



Abacavir dose adjustments in patients with hepatic impairment

Abstract: 1630

Please be aware of this information, but at this time the Benet group is not recommending Abacavir dose adjustments.

re drugs - liver and dose adjustments.

Take home message: ABC dose reduction appears necessary in pts with hepatic impairment with Child Pugh scores > 5-6.

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Pharmacokinetics of, and Tolerability to, a Single, Oral, 600mg Dose of Abacavir in HIV-Positive Subjects with or without Liver Disease.

Abacavir, a synthetic carbocyclic nucleoside analog with specific anti HIV activity, is extensively metabolized by the liver. Primary pathway for metabolism in man is by alcohol-aldehyde dehydrogenase and by glucuronidation to produce the 5-carboxylate (2269W93) and the 5-glucuronide (361W94) metabolites. Because changes in the metabolism due to hepatic insufficiency could potentially be of clinical significance, a study was designed to evaluate the kinetics of, and tolerability to, a single, oral, 600mg dose of abacavir in HIV+ subjects with or without liver disease. Pharmacokinetic (PK) parameters of abacavir and its two major metabolites were determined in 9 HIV+ subjects with clinically diagnosed moderate cirrhosis and 9 normal controls, matched for sex, age and weight. PK analyses were performed using model-independent methods and statistical analysis of primary PK parameters was performed by analysis of variance. All adverse events (AEs) were recorded throughout the study. Results: All patients in the moderate cirrhosis group had Child-Pugh scores of 5-6 (mild impairment). Results showed that the PK profile of abacavir was altered in subjects with cirrhosis. There were concomitant increases in AUC_∞ and t_{1/2} of abacavir, 89% and 58% respectively, and a 47% decrease in CL/F of abacavir in the cirrhosis group compared with the control group (p<0.01). Furthermore, there were marked increases in t_{1/2} of 2269W93 (31%; p<0.05) and in t_{1/2} of 361W94 (21%) but no statistically significant differences for AUC_∞ of the metabolites. No previously unknown AEs related to abacavir were observed during this study. Conclusion: The changes in abacavir kinetics suggest that abacavir daily dose should be reduced to 150mg BID in patients with mild hepatic impairment with cirrhosis.

Key Words

Abacavir
Human pharmacokinetics
Liver

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