Title: Transitioning from single- to multi-gene testing for hereditary cancer predisposition: an advanced practice nurse's experience

Authors: Phyllis Everett, MSN, RN, AOCN, APNG, NP-C; Kelly Fulk, MS, CGC; Virginia Speare, PhD, CGC; Holly LaDuca, MS, CGC; Laura Panos, MS, CGC; Elizabeth Chao, MD, FACMG

Primary Contact: Kelly Fulk, MS CGC kfulk@ambrygen.com Phone: (804) 892-1351

Category: I - Breast Center Operations, Administration, and Programs

Subcategory: C. Programs 4. High Risk Program

Objectives: Nurses, physician assistants, and non-geneticist providers are exploring ways to incorporate genetic testing into patient care. Based on the availability of next generation sequencing, multi-gene panels are rapidly replacing the single-gene approach to testing for hereditary cancer predisposition. We describe an advanced practice nurse's (APN) experience transitioning from single gene test ordering to the utilization of multi-gene testing in her community-based oncology clinic.

Methods: Test results and clinical history were reviewed for cases referred for multi-gene panel testing to a single commercial laboratory within the first year of panel testing being offered at this clinic. Panels included comprehensive analysis of 6-28 genes, depending on the test ordered. Qualitative analysis was used to identify challenges encountered by the APN while transitioning from utilizing single-gene to multi-gene testing.

Results: A total of 113 multi-gene panel tests were ordered, with a personal +/- family history of breast cancer being the most frequent testing indication. For the majority of patients, panels included a combination of high- and moderate-risk hereditary cancer genes (n=104; 92%). The remaining 8% (n= 9) of patients underwent a panel of 6 high-risk breast cancer genes. Seven patients (6%) were found to carry a pathogenic or likely pathogenic germline mutation, five of which were identified in genes other than *BRCA1* and *BRCA2*: *NBN*, *ATM*, *APC*, *PALB2*, and *TP53*. Twenty-six patients (23%) were identified to carry at least one variant of unknown significance, including four who also had a mutation detected. Multiple challenges were encountered during the implementation of multi-gene panels, including a need to become knowledgeable about genes beyond *BRCA1* and *BRCA2*, both for herself and for physician colleagues. Patient education and counseling required modification to include concepts of uncertainty related to a lack of management guidelines for lesser known breast cancer genes and the greater possibility of an uncertain result.

Conclusions: The experience of an APN who incorporated the use of multi-gene testing highlights the need for continuing education about genes other than *BRCA1* and *BRCA2* and the potential need to modify counseling practices. The detection of mutation-positive patients presents an opportunity for early detection and possible cancer prevention; however, management guidelines for lesser known genes are needed.