Patient information

Genetic testing for Lynch syndrome

Why have I been given this information sheet?

You have been given this information sheet because you have been diagnosed with bowel cancer or endometrial cancer. Initial testing on a stored sample of your tumour have suggested an inherited condition called Lynch syndrome **might** be the cause of your cancer. We can now offer you a genetic test on a blood sample to help determine whether or not you have Lynch syndrome.

How often is cancer hereditary?

Cancer is very common. One in two people in the general population are diagnosed with cancer during their lifetime. Most cancer is not hereditary. In a minority of families, there is a gene alteration running in the family that significantly increases the risk of certain cancers. One of the more common hereditary causes of bowel and endometrial cancer is a condition called Lynch syndrome. Lynch syndrome is caused by an inherited gene alteration in one of five genes. Many different words are used to describe cancer-causing gene alterations: “mutation,” “disease-causing alteration”, or “pathogenic variant” are all terms you may come across. We will use the term “pathogenic variant” to describe an alteration in a gene which is known to cause Lynch syndrome. How likely this is, depends on the number of people in a family affected, how closely related they are, the age at which they were diagnosed and the pathology of the cancer.

Lynch syndrome

Lynch syndrome is caused by pathogenic variants in genes (called *MLH1, MSH2, MSH6, PMS2* and *EPCAM*) that usually repair a type of DNA damage. Lynch syndrome mainly increases the risk of bowel and endometrial cancer. The risk of some other cancers, including ovary, pancreas, brain, kidney and urinary tract is also slightly increased, but are not as high as for bowel and endometrial cancer. Individuals with Lynch syndrome are eligible for bowel screening by colonoscopy every two years. Women with Lynch syndrome may also wish to be referred to a gynaecologist to discuss managing the risk of endometrial and ovarian cancer.

Inheritance pattern

We all have two copies of each of the Lynch syndrome genes, one inherited from each of our parents. Someone with Lynch syndrome will have one working copy and one copy with a pathogenic variant. Lynch syndrome is inherited in a 'dominant' way. This means that children of someone with a Lynch syndrome pathogenic variant have a 50% (1 in 2) chance of having inherited it and being at increased cancer risk. They also have a 50% (1 in 2) chance of having inherited the working copy of the gene.

What are the possible results of a genetic test for Lynch syndrome?

There are three possible results of this genetic test:

1. We may find a pathogenic variant in one of the Lynch syndrome genes that causes a significant change to the gene. This would mean you have a diagnosis of Lynch syndrome and would very likely provide an explanation for your cancer. Your oncology team may use this result to inform their management decisions and will discuss this with you further. You will also be referred to the Clinical Genetics service who will discuss what your result means for you and your relatives in more detail. Genetic testing would be available for other members of your family who wished to know whether or not they had inherited Lynch syndrome.

2. The test may identify one or more small gene alterations, termed variants of unknown significance. In this case, it is not clear whether or not these would disrupt the gene enough to cause Lynch syndrome and we would not be able to offer testing to your relatives. However, close relatives may still be recommended to have additional screening.

3. We may not find any variants in the Lynch syndrome genes. This would make it less likely that Lynch syndrome was the cause of your cancer but could not rule it out entirely. You will be referred to the Clinical Genetics service who will assess your personal and family history to advise whether any further testing is indicated and if any cancer screening is recommended for you or your family.

What happens next?

If you decide to have the test, your cancer team will arrange for you to have a blood sample taken. The test usually takes 2 - 3 months to complete and you will be informed of the result by your cancer team.

After you have received your result, your cancer team will refer you to your local Clinical Genetics service. If you have a confirmed diagnosis of Lynch syndrome, the Genetics service will arrange an appointment with you to discuss this in more detail. If your test did not identify any gene alterations, or detected a variant of uncertain significance, the Genetics service will review your personal and family history

information and either send you an appointment for further discussion or provide information by letter. They may suggest further testing to help clarify your results or may provide recommendations for your family members.

If you have any further questions about this test, or in relation to your ongoing cancer treatment, please contact your cancer team.

Acknowledgement

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