Ambry Genetics

RESEARCH SUMMARY

Improvements to Patient Care through Hereditary Cancer Panels

NOVEMBER 2017

Multigene panels for hereditary cancer have become widely accepted and utilized. Ambry continues to lead important studies highlighting the clinical benefit of these panels, as well as the importance of using an experienced lab to obtain accurate, informative results.

Larger multigene panel tests increase the detection of patients with hereditary cancer[1]

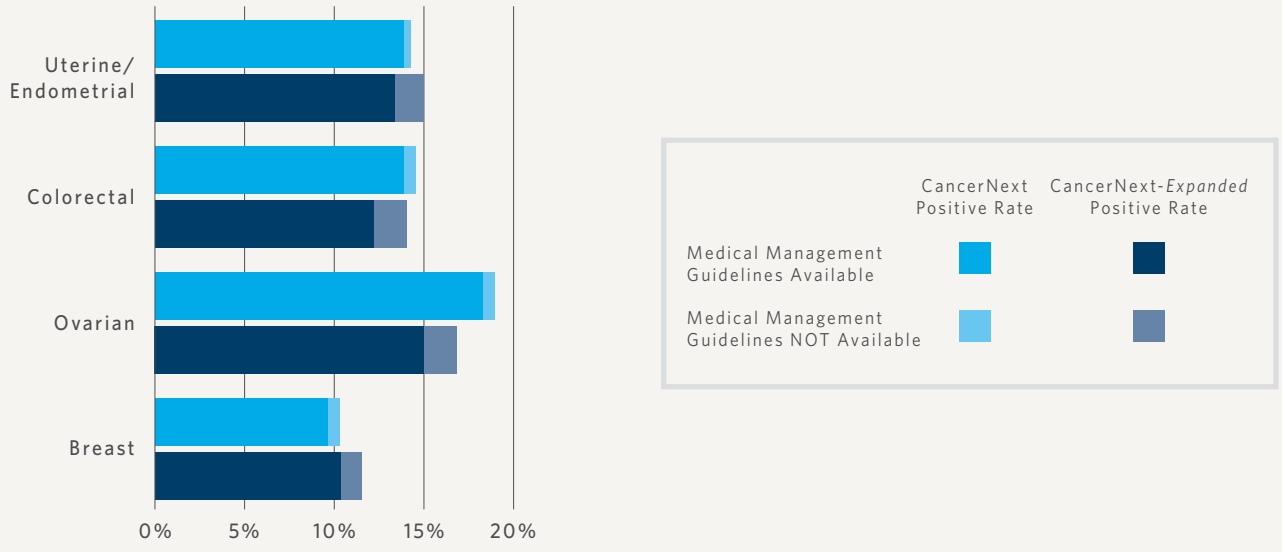
KEY STUDY FINDINGS

- Over 93% of patients who test positive may need to alter medical management based on published recommendations
- Larger gene panels increase the detection rate of patients with hereditary cancer by 5-10% compared to smaller gene panels in patients with breast, colon, and endometrial cancer

POINTS FOR YOUR PRACTICE

- Using a larger gene panel, like CancerNext™, can help you identify more patients with hereditary cancer. Another important benefit of larger panels is that most often positive results are clinically actionable, influencing patient care.

Frequency of Positive Results and Availability of Medical Management Recommendations



Utilizing an experienced lab for multigene panel testing can increase confidence in results and minimize the burden of variants of uncertain significance

KEY FINDINGS FROM MULTIPLE STUDIES

Study 1: VUS Rates by Ethnicity

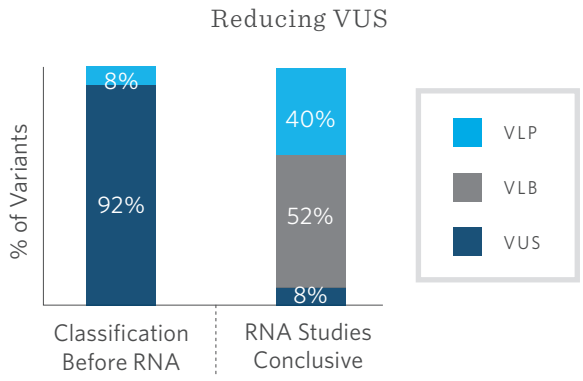
- Rates of variants of uncertain significance (VUS) vary by the number of genes on a panel and by ethnic background, with individuals of Asian, African American, and Hispanic background having the highest VUS rates[2]

MGPT	Caucasian (n=37,151)	African American (n=3,079)	Ashkenazi Jewish (n=3,281)	Asian (n=1,873)	Hispanic (n=2,722)	Overall (n=48,106)
BRCAplus	4.4	8.9	2.6	13.7	8.0	5.20
BreastNext	22.0	37.1	24.7	42.0	29.0	21.92
CancerNext	29.9	48.3	33.1	59.1	36.8	28.08

→ Ambry's BRCAplus panel has the lowest VUS rate across all ethnicities, largely attributed to the small size of the panel

Study 2: Ambry's ATG Lab

- Ambry's Translational Genomics (ATG) lab performs functional studies to determine the effects of certain variants on the gene. Of variants that have been assessed in the ATG lab, 92% were reclassified from a VUS to an informative result.[3]



Study 3: Re-analysis of Direct-to-Consumer Test (DTC) Results

- 40% of DTC test results sent to Ambry for confirmation testing were found to be false positive results[4]

POINTS FOR YOUR PRACTICE

- The ATG lab provides our variant assessment team with additional data and can help lower VUS rates across all ethnicities. This, combined with Ambry's vast experience in panel testing, ensures lower VUS rates compared to other labs, which minimizes uncertainty and provides patients with accurate, actionable results.
- When discussing the potential for a VUS with your patients, it is important to know that smaller panel options can limit the number of VUS; however, patients of non-Caucasian ethnicities may have a higher likelihood of receiving a VUS.

REFERENCES

1. Panos Smith L, *et al.* Is Bigger Always Better? An Updated Comparison of Multi-gene Panel Results for Common Cancers. NSGC 2017
2. Panos L, *et al.* Variant of Unknown Significance Rates Vary by Ethnicity and Genes Analyzed. ASHG 2015 Annual Meeting, Baltimore, MD, October 6-10, 2015
3. Karam R, *et al.* RNA Studies Improves the Classification of Splicing Variants. American College of Medical Genetics 2017, Phoenix, AZ, March 21-25, 2017
4. Tandy-Connor S, *et al.* False Positive Results Reported by Direct-To-Consumer Genetic Tests Highlight the Importance of Clinical Confirmation Testing for Appropriate Patient Care. American College of Medical Genetics 2017, Phoenix, AZ, March 21-25, 2017