HLA-B*57:01 for Abacavir Sensitivity

Disease Overview

Allele Frequency

The frequency of the HLA-B*57:01 allele varies by population; specific frequencies have been reported as:\(^1\):

- 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

<table>
<thead>
<tr>
<th>Result</th>
<th>Allele Detected</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>HLA-B*57:01 heterozygous or homozygous</td>
<td>Predicts significantly increased risk for abacavir hypersensitivity. Avoidance or discontinuation of abacavir is advised</td>
</tr>
<tr>
<td>Negative</td>
<td>HLA-B*57:01 not detected</td>
<td>Predicts no increased risk for abacavir hypersensitivity</td>
</tr>
</tbody>
</table>

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


Related Information

Germline Pharmacogenetics - PGx
Human Immunodeficiency Virus - HIV