Abacavir (Ziagen) Sensitivity

Pharmacologic agent: Abacavir is a synthetic carbocyclic nucleoside analogue with inhibitory activity against HIV-1. It, in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection.

WARNING: RISK OF HYPERSENSITIVITY REACTIONS, LACTIC ACIDOSIS, AND SEVERE HEPATOMEGALY

Serious and sometimes fatal hypersensitivity reactions have been associated with abacavir. Hypersensitivity to abacavir is a multi-organ clinical syndrome usually characterized by a sign or symptom in 2 or more of the following groups: (1) fever, (2) rash, (3) gastrointestinal (including nausea, vomiting, diarrhea, or abdominal pain), (4) constitutional (including generalized malaise, fatigue, or achiness), and (5) respiratory (including dyspnea, cough, or pharyngitis).

Pharmacogenomic information: Patients who carry the HLA-B*5701 allele are at high risk for experiencing a hypersensitivity reaction to abacavir¹⁻³. Only 0-0.5% of patients who are HLA-B*5701 negative will develop hypersensitivity, while >70% who are HLA-B*5701 positive will develop hypersensitivity. The FDA issued an alert in July of 2008 about this and information was added to the boxed warning

Action required⁴:

- Screening for the HLA-B*5701 allele is recommended for all patients prior to starting abacavir therapy. This approach has been found to decrease the risk of a hypersensitivity reaction.
- Patients who previously took abacavir and tolerated it have developed abacavir HSR upon restarting abacavir-containing therapy. Screening is recommended prior to reinitiation of abacavir in patients of unknown HLA-B*5701 status who have previously tolerated abacavir.
- For HLA-B*5701-positive patients, treatment with an abacavir-containing regimen is not recommended and should be considered only under exceptional circumstances when the potential benefit outweighs the risk.

Reference/Resources

- 1. Mallal, S. et al. (2008) HLA-B*5701 <u>Screening for Hypersensitivity to Abacavir</u>. N Engl J Med. 358(6):568-579. (http://content.nejm.org/cgi/content/short/358/6/568)
- 2. Hughes, C.A. et al. (2008) <u>Abacavir Hypersensitivity Reaction: an Update</u>. The Annals of Pharmacotherapy, 44:387-396. (http://www.theannals.com/cgi/content/abstract/aph.1K522v1)
- 3. Saag, M., et al. (2008) <u>High Sensitivity of Human Leukocyte Antigen-B*5701 as a Marker for Immunologically Confirmed Abacavir Hypersensitivity in White and Black Patients</u>. Clinical Infectious Diseases (CID), 46:1111-1118. (http://www.ncbi.nlm.nih.gov/pubmed/18444831)

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2010

- 4. Information for Healthcare Professionals: Abacavir (marketed as Ziagen) and Abacavir-Containing Medications(http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsand Providers/ucm123927.htm)
- 5. Ma, J. et al (2010) HLA-B*5701 Testing to understand Abacavir Sensitivity. (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000684/?tool=pubmed)

General drug information obtained from RxList: http://www.rxlist.com/ziagen-drug.htm