Comprehensive germline multigene panel testing changes clinical care for patients with breast cancer: Untapped clinical utility and PARP inhibitor trial eligibility.


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BACKGROUND
- Guidelines for testing hereditary breast and ovarian cancer (HBOC) patients for BRCA1/2 were established years ago to identify patients with clinically actionable variants and limit the economic burden.
- The cost of genetic testing has plummeted, and the number of breast cancer-risk genes with management guidelines has expanded.
- A community-based registry was established to test all breast cancer patients on a comprehensive multigene panel.
- We report the potential impact of germline tests on health outcomes based on clinical decision making and treatment interventions.

METHODS
- An IRB-approved multicenter prospective registry was initiated with 20 community-based and academic breast sites.
- Patients with current or prior breast cancer were tested with an 80-gene panel.
- Clinical information was collected, including pretesting risk assessment and physician management recommendations after test results were received.

PHYSICIAN MANAGEMENT CHANGES UPON RECEIVING GENETIC TESTING RESULTS
- Pathogenic/likely pathogenic (P/LP) germline mutations were found in 8.7% of patients.
- There was no significant difference in P/LP rate between patients who meet the NCCN testing guidelines and those who do not meet the guidelines (p = 0.44).
- For 62.4% of patients with a P/LP germline mutation, clinicians reported germline results impacted patients' health outcomes, and 69.4% of patients P/LP results impacted the health outcomes of patients' relatives.
- Physician-reported impact on patient outcome associated significantly with the presence of P/LP germline findings (p < 0.0001).
- There was no significant difference in the reported clinical utility of variants of uncertain significance (VUS) compared to negative results (p = 0.49).

CONCLUSIONS
- This study shows that comprehensive panel testing of breast cancer patients impacts physician assessed patient outcomes, and informs changes in surgical treatment strategy, medical therapies and proactive screening.
- The data suggest that BRCAPRO calculators are poor predictors of germline presence of P/LP findings.
- Physicians in this study also demonstrate the ability to discern the clinically actionable value of P/LP mutations from non-actionable VUS, and act accordingly.
- This study suggests multigene panels impact breast cancer patient care by informing implementation of precise medicine treatment interventions, and guiding long-term medical management and preventive surveillance for patients and their family members.