Ambry’s Multigene Panel Testing Finds Families with Unexpected CDH1 Mutations

HOW DO WE BEST MANAGE THESE FAMILIES? AMBRY HELPS FIND THE ANSWER.

A recent collaboration between Ambry Genetics, University of Southern California, and Stanford University published in JCO Precision Oncology describes the incidence and clinical characteristics of CDH1 mutation carriers found through multigene panel testing (MGPT).

WHY THIS MATTERS TO YOU

Some patients found to have a CDH1 mutation via MGPT do not meet clinical criteria for hereditary diffuse gastric cancer (HDGC), posing a management challenge. We studied different families with a CDH1 mutation and offered management recommendations.

BACKGROUND

HDGC is a rare condition caused by CDH1 mutations, and associated with up to an 80% lifetime risk of diffuse gastric cancer (DGC) and up to a 60% lifetime risk for female invasive lobular breast cancer (ILC), therefore needing increased breast cancer screening and to consider prophylactic gastrectomy.

Providers are increasingly ordering MGPT, which often includes CDH1, resulting in the identification of unexpected mutations in patients who do not meet the International Gastric Cancer Linkage Consortium (IGCLC) criteria. Given the serious nature of a gastrectomy, providers question whether these patients should be treated with the same surgical measures used for those with classic HDGC.

This study assessed the clinical histories of 20 CDH1 mutation carriers identified by MGPT (out of 27,254 tested) to determine if they met IGCLC criteria and offer informed recommendations for medical management.

POINTS FOR YOUR PRACTICE

- IGCLC criteria may miss patients with CDH1 mutations; however, MGPT may help to identify these families
- Ambry includes analysis of CDH1 on several panels, including BreastNext, ColoNext, and CancerNext
- Many healthcare providers, including expert authors on this study, continue to manage all CDH1 mutation carriers according to current guidelines, with consideration of prophylactic gastrectomy between 20-30y and annual breast MRI beginning at 30y.

“These guidelines may change as we gain additional knowledge on the cancer risks, and until then, counseling and support balanced by consideration of risks, benefits and costs are integral to partnering with these patients in shared decision-making.” – Study Author
**SIGNIFICANT FINDINGS**

- Breast cancer was the most prevalent cancer, present in 73% of mutation carriers
  - 21% of mutation carriers had ductal breast cancer, not the typical lobular breast cancer associated with CDH1 mutations
- 65% of patients did not meet IGCLC criteria for consideration of CDH1 testing
- 3 patients had prophylactic gastrectomy, and all had pathologic evidence of DGC, despite not meeting IGCLC criteria, highlighting the importance of a well-informed management plan

Learn more about our research [here](#).

**REFERENCES**