Clinician Management Resource for CDH1 (Hereditary diffuse gastric cancer)

This overview of clinical management guidelines is based on this patient’s positive test result for a CDH1 gene mutation. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient’s past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

### SCREENING/SURGICAL CONSIDERATIONS

<table>
<thead>
<tr>
<th>Gastric Cancer</th>
<th>AGE TO START</th>
<th>FREQUENCY</th>
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</table>
| Prophylactic gastrectomy is recommended.  
  • Baseline endoscopy prior to prophylactic total gastrectomy  
  • Intraoperative frozen sections should be performed to verify proximal margin contains esophageal squamous mucosa and distal margin contains duodenal mucosa, to ensure complete removal of gastric tissue. A D2 lymph node dissection is not necessary for prophylactic total gastrectomy.  
  • Not recommended under 18 years of age, but may be considered for certain patients (i.e. family history of gastric cancer diagnosed under age 25) | Between 18-40 years old | N/A |
| Patients who elect not to undergo prophylactic gastrectomy should be offered upper endoscopy with multiple random biopsies | Individualized | Every 6-12 months |

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<th>Female Breast Cancer</th>
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| Breast Screening  
  • Mammography  
  • Consider breast MRI with and without contrast | 30 years old, or 5-10 years before the earliest known breast cancer in the family | Annually |
| Discuss option of risk reducing mastectomy | Individualized | N/A |

* Due to limited data, the management of gastric cancer risk in individuals with pathogenic/likely pathogenic variants in CDH1 in the absence of a family history of gastric cancer is not straightforward. However, studies have shown that some apparently unaffected individuals in breast cancer-only families had early stage diffuse gastric cancer at the time of prophylactic gastrectomy (Jacobs MF, et al. *Gastroenterology* 2019; 157:87-96). Annual endoscopic surveillance should be offered to these individuals, and prophylactic gastrectomy can be considered (Blair V et al. *Lancet Oncol.* 2020 Aug;21(8):e386-e397).

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Understanding Your Positive CDH1 Genetic Test Result

INFORMATION FOR PATIENTS WITH A PATHOGENIC MUTATION OR VARIANT, LIKELY PATHOGENIC

5 Things To Know

<table>
<thead>
<tr>
<th>No.</th>
<th>Topic</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>CDH1 mutation</td>
<td>Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the CDH1 gene.</td>
</tr>
<tr>
<td>2</td>
<td>CDH1-related diffuse gastric and lobular breast cancer (DGLBC)</td>
<td>People with CDH1 mutations have CDH1-related diffuse gastric and lobular breast cancer (DGLBC).</td>
</tr>
<tr>
<td>3</td>
<td>Cancer risks</td>
<td>You have an increased chance to develop a particular type of gastric cancer (diffuse) and a particular type of female breast cancer (lobular).</td>
</tr>
<tr>
<td>4</td>
<td>What you can do</td>
<td>Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor and decide on a plan that works for you.</td>
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<td>5</td>
<td>Family</td>
<td>Family members may also be at risk—they can be tested for the CDH1 mutation that was identified in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.</td>
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</tbody>
</table>

CDH1 Mutation Lifetime Cancer Risks (%)*

- General Population
- CDH1 Mutation Carrier

CDH1 Mutations in the Family

There is a 50/50 random chance to pass on a CDH1 mutation to each of your children. The image below shows that everyone can carry and pass on these mutations, regardless of their sex at birth.

RESOURCES

- Ambry’s Hereditary Cancer Site for Families patients.ambrygen.com/cancer
- No Stomach for Cancer nostomachforcancer.org
- Bright Pink brightpink.org
- HDGC advocacy hereditarydiffusegastriccancer.org
- Imerman Angels imermanangels.org
- Susan G. Komen Foundation komen.org
- Genetic Information Nondiscrimination Act (GINA) ginahelp.org
- National Society of Genetic Counsellors nsgc.org
- Canadian Society of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your CDH1 result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.