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Abacavir

A Viewpoint by Walter T. Hughes

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The strategy currently applied to the treatment of HIV infection is to reduce the viral burden (HIV RNA) to undetectable levels and to reconstitute the immune system. To date, the greatest success has been reported with the combination of 3 antiretroviral drugs, most commonly a protease inhibitor plus at least 1 nucleoside analogue reverse transcriptase (RT) inhibitor (NRTI). Monotherapy is used only in unusual circumstances. Thus, any new drug must be viewed for its role in combination with other drugs. Emergence of resistance mutations, noncompliance and adverse effects are the main causes of therapeutic failure.

The main advantages of abacavir include its high oral bioavailability, twice daily dosage, penetration into the cerebrospinal fluid, relatively slow development of drug-resistant mutants and seemingly low rate of serious adverse effects. Clinical trials have supported the *in vitro* observation that abacavir acts synergistically with zidovudine and the protease inhibitor 141W94 (VX-478). Forthcoming studies will provide further information on abacavir in combination with non-nucleoside RT inhibitors and protease inhibitors. These will be necessary to properly assess the place of abacavir in the management of HIV infection.

Paediatricians will be pleased that the drug has been developed with studies in infants and children being conducted concomitantly with studies in adults. The pharmacokinetic parameters are similar. Whether or not efficacy is similar remains to be seen. When adults were given abacavir alone, decreases in HIV RNA copies >1.4 $\log_{10}$ copies/ml were observed after 4 weeks at all doses studied.[1] However, in a recently terminated Pediatric ACTG trial (Protocol 330), 27 HIV-infected children given 4 and 8 mg/kg every 8 hours for 12 weeks had no significant change in viral load. An explanation for the difference in these results is lacking; however, the adults were generally antiretroviral treatment-naive, whereas the children had received prior therapy.

It is reasonable to consider abacavir as an important addition to combined antiretroviral drug therapy in HIV-infected patients. Assessment of the extent of its value awaits further studies, many of which are already in progress. ▲

References

1. Harrington R, Stone C, Griffin P, et al. Antiretroviral activity and response profile of the carbocyclic nucleoside HIV reverse transcriptase inhibitor 1592U89 [abstract no. 15]. Fourth Conference on Retroviruses and Opportunistic Infections; 1997 Jan 22-26; Washington, DC, USA, 67