

## 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 Caucasians and 2-3% of African Americans.<sup>1</sup> Administration of abacavir following ABC HSR is contraindicated because continued treatment can cause a more severe reaction.<sup>1</sup>

### Disease Overview

#### Allele Frequency

The frequency of the HLA-B\*57:01 allele varies by population; specific frequencies have been reported as<sup>2</sup>:

- 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<sup>2</sup>:

- 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.<sup>2</sup> 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

### 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

## 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: Jun 2020]

## Related Information

[Germline Pharmacogenetics - PGx](#)  
[Human Immunodeficiency Virus 1, Antiretroviral Drug Resistance Testing - HIV Drug Resistance](#)

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology, 500 Chipeta Way, Salt Lake City, UT 84108  
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com  
Content Review February 2020 | Last Update July 2020