Hereditary Breast, Ovarian and Pancreatic cancers: looking beyond the *BRCA1/2* genes

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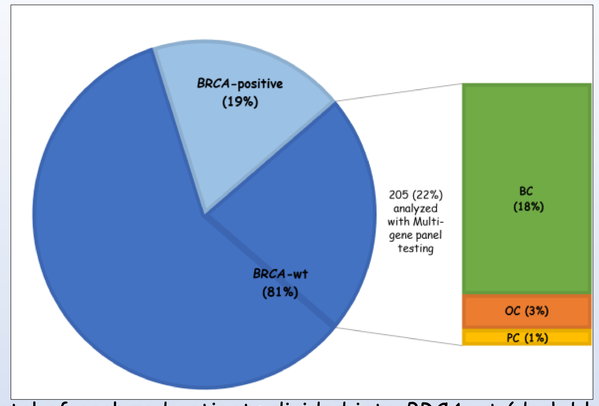
BACKGROUND

Hereditary breast (BC), ovarian (OC) and pancreatic (PC) cancers are the major *BRCA*-associated tumours. However, some *BRCA1/2*-non informative patients with a strong cancer personal and/or family history need a further genetic testing through a multi-gene panel including other high- and moderate-risk susceptibility genes

METHODS

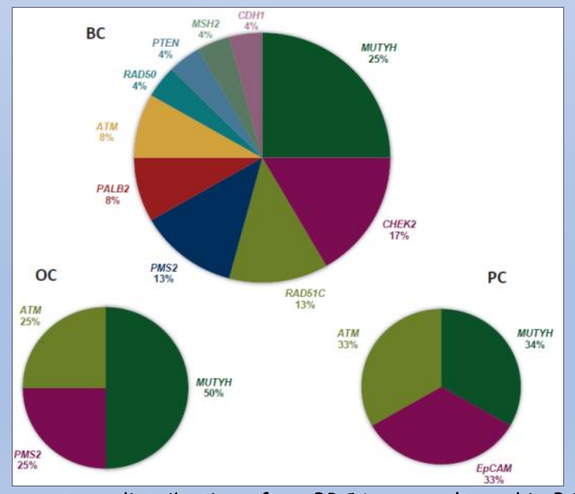
We evaluate if some BC, OC and PC patients should be offered multi-gene panel testing, based on well-defined criteria regarding their cancer personal and/or family history. 205 out of 915 BC, OC and PC patients, resulted *BRCA1/2* non-informative and with significant cancer personal and/or family history, were genetically tested for germline pathogenic or likely pathogenic variants(PVs/LPVs) in genes different from *BRCA1/2*



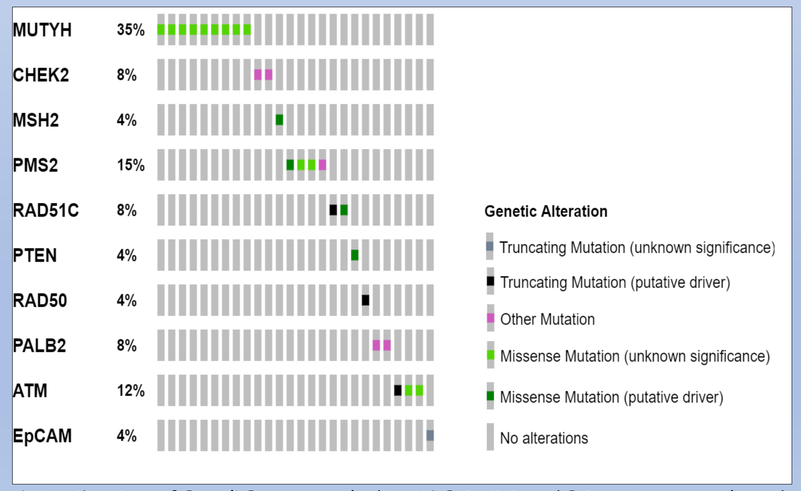
Total of analyzed patients divided into *BRCA*-wt (dark blue) and *BRCA*-positive (light blue).
Patients analyzed with multi-gene panel divided into Breast cancer (green), Ovarian cancer (orange) and Pancreatic cancer (yellow)

RESULTS

We revealed that 31 (15.1%) out of 205 patients harboured germline PVs/LPVs in no-*BRCA* genes, including *PALB2*, *CHEK2*, *ATM*, *MUTYH*, *MSH2*, *RAD51C*. In particular, we found that 11 out of 24 (45.8%) BC patients harbouring PVs/LPVs in no-*BRCA* genes showed a bilateral breast cancer



Percentage distribution of *no-BRCA* genes altered in BC, OC, or PC patients detected by multi-gene panel testing.



Distribution of PVs/LPVs revealed in 31 BC, OC and PC patients analyzed with multi-gene panel testing.

CONCLUSIONS

Providing a multi-gene panel testing to *BRCA1/2*-non informative BC, OC and PC patients with a strong cancer personal and/or family history could significantly increase the detection rates of germline PVs/LPVs in other cancer predisposition genes beyond *BRCA1/2*. The use of a multi-gene panel testing could improve the inherited cancer risk estimation and clinical management of patients and unaffected family members

References:
1. Bono, M., et al (2021). Impact of deleterious variants in other genes beyond BRCA1/2 detected in breast/ovarian and pancreatic cancer patients by NGS-based multi-gene panel testing: looking over the hedge. ESMO open
2. Germani, A.,et al (2020). Beyond BRCA1 and BRCA2: Deleterious Variants in DNA Repair Pathway Genes in Italian Families with Breast/Ovarian and Pancreatic Cancers. Journal of clinical medicine
3. Fanale, D., et al (2020). Detection of Germline Mutations in a Cohort of 139 Patients with Bilateral Breast Cancer by Multi-Gene Panel Testing: Impact of Pathogenic Variants in Other Genes beyond BRCA1/2. Cancers

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DISCLOSURE the authors have declared no conflicts of interest.