Key Summary of Conference Abstract

Frequency of Pathogenic and Likely Pathogenic Variants in Breast and Ovarian Cancer Genes Identified in a 34-Gene Hereditary Multi-Cancer Panel at a Diagnostic Reference Laboratory

Background

- Multigene panels allow assessment of many genes simultaneously and have demonstrated clinical utility for identifying pathogenic variants in cancer genes.[1]
- Information gleaned from these panels could improve knowledge about variants associated with diseases and multigene panels.
- **Objective:** The investigators of this study report the frequency of pathogenic/likely pathogenic variants (P/LPVs) detected by a 34-gene hereditary cancer panel at a diagnostic laboratory.

Methods

- The investigators retrospectively analyzed variants identified in specimens submitted for genetic testing with a 34-gene hereditary cancer panel at Quest Diagnostics. The panel included the following genes:
  - *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RET, SDHB, SDHC, SDHD, SMAD4, STK11, TP53,* and *VHL*.
- P/LPVs in the 34 genes were identified by next-generation sequencing; copy number variants were confirmed by DNA microarray analysis.

Results

- Among 3,805 individuals in the study cohort, 422 (11%) had a total of 450 P/LPVs (386 P/64 LP).
- Of the 450 P/LPVs detected
  - 323 (72%) were in breast cancer genes
  - 264 (59%) were in ovarian cancer genes (overlap with breast cancer genes)
  - 83 (18%) were in genes not associated with breast or ovarian cancer
- Of the 353 P/LPVs found in breast and/or ovarian cancer genes, 216 (61%) were in non-*BRCA1/2* genes.

Conclusions

- In this study, most P/LPVs detected with the 34-gene hereditary cancer panel were in breast and ovarian cancer genes.
- Most P/LPVs detected in breast and ovarian cancer genes were in non-*BRCA1/2* genes.

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Reference

1. LaDuca H, Polley EC, Yussuf A, et al. A clinical guide to hereditary cancer panel testing: evaluation of gene-specific cancer associations and sensitivity of genetic testing criteria in a cohort of 165,000 high-risk patients. *Genet Med*. 2020;22(2):407-415. doi:10.1038/s41436-019-0633-8