Discussion. SPOP was found to be mutated in 8,54% of our samples, confirming the literature data that showed a strong association with high expression of PDL-1, independently from specific mutations. Interestingly, we found that SPOP mutated samples had also the highest expression profiles of our samples. This data seems to confirm the possible role of SPOP and the cullin-based E3 ubiquitin ligase in the regulation of PDL-1 expression, becoming a possible molecular marker in the cancer immunotherapy. Moreover, we found PDL-1 to be associated with higher Gleason grades, such a result is probably linked to the higher tumor mutational burden of this prostate cancer subgroup. Nothwithstanding, we found that 35,4% of SPOP wild-type prostate cancer have an overexpression of PDL-1, suggesting that other molecular pathways could be implicated in the upregulation of PDL-1 in prostate cancer. However, our SPOP mutated specimens were not numerous enough in order to make definitive statements and further research is needed in order to get more conclusive Results.

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BRCA AND OVARIAN CANCER: IMPLEMENTING ROUTINE GENETIC TESTING. THE GENOA EXPERIENCE

M.Paudice[1], D.Rivera[2], G.Anselmi[3], C.Dellepiane[4], M.G.Centurioni[5], S.Mammoliti[6], V.Gismondi[2], L.Varesco[2], V.G.Vellone[1,3]

[1] Univ. of Genoa, Dept. of Surgical Sciences and Integrated Diagnostics, Genoa; [2] Unit of Hereditary Cancer, IRCCS Osp. Policlinico S. Martino, Genoa; [3] Unit of Academic Pathology, IRCCS Osp. Policlinico S. Martino, Genoa; [4] UO Oncologia Medica 2, IRCCS Osp. Policlinico S. Martino, Genoa; [5] Unit of Obstetrics and Ginecology, IRCCS Osp. Policlinico S. Martino, Genoa; 6 UO Oncologia Medica 1, IRCCS Osp. Policlinico S. Martino, Genoa

Objectives. Ovarian cancer (OC) is the fifth cause of cancer death among women in western countries. The advanced stage at diagnosis (FIGO III-IV) is the main cause of its high mortality rate. The evaluation of OC BRCA status has important therapeutic and prognostic implications, therefore genetic testing is recommended at diagnosis of OC. Our Institute (Policlinico San Martino, Genoa) investigated the reliability of the detection of germline and somatic BRCAm from formalin-fixed-paraffin-embedded (FFPE) specimens in a routine lab set.
Materials and methods. We included patients who underwent germline BRCA testing for the period 2017-2019 and with histological diagnosis of High Grade Serous Ovarian Cancer (HGSOC) (n=19). All the cases were reviewed by a pathologist expert in gynecological pathology. The paraffin block for each patient was chosen according to: optimal fixation and storage, high representativeness of the entire neoplasia, high tumor cellularity (>20%), low percentage of stroma cell, fibrosis and necrosis. From each selected sample, macro sections (six sections of 10 µm thickness) were obtained for molecular analyses. DNA was isolated using the QS GeneRead DNA FFPE treatment kit and its quality was assessed by the Qubit 3.0 Fluorometer. Somatic BRCA analysis was performed with Oncomine BRCA panel on the Ion GeneStudio S5 System. Parameters for analysis excluded SNVs with: variant allele frequency (VAF) <5%, coverage <500X, quality score (PHRED) < 30. Pathogenetic variants (PVs) were validated by Sanger sequencing. Samples were analyzed blindly to their germline status.
Results. PVs were detected in 10 of 19 cases (52,63%): of these, 8 (80%) were germline. All known germline variants were detected by the somatic analysis.
Conclusions. The implementation of BRCA testing in the routine diagnostic workflow of OC benefits from the strict collaboration of skilled clinician, geneticist and pathologist. An optimal preanalytical phase is required to obtain satisfactory genetic Results from FFPE specimens.