Talking to Your Patient About a Germline Variant of Uncertain Significance (VUS)

What is a VUS?

A VUS is a variation in a genetic sequence for which the association with disease risk is unclear. **This means there is not enough information to determine if a variant is benign or pathogenic.**

How common is a VUS?

Testing for a panel of genes is common in germline testing. **About 10%–20% of broad panel genetic tests identify a VUS.** The more genes analyzed, the more likely a VUS will be detected.

What should I tell a patient about management?

A VUS is not actionable. Management and recommendations for cancer prevention and detection will be based on the patient's personal medical history and family history of malignancy—not the results of genetic testing. Talk to a genetics professional for next steps and management recommendations for the patient and family.

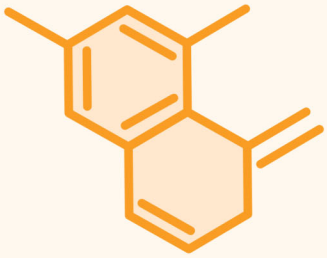
Should family members be tested to determine if they have the VUS?

In general, because the meaning of a VUS is not clear or informative, **testing family members is not recommended.** Management of the patient and their family members should be based on personal and/or family history of cancer—not the results of genetic testing.

This resource was developed by ONS through a sponsorship from AstraZeneca.

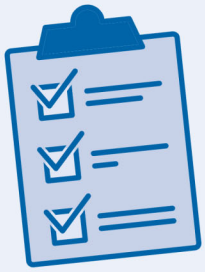
Does a VUS classification ever change?

Laboratories have teams dedicated to the reclassification of variants. **Reclassification occurs when a laboratory determines that a VUS is either a likely pathogenic or pathogenic variant or a likely benign or benign variant.** Some laboratories will study a VUS within a family to see if it is tracking with cancer. They also consider functional assays and other data about the specific variant to facilitate reclassification.



How does a patient know a VUS is reclassified?

Most testing companies will send a revised report to the healthcare provider who ordered the testing, and the healthcare provider will then update the patient. **Genetics professionals instruct individuals with a VUS to check periodically (every 12 to 18 months) for any change in the information.** This check-in also allows the genetics professional to review the family history for changes, update contact information, and determine whether care recommendations are current.



Where can additional VUS information or updates be obtained?

- Information about selected variants can be found in ClinVar: www.ncbi.nlm.nih.gov/clinvar.
- Families may be eligible for participation in an online VUS study, "Prompt," Prospective Registry of Multiplex Testing: https://promptstudy.info.

Bibliography

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