What Are the Acute Hepatic Porphyrias (Also Known as Acute Porphyrias)?[1-4]

There are four types of acute hepatic porphyria: acute intermittent porphyria (AIP), variegate porphyria (VP), hereditary coproporphyria (HCP), and ALAD-deficient porphyria (ADP). The acute hepatic porphyrias (AHPs) are characterized by acute, potentially life-threatening attacks and chronic debilitating symptoms that negatively impact patients' quality of life. Attacks are commonly characterized by severe abdominal pain, vomiting, nausea, rapid heart rate (tachycardia), and constipation. During an attack, a person may also experience muscle weakness or paralysis, seizures, low sodium levels (hyponatremia), and mental changes such as anxiety, confusion, or hallucinations in severe cases. HCP and VP are classified as acute but can also have symptoms that affect the skin—specifically blistering skin lesions on sun-exposed areas. Skin symptoms can be present with or without attacks.

For more information about the acute hepatic porphyrias, visit the American Porphyria Foundation at **www.porphyriafoundation.org**

What Is a Variant of Unknown Significance

Gene mutation testing can give several possible results: a positive result, a negative result, or an ambiguous (or uncertain) result called a variant of unknown significance.

A variant of unknown significance (VUS) indicates that a gene change (mutation) has been identified, but its association with disease is still unknown or unclear. Over time, as its significance becomes better understood, a VUS may be re-classified as either positive or negative.

What Does a Variant of Unknown Significance Result Mean for You[3,5]

Other tests may help clarify the clinical significance of a VUS. Biochemical testing—specifically testing a person's urine for elevated levels of porphobilinogens (PBG) or aminolevulinic acid (ALA)—may be used to diagnose AIP, HCP, and VP.* These tests can be performed in a random urine sample and are more accurate when normalized per gram of urine creatinine—a 24-hour collection is not required. Biochemical testing is typically performed when a person is experiencing a suspected attack, since PBG and/or ALA are most elevated at this time.

Genetic and biochemical testing results should always be interpreted in the context of a person's symptoms, medical history, and family history. If genetic testing reveals a VUS, you are encouraged to follow up with your health care provider to interpret the result as well as to determine whether other tests, such as biochemical testing, may be indicated.

Genetic Counseling

In addition to genetic testing, Alnylam is sponsoring no-charge, third-party genetic counseling in the U.S. for the AHPs.

Genetic counseling is a service that provides information and support to people and families who have, or may be at risk for, genetic diseases. Genetic counselors are trained health care professionals who can explain genetic diseases, genes and inheritance, and genetic test results.

To schedule telephone-based genetic counseling, call **1.888.475.3128** and reference the Alnylam Act™ program.

*Urinary aminolevulinic acid (ALA) is the first-line test for ADP.

AlnylamAct™ The Alnylam Act™ program was developed to reduce barriers to genetic testing and counseling in order to help people make more informed decisions about their health. While Alnylam provides financial support for this program, all tests and services are performed by independent third parties. At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for health care providers who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S.

References: 1. Bissell DM, et al. *J Clin Transl Hepatol*. 2015;3(1):17-26. **2.** Bonkovsky, HL et al. *Am J Med*. 2014;127:1233-1241. **3.** Anderson KE, et al. *Ann Intern Med.* 2005;142(6):439-50. **4.** Anderson, et al. In: Proceedings from AASLD 2016;64(1):285A. **5.** Bissell, et al. *N Engl J Med*. 2017;377:862-872.