EPCAM gene

Associated Syndrome Name: Lynch syndrome/Hereditary Non-Polyposis Colorectal Cancer (HNPCC)

EPCAM Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Colorectal	High Risk
Endometrial	High Risk
Gastric	High Risk
Other	High Risk
Ovarian	High Risk
Skin	High Risk
Pancreatic	Elevated Risk
Prostate	Elevated Risk

EPCAM gene Overview

Lynch syndrome [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]

- Individuals with mutations in *EPCAM* have Lynch syndrome. This condition is also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC).
- Men and women with Lynch syndrome due to mutations in *EPCAM* have a high risk of developing colorectal cancer, often at young ages. Colorectal cancer in patients with Lynch syndrome develops from adenomatous polyps which progress to cancer more quickly than polyps in individuals who do not have Lynch syndrome.
- Women with Lynch syndrome due to mutations in *EPCAM* have a high risk for developing endometrial and ovarian cancer, often at young ages.
- Patients with Lynch syndrome due to mutations in *EPCAM* are also believed to have an increased risk of developing a wide variety of other cancers, including small bowel, urinary tract, hepatobiliary tract, brain (usually glioblastoma), sebaceous gland, prostate, and pancreatic. These risks may be more significant in patients with a family history of these cancers. Therefore, the general screening and management recommendations provided below should be modified based on individualized risk assessment and counseling.
- Patients with Lynch syndrome due to mutations in *EPCAM* have an increased risk for gastric cancer. Screening may be particularly important for patients with additional risk factors for gastric cancer, such as being male, older age, first-degree relative with gastric cancer, Asian ethnicity, residing in, or immigrating from countries with high background incidence of gastric cancer, chronic autoimmune gastritis, gastric intestinal metaplasia, and gastric adenomas.
- Studies have investigated the possibility that patients with Lynch syndrome have an increased risk for other cancers, including breast cancer and adrenocortical carcinoma. However, the data are not conclusive at this time and there are currently no medical management guidelines related to these cancers.
- Patients with Lynch syndrome have a high risk for developing second primary cancers following an initial diagnosis of colorectal or endometrial cancer. This includes a high risk for endometrial cancer in women following colorectal cancer and vice versa, a high risk for a second primary colorectal cancer in any portions of the colon or rectum remaining after surgical treatment, and a high risk for other Lynch associated cancers, such as those of the upper gastrointestinal tract, urinary tract, and other sites.
- Cancer risks for patients with Lynch syndrome due to mutations in *EPCAM* are currently estimated to be similar to those for patients with Lynch syndrome due to mutations in *MSH2*, and medical management guidelines are currently the same for patients with mutations in either gene. However, it is possible that this will change over time as we learn more about the exact risks associated with mutations in *EPCAM*. There are some early indications that endometrial cancer risk may be much lower for women with certain types of mutations in *EPCAM*.
- Although there are high risks for cancer in patients with Lynch syndrome, many of these risks can be greatly reduced with appropriate medical management. Guidelines for the medical management of patients with Lynch syndrome have been developed by the National Comprehensive Cancer Network (NCCN) and other expert groups. These are listed below. It is recommended that patients with an *EPCAM* mutation and a diagnosis of Lynch syndrome be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with this condition.

EPCAM gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 70[1, 2, 12, 13, 14, 15]	33%-51%	1.8%
Endometrial	To age 70[1, 2, 12, 13, 14, 15, 16]	21%-53%	1.9%
Overall cancer risk (Lynch cancers)	Risk for a second Lynch-related cancer after a first cancer diagnosis[17, 18]	Increased risk	NA
Ovarian	To age 70[1, 2, 12, 13, 14, 15, 16]	8%-24%	0.6%
Gastric	To age 70[13, 14, 15, 16]	2%-9%	0.3%
Small Bowel	To age 70[13, 14, 15, 16]	1%-3%	0.1%
Urothelial	To age 70[1, 2, 10, 13, 15, 19]	7%-21%	0.7%
Pancreatic	To age 70[11, 13, 14, 15, 20]	Elevated risk	0.6%
Brain	To age 70[2, 13, 14, 15, 16]	2%-6%	0.4%
Prostate	To age 70[2, 13, 15, 16]	13%-17%	6.1%
Hepatobiliary Tract	To age 70[12, 13, 14, 15, 20]	Elevated risk	0.5%
Lynch-associated Skin Tumors	To age 70[3, 8]	1%-9%	<1.0%

EPCAM 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)
Colorectal	Colonoscopy[3]	20 to 25 years, or 2 to 5 years younger than the earliest colorectal cancer diagnosis in family if it is under age 25	Every 1 to 2 years
	Consider the use of aspirin as a risk-reduction agent[3]	Individualized	Individualized
Endometrial	Patient education about the importance of quickly seeking attention for endometrial cancer symptoms, such as abnormal bleeding or menstrual cycle irregularities[3]	Individualized	Individualized
	Consider pelvic examination, endometrial sampling and transvaginal ultrasound.[3]	30 to 35 years	Every 1 to 2 years
	Consider hysterectomy.[3]	After completion of childbearing	NA
Ovarian	Consider bilateral salpingo-oophorectomy.[3]	After completion of childbearing	NA

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
	Consider transvaginal ultrasound and CA-125 measurement.[3]	30 to 35 years	NA
	Consider options for ovarian cancer risk-reduction agents (i.e. oral contraceptives).[3, 21]	Individualized	NA
	Patient education about ovarian cancer symptoms[3]	Individualized	NA
Gastric	Consider testing and treating Helicobacter pylori infection.[3]	Individualized	NA
	Consider upper endoscopy, particularly for patients with additional risk factors (see clinical overview). Consider biopsy of the proximal and distal stomach.[3, 26]	40 years	Every 3 to 5 years
Small Bowel	Consider upper endoscopy, particularly for patients with additional risk factors for small bowel cancer, such as family history.[3]	30 to 40 years	Every 3 to 5 years
Urothelial	Consider urinalysis.[3]	30 to 35 years	Annually
Pancreatic	For patients with a family history of pancreatic cancer, consider available options for pancreatic cancer screening, including the possibility of endoscopic ultrasonography (EUS) and MRI/magnetic resonance cholangiopancreatography (MRCP). It is recommended that patients who are candidates for pancreatic cancer screening be managed by a multidisciplinary team with experience in screening for pancreatic cancer, preferably within research protocols.[3, 24]	45 to 50 years, or 10 years younger than the earliest diagnosis of pancreatic cancer in the family	Annually
	Provide education about ways to reduce pancreatic cancer risk, such as not smoking and losing weight.[22]	Individualized	Individualized
Brain	Patient education about the importance of quickly seeking attention for signs and symptoms of neurologic cancer[3]	Individualized	NA
Prostate	Incorporating information about increased risk due to gene mutation, start risk and benefit discussion about offering baseline digital rectal examination (DRE) and Prostate Specific Antigen (PSA).[3, 23]	Age 40	Individualized, consider annually
Hepatobiliary Tract	Currently there are no specific medical management guidelines for hepatobiliary cancer risk in mutation carriers.[3]	NA	NA
Lynch-associated Skin Tumors	Consider skin exams[3]	Individualized	Every 1 to 2 years
For Patients With A Cancer Diagnosis	For patients with a gene mutation and a diagnosis of cancer, targeted therapies may be available as a treatment option for certain tumor types (e.g., antibodies to PD-1)[25]	NA	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 *EPCAM* 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.

Parents who are concerned about the possibility of passing on an *EPCAM* mutation to a future child may want to discuss options for prenatal testing and assisted reproduction techniques, such as pre-implantation genetic diagnosis (PGD).[3]

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