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RE: Universal tumor DNA BRCA1/2 testing of ovarian cancer: prescreening PARPi treatment and genetic predisposition

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BRCA1/2 mutations play a predictive role in ovarian cancer risk evaluation. Moreover , patients are today being tested for BRCA1/2 mutations to select a tailored therapy too , because they could benefit from a treatment with PARP inhibitors (PARPi).Therefore in ovarian carcinomas (OCs), BRCA1/2 mutation testing is an important step in planning the correct therapeutic strategy in association with chemotherapy and anti VEGF agents. We read with great interest the paper submitted by Vos et al (1) which investigates the role of universal tumor DNA BRCA1/2 testing of all newly diagnosed OC patients as prescreen for PARPi treatment and cancer predisposition. With the approach described by the authors, both hereditary and somatic aberrations affecting DNA BRCA1/2 could be quickly and correctly detected with tumor BRCA1/2 smMIP-based next generation sequence testing.The authors concluded that this test, as the first step in all newly diagnosed OC patients, could statistically significantly increase the identification rate of eligible patients for treatment with PARPis. Even if this result can contribute to modify the clinical practice, it is appropriate to make some observations. In the paper all 315 patients were not distinguished according to histotype (generically ovarian cancer patients were recruited and investigated). This is a considerable gap if one only considers that in women unselected for family history, germline *BRCA1/2* mutations have been found in 4%–14% of all OCs, 5%–18% of serous OCs, and ~22% of high grade serous cases (2). The Cancer Genome Atlas consortium, detected BRCA1/2 mutations in 20% of 316 high grade serous cases; 9% and 8% were germline BRCA1 and BRCA2 mutations and 3% were somatic mutations (3). OC DNA testing was performed according to methodology described by Weren et al (4). In the paper it is not specified whether some parameters had been evaluated to ensure good quality of formalin-fixed paraffin embedded samples for DNA analysis (as the recommendations for information to be included when reporting tumor BRCA1/2 results), according to Capoluongo, et al. (2). In the section describing the study population the authors declare that in few cases, cells obtained from ascites aspiration were analyzed. Even if there are only a few cases, it should be pointed out that at present there are no mature data supporting the use of the ascitic liquid as a source of cells to carry out mutational

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analysis of BRCA1/2 in OC. Tissue samples from primary carcinomas and metastases, formalin-fixed paraffin embedded and fresh-frozen specimens constitute the most suitable source of material to carry out DNA BRCA1/2 testing (2, 5). It is declared also that universal BRCA1/2 testing is well appreciated by patients and gynecologists. Undoubtedly this statement is correct and shareable but we must not forget that only 13 of 17 patients consented to the telephone interview and only 18 of 41 gynecologists compiled and delivered the evaluation questionnaire. These numbers are decidedly poor to allow us to draw firm conclusions on the compliance and satisfaction of patients and doctors towards the test.

Note

All the authors declare no conflict of interest in preparing and submitting this manuscript.

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