Information for Patients Who Have an Inconclusive Result With a Variant of Unknown Significance (VUS)

Your Genetic Test Results:
You have undergone genetic testing for dilated cardiomyopathy (DCM). Your test identified a variant of unknown significance (VUS).

What is a VUS?
A VUS is a change in one of the genes associated with DCM but, because this variant has never been observed before or because of conflicting information in the medical literature, we cannot yet tell whether this genetic variant is disease-causing or simply a harmless, normal genetic variant.

There are two types of VUSs at GeneDx, VUS likely disease-causing and VUS. These two categories are meant to help guide you and your doctor on the probability that this variant could be the cause of your DCM. VUS likely disease-causing has some evidence to suggest that the change does cause DCM; however, the evidence is insufficient to definitely establish it as a cause of DCM.

What This Test Result Means...

For You:
If you have been diagnosed with dilated cardiomyopathy (DCM), this test result does not change your clinical diagnosis. You should continue the medical management for this condition as recommended by your doctor. It is possible that this genetic variation is disease-causing; however, it is also possible that this variant is a normal genetic variant and does not cause DCM. This test result will not be helpful to clarify the risk for your unaffected family members to develop DCM without further evaluation of your family (see below). Your doctor or genetic counselor should contact GeneDx once a year to see if there is any more information on the VUS.

If you do not currently have dilated cardiomyopathy (DCM), this test result is inconclusive and cannot determine your risk for DCM without further evaluation of your family (see below). It will be important for you to establish care with a cardiologist so that you have regular evaluations to monitor your heart. Your doctor or genetic counselor should check in with GeneDx once a year to see if there is any new information on the VUS.

For Your Family:

• Although you were found to have a VUS, this information is not helpful for determining your family members’ risk for developing DCM. Regardless of whether they have this VUS or not, they may still be at significant risk to develop DCM.

• Share a copy of your test report with your family members to ensure that they are evaluated for the correct genetic variant. Even if some family members are not affected or may not be interested in pursuing genetic testing, it is still important for you to share the information about DCM and this VUS with them, as their doctor may still recommend cardiac surveillance.

Symptomatic family members
• Testing symptomatic family members and your biological parents for this VUS can help clarify the interpretation of your result.
  • The greater the number of affected family members who carry the VUS, the greater is the likelihood that the VUS is the cause of the DCM in your family.
  • If a family member with a diagnosis or suspected diagnosis of DCM tests negative for this VUS, it is less likely that the VUS is the cause of the DCM in your family.

Asymptomatic family members
• It is not recommended that unaffected family members undergo predictive testing for variants of unknown significance to predict their risk of DCM.
  • If an individual has DCM and the VUS if found to be de novo (arose new in that individual and was not inherited from either parent), the variant is likely disease-causing.
### How Can My Affected Family Members and Biological Parents Get Genetic Testing?

Genetic testing of your affected family members and biological parents can be helpful in clarifying the significance of this variant. In most cases targeted testing is performed simply by looking for the particular variant(s) that you have. Targeted testing can be done from a cheek swab or blood, and must be ordered by a doctor or genetic counselor. Bringing a copy of this information as well the genetic test report to the appointment can assist the doctor in obtaining the correct genetic testing. Health care providers can order test kits by going to our website www.genedx.com/kits.

Additional materials are available on the GeneDx website that you may find helpful to use when communicating genetic information to your family members. You can access these materials at www.genedx.com/cardiology.

It is recommended that genetic counseling be provided in conjunction with genetic testing. The National Society of Genetic Counselors maintains a list of national and international genetic counselors. Visit www.nsgc.org to locate a genetic counselor near you.

### Medical Management for DCM

Medical management for DCM varies for each patient. You should discuss whether or not you have the diagnosis of DCM and your specific treatment with your doctor. For patients with DCM, some of the medical management options may include:

**Surveillance:** It is recommended that individuals with DCM, or at risk for DCM, undergo routine cardiac surveillance. Such surveillance may include history and physical examination, as well as routine echocardiography, electrocardiography, and/or cardiac magnetic resonance imaging (MRI). In some patients, holter monitoring or exercise tests may be necessary. The frequency of cardiac surveillance will depend upon the age of the patient, their family history, symptoms, and the extent of their disease.

**Medication(s):** A variety of medications can be used to treat patients with DCM. The most commonly employed medications are ACE inhibitors and beta-blockers, but other medications may be used depending on symptoms and the stage of a patient’s heart disease.

**Implantable cardioverter defibrillator (ICD):** Individuals with DCM may have a higher risk of sudden cardiac arrest due to the occurrence of abnormal heart rhythms. Some patients with DCM require placement of an ICD. This is a small, implantable device that can shock the heart if an abnormal rhythm is detected.

**Activity Restriction:** Patients with DCM may be advised to restrict their participation in strenuous physical activities, such as competitive sports. However, 30 minutes of endurance-type exercise a day may be recommended.

**Cardiac Transplantation:** Some patients with DCM may ultimately need a new heart if heart failure develops and cannot be adequately treated with medication.

### Glossary:

**Gene:** A defined segment of DNA that provides instructions for the cells of the body to make a specific protein.

**Genetic:** Refers to a medical condition that is caused, at least in part, by an alteration (or mutation) in a person’s DNA. Genetic conditions are often inherited, or passed down through the family tree.

**Mutation:** An alteration in DNA. Mutations are often considered to cause the development of a particular disease.

**Autosomal Dominant:** Disorders affect men and women equally. Every family member with the mutation has a significantly increased risk of developing the condition.

### What are some patient resources?

- Cardiomyopathy Association: www.cardiomyopathy.org
- Children’s Cardiomyopathy Foundation: www.childrenscardiomyopathy.org
- GeneDx: www.genedx.com/cardiology

### References:

