among which activation of DNA replication and changes in cell cycle regulation were notable. Organelles which retained regeneration capacity after carboplatin exposure, showed a sustained shift in expression of stemness associated surface marker CD133+ in the subsequent passages as showed by fluorescence-activated cell sorting and Western blot

Conclusion We hereby propose OFE assay as a novel functional readout for carboplatin sensitivity. Furthermore, expression profile changes in organoids during acute response to carboplatin provide insights into specific signaling hallmarks that are associated with resistance to carboplatin, and could help identify the cellular mechanism behind the process.

Conclusion GIScar demonstrated high accuracy with MG data with less inconclusive results and identifies patients who could best benefit from maintenance olaparib added to bevacizumab. GIScar test performances allow the deployment of this test in academic molecular biology laboratories.

Introduction/Background

High-grade serous ovarian cancers with deficiency of homologous recombination DNA repair (HRD) are sensitive to the combination of bevacizumab and olaparib as maintenance therapy in PAOLA-1 trial (NCT02477644). HRD status is determined by mutational scars within tumor genome. Here, we developed a new method called GIScar (Genomic Instability Scar) suitable with the most of the academic molecular biology laboratory constraints.

Methodology

We used sequencing data from a limited panel of 127 genes including genes involved in homologous recombination to detect mutational scars, i.e. chromosomal breaks, genomic deletion/duplication and allelic imbalance. The score was trained among 146 prospective samples from ovarian tumors with HRD status previously defined by Myriad Genetics® (MG). For clinical validation, we sequenced 469 DNA tumor samples from the PAOLA-1 trial and correlated GIScar status with progression free survival (PFS).

Results

On the 146 prospective samples, GIScar reached an accuracy of 92.46% compared to MG HRD status, with a sensitivity of 95.38% and specificity of 90.12%. On the 469 PAOLA-1 samples, patients with GIScar HRD positive (including tBRCAm) tumors showed a significant prolonged PFS in olaparib vs placebo arm (median PFS: 38.7 vs 20.1 months, hazard ratio (HR): 0.470 [95% CI, 0.334–0.661] as well those with GIScar HRD positive tBRCAw tumors (23.9 vs 16.4 months, HR: 0.529 [95% CI, 0.323–0.836]). Patients with negative GIScar HRD tumors did not benefit from addition olaparib (median PFS: 16.6 vs 16.5 months, HR: 1.045 [95% CI, 0.757–1.441]). Furthermore, our approach reduced by 90% (4 vs 47 tumors) the number of inconclusive status compared to MG.

Conclusion

GIScar demonstrated high accuracy with MG data with less inconclusive results and identifies patients who could best benefit from maintenance olaparib added to bevacizumab. GIScar test performances allow the deployment of this test in academic molecular biology laboratories.

Introduction/Background

Ovarian cancer (OC) is the fifth most common cause of death from cancer in women in Europe, with most patients being diagnosed in advanced stages. The most common histological subtype is high grade serous OC, which is characterised by deficiency in homologous recombination. The current standard therapy for advanced OC patients is debulking surgery, followed by platinum based chemotherapy and bevacizumab (bev), followed by maintenance therapy with bev or monotherapy with PARPi inhibitors (PARPi). The anticancer effects of PARPi seem to be increased by the addition of antiangiogenic drugs. Preclinical data showed increased HRD in tumours pre-treated with bev, and clinical trials showed a benefit of the combination of antiangiogenic drugs and PARPi vs. PARPi alone. Hence, in this placebo-controlled study we will evaluate rucaparib maintenance following bevacizumab maintenance for the treatment of advanced primary high grade BRCAwt OC (centrally tested by NGS analysis).

Methodology

This study will randomise 190 patients with histologically confirmed advanced (FIGO stage IIIA- IV) high grade serous or high grade endometrioid OC, fallopian tube cancer, primary peritoneal cancer or clear cell carcinoma of the ovary at the ration of 2:1 to receive either rucaparib 600 mg BID or placebo as maintenance therapy following first line chemotherapy with 6 cycles of Carboplatin/Paclitaxel and at least 12 months of bevacizumab. Subsequent maintenance therapy with rucaparib will continue for 24 months or until disease progression, unacceptable toxicity, or withdrawal.
Abstracts

INFLUENCE OF CANCER AND SURGERY TO IMMUNOSUPPRESSIVE AND PROINFLAMMATORY FACTORS IN OVARIAN CANCER PATIENTS’ PBMCs

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Introduction/Background Heme-oxygenase 1 (HO-1), programmed cell death protein 1 (PD-1) and its ligand (PD-L1) along with cytokines play an important role in ovarian cancer development. The changes of anti-cancer immunity in post-surgical period and its role in cancer progression are poorly understood. We intended to investigate HO-1, PD-1, PD-L1, immunosuppressive (IL-4) and proinflammatory (IL-1β, IL-6) interleukins expression in peripheral blood mononuclear cells (PBMCs).

