Abacavir

Abacavir is a drug used for the treatment of HIV infection. It belongs to a family of antiretroviral drugs called nucleoside analogue reverse transcriptase inhibitors (NRTIs).

Other Names

Abacavir sulfate is sold in the U.S. under the trade name Ziagen, by GlaxoSmithKline. It is sometimes referred to as ABC.

It is also available combined with other antiretroviral drugs in a single tablet form.

- Abacavir and lamivudine are available in a single tablet called Epzicom.
- Abacavir, lamivudine, and zidovudine are available in a single tablet called Trizivir.

Uses

Abacavir is used, in combination with other antiretroviral agents (drugs that work against HIV), for the treatment of HIV infection. It is available as tablets containing 300 mg of the active drug, or as an oral solution containing 20 mg of drug per 1 mL. Abacavir was approved by the Food and Drug Administration (FDA) on December 17, 1998.

Abacavir does not cure HIV infection or AIDS and does not reduce the risk of passing the virus to other people.

How Abacavir is Taken

Abacavir is taken orally (by mouth).

In combination with other antiretroviral drugs, the recommended oral dose for adults is 600 mg daily, given either 300 mg twice daily or 600 mg once daily.

For children up to 16 years of age, the recommended dose is 8 mg/kg twice daily (up to a maximum of 300 mg twice daily) in combination with other antiretroviral agents.

The recommended dose in patients with mild liver impairment is 200 mg twice daily. Abacavir oral solution (10 mL twice daily) is typically used for the treatment of these patients.

How Abacavir Works

Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) of human immunodeficiency virus type 1 (HIV-1). It has no activity against a related virus, HIV-2.

The drug works by imitating an essential building block of DNA (or nucleoside) called guanosine, which HIV-1 needs in order to make more copies of itself. Unlike guanosine, abacavir can't make connections with the next building block, so when the virus uses abacavir as a building block, the DNA chain stops building and that copy of the virus stops forming. The enzyme that does the building of DNA in retroviruses is called reverse transcriptase, so the drug is a reverse transcriptase inhibitor.

Other drugs in this class include zidovudine (AZT, the first antiretroviral drug approved by the FDA to treat HIV), didanosine(ddI, the second FDA-approved antiretroviral drug), stavudine, lamivudine, and emtricitabine.

How the body affects abacavir

Abacavir is rapidly absorbed into the body after oral administration. Taking abacavir with or without food does not alter the blood level of the drug. Furthermore, the tablet form and oral solution form provide the same level of active drug in the body.

Abacavir is metabolized (broken down) in the liver by the enzyme alcohol dehydrogenase. Most of these metabolites are removed from the body in the urine, and the remainder is eliminated in the feces.

Side Effects

Like the other drugs of its class, abacavir is generally well tolerated.[[[1]]] But severe side effects can occur. The most notable is a hypersensitivity reaction.

Hypersensitivity reaction

About five to eight percent of adults and children taking the drug experience a hypersensitivity syndrome that can include the following symptoms:

- High fever
- Skin rash
- Tiredness
- Nausea, vomiting, and diarrhea
- Painin the abdomen
- Sore throat
- Shortness of breath
- Dry cough
- Muscle and joint pains
- Sores in the mouth
- Conjunctivitis

Symptoms usually appear within the first 6 weeks of treatment with abacavir, and in prior studies, 95% of people on the drug reported at least two of the above symptoms.

This syndrome can be unexpected and can occur in people who have never had abacavir before, as well as in people who have been taking it for months. Hypersensitivity usually starts within six weeks of beginning abacavir but may take up to a year to appear. The most common time is about eleven days into therapy. If this syndrome is not aggressively treated and abacavir stopped, complications can arise including liver and kidney failure, shock, and death. Unfortunately, the symptoms can vary, which makes diagnosis tricky.

