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335 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 serous 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, BRIP1, 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 serous 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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336 IS A VAGINECTOMY ENOUGH OR IS A PELVIC EXENTERATION ALWAYS REQUIRED FOR SURGICAL TREATMENT OF RECURRENT CERVICAL CANCER?

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Introduction No consensus has yet been reached on the best strategy for treatment of cervical cancer local recurrence. Vaginectomy could be a salvage treatment in selected patients.

Methods The records of vaginal recurrent cervical cancer patients admitted at Fondazione Policlinico 'Agostino Gemelli' IRCCS in Rome from January 2010 to June 2019 were retrospectively analyzed. We reported perioperative and survival outcomes of vaginectomy with respect to a matched series of pelvic exenteration (PE).

Results Fifteen women underwent vaginectomy and 30 patients were submitted to PE. No statistical differences were observed between the two groups at baseline characteristics. The vaginectomy procedures were successfully performed in all women, and no case required conversion to PE. Moreover, a higher rate of major postoperative complications after PE with respect to vaginectomy ($p=0.027$) were recorded: among them, 3 women required a reoperation within 30 postoperative days, and 4 experienced two or more complications. Twenty-five (55.6%) women experienced recurrence: 8/25 (32.0%) in the vaginectomy group, and 17/25 (68%) in the PE group, with a median progression-free survival of 20 months and 13 months, respectively ($p=0.169$). In total, 5/15 (33.3%) died of disease in the vaginectomy group and 13/30 (43.3%) in the PE group, with a median overall survival of 39 and 18 months for vaginectomy and PE, respectively ($p=0.161$).

Conclusions The vaginectomy seems to allow for salvage treatment, like radiotherapy and/or PE, but with a minimal impact on quality of life in appropriately selected women with local recurrent cervical cancer.

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337 TREATMENT OF OVARIAN CANCER VIA INDUCTION OF CELLULAR STRESS AND THE UNFOLDED PROTEIN RESPONSE (UPR)

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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 and LG OVCA cells 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