HLA-B*57:01 for Abacavir Sensitivity

Indications for Ordering

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

Test Description

Polymerase chain reaction (PCR) and fluorescence monitoring
- Tests for presence or absence of the HLA-B*57:01 allele

Tests to Consider

Primary test

HLA-B*57:01 for Abacavir Sensitivity 2002429
- Identify individuals at risk for abacavir sulfate hypersensitivity reaction (ABC HSR)

Disease Overview

HLA-B*57:01 allele frequency – varies by ethnicity
- Southwest Asian – 11%
  - Other Asian – 0 to 6.7%
- European – 6.8%
- South American – 2.6%
- Middle Eastern – 2.5%
- Mexican – 2.2%
- African – 1%

Symptoms
- Fatal ABC HSR is often associated with ≥2 of the following symptoms
  - Fever
  - Rash
  - Malaise/fatigue
  - Respiratory symptoms
  - Gastrointestinal symptoms (nausea, vomiting, diarrhea)
- Symptoms typically appear suddenly and worsen with each subsequent dose of abacavir
- Symptoms improve within 48-72 hours of discontinuation of abacavir

Treatment issues
- Abacavir sulfate – nucleoside reverse transcriptase inhibitor (NRTI) used in combination with other antivirals in treatment of HIV infection
- Serious and sometimes fatal ABC HSR occurs in
  - First 6 weeks of treatment
  - 5-8% of Caucasians
  - 2-3% of African Americans
- Administration of abacavir following ABC HSR is contraindicated
  - Continued treatment can cause a more severe reaction
- 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 serological testing
  - Monoclonal antibodies may show cross-reactivity with other HLA subtypes
- FDA recommends pretherapeutic screening for the HLA-B*57:01 allele
  - Patients testing positive should not be treated with a regimen containing abacavir
  - Routine screening has been shown to reduce the incidence of ABC HSR from 8% to <0.5% in abacavir-naïve patients
  - ~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 manifestation 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
- 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

- Mallal S, Phillips E, et al. HLA-B*5701 screening for hypersensitivity to abacavir. N Engl J Med. 2008;358(6):568-79
- Saag M, Balu R, et al. Study of Hypersensitivity to Abacavir and Pharmacogenetic Evaluation Study Team. High sensitivity of human leukocyte antigen-b*5701 as a marker for immunologically confirmed abacavir hypersensitivity in white and black patients. Clin Infect Dis. 2008;46(7):1111-8