V122I PATIENTS ARE AT HIGHER RISK OF hATTR PROGRESSION[1]

Identifying patients with the V122I variant is urgent

2.6 years

is the **median survival time** for V122I patients, compared to 5.8 years for patients with other variants, following an hATTR diagnosis.[2-4]

PREVALENCE[1,5-9]

V122I (V142I) is one of 120 inherited gene variants associated with hATTR. It's the **most common variant** in the United States, and ~**4% of African Americans** are carriers.[5-8]

Disease Progression

The V122I variant is also associated with more aggressive disease progression compared with other variants or wild-type ATTR, with patients at higher risk of the following[1,9]:

- Heart failure
- Cardiovascular death
- All-cause mortality

V122I PATIENTS OFTEN PRESENT WITH MIXED PHENOTYPE[3,6,10,11]

In patients with the V122I variant, cardiomyopathy may coincide with or follow polyneuropathy.[10]

Cardiac complications[3,11]

Sensory neuropathy[3,11]

Gastrointestinal symptoms[3,11]

Renal impairment[6]

Motor neuropathy[3,11]

Early diagnosis and intervention are critical to slow disease progression.[12]

ATTR=transthyretin-mediated amyloidosis; hATTR=hereditary transthyretin-mediated amyloidosis.

CONFIRMING A DIAGNOSIS OF hATTR

Establish a diagnosis in 3 steps[1,3,13]

1 **Rule out AL amyloidosis** with simple monoclonal light-chain assays

2 **Detect amyloid deposition** in myocardial tissue with nuclear scintigraphy (eg, ^{99m}Tc-PYP) or cardiac biopsy

3 Once ATTR-CM is confirmed, **use genetic testing** to determine if it is hereditary

Use genetic testing to detect TTR variants and distinguish hATTR from wtATTR[1,14]

Following a diagnosis, genetic testing can accurately distinguish hATTR from wtATTR, with current techniques **detecting over 99% of TTR variants.**[1,14] Clinical testing kits can be ordered at no cost through the Alnylam Act® Program.

ALNYLAM ACT®–US GENETIC TESTING AND COUNSELING PROGRAM

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

Click here to order a genetic test and learn more about Alnylam Act®.

AL=amyloid light chain; ^{99m}Tc-PYP=technetium-^{99m} pyrophosphate; ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis; TTR=transthyretin; wtATTR=wild-type transthyretin-mediated amyloidosis.

Diagnosis is based on the independent medical judgment of the healthcare professional.

References: 1. Kittleson et al. *Circulation*. 2020;142:e7-22. **2**. Lane et al. *Circulation*. 2019;140:16-26. **3**. Kittleson et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126. **4**. Rozenbaum et al. *Cardiol Ther*. 2021;10(1):141-159. **5**. Hawkins et al. *Ann Med*. 2015;47(8):625-638. **6**. Maurer et al. *J Am Coll Cardiol*. 2016;68(2):161-172. **7**. Sekijima Y. *J Neurol Neurosurg Psychiatry*. 2015;86(9):1036-1043. **8**. Maurer et al. *Circ Heart Fail*. 2019;12(9):e006075. **9**. Kozlitina et al. *J Card Fail*. 2022;28(3):403-414. **10**. Grogan et al, Presented at: HFSA, 2019. **11**. Wixner et al. *Orphanet J Rare Dis*. 2014;9:61. **12**. Conceição et al. *Amyloid*. 2019;26(1):3-9. **13**. McDonagh et al. *Eur Heart J*. 2021;42(36):3599-3726. **14**. Ando et al. *Orphanet J Rare Dis*. 2013;8:31.

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