



Abacavir Hypersensitivity Screening

Summary

The abacavir hypersensitivity screening test can help to identify people who are at high risk for a serious adverse reaction to abacavir or any drug containing abacavir. This test is meant to be used in people living with HIV/AIDS who have never previously been exposed to abacavir. If the test is positive, you should not use abacavir or any drug containing abacavir. If the test is negative, there is a relatively low risk that you will have a reaction to abacavir, although a reaction is still possible. If you take abacavir or any drug containing abacavir, it is important for you to be able to recognize the symptoms of a hypersensitivity reaction.

Symptoms of abacavir hypersensitivity

Abacavir (Ziagen, ABC) is a nucleoside analogue commonly used as part of combination therapy for HIV/AIDS. Abacavir is also found in the following medicines:

- Kivexa – contains both ABC and another anti-HIV drug called 3TC (EpiVir, lamivudine) in one tablet
- Trizivir – contains three anti-HIV drugs in one tablet: ABC, 3TC and AZT (Retrovir, zidovudine)

In up to 8% of people with HIV/AIDS (PHAs) who use abacavir, an exaggerated reaction against abacavir by the immune system—abacavir hypersensitivity—can occur. **This reaction is very serious and can be fatal.**

Although the hypersensitivity reaction can occur at any time while a person is taking abacavir, on average it occurs within the first six weeks of use. The reaction can include the following:

- fever
- rash

- gastrointestinal symptoms (including nausea, vomiting, diarrhea, stomach pain)
- general symptoms (including unexpected lack of energy or tiredness, muscle pain, bone pain)
- respiratory symptoms (including cough, shortness of breath, sore throat)

If any of these symptoms occur while you are taking abacavir or any drug containing abacavir, you should stop taking this medicine and contact your doctor right away. If a hypersensitivity reaction to abacavir has indeed happened, then abacavir should never be restarted, as a fatal reaction could occur within hours. You should also never take any other drug that contains abacavir.

Abacavir has been available since the late 1990s. Historically, doctors in Canada and the rest of the world have dealt with the possibility of an allergic reaction to abacavir by educating their patients, before prescribing this medication, on how to recognize the potential reaction. They have also emphasized the need for those who suspect that they may be experiencing this reaction to call their doctor right away.



Screening is possible

In 2002, researchers in Western Australia at the Royal Perth Hospital made a major breakthrough. They found a link between the presence of certain genetic material in some PHAs and the risk of having a hypersensitivity reaction to abacavir. Other groups have confirmed this work and more recent studies from Western Australia and the United Kingdom have suggested a marked decrease in abacavir hypersensitivity reaction with the implementation of genetic testing or screening.

Now, in large HIV/AIDS clinics across Canada, researchers are conducting abacavir hypersensitivity testing. This testing is often done as part of a research program, sometimes integrated into other evolving genetic screening programs. In Quebec, the test is offered as a standard of care. The good news for PHAs across the country is that there is no charge for the test.

The abacavir hypersensitivity screening test

The likelihood of developing hypersensitivity to abacavir can now be assessed with a simple blood test. This test is meant to be used in PHAs who have never previously been exposed to abacavir. The test should not be used in PHAs who received a diagnosis of abacavir hypersensitivity reaction in the past.

A small sample of blood is drawn and sent to the clinic's lab. The test checks for the presence of specific genetic material, called HLA-B*5701, which has been associated with the abacavir hypersensitivity reaction.

What the test results mean

The results of the blood test are sent to the physician's office after two or three weeks. The results can appear in one of two ways:

- Negative — This does not mean that you will never get a hypersensitivity reaction. But it does mean that there is a relatively

low risk (less than 1%) of developing an abacavir hypersensitivity reaction should your doctor prescribe abacavir.

- Positive — There is a high risk of having a hypersensitivity reaction to abacavir and you should not use this drug or any other drug that contains abacavir.

The availability of this test should greatly reduce the concerns of both doctors and their patients when the use of abacavir is being discussed. However, education about the symptoms of the hypersensitivity reaction remains important in the unlikely case that there is a reaction.

Genes and abacavir hypersensitivity screening

When abacavir hypersensitivity testing was initially done, researchers in Australia used PHAs whose ancestors were mainly from northwest Europe and found that HLA-B*5701 (genetic material) was relatively common. There is some concern about the usefulness of the test in different groups of people. For instance, in the major cities of many high-income countries there are people from all parts of the world and there are concerns that the genetic material linked to abacavir hypersensitivity in people of western European ancestry might be different than that in people from sub-Saharan Africa, Asia and South America.

Part of the problem in solving this issue has been that the clinical diagnosis of abacavir hypersensitivity syndrome can be confused with adverse reactions to other drugs or other changes in the immune system that can occur soon after starting HIV treatment. A skin test, called a patch test, was developed in Canada and has been used to confirm the clinical diagnosis of abacavir hypersensitivity. The patch test is being used as part of two major studies:

- SHAPE study: an American study looking at associations between HLA-B*5701 and



abacavir hypersensitivity reaction in black and white people

- Predict-1 study: a randomized, controlled study conducted throughout sites in Europe and Australia to look at the usefulness of genetic screening for HLA-B*5701 in preventing abacavir hypersensitivity

These studies will be important in validating the feasibility of genetic screening in everyday clinical practice.

