Key Summary of Conference Abstract

Detection of Germline and Somatic *BRCA* Mutations Using a 50-Gene Next-Generation Sequencing Panel

Background

- Genetic variants in *BRCA1* and *BRCA2* are often detected in breast and ovarian cancer patients; *BRCA1* variants are commonly associated with *TP53* variants.[1]
- Investigators previously developed a 50-gene, next-generation sequencing (NGS) panel that can detect mutations in breast and ovarian tumor specimens.[2]
- The frequency of variants identified by individual panels in a clinical setting is an important measure of panel performance.
- **Objective:** In this study, the investigators at a national reference laboratory used the 50-gene NGS panel to examine the frequency of *BRCA1/2* and *TP53* mutations in tumor specimens.

Methods

- The investigators conducted a retrospective analysis of deidentified results from consecutive fixed formalin-fixed and paraffin-embedded (FFPE) tissue specimens submitted to Quest Diagnostics for testing with a 50-gene NGS panel.
  - Targeted exon capture and NGS were used to detect variants in *BRCA1*, *BRCA2*, *TP53*, and 47 other actionable genes with variants often found in solid tumors.
  - Variant analysis included single nucleotide variants, insertions/deletions, translocations, and copy number variants; tumor mutation burden and microsatellite instability were also analyzed.

Results

- A total of 240 FFPE specimens were included:
  - 123 from patients with breast cancer (median age 54 years)
  - 116 from patients with ovarian cancer (median age 63 years)
  - 1 from a patient with breast and ovarian cancer (age 48 years)
- Pathogenic *BRCA1/2* mutations were identified in
  - 4.8% (6/124) of breast cancer patients
  - 13.9% (16/115) of ovarian cancer patients
- Variants of unknown significance were identified in
  - 10.5% (13/124) of breast cancer patients
  - 7.0% (8/115) of ovarian cancer patients
- Pathogenic *TP53* mutations were identified in
  - 93.3% (14/15) of patients with *BRCA1* mutations
  - 62.8% (137/218) of patients without *BRCA1/2* mutations (*P*=0.016)

Conclusions

- With the previously developed and optimized 50-gene NGS panel, the prevalence of pathogenic *BRCA1/2* mutations in this study population was 4.8% in breast cancer patients and 13.9% in ovarian cancer patients; these frequencies are similar to findings of other studies.[3]
- Most (93%) breast and ovarian tumors with *BRCA1* mutations also had a pathogenic *TP53* mutation.

Poster presentation at the 8th International Symposium on Hereditary Breast and Ovarian Cancer

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8th International Symposium on Hereditary Breast and Ovarian Cancer, Virtual Edition, May 4-7, 2021
Date: May 6
Time: 11:30-13:00 EDT

Webpage
TBD

References

1. Peng L, Xu T, Long T, et al. Association between *BRCA* status and p53 status in breast cancer: a meta-analysis. *Med Sci Monit*. 2016;22:1939-1945.
2. Ma L, Hua M, Rivera S, et al. Validation of a clinically actionable core cancer gene test for solid tumors facilitating targeted molecular therapy and immunotherapy. Abstract presented at American Association for Cancer Research Annual Meeting 2017; April 1-5, 2017; Washington, DC. https://cancerres.aacrjournals.org/content/77/13_Supplement/5356
3. Kurian AW, Ward KC, Howlader N, et al. Genetic testing and results in a population-based cohort of breast cancer patients and ovarian cancer patients. *J Clin Oncol*. 2019;37(15):1305-1315. doi:10.1200/JCO.18.01854

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