Pre-Test Counseling Guide: Anti-AAV9 Antibody Testing

A resource to support conversations between health care providers and families regarding AAV9 testing.

Key Takeaways

- **Testing for AAV9-specific antibodies** is an important step in understanding what treatment options may be appropriate for an individual being considered for an AAV9-based gene therapy
- **Discussing potential test results and their implications with the patient's family prior to ordering the test** is strongly recommended. This could involve discussing AAV9 antibody titer levels and potential implications on clinical management based on the Prescribing Information of the specific gene therapy and the clinical presentation of the individual patient
- **Having an elevated anti-AAV9 antibody test result** may limit treatment options or require additional steps prior to receiving gene therapy. Test results should be interpreted by the treating health care provider (HCP) to determine the appropriate management plan
- **While exposure to AAV9 in everyday environments is very common**, taking simple health precautions before treatment (eg, washing hands and avoiding crowded places) can help reduce exposure to the AAV9 virus, which could reduce the likelihood of an 'Elevated' AAV9 antibody test

Topic	Talking points to discuss with families
Review of AAV9 testing	• Adeno-associated viruses (AAVs) are common in the environment, and many people have been exposed to them naturally[1-3] • AAV capsids* are often modified and used in gene therapy to deliver a transgene.†[1,3] Antibody testing is intended to assess prior exposure to the AAV capsid, and is not intended to diagnose a disease or condition[4,5] • There are different types of AAVs, which are given different numbers, such as AAV9.[4] When someone has been exposed to AAV9, the body's immune system can create antibodies specific to AAV9.[5,6] These AAV9-specific antibodies can be detected through a simple blood test[7] • The presence of pre-existing AAV9 antibodies does not cause disease on its own. However, if an individual with pre-existing antibodies receives AAV9-based gene therapy, their body's immune response could cause serious safety concerns or reduce the gene therapy's efficacy[2,3,5,7]
Why anti-AAV9 antibody testing matters	• AAV9-based gene therapies use a modified AAV9 capsid* to deliver a transgene.†[8] A test result showing elevated antibodies suggests that the immune system may recognize the capsid as foreign when it enters the body and react to it, potentially causing serious safety concerns or causing the gene therapy to be less effective[5,7] • It is important to interpret the anti-AAV9 antibody titer result in the context of the specific gene therapy's safety and efficacy data, which may include dosing information for patients with elevated anti-AAV9 antibodies

*A capsid is the outer protein shell enclosing the viral genetic material.[7]
†A transgene in AAV gene therapy is the therapeutic genetic sequence packaged into the AAV capsid and delivered to a cell in order to produce a desired protein or biological effect.[3]

Navigating the uncertainty

Waiting for test results and learning about their implications can cause concern or anxiety for patients' families. **Discussing these possibilities with the patient's family prior to testing may help ease their concern.** Typical turnaround time for AAV9 testing is under 1 week.[9]

Considerations for conversations with patients and families

- Anxiety and other emotions (eg, relief, disappointment, confusion) around test results and their implications are normal and expected
- Families may benefit from reassurance that their HCP will help them navigate the next steps in the patient's care regardless of the test results
  - Patients' families may express concern about an 'Elevated' AAV9 test result. It may be helpful for them to know that results are interpreted based on the AAV9 titer level, the specific gene therapy's Prescribing Information, the individual patient's clinical presentation, and any other relevant clinical guidance
- Families may find it helpful to process the information with their trusted support system
- AAV9 results are one of many factors that determine the best treatment plan for patients

Resources to help support patients and their families through this process:

- Organizations such as the American Society of Gene & Cell Therapy (ASGCT) can provide education about AAV-based gene therapy and AAV testing, and Global Genes can help direct patients and families to disease-specific patient advocacy organizations‡
- Some families may also find it helpful to speak with mental health professionals or family counselors
- Please note that Ultragenyx may not have additional AAV9 testing materials or resources available for patients and families

‡This is not an exhaustive list and is for informational purposes only. Other relevant organizations may exist, Ultragenyx does not endorse any individual organization.