A great deal is at stake in diagnosing an abacavir reaction. This is because, although the best treatment is to stop the drug, it cannot safely be restarted after being stopped because a much worse reaction followed by death may result.[[[2]]] Because patient safety and the loss of one drug in the treatment arsenal is at stake, the diagnosis of hypersensitivity and the decision to stop abacavir must be made in close consultation with the patient's HIV doctor.

There are recent data to suggest that there may be genetic factors which influence the development of the hypersensitivity syndrome in people taking abacavir.[[[3]]] One of the types of genes (alleles) that is associated with hypersensitivity, HLA-B*5701, is much more common in some parts of the world than others. For example, in Caucasians, about 4% of people have that allele.

Recent studies have found that screening people to see who had the HLA-B*5701 allele, and avoiding the drug in people who did, greatly reduced the incidence of the hypersensitivity reaction. These studies are examples of how to use pharmacogenetics to enhance patient safety.[[[4]]][[[5]]]

Other side effects

Other side effects in people taking abacavir include the following:

- Sleep disorders
- Headache
- Nausea, vomiting, or diarrhea
- Tiredness
- Rashes
- Discomfort or pain in the abdomen
- Depressive disorders
- Dizziness
- Pain in the muscles or joints

These side effects have been reported in people taking abacavir along with other antiretroviral agents such as lamivudine, efavirenz, and zidovudine.

Risks

Cross-resistance

HIV can become resistant to all of the NRTIs. To prevent HIV drug resistance, abacavir is used in combination with other antiretroviral drugs.

Immune reconstitution syndrome

Immune reconstitution syndrome (an aggressive immune response to a hidden, or residual opportunistic infection) has been reported in people treated with combination antiretroviral therapy, including abacavir.[[[6]]]

Fat redistribution

Redistribution of body fat, including central obesity; fat enlargement on the back of the neck and upper back (sometimes called a "buffalo hump"); wasting of the arms, legs, and face; breast enlargement; and a “cushingoid appearance” have been observed in patients receiving antiretroviral therapy.[[[7]]]

Nursing mothers

The Centers for Disease Control and Prevention (CDC) recommends that HIV-infected mothers not breast-feed their infants to avoid risking transmission of HIV, even if they are taking abacavir and other antiretroviral medications.

Drug interactions

There is some suggestion that alcohol may inhibit the liver's ability to break down abacavir. It is not known whether this reaction is significant.[[[8]]]

Alternatives

There are six classes of antiretroviral drugs that inhibit the growth and replication of HIV:

- Other nucleoside analogue reverse transcriptase inhibitors (NRTIs), including zidovudine (Retrovir), lamivudine (Epivir), didanosine (Videx), zalcitabine (Hivid), and stavudine (Zerit).
- Protease inhibitors (PIs), including saquinavir (Invirase), ritonavir (Norvir), indinavir (Crixivan), nelfinavir (Viracept), amprenavir (Agenerase), lopinavir + ritonavir (Kaletra), atazanavir (Reyataz) and tipranavir (Aptivus).
- Non-nucleoside reverse transcriptase inhibitor (NNRTIs), including nevirapine (Viramune), delavirdine (Rescriptor), efavirenz (Sustiva) and etravirine (Intelence).
- Nucleotide reverse transcriptase inhibitors (NtRTIs), including tenofovir (Viread).
- Fusion inhibitors, including enfuvirtide (Fuzeon).
- Integrase inhibitors, including raltegravir (Isentress).

The decision to use one or more HIV drugs should take into account the patient's health history, his or her HIV severity, and the known sensitivity of the virus to one or another class of drugs.

Research

There were two major trials that studied the effectiveness of abacavir, called CNA3005 and CNA30021.

- CNA3005 was a study in which 562 HIV-infected, never-before-treated adults received either abacavir (300 mg twice daily) plus Combivir (lamivudine 150 mg/zidovudine 300 mg twice daily), or indinavir (800 mg 3 times a day) plus Combivir twice daily. An overall average increase in CD4+ cell count of about 150 cells/mm³ was observed in both groups, showing that both treatment combinations are equally effective.[[[9]]]
- CNA30021 was an international study in which 770 HIV-infected never-before-treated adults received either abacavir (600 mg once daily) or abacavir (300 mg twice daily), both in combination with lamivudine (300 mg once daily) and efavirenz (600 mg once daily). The median CD4+ cell count increases were 188 cells/mm³ in the group receiving abacavir 600 mg once daily and 200 cells/mm³ in the group receiving abacavir 300 mg twice daily. This study showed that the abacavir treatment 300 mg twice daily (in combination with other antiretroviral drugs) is slightly more effective.[[[10]]]

A recent study has suggested that using abacavir as the third drug in combination regimens may not be as effective as using efavirenz.[[[11]]] Of 744 patients in the study, those taking abacavir as the third drug in their regimens had a virologic failure rate of 2.17 compared to those taking efavirenz as the third drug. Further research in this area is needed to determine the most effective drug combinations.

Clinical Trials

For information on clinical research trials studying abacavir, visit Abacavir Studies.

References

1. ↑ Zapor MJ, Cozza KL, Wynn GH, Wortmann GW, Armstrong SC. Antiretrovirals, Part II: focus on non-protease inhibitor antiretrovirals (NRTIs, NNRTIs, and fusion inhibitors). *Psychosomatics.* 2004 Nov-Dec;45(6):524-35.
2. ↑ Clay PG. The abacavir hypersensitivity reaction: a review. *Clin Ther.* 2002;24:1502–1514.
3. ↑ 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.
4. ↑ Rauch A, Nolan D, Martin A, McKinnon E, Almeida C, Mallal S. Prospective genetic screening decreases the incidence of abacavir hypersensitivity reactions in the Western Australian HIV cohort study. *Clin Infect Dis.* 2006 Jul 1;43(1):99-102. Epub 2006 May 26.
5. ↑ Mallal S, Phillips E, Carosi G et al; PREDICT-1 Study Team. HLA-B*5701 screening for hypersensitivity to abacavir. *N Engl J Med.* 2008 Feb 7;358(6):568-79.
6. ↑ Taniguchi H, Izumi S. [A case of tuberculosis showing immune reconstitution syndrome after the initiation of antiretroviral therapy for HIV infection]. *Kekkaku.* 2007 Jan;82(1):27-31.
7. ↑ Wohl DA. Diagnosis and management of body morphology changes and lipid abnormalities associated with HIV Infection and its therapies. *Top HIV Med.* 2004 Jul-Aug;12(3):89-93.
8. ↑ Jang GR, Harris RZ. Drug interactions involving ethanol and alcoholic beverages. *Expert Opin Drug Metab Toxicol.* 2007 Oct;3(5):719-31.
9. ↑ Staszewski S, Keiser P, Montaner J, et al. Abacavir-lamivudine-zidovudine vs indinavir-lamivudine-zidovudine in antiretroviral-naive HIV-infected adults: A randomized equivalence trial. *JAMA.* 2001 Mar 7;285(9):1155-63.

10. ↑ Moyle GJ, DeJesus E, Cahn P et al; Ziagen Once-Daily in Antiretroviral Combination Therapy (CNA30021) Study Team. Abacavir once or twice daily combined with once-daily lamivudine and efavirenz for the treatment of antiretroviral-naive HIV-infected adults: results of the Ziagen Once Daily in Antiretroviral Combination Study. *J Acquir Immune Defic Syndr.* 2005 Apr 1;38(4):417-25.
11. ↑ Cozzi-Lepri A, De Luca A, Phillips AN, et al. A comparison between abacavir and efavirenz as the third drug used in combination with a background therapy regimen of 2 nucleoside reverse-transcriptase inhibitors in patients with initially suppressed viral loads. *J Infect Dis*. 2006 Jul 1;194(1):20-8.

External links

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