


10. Saiman L, O’Keefe M, Graham PL 3rd, et al. The changing epidemiology of moderate hepatic impairment (defined as Child-Pugh scores of 5–6) [2]. In this study, the pharmacokinetics of single 600-mg doses of abacavir administered to 9 subjects with HIV infection who had received a diagnosis of moderate cirrhosis were compared with those of 9 controls who were matched for age, sex, and weight. In patients with mild hepatic dysfunction, the area under the concentration (AUC)–time curve increased by 89% and the half-life increased by 58%. In addition, the half-life of inactive metabolites increased by 21% to 31%. Although there were no adverse events after a single dose, the authors recommended a decrease of the abacavir dose to 150 mg twice per day. Similarly, the abacavir prescribing information specifies that a dose of 200 mg twice per day should be used in mild hepatic impairment and that abacavir is contraindicated in moderate to severe hepatic impairment [3].

Finally, the association between alcohol dehydrogenase activity and liver disease is not certain in cases of nonalcoholic liver disease. It is relevant that in an open-label, randomized, 3-way crossover study of 25 HIV-infected subjects, ethanol induced an increase in the abacavir AUC of 41% and an increase in the elimination half-life of 26% [4].

In summary, when used in patients with mild hepatic dysfunction in the presence of cirrhosis, a dose of 150–200 mg twice per day should be considered, especially for those who use alcohol. Abacavir should be avoided in those with more severe hepatic impairment.

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Reply to Graham and Goetz

Sir—We appreciate the comments of Drs. Graham and Goetz [1] regarding the pharmacokinetics of abacavir in the presence of hepatic dysfunction and the altered prescribing information that was published shortly after our article was accepted for publication. Though we were unaware of the original data that was presented in abstract form in 2000, it should be noted that the abacavir package insert did not recommend any dose adjustment for hepatic dysfunction until this most recent change in August 2004 [2]. In fact, we recently submitted a letter to the editor that highlights the same data and altered dosing recommendations for abacavir in the presence of mild hepatic dysfunction [3].

A word of caution, however, is necessary. The package insert states that abacavir is contraindicated in people with moderate to severe hepatic impairment (because of a lack of data) [2], and Graham and Goetz echo this statement, writing that “Abacavir should be avoided in those with more severe liver disease” [1]. But 3 points need to be made: (1) abacavir...