

EXTREME DRUG RESISTANCE FOR CARBOPLATIN PREDICTS RESISTANCE TO FIRST-LINE THERAPY IN ADVANCED-STAGE OVARIAN CANCER: RESULTS FROM THE EORTC-GCG/NCIC-CTG NEOADJUVANT TRIAL

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Introduction: The EORTC 55971/NCIC OV13 trial included 719 patients with stage IIIc-IV epithelial ovarian cancer who all received platinum-based chemotherapy. Patients were randomized to primary or interval debulking surgery. More than one third of included patients appeared to be platinum resistant (progression during or within 6 months after first-line chemotherapy). A predictive test identifying patients' resistance to standard treatment would allow for more individualized treatment, including non-platinum based chemotherapy. We therefore investigated if the Extreme Drug Resistance (EDR) Assay (Oncotech - Exiqon AS Copenhagen) could predict resistance to platinum-based chemotherapy.

Patients and methods: Tumor tissue biopsies were taken during cytoreductive surgery and tested with the EDR assay against 11 chemotherapeutic agents, including carboplatin and paclitaxel. In vitro drug resistance was based on the percentage of chemotherapy induced cell growth inhibition. Clinical response to first line treatment was assessed according to the RECIST criteria.

Results: Biopsies were obtained from 246 patients. EDR based resistance to cisplatin and topotecan showed a positive relationship with WHO performance status; resistance to gemcitabine was positively linked to FIGO stage ($p < 0.05$). In vitro EDR to carboplatin showed a significant association with resistance to first-line treatment ($p < 0.05$). Multivariate analysis revealed residual disease after surgery ($p < 0.0001$), number of chemotherapy cycles received ($p = 0.007$) and EDR to carboplatin ($p = 0.008$) as independent predictors of response.

Conclusion: EDR to carboplatin was an independent significant predictive factor for failure of response to first-line platinum-based treatment in advanced ovarian cancer.