British Columbia Centre for Excellence in HIV/AIDS
Providence HEALTH CARE How you want to be treated.
Pharmacovigilance Program
SAFETY ALERT
No.1, July 2009

Abacavir use in HLA-B*5701 positive patients and untested patients

Sentinel event

The Pharmacovigilance Program received a report of an HLA-B*5701 positive patient who had tolerated long term abacavir therapy, discontinued antiretroviral drugs for several months, then developed a diffuse rash, respiratory distress and fever shortly after re-initiating an abacavir-containing regimen. The symptoms and rapid onset were consistent with a clinical diagnosis of abacavir hypersensitivity reaction.

Background

- Abacavir hypersensitivity reaction (HSR) is diagnosed clinically if the patient has symptoms in at least two of the following categories: fever, rash, gastrointestinal symptoms, constitutional symptoms (e.g. malaise, fatigue) or respiratory symptoms.
- Persons who carry the HLA-B*5701 allele are at high risk of developing abacavir HSR.
- Pre-screening for HLA-B*5701 status and avoiding abacavir in persons who test positive significantly reduces the incidence of HSR diagnosis within the first six weeks of therapy.
- Although abacavir HSR usually develops within six weeks after the first dose, HSR may occur at any time during therapy. Several published case reports describe HSR associated with re-starting abacavir in patients who had previously tolerated the drug. The HLA status was unknown in these cases.
- There is uncertainty regarding the effect of interrupting and re-starting abacavir on the frequency or severity of HSR in patients who have previously tolerated abacavir.
- The predictive value of HLA-B*5701 status has not been studied for late onset or re-challenge reactions; however, HLA testing is presently the best available tool for predicting risk of HSR.
- The abacavir (Ziagen™) monograph boxed warning recommends *HLA-B*5701 testing* ***prior to starting or re-starting*** *abacavir in all patients and avoiding abacavir in those who test positive.*

Recommendations

BC-CfE recommends HLA-B*5701 testing for:

- All patients prior to initiating abacavir.
  - If positive for HLA-B*5701, abacavir is NOT recommended.
- Patients with unknown HLA status, prior to re-starting abacavir
  - If positive for HLA-B*5701, abacavir is NOT recommended (even if previously tolerated).
- Previously untested patients receiving ongoing abacavir therapy.
  - If positive for HLA-B*5701, re-evaluate therapeutic options.
  - If the benefits of continuing abacavir outweigh the risks, counsel the patient on how to recognize and respond to possible HSR symptoms.
  - If abacavir is interrupted or discontinued, re-starting is NOT recommended.
- If signs and symptoms of abacavir hypersensitivity reaction develop, discontinue abacavir and NEVER RE-START abacavir, regardless of the patient's HLA-B*5701 status.

FAQs: HLA-B*5701 testing in BC

- **How do I order this test?** The HLA-B*5701 laboratory requisition form may be downloaded from the BC-CfE website: http://cfenet.ubc.ca/our-work/programs/laboratory-program/clinical-tests/hla-b5701-screening
- **Is there a charge for testing?** There is no charge for HIV positive, BC residents.
- **Is it necessary to wait until planning to start abacavir before ordering the test?** No. The BC-CfE laboratory encourages physicians to order the HLA-B*5701 test at the time of the initial work-up for HIV diagnosis, in order to plan future treatment options.
- **How often does a patient require HLA-B*5701 testing?** This test is only required once. The result is stable over the patient's lifetime.
- **Who do I contact to obtain test results?** Test results will be mailed to the requesting physician. Clinicians who are directly involved in a patient's care may verify results by contacting the BC-CfE laboratory at 604-806-8281.

Selected references

- Mallal S, Phillips E, Carosi G, et al. HLA-B*5701 screening for hypersensitivity to abacavir. New England Journal of Medicine 2008; 358(6): 568-579.
- Frissen JPH, de Vries J, Weigel HM et. al. Severe anaphylactic shock after rechallenge with abacavir without preceding hypersensitivity. AIDS 2001; 15(2):289.
- Hetherington S, McGuirk S, Powell G, et. al. Hypersensitivity reactions during therapy with the nucleoside reverse transcriptase inhibitor abacavir. Clinical Therapeutics 2001; 23(10):1603-1614.
- Loeliger AE, Steel H, McGuirk S, et al. The abacavir hypersensitivity reaction and interruptions in therapy. AIDS 2001; 15(10):1325-6
- El Sahly HM. Development of abacavir hypersensitivity reaction after rechallenge in a previously asymptomatic patient. AIDS 2004; 18(2): 361-2.
- Gervasoni C, Vigano O, Grinelli E, et al. Abacavir hypersensitivity reaction after switching from the twice daily to the once daily formulation. AIDS Patient Care 2007; 21(1):1-2

Thank you for reporting suspected adverse reactions to antiretroviral drugs

The BC-CfE Pharmacovigilance Program conducts ongoing monitoring of adverse reactions to antiretroviral drugs in order to identify drug-related problems and alert health care providers and patients regarding safety concerns.

How to report: Complete the adverse reaction section on the HIV drug prescription request or therapy discontinuation form (available to HIV care providers) or download an adverse reaction report form at www.cfenet.ubc.ca (available to any health care provider, patient or caregiver).

Contact the BC-CfE Pharmacovigilance program:
Telephone: 604-806-8663 Fax: 604-806-8938 E-mail: ADR@cfenet.ubc.ca

***SAFETY ALERT* editors:**
Ms Kathy Lepik BSc(Pharm), MSc; Research Coordinator, Pharmacovigilance Program
Dr. Rolando Barrios MD; Director Pharmacovigilance Program, Assistant Director BC Centre for Excellence in HIV/AIDS