HLA-B*57:01 for Abacavir Sensitivity

Abacavir sulfate is a nucleoside reverse transcriptase inhibitor (NRTI) used in combination with other antivirals in treatment of HIV infection. Serious and sometimes fatal abacavir hypersensitivity reaction (ABC HSR) occurs within the first 6 weeks of treatment in 5-8% of Whites and 2-3% of African Americans.[1] Administration of abacavir following ABC HSR is contraindicated because continued treatment can cause a more severe reaction.[1]

Tests to Consider

HLA-B*57:01 for Abacavir Sensitivity 2002429

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Standard of care before abacavir therapy per FDA
- Predicts risk of abacavir hypersensitivity syndrome
- Screening before reinitiation of treatment in individuals who have previously tolerated abacavir but whose HLA-B*57:01 status is unknown
- Relevant to most populations

Disease Overview

Allele Frequency

The frequency of the HLA-B*57:01 allele varies by population; specific frequencies have been reported as[2]:

- Southwest Asian: 11%
- Other Asian: 0-6.7%
- European: 6.8%
- South American: 2.6%
- Middle Eastern: 2.5%
- Mexican: 2.2%
- African: 1%

Symptoms

Symptoms typically appear suddenly, worsen with each subsequent dose of abacavir, and improve within 48-72 hours of abacavir discontinuation. ABC HSR is often associated with two or more of the following symptoms[2]:

- Fever
- Rash
- Malaise/fatigue
- Headache
- Respiratory symptoms
- Gastrointestinal symptoms (nausea, vomiting, abdominal pain)

Treatment Issues

Hypersensitivity to abacavir has been strongly associated with the major histocompatibility complex class I human leukocyte antigen (HLA), specifically the HLA-B*57:01 allele. DNA-based testing to assess the presence of HLA-B*57:01 offers higher specificity than serologic testing because monoclonal antibodies may show cross-reactivity with other HLA subtypes. The U.S. Food and Drug Administration (FDA) recommends pretherapeutic screening for the HLA-B*57:01 allele. Patients testing positive should not be treated with a regimen containing abacavir.[2] Routine screening has been shown to reduce the incidence of ABC HSR from 8% to <0.5% in abacavir-naïve patients. Because ~2% of individuals who are HLA-B*57:01 positive are tolerant to abacavir, HLA-B*57:01 status is necessary, but not sufficient by itself, for development of ABC HSR.

Genetics

Gene

HLA-B

Inheritance

Autosomal dominant

Allele

HLA-B*57:01 is strongly associated with ABC HSR.

Test Interpretation

Sensitivity/Specificity

Clinical sensitivity/specificity: 100% for immunologically confirmed hypersensitivity reaction

Analytical sensitivity/specificity: >99%

Results

Result	Allele Detected	Clinical Significance
Positive	HLA-B*57:01 heterozygous or homozygous	Predicts significantly increased risk for abacavir hypersensitivity Avoidance or discontinuation of abacavir is advised
Negative	HLA-B*57:01 not detected	Predicts no increased risk for abacavir hypersensitivity

Limitations

- Alleles other than HLA-B*57:01 will not be evaluated
- Does not distinguish between heterozygote and homozygote carriers
- Diagnostic errors can occur due to rare sequence variations
- Risk of therapeutic failure or adverse reactions with abacavir may be affected by genetic and nongenetic factors not detected by this test
- This test does not replace the need for therapeutic drug or clinical monitoring

References

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. [Last updated: Dec 2019; Accessed: Feb 2020]

2. Clinical Pharmacogenetics Implementation Consortium. CPIC guideline for abacavir and HLA-B. [Updated: May 2014; Accessed: Jul 2022]

Related Information

Germline Pharmacogenetics - PGx
Human Immunodeficiency Virus - HIV

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