Ambry Genetics®
A TEMPUS COMPANY

Clinician Management Resource for *VHL*

This overview of clinical management guidelines is based on this patient's positive test result for a pathogenic or likely pathogenic variant in the *VHL* gene. Unless otherwise stated, medical management guidelines used here are limited to those published in the VHLA Suggested Active Surveillance Guidelines[1]. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries, and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decision but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider and may change.

SURVEILLANCE CONSIDERATIONS[1]	AGE TO START*	FREQUENCY*
von Hippel-Lindau syndrome (VHL)		
Age-appropriate history and physical examination	Birth	Annually from age 1 year
Measurement of blood pressure and pulse rate to monitor for pheochromocytomas/paragangliomas	2 years old	Annually
Dilated eye examination including ophthalmoscopy performed by a specialist with experience in retinal manifestations of VHL to monitor for retinal hemangioblastomas	1 year old	Every 6-12 months until age 30, then annually
Measurement of plasma free metanephrines (preferred), or fractionated 24-hour urinary free metanephrines to monitor for pheochromocytomas/paragangliomas	5 years old	Annually until age 65**
MRI of the brain and spine with or without contrast to monitor for CNS hemangioblastomas^	11 years old	Every 2 years until age 65**
Audiogram to monitor for endolymphatic sac tumors	11 years old	Every 2 years until age 65**
MRI of the abdomen with and without contrast to monitor for renal cell carcinomas, pheochromocytomas/paragangliomas, and pancreatic neuroendocrine tumors/cysts^	15 years old	Every 2 years until age 65**
High-resolution MRI of the internal auditory canal to monitor for endolymphatic sac tumors	Once, at 15 years old	Add on to the MRI of the neuroaxis between 15-20 years old

* Modifications of surveillance schedules may sometimes be made by physicians familiar with individual patients and their family histories. Once a patient has a known manifestation of VHL, or develops a symptom, the follow-up plan should be determined by their medical team. More frequent testing may be needed to track the growth of known lesions.

** Beginning at age 65, routine laboratory and radiologic screening for patients who have never had specific VHL manifestations may cease. However, patients presenting with signs/symptoms should be evaluated with appropriate testing/imaging regardless of age.

^ Refer to the VHLA Suggested Active Surveillance Guidelines[1] for specific MRI recommendations regarding contrast agents, order of imaging priority, timing of contrast administration, and surveillance timelines.

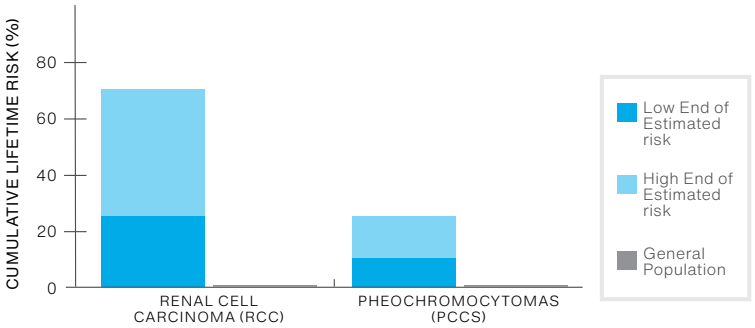
1. The VHL Alliance. "VHLA Suggested Active Surveillance Guidelines." VHL.org. Updated 10/09/2020. https://www.vhl.org/wp-content/uploads/forms/vhla-active-surveillance-guidelines.pdf

Understanding Your Positive *VHL* Genetic Test Result

INFORMATION FOR PATIENTS WITH A PATHOGENIC OR LIKELY PATHOGENIC VARIANT

1	Result	Your testing shows that you have a pathogenic or likely pathogenic variant in the *VHL* gene.
2	von Hippel-Lindau disease	People with a pathogenic or likely pathogenic variant in this gene have von Hippel-Lindau (VHL) disease.
3	Cancer risks and noncancerous tumor risks	You have an increased chance to develop kidney cancer, pheochromocytomas (PCCs), and neuroendocrine tumors of the pancreas (PNETs), as well as other noncancerous tumors or cysts in the eyes, ears, brain, spine, pancreas, and reproductive system.
4	Other Information About VHL	There are different subtypes of VHL. Each type has different cancer and tumor risks: • VHL type 1: kidney cancer, PNET, noncancerous tumors of the eyes, brain, spine, and pancreas • VHL type 2A: PCC, noncancerous tumors of the eyes, brain, and spine • VHL type 2B: PCC, kidney cancer (high risk), PNET, and noncancerous tumors of the eyes, brain, spine, and pancreas • VHL type 2C: PCC only Your specific variant may help clarify which type of VHL you have. It is important to talk to your healthcare provider about which tumors and cancers you are at risk for.
5	What you can do	Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your healthcare provider and decide on a plan that works for you.
6	Family	Family members may also be at risk – they can be tested for the pathogenic or likely pathogenic *VHL* variant that was found in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.

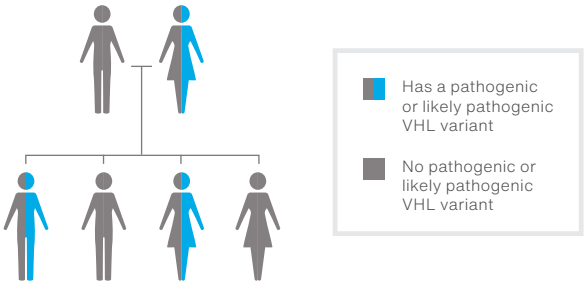
VHL Lifetime Cancer Risks*



* Because risk estimates vary in different studies, only approximate risks are given. Cancer risks will differ based on individual and family history.

VHL in the Family

There is up to a 50/50 random chance to pass on the pathogenic or likely pathogenic *VHL* variant to each of your children.



RESOURCES	
	• VHL Alliance vhl.org • National Society of Genetic Counselors nsgc.org • Canadian Society 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 *VHL* result, medical recommendations, 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.

1 Enterprise, Aliso Viejo, CA 92656 USA Toll Free +1.866.262.7943 Fax +1.949.900.5501 **ambrygen.com**

MKT-ONCO-FLYR-10096-EN v5 05.05.26