Topic	Talking points to discuss with families	
Potential test results and implications[9]	**Test result**	**Implications**
	'Not elevated' Anti-AAV9 antibody titer < 1:25	AAV9-specific antibodies are not present or are below the threshold of the test.
	'Elevated' Anti-AAV9 antibody titer = 1:25, 1:50, 1:100, 1:200 or > 1:200	AAV9-specific antibodies are present at a detectable and potentially elevated level. • Laboratories may report an 'Elevated' test result based on the analytical threshold established for a specific assay • Interpretation of an 'Elevated' test result takes into account the reported titer level, the specific gene therapy's Prescribing Information, the individual patient's clinical presentation, and any other relevant clinical guidance, as part of clinical management and treatment decisions
Communicating test results	• Test results are typically available in under 1 week.[9] Before ordering the test, HCPs are encouraged to discuss with families when and how results will be shared, including whether a follow-up visit will be scheduled to review the results and their implications on the management plan • Test results are often sent to patients automatically through electronic health record systems. If the institution allows it, HCPs can consider delaying this automatic release when ordering tests, until results have been shared with the family (eg, via phone call or office visit) • If the practice allows, it may be helpful to offer families the option to receive results in person or by phone call, as the HCP deems most appropriate. Regardless of how test results are shared, HCPs are encouraged to approach the conversation with compassion and provide a safe space for families to process the results.[10] Before notifying families of test results, the patient's clinical presentation and the specific gene therapy's Prescribing Information should be reviewed to help interpret the clinical implications of the AAV9 test result	
Avoiding AAV9 exposure	Because AAV9 is common in our environment, many people have been exposed at some point, often without realizing it.[2,3] For patients who do not have pre-existing AAV9 antibodies, HCPs may consider discussing typical precautionary measures to avoid viral infection, including avoiding large crowds and frequent hand washing. Complete isolation until dosing is often not necessary but left to the discretion of the health care team to find a solution with the patient's family. In families where siblings may be eligible for gene therapy and sibling dosing cannot occur concurrently, precautionary measures, such as limiting sharing food, bathrooms, and other activities or spaces where oral or fecal spread can occur, are encouraged.	

Frequently asked questions (FAQs) from families/caregivers

Q: How common is it to receive an 'Elevated' (or equivalent) test result for AAV9 antibodies?
A: AAV9 antibodies are quite common since AAV9 viruses are found everywhere in our environment.[2] Studies show that many people have been exposed to AAV9 through normal daily life, though most people don't know it because AAV9 doesn't cause illness.[1,3] Exposure to AAV9 can vary around the world, but in the United States the estimate is around 50%.[2]

Q: Can I do anything to lower antibody levels?
A: There are no standardized methods to lower AAV9 antibody levels. Generally, individuals who have a positive antibody test result will stay positive. Less commonly, antibody levels may drop naturally over time. Retesting at a future time may be considered, though the timing depends on the patient's individual circumstances and the HCP's clinical judgment.[5,7]

Q: What happens if my child receives an 'Elevated' test result?
A: An 'Elevated' AAV9 test result may limit treatment options such as gene therapy depending on the patient's specific titer level and individual circumstances. Alternative management approaches and retesting at a future time may be considered in some cases.[5,7]

Q: How long is a 'Not Elevated' AAV9 antibody test valid for?
A: To minimize the risk of being exposed to AAV9 in the environment, it is recommended for eligible patients to receive the AAV9-based gene therapy as soon as feasible after a 'Not Elevated' or equivalent AAV9 antibody test result.[11] If necessary, retesting AAV9 antibodies closer to the date of planned gene therapy administration may be considered.[5,7]

HCPs with questions about the anti-AAV9 antibody test may contact Athena Client Services by phone (**1-800-394-4493, select option 2**). Questions about a specific AAV9-based gene therapy should be directed to the appropriate pharmaceutical company.

References:
1. Sant'Anna TB, Araujo NM. *Virol J*. 2022;19(1):173. **2.** Chhabra A, et al. *Mol Ther Methods Clin Dev*. 2024;32(3):101273. **3.** Earley J, et al. *Trends Biotechnol*. 2023;41(6):836-845. **4.** Issa SS, et al. *Cells*. 2023;12(5):785. **5.** Braun M, et al. *Mol Ther Methods Clin Dev*. 2024;32(1):101217. **6.** Weber T. *Front Immunol*. 2021:12:658399. **7.** Mendell JR, et al. *Mol Ther Methods Clin Dev*. 2022;25:74-83. **8.** Lau HA, et al. Oral presentation at: WORLD*Symposium*; February 2-6, 2026; San Diego, CA, USA. **9.** Ultragenyx Inc. AAV9 antibody test [report sample]. Data on file. Athena Diagnostics, Inc.; 2024. **10.** Voorhees K, et al. Poster presented at: American Society of Gene & Cell Therapy (ASGCT) Annual Meeting; May 11-15, 2026; Boston, MA, USA. Poster #1196. **11.** Schulz M, et al. *Mol Ther*. 2023;31(3):616-630.

© 2026 Ultragenyx Inc. All Rights Reserved.