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RESEARCH SUMMARY

Genetic Testing Indicated for All Patients with Pancreatic Cancer

SEPTEMBER 2018

Recent studies by Ambry Genetics and other investigators have demonstrated a high prevalence of hereditary pancreatic cancer, highlighting the importance of multigene panel testing (MGPT) for all patients diagnosed with pancreatic cancer.

WHY THIS MATTERS TO YOU

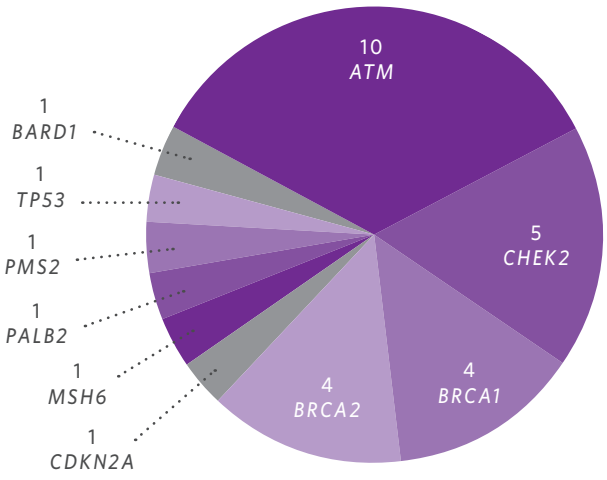
Due to these recent studies, NCCN® guidelines now recommend *BRCA1/2* testing for patients with a personal and/or family history of pancreatic cancer diagnosed at any age[1]. These studies also suggest that MGPT should be considered to identify more patients with hereditary pancreatic cancer.

Prospective Study of Germline Genetic Testing for Pancreatic Cancer*

KEY STUDY FINDINGS[2]

- In the first multi-center, prospective study of its kind, 298 consecutive, unselected patients with pancreatic ductal adenocarcinoma (PDAC) underwent MGPT for 32 genes.
- 41/298 (14%) patients were identified to have a mutation in a cancer susceptibility gene.
- 29/41 (70.7%) mutations were considered clinically actionable. (Figure 1)
- Using then current guideline-based testing, 52% of mutations in known PDAC genes would have been missed.

Figure 1. Breakdown of Clinically-Actionable Positive Results



** Ambry Genetics study*

RESEARCH SUMMARY

Multigene Hereditary Cancer Panels Reveal High-Risk Pancreatic Cancer Susceptibility Genes*

KEY STUDY FINDINGS[3]

- A case-control study of 1,652 patients with pancreatic cancer undergoing MGPT estimated the risk of pancreatic cancer associated with mutations in cancer susceptibility genes.
- 20.73% of patients were found to have a germline mutation.
- *ATM*, *BRCA2*, *CDKN2A*, MSH2, *MSH6*, *PALB2*, *TP53* were associated with high risk (OR >5) of pancreatic cancer.

Gene	Odds Ratio (OR)	95% CI	*P*-value
ATM	8.96	6.12-12.98	< .001
BRCA1	2.95	1.49-5.60	.002
BRCA2	9.07	6.33-12.98	<.001
CDKN2A	35.97	14.68-85.93	<.001
CHEK2	2.08	1.15-3.67	.02
MSH2	7.10	1.04-37.16	.047
MSH6	7.79	3.85-15.16	<.001
PALB2	14.82	8.12-26.22	<.001
TP53	7.15	2.78-18.13	<.001

KEY FINDINGS FROM OTHER SUPPORTING STUDIES

- Case-control study of 3,030 pancreatic cancer patients undergoing germline MGPT found significant associations between pancreatic cancer and mutations in *ATM, BRCA1, BRCA2, CDKN2A, MLH1,* and *TP53*.[4]
- Study of 289 unselected PDAC patients undergoing germline and somatic MGPT found that 9.7% of patients had a mutation.[5]

POINTS FOR YOUR PRACTICE

- Roughly 5-20% of pancreatic cancer patients have a mutation in a cancer susceptibility gene, and identification of these patients is critical for appropriate medical management, including determining clinical trial eligibility.
- NCCN® guidelines now indicate that *BRCA1/2* testing should be considered for **all** patients with pancreatic cancer.
- Patients with pancreatic cancer are at-risk for clinically actionable mutations in genes beyond *BRCA1/2*, therefore, MGPT may be an appropriate option for identifying cancer susceptibility.

** Ambry Genetics study*

REFERENCES

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3. Hu *et al.* Multigene Hereditary Cancer Panels Reveal High-Risk Pancreatic Cancer Susceptibility Genes. JCO Precision Oncology. July 2018.
4. Hu *et al.* Association Between Inherited Germline Mutations in Cancer Predisposition Genes and Risk of Pancreatic Cancer. AMA. 2018.
5. Yurgelun *et al.* Germline cancer susceptibility gene variants, somatic second hits, and survival outcomes in patients with resected pancreatic cancer. Genetics in Medicine. July 2018.

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