Transitioning from Single- to Multi-gene Testing for Hereditary Cancer Predisposition: An Advanced Practice Nurse's Experience

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BACKGROUND

- Nurses, physician assistants, and non-geneticist providers are incorporating genetic testing into patient care more now than ever before.
- 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 ordering single gene tests to the utilization of multi-gene testing in her community-based oncology clinic.

METHODS

- Test results and clinical histories were reviewed for 113 cases referred for multi-gene panel testing to a single commercial laboratory within the first two years (2012 to 2014) of panel testing being offered at this clinic.
- Panels included comprehensive analysis (sequencing and deletion/duplication analysis) of 6-28 genes, depending on the test ordered.
- Qualitative analysis was used to identify challenges encountered by the APN while introducing multi-gene testing into her practice.

TABLE 1. DEMOGRAPHICS

Ethnicity	n	%		Cancer History	n	%
African American	16	14.2		Yes	105	92.9
Caucasian	80	70.8		No	8	7.1
Unknown	14	12.4		Breast cancer	71	62.8
Mixed Ethnicity	2	1.8		Ovarian cancer	7	6.2
Gender				Endometrial cancer	6	5.3
Female	102	90.3		Colorectal cancer	17	15.0
Male	11	9.7		Adenomatous polyps	12	10.6
Age at testing				**Test Ordered**		
21-30	2	1.8		BRCAplus	9	8.0
31-40	7	6.2		BreastNext	17	15.0
41-50	15	13.3		OvaNext	35	31.0
51-60	21	18.6		ColoNext	5	4.4
61-70	33	29.2		CancerNext	46	40.7
71-80	26	23.0		RenalNext	1	0.9
81-90	8	7.1				
91+	1	0.9				

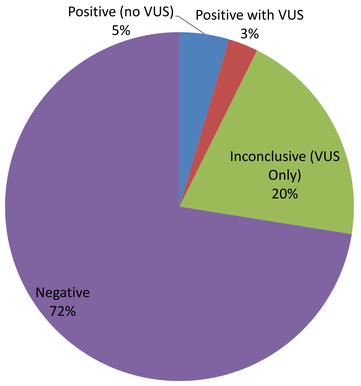
Total number of patients = 113

TABLE 2. GENES BY PANEL

	Panel					
	BRCAplus	BreastNext	OvaNext	ColoNext	RenalNext	CancerNext
APC				x		x
ATM		x	x			x
BARD1		x	x			x
BMPR1A				x		x
BRCA1	x	x	x			x
BRCA2	x	x	x			x
BRIP1		x	x			x
CDH1	x	x	x	x		x
CDK4						x
CDKN2A						x
CHEK2		x	x	x		x
*EPCAM**			x	x	x	x
MLH1			x	x	x	x
MRE11A		x	x			x
MSH2			x	x	x	x
MSH6			x	x	x	x
MUTYH		x	x	x		x
NBN		x	x			x
NF1		x	x			x
PALB2		x	x			x
PMS2			x	x	x	x
PTEN	x	x	x	x	x	x
RAD50		x	x			x
RAD51C		x	x			x
RAD51D		x	x			x
SMAD4				x		x
STK11	x	x	x	x		x
TP53	x	x	x	x	x	x
FH					x	
FLCN					x	
MET					x	
MITF					x	
SDHA					x	
SDHB					x	
SDHC					x	
SDHD					x	
TSC1					x	
TSC2					x	
VHL					x	

**EPCAM* testing is del/dup only.

FIGURE 1. MULTI-GENE PANEL RESULTS



N= 113

RESULTS

- A total of 113 multi-gene panel tests were ordered, with a personal and/or 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 with known management guidelines.
- 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.

CHALLENGES ENCOUNTERED IN IMPLEMENTING PANEL TESTING

- There is now a need to become personally knowledgeable about genes beyond *BRCA1* and *BRCA2* and to educate physician colleagues in order to properly manage patient care.
- Additional patient pre- and post-test counseling is needed to incorporate concepts of uncertainty related to a lack of management guidelines for lesser known breast cancer genes and the greater possibility of an uncertain result.
- Initially, there was some difficulty obtaining insurance coverage for panels.
- Become knowledgeable about the various labs offering multi-gene panels and deciding which lab to choose is crucial in order to ensure patients are offered the most appropriate testing options.[1]

TAKE-HOME POINTS

- Expanded educational opportunities are needed for non-geneticist providers who are incorporating the use of multi-gene testing into clinical practice, including training about genes other than *BRCA1* and *BRCA2* and modified counseling practices.
- The detection of a greater percentage of mutation-positive patients presents an opportunity for early detection and possible cancer prevention.[2]
- Gene variants of uncertain significance (VUS) and limited understanding of the clinical significance of some lesser known genes included in multi-gene tests continue to pose challenges for clinicians; however, appropriate patient management plans can be achieved using the ever-improving knowledge of these genes in combination with the patients' family histories.
- Community clinics can play an important role in identifying patients at risk for hereditary cancer syndromes when providers, such as APN's, are able to effectively utilize multi-gene panels and provide appropriate counseling.

REFERENCES

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2. Minion L, Dolinsky J, Chase D, Dunlop C, Chao E and Monk B. Hereditary predisposition to ovarian cancer, looking beyond BRCA1/BRCA2. Gynecologic Oncology (2015).