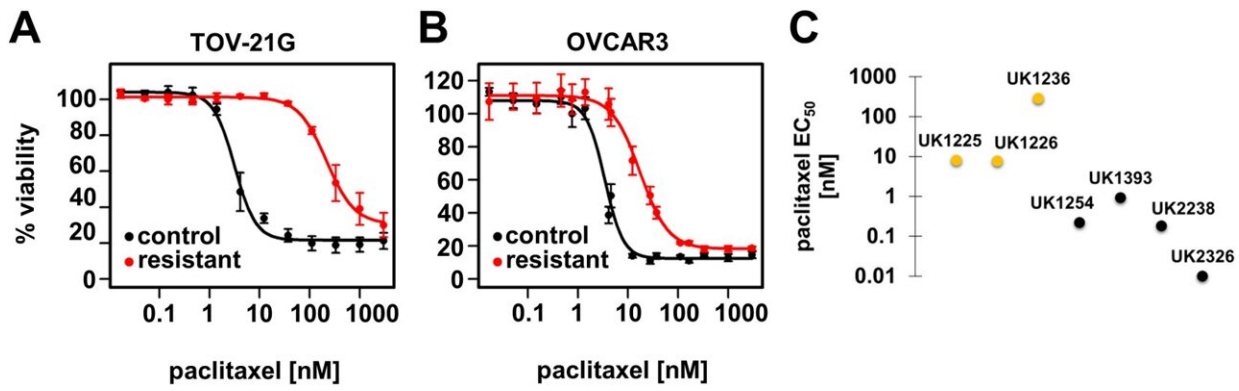

Fig 1. Ovarian cancer cell lines exhibit varied responses to paclitaxel treatment. Paclitaxel-resistant (PacR) and parental control ovarian cancer cell lines, TOV-21G and OVCAR3, were treated with serially diluted doses of paclitaxel for 96 hours in vitro. Cell viability is displayed at each concentration tested relative to untreated cells for the control (black) and PacR (red) cell lines of (A) TOV-21G and (B) OVCAR3 cells. Dose response curves were fit to the data and IC50 values were calculated using four-parameter log-logistic models. (C) Ovarian tumor organoid cell lines' paclitaxel EC50 values. Resistant lines are shown in gold and sensitive lines are shown in black. Credit: DOI: 10.1371/journal.pone.0254205

A new study from University of Kentucky Markey Cancer researchers demonstrates a combination of two drugs may be useful to treat ovarian cancers that are resistant to paclitaxel.

Recently published in *PLOS ONE*, the study demonstrates the combination of paclitaxel and lapatinib is synergistic, or when used together, the combined effect is better than expected; which may be a promising treatment strategy for patients with recurrent ovarian cancer.

Ovarian cancer is the most deadly gynecologic malignancy, with 1 in 70 women affected during their lifetime and with a five-year survival rate of less than 50%. Individuals with recurrent disease commonly receive paclitaxel, although only 20–30% benefit. The lack of response to paclitaxel is multifactorial, but one big reason is overexpression of ABCB1, a protein that essentially pumps drugs like paclitaxel out of cancer cells. This results in paclitaxel being eliminated from the body and unable to kill the cancer cells.

The team of researchers, led by Jill Kolesar, Pharm.D., professor in the UK College of Pharmacy and administrative director of Markey's Precision Medicine Clinic, demonstrated that inhibitors of ABCB1 in combination with paclitaxel were able to kill cancer cells that had previously been resistant to paclitaxel. The medications tested in this study, lapatinib and poziotinib, have both been previously shown to inhibit ABCB1 activity, though this study was the first to demonstrate activity in ovarian cancer.

"This combination may benefit patients with recurrent ovarian cancer who have received paclitaxel as their first line of treatment," Kolesar said. "More than 14,000 women will be diagnosed with ovarian cancer this year and the majority will have a recurrence, so developing effective treatment strategies is critical."

Kolesar's research led to the development of an ongoing clinical trial at the Markey Cancer Center for patients with who have recurred after platinum based chemotherapy.

"We are excited to evaluate another innovative treatment option for our patients with ovarian cancer, particularly since the combination of lapatinib and paclitaxel was discovered by Dr. Kolesar and team in one of our collaborative Markey Cancer Center labs," said Frederick Ueland, M.D., chief of gynecologic oncology and director of clinical operations at the UK Markey Cancer Center.

More information: J. Robert McCorkle et al, Lapatinib and poziotinib overcome ABCB1-mediated paclitaxel resistance in ovarian cancer, *PLOS ONE* (2021). DOI: 10.1371/journal.pone.0254205

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