ONCOLOGICAL OUTCOMES IN PATIENTS HAVING NEOADJUVANT CHEMOTHERAPY WHO DO NOT UNDERGO INTENDED INTERVAL DEBULKING SURGERY

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Introduction/Background A common treatment approach for patients with FIGO stage III/IV ovarian cancer is neoadjuvant chemotherapy (NACT) with interval debulking surgery (IDS) with subsequent adjuvant chemotherapy. 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 90.00%, 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,
**Introduction/Background** MicroRNAs (miRNAs) are small non-coding RNA molecules regulating gene expression that may have diagnostic potential by being associated with different diseases, including epithelial ovarian carcinomas (EOC). However, there is a lack of consensus how to accurately quantify miRNA levels, which hinders their implementation in diagnostics. Real-time qRT-PCR is often considered as the golden method; however, the results might be biased by various handling of missing data and normalization approaches. Only a few studies have been published to date on the identification of endogenous miRNA controls in EOC. Therefore, our aim was to identify stable candidates based on own, previously published- and three public miRNA-microarray datasets and verify their stability in a new cohort of EOC patients. Moreover, our goal was to compare different missing data and normalization approaches to investigate their impact on the results.

**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 (GeNorm, BestKeeper, NormFinder, the comparative ΔCt 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.

**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.

**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.