BLOOD-BASED DETECTION OF CIRCULATING DICKKOPF-1 AS A PROGNOSTIC BIOMARKER IN OVARIAN CANCER PATIENTS

Introduction/Background Dickkopf-1 (DKK-1) is a secreted protein, known for suppressing the differentiation and activity of bone-building osteoblasts by acting as an inhibitor of Wnt-signalling. Soluble DKK-1 (sDKK-1) has been proposed as a prognostic biomarker for a wide range of malignancies, however, clinical relevance of sDKK-1 as potential blood-based marker for ovarian cancer is unknown.

Methodology sDKK-1 levels were quantified in a cohort of 150 clinically documented ovarian cancer patients by a commercially available DKK-1 ELISA (Biomedica, Vienna, Austria). Median sDKK-1 level was significantly elevated at 150 clinically documented ovarian cancer patients by a commercially available DKK-1 ELISA (Biomedica, Vienna, Austria). Median sDKK-1 level was significantly elevated at 150 clinically documented ovarian cancer patients by a commercially available DKK-1 ELISA (Biomedica, Vienna, Austria).

Result(s) Median sDKK-1 level was significantly elevated at primary diagnosis of ovarian cancer compared to healthy controls (estimated difference (ED) of 7.75 ng/mL (95%CI: 3.01 – 12.30 ng/mL, p = 0.001)). Higher levels of sDKK-1 at diagnosis indicated an increased volume of intraoperative malignant ascites (ED 7.08 pmol/L, 95%CI: 1.46 – 13.05, p = 0.02) and predicted suboptimal debulking surgery (ED 6.88 pmol/L, 95%CI: 1.73 – 11.87, p = 0.01). sDKK-1 did not correlate with CA125, and higher sDKK-1 levels predicted a higher risk of recurrence and poor survival (PFS: HR = 0.507, 95%CI: 0.317 – 0.809; p = 0.004; OS: HR = 0.561, 95%CI: 0.320 – 0.986; p = 0.044). Prognostic relevance of sDKK-1 was partly sustained in wtBRCA patients (PFS: HR = 0.507, 95%CI: 0.317 – 0.809; p = 0.004).

Conclusion This is the first study demonstrating the prognostic relevance of sDKK-1 in ovarian cancer patients, including those with wtBRCA1/2 status. Our data encourage further evaluation of sDKK-1 in ovarian cancer patients, possibly in terms of a therapy monitoring marker or a response predictor for sDKK-1-directed targeted therapies.

BRCA GERMLINE MUTATION FREQUENCY AND THE EFFECTS ON ONCOLOGIC OUTCOMES AMONG NORWEGIAN OVARIAN CANCER PATIENTS

Introduction/Background Germline mutations in the BRCA1 and BRCA2 genes (BRCAg) are a known risk factor for development of breast and epithelial ovarian cancer (OC). We describe the frequency of BRCAg carriers, the clinical features and survival in Norwegian OC patients.

Methodology This is a prospective cohort study including OC patients at the Norwegian Radium Hospital (covering 50% of the Norwegian population) from Jan 1st 2014 to Dec 31st 2019. Included are the patients which accepted BRCAg test after giving informed consent. DNA was isolated from peripheral blood, and mutation analyses performed with Sanger sequencing and multiplex ligation probe amplification. Data on family history, BRCAg test results was registered and data on clinical features and histopathology was collected from the department’s quality database. All statistical analyses were performed using the Stata (Stata/MP 17.1) program, Chi-square
test for independence of groups and Kaplan-Meier survival analysis.

Result(s)* Altogether 73% of OC patients accepted BRCAg test and were included in the study (n=1049), 83 (7.9%) had a BRCAg, of which 46 (4.4%) had mutation in BRCA1 and 37 (3.5%) in BRCA2. Assuming that the BRCAg frequency is not higher among the not tested compared to the tested and lowest 0, we estimate 5.7-7.9% BRCAg frequency in our OC population.

The patients with BRCAg were younger at diagnosis (mean age 59.9 y vs. 63.3 y p=0.005), had more often high-grade serous histology (95% vs. 67% p<0.0001), had more advanced disease (FIGO stage III-IV) at the time of diagnosis (83% vs. 71% p=0.003) and more often received neoadjuvant chemotherapy (28% vs. 5% p=0.04) compared to non-mutation carriers. Patients with FIGO stage III-IV and BRCAg had a better overall survival compared to non-mutation carriers (median OS 76.4 months vs. 42.1 months p=0.03, figure 1). However, the difference in progression free survival between the two groups was non-significant (median PFS 31.1 months vs. 30.3 months p=0.87).

Conclusion* In our study population the BRCAg frequency was 7.9% and BRCAg was found to be a significant prognostic factor.

1086 ABSTRACT WITHDRAWN

1094 MIRRORS STUDY: A PROSPECTIVE COHORT STUDY ASSESSING THE FEASIBILITY OF ROBOTIC INTERVAL DEBULKING SURGERY FOR ADVANCED-STAGE OVARIAN CANCER

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Introduction/Background* MIRRORS (Minimally Invasive Robotic surgery, Role in optimal debulking Ovarian cancer, Recovery & Survival) is the largest prospective cohort study of robotic interval debulking surgery (IDS) in women with advanced-stage epithelial ovarian cancer (EOC) to date. MIRRORS has investigated the feasibility of obtaining consent from women, the acceptability and success of robotic IDS and its impact on short-term surgical outcomes and quality of life.

Methodology Eligibility Women with FIGO IIIc-IVb EOC undergoing neo-adjuvant chemotherapy and suitable for IDS. Exclusions: pelvic mass >8cm, extensive HPB and/or extensive bowel involvement.

Surgery commenced with an initial laparoscopic assessment, for all women recruited, followed by a decision to proceed immediately to robotic or open IDS.

Result(s)* 23/24 eligible women recruited. Following initial diagnostic laparoscopy, 20 women proceeded directly to robotic IDS, 3 women received open IDS. All patients were debulked with maximal surgical effort to R<1, 39% to R=0. No robotic cases were converted to open. Median EBL for robotic IDS: 50ml, open: 2026ml, median operating time 05:58 robotic vs 05:38 open, length of stay (LOS) 1.5 days robotic vs 6 days open. Bowel resection with stapled anastomosis 15% (3/20), diaphragmatic stripping 60% (12/20), full-thickness diaphragmatic resection 5% (1/20), pelvic peritoneal stripping 70% (14/20).

Conclusion* MIRRORS has shown significantly enhanced recovery with short LOS, reduced blood loss and reduced HDU/ITU demands, enabling faster re-commencement of chemotherapy in women with FIGO IIIc-IVb EOC. This proved to be greatly beneficial during the COVID-19 pandemic.