Abstracts

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LOW BRCA 1/2 GERMLINE MUTATION RATE IN A FRENCH CANADIAN POPULATION

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Objective Universal genetic testing has become increasingly important in the management of women with epithelial tubo-ovarian and peritoneal carcinoma. Worldwide, the reported rates of deleterious BRCA mutation rate vary between 12–15%. We wanted to evaluate the mutation rate in our population considering its specific genetic background (French Canadian ascent).

Method Mainstreaming genetic testing was implemented in our service in Mai 2017 and offered to all patients with epithelial tubo-ovarian or peritoneal carcinomas, except mucinous and borderline tumors. The data was prospectively collected in a database and retrospectively analyzed.

Results A total of 214 patients were tested in our center, 169 (79%) were high grade serious carcinomas (HGSC). Overall, 137 patients had no mutation (64%). Deleterious BRCA 1/2 mutations were observed in 10 patients (4,7%), 4 BRCA1 and 6 BRCA2, nearly all were in HGSC (9). Other non BRCA-mutations (ATM, RAD51C, RAD51D, BRIPI, CDH1, MRE11, MSH6, MUTYH, PALB2 and PMS2) were observed in an additional 18 patients (8,4%): 16 HGSC, 1 endometrioid and 1 carcinosarcoma. VUS were seen in 57 patients (26,7%) of which 4 were BRCA1/2 VUS. No deleterious mutations were identified in clear cell carcinomas and seen in only one low grade serious carcinoma.

Conclusion In our specific French Canadian population, the deleterious germline BRCA mutation rate was surprisingly low (4,7%), less than half the rate reported in the literature. Based on Health Canada’s current approval, only a small proportion of our patients could access PARPi therapy. Hopefully canadian indications for PARPi will soon include non-BRCA and somatic mutations.

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IS A VAGINECTOMY ENOUGH OR IS A PELVIC EXENTERATION ALWAYS REQUIRED FOR SURGICAL TREATMENT OF RECURRENT CERVICAL CANCER?

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Introduction Ovarian cancer (OVCA) is a lethal gynecologic malignancy. Patients with high-grade and low-grade disease carry a poor prognosis from chemoresistance and decreased induction of apoptosis. We hypothesized persistent activation of the unfolded protein response (UPR) with upregulation of CHOP and XAF-1 arms, would overcome apoptotic arrest, leading to death in chemo-sensitive and resistant OVCA.

Methods Patient-derived and commercially available HG OVCA and LG OVCA single cell lines were cultured and treated with celastrol, a potent UPR activator. Cell viability was assessed using Incucyte. Protein lysates of cells treated with celastrol were analyzed using Western blot and Caspase-Glo. RNA was analyzed using real-time PCR. Transient knock down (KD) of XAF-1 and CHOP was performed using siRNA.

Results Celastrol induced cell death in chemo-sensitive and resistant OVCA lines in the nanomolar range. Celastrol induced the UPR. CHOP was preferentially upregulated upstream of mitochondrial depolarization and induction of the intrinsic apoptotic pathway. There was a reciprocal rise in XAF-1 RNA/protein levels and fall in XIAP with UPR activation. KD of XAF-1 decreased the cytotoxic effect of celastrol. KD of...
CHOP resulted in a lack of rise in XAF-1 with UPR activation.

Conclusions Activating UPR with agents that upregulate the CHOP/XAF-1 axis induce death in chemo-sensitive/resistant OVCA lines. XAF-1 is presumptively regulated by CHOP and a major effector of UPR, required for full cytotoxic activity. The CHOP/XAF-1 arm of UPR is a promising targetable pathway for treating HG/LG OVCA.

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CHOP resulted in a lack of rise in XAF-1 with UPR activation.

Conclusions Activating UPR with agents that upregulate the CHOP/XAF-1 axis induce death in chemo-sensitive/resistant OVCA lines. XAF-1 is presumptively regulated by CHOP and a major effector of UPR, required for full cytotoxic activity. The CHOP/XAF-1 arm of UPR is a promising targetable pathway for treating HG/LG OVCA.

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Objectives Breast cancer is the most frequent solid cancer among menopausal women. The main objective of this study is to evaluate the body image and the sexual function in menopausal women diagnosed with nonmetastatic and operable breast cancer.

Methods This is a prospective cohort-type study of 200 menopausal women diagnosed then operated on for breast carcinoma between January 2017 and January 2019 in the department of Gynecology and Obstetrics of Farhat Hached Teaching Hospital Sousse, Tunisia. Patients were stratified based on whether they underwent conservative (G1) or radical (G2) breast surgery.

The data collection used 2 standardized psychometric assessment scales validated in Arabic:

- The Body-Esteem Scale for Adolescents and Adults (BESAA) for the evaluation of the body image.
- The Arab Female Sexual Function Index (ArFSFI) for evaluation of sexual function.

Results The two groups were comparable in terms of age and socio-economic characteristics of the patients and their spouses. The median tumor size at the time of cancer diagnosis was 3.6 cm (± 1.2) in G1 and 6.1 cm (± 2.6). The body image was lower after mastectomy with a significant difference for the item appearance (p = 0.047); without influencing any aspect of the sexual function. The results

- Table 1 Comparison of the sexual function scores according to the Arab Female Sexual Function Index (ArFSFI)