Ambry Genetics®

Understanding Your VUS Hereditary Cancer Genetic Test Result

INFORMATION FOR PATIENTS WITH A **VARIANT OF UNKNOWN SIGNIFICANCE**

Result	**VUS**	Your testing found at least one variant of unknown significance (VUS) in a gene tested. A VUS is a change in a gene from what we expect to see, but we do not know if it causes an increased risk for cancer or not.
Reclassification	**POSSIBLE**	Collecting information about a VUS is an ongoing process, so it is possible that your result may be better understood in the future. The healthcare provider that ordered your test will be notified if new information becomes available about your VUS.
Cancer Risk	**VARIES**	Even though your genetic test result was a VUS, you and your relatives may still have an increased risk of developing cancer based on other factors, including your medical and/or family history. Your healthcare provider can help you learn more about this.
Risk Management	**VARIES**	Risk management decisions are very personal and depend on many factors. Talk to your doctor about which, if any, options may be right for you.
Family Members	**POSSIBLE FURTHER TESTING**	Certain family members may be eligible for genetic testing through our Family Studies Program. In some cases, this may help add to the understanding of your result. If you and your relatives are interested in this, please speak to your healthcare provider about it.
Next Steps	**DISCUSS**	It is recommended that you stay in contact with your healthcare provider on a regular basis for possible new information about your result.
Reach Out	**RESOURCES**	• Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer • American Cancer Society cancer.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Association 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 genetic test result, medical recommendations, genetic testing options, 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.

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PATHOGENIC MUTATION (POSITIVE TEST RESULT)	Contains enough evidence showing it can cause a disease
VARIANT, LIKELY PATHOGENIC (VLP, POSITIVE TEST RESULT)	Strong evidence to suggest it causes a disease
VARIANT UNKNOWN SIGNIFICANCE (VUS)	Limited and/or conflicting evidence to suggest it may cause a disease
VARIANT, LIKELY BENIGN (VLB, NEGATIVE TEST RESULT)	Strong evidence to suggest it does not cause a disease
BENIGN (NEGATIVE TEST RESULT)	Contains enough evidence to show it does not cause a disease

1. **Does finding a VUS on genetic testing change medical management recommendations?**

   VUS by definition have not been proven to increase an individual's risk for disease or to be the cause of the disease within a family. Medical recommendations should be based on personal and/or family history of a specific disease.

2. **What percentage of VUS are reclassified?**

   Of the VUS that are reclassified, the vast majority will be reclassified to VLB or benign, although many VUS will not be reclassified at all due to lack of additional information. Only a small percentage of VUS will ultimately be reclassified to VLP or pathogenic.

3. **How long does it take to reclassify a VUS?**

   This depends upon several factors:
   - How often the VUS is found in individuals (rare variants may take longer to reclassify)
   - How common the disease is in the general population and how strongly the gene has been linked to the disease
   - Participation of certain families with the VUS in our Family Studies Program
   - Eligibility for additional specialized testing performed by Ambry's Translational Genomics (ATG) laboratory
   - Amount of active research taking place on a particular gene or VUS

4. **Who is notified if a VUS gets reclassified?**

   When enough evidence becomes available to cause a significant change, Ambry will make every attempt to send reclassification alerts for a VUS that gets reclassified to the healthcare provider.

5. **What is Ambry's Family Studies Program, and is it worth participating in it?**

   Our Family Studies Program and ATG lab include follow-up testing for you or certain family members after a VUS has been found. These studies can be worthwhile if many family members (especially those with the disease) are willing to participate. For more information, please visit our website for the Family Studies Program or ATG lab.

6. **Does Ambry perform family studies for VUS in all genes?**

   Not all genes are well suited for family studies. To find out if the VUS found is eligible for family studies contact FamilyStudies@ambrygen.com

7. **How often does Ambry check to see if there is new information about a VUS?**

   Ambry regularly assesses the data and emerging evidence related to a specific variant. Healthcare providers are welcome to contact Ambry Genetics at +1.866.262.7943 on a yearly basis to request the most current assessment of a particular variant.

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