Similarly, an important part of the abacavir research testing underway in parts of Canada will be to find if HLA-B*5701 is linked to hypersensitivity reactions among different races and ethnic groups. Researchers in Montreal hope to analyse their results to find out more about this issue.

Research on abacavir hypersensitivity continues around the world, with several teams in Australia and British Columbia trying to find other ways of conducting screening for this condition. Much of this work in Canada has involved collaboration with the Western Australian group to assess the quality and accuracy of diagnostic kits for HLA-B*5701. The quality assurance of these and other quicker and cheaper methods for HLA-B*5701 will hopefully facilitate the incorporation of abacavir genetic screening into routine HIV care across Canada.

Access to abacavir hypersensitivity screening in Canada

Across the country, several major clinics and research centres are assessing the risk for abacavir hypersensitivity using the screening test, sometimes as part of other integrated programs of genetic screening. In Quebec, this program is being offered as part of regular HIV care. The locations of these programs are as follows:

- Montreal Chest Institute
- Ottawa Hospital

- Sunnybrook Hospital (Toronto)
- Southern Alberta Clinic of the Calgary Health Region
- St. Paul's Hospital (Vancouver)

PHAs interested in getting access to screening do not need to be patients at these clinics and can speak to their doctors about how to get tested for abacavir hypersensitivity reaction.

Acknowledgements

CATIE would like to thank the following researchers for their time and effort in helping us to produce this fact sheet:

- Richard Harrigan, PhD, British Columbia Centre for Excellence in HIV/AIDS
- John Gill, MD, Southern Alberta Clinic of the Calgary Health Region
- Jonathan Angel, MD, Ottawa Hospital
- Anita Rachlis, MD, Sunnybrook Hospital
- Richard Lalonde, MD, Montreal Chest Institute
- Annalise Martin, PhD, Centre for Clinical Immunology and Biomedical Statistics, Royal Perth Hospital, Perth, Australia
- Elizabeth Phillips, MD, Centre for Clinical Immunology and Biomedical Statistics, Royal Perth Hospital, Perth, Australia

Author: Sean R. Hosein

Design: Renata Lipovitch

2007

REFERENCES:

1. Shikuma CM, Yang Y, Glesby MJ, et al. Metabolic Effects of Protease Inhibitor-Sparing Antiretroviral Regimens Given as Initial Treatment of HIV-1 Infection (AIDS Clinical Trials Group Study A5095). *Journal of Acquired Immune Deficiency Syndromes* 2007 in press.
2. Mallal S, Nolan D, Witt C, et al. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1-reverse-transcriptase inhibitor abacavir. *Lancet* 2002 Mar 2;359(9308):727-32.
3. Martin AM, Nolan D, Gaudieri S, et al. Predisposition to abacavir hypersensitivity conferred by HLA-B*5701 and a haplotypic Hsp70-Hom variant. *Proceedings of the National Academy of Sciences USA* 2004 Mar 23;101(12):4180-5.



4. Phillips EJ. Genetic screening to prevent abacavir hypersensitivity reaction: are we there yet? *Clinical Infectious Diseases* 2006 Jul 1;43(1):103-5.
5. Rauch A, Nolan D, Martin A, et al. Prospective genetic screening decreases the incidence of abacavir hypersensitivity reactions in the Western Australian HIV cohort study. *Clinical Infectious Diseases* 2006 Jul 1;43(1):99-102.
6. Martin AM, Krueger R, Almeida CA, et al. A sensitive and rapid alternative to HLA typing as a genetic screening test for abacavir hypersensitivity syndrome. *Pharmacogenetics and Genomics* 2006 May;16(5):353-7.
7. Sadiq ST and Pakianathan MR. Uncertainties of routine HLA-B*5701 testing in black African HIV cohorts in the UK. *Sexually Transmitted Infections* 2007 in press.
8. Gewin V. Crunch time for multiple-gene tests. *Nature* 2007 Jan 25;445(7126):354-5.
9. GlaxoSmithKline. Ziagen: abacavir sulfate tablets. Product Monograph. *Compendium of Pharmaceuticals and Specialties* 2006; 2512-4.

Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

The Canadian AIDS Treatment Information Exchange (CATIE) in good faith provides information resources to help people living with HIV/AIDS who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

We do not guarantee the accuracy or completeness of any information accessed through or published or provided by CATIE. Users relying on this information do so entirely at their own risk. Neither CATIE nor the Public Health Agency of Canada nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE are solely those of the authors and do not reflect the policies or opinions of CATIE or the official policy of the Minister of Health Canada.

Permission to reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1.800.263.1638.*

Contact CATIE

by telephone
1.800.263.1638
416.203.7122

by fax
416.203.8284

by e-mail
info@catie.ca

on the Web
<http://www.catie.ca>

by mail
505-555 Richmond Street West
Box 1104
Toronto, ON M5V 3B1
Canada

Funding has been provided by the Public Health Agency of Canada.

