Abacavir (Ziagen)

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Drug Summary

Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) that has played a significant role in the NRTI backbone component of antiretroviral regimens. The primary current uses for abacavir are (1) in the well-tolerated and highly effective single tablet regimen dolutegravir-abacavir-lamivudine or (2) with lamivudine as an alternative to tenofovir DF-emtricitabine in patients with renal insufficiency or osteoporosis. For patients with a baseline HIV RNA level greater than 100,000 copies/mL, the abacavir-lamivudine NRTI backbone should be avoided if used with efavirenz, raltegravir, atazanavir-cobicistat, or atazanavir boosted with ritonavir. A life-threatening hypersensitivity reaction can occur with abacavir in individuals who are HLA-B*5701 positive. All patients need to undergo testing for HLA-B*5701 prior to receiving abacavir and those who test positive for HLA-B*5701 should not take abacavir. Several studies have suggested that abacavir may increase the risk of ischemic cardiovascular events, but the data overall have been inconclusive. Nevertheless, based on available information, most experts avoid the use of abacavir in patients with ischemic cardiovascular disease if effective alternatives exist. The dose of abacavir should be reduced for patients with mild hepatic impairment (Child-Turcotte-Pugh class A cirrhosis) and the medication should be avoided in the setting of more advanced impairment (Child-Turcotte-Pugh class B or C cirrhosis).

Key Clinical Trials

Abacavir-lamivudine and tenofovir DF-emtricitabine had comparable virologic efficacy when either was combined with lopinavir-ritonavir [HEAT] or darunavir plus ritonavir [FLAMINGO]. In contrast, abacavir-lamivudine had inferior virologic response compared with tenofovir DF-emtricitabine when both were given with efavirenz [ASSERT]. In a trial that randomized participants to abacavir-lamivudine or tenofovir DF-emtricitabine, combined with efavirenz or ritonavir-boosted atazanavir, virologic outcomes were inferior for those receiving abacavir-lamivudine if the baseline HIV RNA level was greater than 100,000 copies/mL [ACTG 5202]. However, participants in a trial of abacavir-lamivudine plus dolutegravir versus abacavir-lamivudine plus ritonavir-boosted darunavir had excellent virologic responses, even with baseline HIV RNA levels greater than 100,000 copies/mL [FLAMINGO]. Screening for HLA-B*5701 prior to initiating abacavir markedly reduces the risk of persons developing the abacavir hypersensitivity reaction [PREDICT-1].
**Adverse Effects**

Abacavir can cause a life-threatening hypersensitivity reaction; this reaction manifests as flu-like symptoms with or without rash and gastrointestinal symptoms, all of which worsen with each dosage. The abacavir hypersensitivity reaction may occur in individuals who are positive for HLA-B*5701. Screening for HLA-B*5701 should be done before initiating abacavir; avoidance of abacavir in persons who are positive for HLA-B*5701 eliminates the occurrence of immunologically confirmed hypersensitivity. Other possible side effects include rash, malaise, fatigue, anxiety, and elevations in hepatic aminotransferase levels. Some clinical trials have shown that abacavir leads to an increased risk of ischemic cardiovascular events, while other trials have failed to confirm this finding; thus, data are conflicting regarding effects of abacavir on cardiovascular risk profile.

**Resistance**

For a listing of the most common clinically significant mutations associated with abacavir (ABC) resistance, see the NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database.

**Key Drug Interactions**

For complete information on abacavir-related drug interactions, see the Drug Interactions section in the Abacavir (Ziagen) Prescribing Information.