Histologically, they are defined by the WHO as a category of tumors intermediate between morphologically benign lesions and those that are obviously malignant.

Methodology This retrospective cohort study included 10 women with borderline ovarian tumor treated in at chu hassan II Uni between 2019 and 2023. Clinicopathological characteristics, treatment, recurrence and survival data were collected

Results The average age is 38 years, 30% of our patients were nulligest, the serous subtype represents 70% and the mucinous 20%, all our patients have benefited from a surgical treatment

Conclusion OBRT most often affects young women. The majority are diagnosed at an early stage (stage I). The prognosis is excellent and the overall survival rate of OBRT is much higher compared to ovarian carcinomas.

Disclosures Frontier tumors of the ovary are clinically distinguished from malignant tumors by an earlier age of onset (mean age: 35–38 years) and a better prognosis. These tumors are almost always limited to the ovary (stage I) and often require less radical treatment than carcinomas, because of their non-invasive character.

#471 PARP-INHIBITORS CAN BE APPLIED TOGETHER WITH TUMOR TREATING FIELDS (TTFIELDS) TO PROLONG SURVIVAL IN AN OVARIAN CANCER MOUSE MODEL

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Introduction/Background Tumor Treating Fields (TTFields) provide non-invasive cancer treatment through continuous delivery of alternating electrical fields, administered through arrays on the skin of patients. TTFields have been investigated in combination with weekly paclitaxel for the treatment of recurrent ovarian cancer (OC) (INNOVATE, NCT02244502). This phase 2 study showed good tolerability and promising survival results and provided motivation for the ongoing phase 3 study (INNOVATE-3/ENGOT-ov50/GOG-3029, NCT03940196). Besides the originally hypothesized anti-mitotic mechanism, induction of double-stranded DNA breaks and inhibition of DNA damage repair were reported as a result of TTFields in vitro. Therefore, this study aimed to evaluate combination treatment with TTFields and concomitant poly ADP ribose polymerase (PARP) inhibition (Olaparib) in a high-grade serous OC mouse model.

Methodology C57BL/6 mice (N= 4 or 5) were inoculated with 5x106 ID8-fLuc OC cells intraperitoneally. One week post inoculation, transducer arrays were applied to the shaven skin of the mice and TTFields treatment (200 kHz) was initiated for a period of four weeks. Concomitantly, Olaparib (50mg/kg) was administered through daily oral gavage. Bioluminescent imaging (BLI) analysis was performed before, during and after treatment to observe tumor growth. Mice were analyzed for survival using endpoint criteria described previously.

Results TTFields combined with Olaparib resulted in a survival benefit compared to non-treated, TTFields only treated and Olaparib only treated tumor-bearing mice (median survival 97 vs 76, 74 and 80.5 days respectively). A repeat study showed similar prolongation of the combination treatment compared to TTFields alone (median survival 92 vs 76 days). These results were underscored by BLI analysis showing reduced tumor growth in Olaparib + TTFields treated mice in both experiments.

Conclusion Our experiments provide first in vivo evidence that a combination of TTFields and PARP inhibition can result in a survival benefit in OC. Further research is needed to confirm and expand these findings.

Disclosures AC is a contracted researcher for Oncoinvent AS and Novocure and a consultant for Sotio a.s. and Epics Therapeutics SA.

#472 ESTABLISHING HIGH GRADE SEROUS OVARIAN CANCER PATIENT-DERIVED ORGANOIDS AS MODELS FOR PRE-CLINICAL RESEARCH

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Introduction/Background Given their genotypic and phenotypic correlation with in vivo tumour, patient-derived organoids (PDOs) are in increasing use as pre-clinical models for High Grade Serous Ovarian Cancer (HGSOC) and other malignancies, including as putative predictive biomarkers. We sought to demonstrate inter- and intra-patient heterogeneity in PDOs from disseminated HGSOC tumours.

Methodology Multi-site tumour samples were obtained from patients undergoing primary cytoreductive surgery, tumour cells were extracted and PDOs propagated using different media conditions (± R-spondin supplementation). Once established, PDOs were assessed against conventional and targeted therapeutics using IC50 and AUC for comparison. RNA sequencing was also performed to characterise transcriptomic differences between PDOs.

Results Multi-site PDOs were grown from 14 patients with a mean of 5 sites cultured per patient, successfully established (≥5 passages) in 8/14 cases (57%) and immortalised in 5/14 cases (36%). Large variation was observed in IC50 and AUC values for platinum compounds and PARP inhibitors between patients, and between different tumour PDOs from the same patient. Interpatient heterogeneity was observed with cisplatin sensitivity varying up to 20-fold across 8 different PDO lines ($p<0.0001$). Intra-patient heterogeneity was observed with variations in carboplatin sensitivity by almost 10-fold between anatomical sites in one case ($p<0.0001$). Heterogeneity in rucaparib sensitivity was also demonstrated between cases and between sites from the same case ($p<0.001$). Dependence on R-spondin for growth was variable and influenced treatment sensitivity. Resistance was induced in 2 PDO lines through growth in low-dose conditions, with increments in AUC observed for cisplatin ($p<0.01$) and rucaparib ($p<0.05$) compared to controls.

Conclusion HGSOC PDOs are a reliable model for drug screening and enable characterisation of inter and intra-patient heterogeneity ex vivo. The extent of intra-patient heterogeneity is a likely contributory factor to the high rates of treatment resistance and relapse observed with HGSOC.

Disclosures JC received honoraria from Novartis and Pfizer, outside of the submitted work. CF received honoraria from Ethicon, GSK, Astra Zeneca/MSD, Tesaro, Clovis, Sequana and Roche, outside of the submitted work.