CTNNA1 gene

Associated Syndrome Name: Hereditary diffuse gastric cancer (HDGC) syndrome

CTNNA1 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Gastric	High Risk

CTNNA1 gene Overview

Hereditary diffuse gastric cancer (HDGC) syndrome [1, 2]

- Individuals with mutations in *CTNNA1* have hereditary diffuse gastric cancer syndrome (HDGC).
- Individuals with *CTNNA1* mutations have a high risk for diffuse gastric cancer. Although the exact risk is not known, it may be similar to that for individuals with HDGC due to mutations in the *CDH1* gene, which has been estimated to be as high as 83%. Gastric cancer has been reported in individuals ranging from teens to late adulthood.
- The diffuse form of gastric cancer, which is less common than the intestinal type of gastric cancer, is more difficult to detect with endoscopic screening because it typically forms without a distinct mass.
- Women with HDGC due to mutations in the *CDH1* gene have a high risk for lobular breast cancer. At this time, it is not known if there is also an increased risk for breast cancer in women with HDGC due to mutations in *CTNNA1* and there are currently no medical management recommendations for breast cancer risk.
- Guidelines for the medical management of patients with HDGC have been developed by the International Gastric Cancer Linkage Consortium (IGCLC). These are listed below. Due to the complexity of this condition, it is recommended that patients with *CTNNA1* mutations and a diagnosis of HDGC be managed by a multidisciplinary team with expertise in medical genetics, gastric surgery, gastroenterology, pathology, and nutrition.

CTNNA1 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Gastric	To age 80[1, 2, 3, 4]	49%-57%	0.6%

CTNNA1 Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Gastric	Endoscopy with targeted and random biopsies[2]	Individualized	Annually
	Consider gastrectomy, after baseline endoscopy[2]	Individualized	NA
	Consider testing and treating for Helicobacter pylori infection if present[2]	Individualized	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the CTNNA1 gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

References

1. van der Post RS, et al. Hereditary gastric cancer: what's new? Update 2013-2018. Fam Cancer. 2019 18:363-367. PMID: 30989426.

2. Blair VR, et al. Hereditary diffuse gastric cancer: updated clinical practice guidelines. Lancet Oncol. 2020 21:e386-e397. PMID: 32758476.

3. Coudert M, et al. First estimates of diffuse gastric cancer risks for carriers of *CTNNA1* germline pathogenic variants. J Med Genet. 2022 Dec;59(12):1189-1195. PMID: 36038258.

4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2025 Apr 1]. Available from https://seer.cancer.gov/explorer/.

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