Oncological outcomes in patients having neoadjuvant chemotherapy who do not undergo intended interval debulking surgery

**Introduction/Background** A common treatment approach for patients with FIGO stage III/IV ovarian cancer is neoadjuvant chemotherapy (NACT) with interval debulking surgery (IDS) following NACT for stage III/IV ovarian cancer. However, not all patients undergo the intended surgery for multiple reasons. Outcome data for these patients is limited, however, reduced survival has been reported in literature. This study aimed to assess and compare the oncological outcomes of patients who did not undergo IDS following NACT for stage III/IV ovarian cancer in Wales.

**Methodology** The Wales Cancer Network identified all patients with stage III/IV ovarian cancer scheduled for NACT across the three Cancer centres in Wales in 2018 and 2019. The Welsh Clinical Portal and CANISC were used to gather data on patients’ demographics, disease stage, treatment plans, complications, reasons for not having surgery, and oncological outcomes.

**Results** 197 patients were included, of which 128 (65%) underwent surgery and 69 (35%) did not. Across Wales, the patients who had surgery were on average younger (64.2 vs 70.8 years), had fewer comorbidities (average 2.7 vs 3.0), a better performance status at diagnosis (average 0.8 vs 1.5), but had the same average BMI (28.9) compared to those who did not. The majority of patients who underwent surgery had zero complications (58.6%). Across Wales, 99.13%, 93.91%, 74.78%, and 58.26% of patients who underwent IDS survived at 6, 12, 24, and 36 months, respectively, compared to 90.0%, 73.33%, 40.00%, and 20.00% who did not (p=0.0034, 0.0001, 0.0001, 0.0001 respectively).

**Conclusion** Across Wales, 35% of women with stage III/IV ovarian cancer did not undergo their intended surgery after NACT. In this retrospective cohort, the survival was lower in those who did not have surgery. Common reasons for not proceeding with surgery included disease progression, fitness for surgery, and patient choice.

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**CHITINASE RESPONSE AFTER 3 CYCLES OF CHEMOTHERAPY AS A PROMISING MARKER OF CHEMOSENSITIVITY AN ANCILLARY ANALYSIS OF THE GINECO-ENGOT EWOC-1 TRIAL

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**Introduction/Background** Older patients with ovarian cancer have poor outcomes; the geriatric vulnerability score (GVS) was validated as a prognostic factor for survival. During aging the circulating Chitinase 3-like-1 (CHI3L1), and its related chitinase enzymatic activity increase, leading to propose them as ‘aging biomarkers’. However, recent data supported the implication of chitinase-like proteins in the proliferation of several cancers. The EWOC-1 trial (NCT02001272) showed a lower efficacy of the carboplatin monotherapy (Cmono) arm compared to carboplatin-paclitaxel (CP) in vulnerable patients; a serum sampling was provided on inclusion, after 3 and 6 courses of chemotherapy for the measurement of chitinase activity in each arm (A: standard CP; B: Cmono; C: 3weeks/4 CP), to identify whether its association with patients’ outcomes and inversely, the differential impact of the distinct treatment regimens on it.

**Methodology** Chitinase activity was assessed as previously published. Were analyzed both its absolute value on inclusion and its kinetics after 3 chemotherapy courses (chitinase response).

**Results** Serum samples could be retrieved for 46/120 patients on inclusion and 33 after 3 chemotherapy courses. Chitinase baseline median activity (in U/L, IQR) was 1727.9 (1459.3; 1878.3) at inclusion, similar in the 3 arms; no association was shown with any of the geriatric vulnerability parameters, nor the GVS, nor overall survival. Chitinase response was significantly different in the 3 arms, with a median (in U/L,
IQR) of -160 (-297; 35.2) in the total cohort, -272 (-376; -122) in arm A, 105 (-109; 221) in arm B and -160 (-663; -109) in arm C, p=0.008. High chitinase response was associated with high CA-125 ELIMination rate constant K (KELIM), a marker of chemosensitivity (Fisher exact test, p=0.042).

Conclusion Chitinase activity should not be considered, in the context of ovarian cancer as an aging biomarker, but chitinase response appears as a promising marker of chemosensitivity.

Identification and Validation of MicroRNAs as Endogenous Controls in Epithelial Ovarian Cancer

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Methodology Following RNA extraction from formalin-fixed paraffin embedded tissues from 80 high-grade EOC patients, a custom designed panel of 48 miRNAs was investigated by RT-qPCR and analyzed by applying various strategies regarding missing data (a listwise/pairwise deletion, mean substitution, replacing non-detects with a Cp value of 40, multiple imputation), choosing stable endogenous controls (GeoNorm, BestKeeper, NormFinder, the comparative Ct method and RefFinder) and normalization based on endogenous controls, spike-ins or global mean.

Results We identified 20 endogenous control candidates by combining miRNA microarray data analyses of four datasets and literature screening. Among these candidates, hsa-miR-101-3p, hsa-miR-191-5p, and hsa-miR-193a-5p were subsequently validated as most stable in 80 EOC patients. Moreover, we present how different approaches of data handling affect results, e.g. common practice of setting missing Cp values to 40 might lead to large (likely false) differences in miRNA expression between patients.

Conclusion Our data demonstrated the challenge of miRNA qRT-PCR data analysis and the need for standardization if comparison/conclusions across datasets are performed.

Implementation of a Tri-modal Prehabilitation Intervention – KORE-INNOVATION: The First Prospective Clinical Trial to Assess a Perioperative Pathway to Reduce Postoperative Complications in Ovarian Cancer Patients

Introduction/Background The effectiveness of prehabilitation in improving physical capacity for patients undergoing surgery has been shown for patients in orthopedic, abdominal, or cardiothoracic surgeries. Ovarian cancer patients have an exceptionally high risk for severe postoperative complications due to the extent of the surgical treatment, often including multivisceral resection. We report our first experiences of implementing a tri-modal prehabilitation intervention as part of the KORE-INNOVATION trial.

Methodology KORE-INNOVATION is an ongoing clinical trial to implement and assess an innovative perioperative care pathway to reduce complications (primary endpoint) for patients undergoing surgery for ovarian cancer through the implementation of a prehabilitation strategy combined with the ‘enhanced recovery after surgery’ (ERAS)-pathway. The prehabilitation intervention consists of three modules: a personalized empowerment intervention, a personalized physical exercise-program, and a personalized metabolic screening and diet.