Methodology The peripheral venous blood samples were collected before and after surgery on the 1st, 3rd and 5th day from 10 controls and 9 ovarian cancer patients (FIGO stage III-IV) for PBMCs isolation with FICOL Paque Premium and targets mRNA expression analysis. RNA extraction and synthesis of cDNA, quantitative real-time PCR assays were performed. Results are presented as median with interquartile range.

Abstract 2022-RA-939-ESGO Figure 1 Relative mRNA expression of HO-1, IL-1β, IL-4, IL-6, PD-1, PD-L1 genes in PBMCs from ovarian cancer patients on the 1st, 3rd and 5th day after surgery compared to the expression before the treatment. Bar graphs show median value and interquartile range *p<0.05.

Results Median age of controls and cancer patients were 59 (26) and 58 (14) years respectively (p>0.05). The mRNA expression of all markers in PBMCs were significantly down-regulated in cancer patients before surgery comparing to controls (p<0.05). Relative median expression of HO-1, IL-1β, IL-4, IL-6, PD-1 and PD-L1 in controls and cancer patients respectively were 0.97 (0.33) vs 0.66 (0.5), 0.87 (1.95) vs 0.07 (0.16), 0.86 (1.39) vs 0.43 (0.61), 0.98 (1.15) vs 0.03 (0.03), 0.99 (0.94) vs 0.32 (0.50), 1.18 (0.66) vs 0.26 (0.36). Significant post-surgical changes in IL-6 and PD-L1 expression were observed along with not significant fluctuations of other targets expression (figure 1).

Conclusion Investigated components of anticancer immunity and immunosuppression mechanisms are affected by cancer and surgical treatment. Therefore, PBMCs are worthy targets for detailed investigation in this field.

CEBOC, A SINGLE-ARM PHASE II TRIAL TO EVALUATE THE SAFETY OF CEDIRANIB IN THE PREVENTION OF BOWEL PERFORATION IN PLATINUM RESISTANT OVARIAN CANCER

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Introduction/Background Systemic treatment of platinum-resistant advanced ovarian cancers (PROC) utilises cytotoxic chemotherapy and vascular endothelial growth factor receptor (VEGFR) inhibitors. However, patients at risk for malignant bowel obstruction (MBO) are excluded from this efficacious combination due to risk of bowel perforation.

Methodology We conducted a Simon’s two-stage trial combining oral VEGF inhibitor cediranib (20 mg/day) with weekly paclitaxel (70 mg/m²), in participants with recurrent PROC and clinical and/or radiological features indicating an increased risk of developing MBO. Primary endpoint was number of patients free of grade 3–5 gastrointestinal perforation (GIP) or fistula, from those who received ≥5 days and ≤18 weeks cediranib, causally related to cediranib. With 90% power and 5% significance, 24 evaluable patients were required, with 22 free of GIP or fistula to demonstrate safety. Cediranib could start with chemotherapy, or at cycle 2 or 3, once bowel symptoms were CTCAE grade ≤2. Previous bevacizumab exposure and prior MBO were permitted. Patients were continued on cediranib maintenance after paclitaxel completion, and optionally proceeded to cediranib plus olaparib (300 mg bd) at disease progression.

Results 30 participants were enrolled from March 2018 to February 2021. 90% ECOG 0–1, 97% had symptoms showing risk of bowel obstruction. 1 patient died before any treatment. 12 received paclitaxel only (bowel symptoms didn’t improve or deterioration) and subsequently progressed. 17 patients were evaluable for primary endpoint; none developed GIP or fistula. Three cediranib+paclitaxel participants developed bowel obstruction (any grade; including one receiving cediranib+olaparib). Three participants had grade 3+ SAEs causally related to cediranib+/-olaparib (one diarrhoea; one diarrhoea and TIA; one vomiting). Median progression-free survival was 5.4 months (95%CI: 4.18–8.25), and overall survival 15.2 months (95%CI: 8.52–20.5).