

Poster 26: The patient-derived ovarian cancer spheroid model predicts response to first-line chemotherapy of newly diagnosed primary ovarian cancer patients - clinical validation in the Spheroid study

Franziska Kusstatscher¹, Nicole Sigrüner¹, Kathrin Halfter², Bastian Czogalla², Barbara Mayer¹

¹Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, LMU Klinikum München, Deutschland

²LMU Klinikum München, Deutschland

Background

The diagnosis of advanced primary ovarian cancer is associated with poor prognosis despite intensive treatment with surgery followed by a combination therapy of carboplatin and paclitaxel. Most of the patients experience early recurrence and 5-year overall survival rate is less than 30%. This unfavorable outcome underlines the high need for new therapeutic strategies selected for the individual patient.

Objectives

The prospective multicenter Spheroid study was conducted to evaluate the chemopredictivity of the patient-derived ovarian cancer (PDOC) spheroid model for the 5-year overall survival (5-y OS, primary endpoint) and the 5-year progression free survival (5-y PFS, secondary endpoint) in newly diagnosed, primary ovarian cancers.

Results

101 patients newly diagnosed with advanced primary ovarian cancer were included in the Spheroid study. PDOC spheroids were prepared with a take rate of 97%. The cutoff of the residual metabolic activity after treatment of the PDOC spheroids with the first-line chemotherapy carboplatin combined with paclitaxel was 14.93%, AUC 0.734 (CI95% 0.627-0.841). This cutoff had an impact on the 5-year OS in primary ovarian cancer (log rank, $p < 0.001$). Cox regression model confirmed the cutoff as a prognostic factor (HR 2.94, CI95% 1.51-5.75, $p = 0.002$) independent from the FIGO-stage and macroscopic residual tumor. Overall, sensitivity of the drug testing in the PDOC spheroid model was 81.5% (CI95% 70.0%-90.1%) and specificity was 64.7% (46.5%-80.3%). Subgroup analysis identified several vulnerable subgroups gaining higher benefit from drug testing in the PDOC spheroid model, i.e. elder patients (>66 years, $n = 51$), patients with distant metastasis (FIGO IV, $n = 30$) and patients with an HGSOc histology ($n = 79$). Twelve out of 101 patients (11.9%) were classified chemo-resistant due to poor response to all tested chemotherapies.

Conclusion

The data suggest preclinical testing of first- and second-line therapies in the predictive PDOC spheroid model for each newly diagnosed primary ovarian cancer patient. This strategy could prevent treatment failure due to ineffective treatment reduction and chemoresistance.