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Tipranavir: A Ritonavir-Boosted Protease Inhibitor

A Viewpoint by Charles Hicks

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The introduction of HIV-1 protease inhibitors into clinical practice in late 1995 revolutionised the treatment of persons with HIV infection. An infection considered to be uniformly fatal was transformed into a chronic manageable disease for many patients. Some lay publications even speculated about "the end of AIDS". Unfortunately HIV proved to be a much more challenging adversary than anticipated and a variety of issues soon made it clear that HIV treatment would be a long-term process with many hurdles to overcome. One major issue that continues to plague clinical care is viral resistance to antiretroviral agents.

Persons starting combination antiretroviral therapy in 2005 have the advantage of benefiting from lessons learned over the 18 years since the first antiretroviral agent, zidovudine, was approved for use. One major lesson is that it is critical to use a sufficiently potent combination to suppress viral replication to the greatest extent possible, a requirement that typically necessitates the use of three drugs simultaneously. Less potent regimens such as those commonly used prior to 1995 virtually always lead to selection of resistant strains of HIV and subsequent treatment failure. In addition, successful therapy requires close adherence to the treatment regimen to maintain viral suppression; lesser degrees of adherence may also promote resistance. As a consequence there are now large numbers of HIV-infected patients infected with resistant HIV who require new drugs active against such strains of virus.

Tipranavir is a non-peptidic HIV-1 protease inhibitor with excellent *in vitro* activity against strains of HIV that have developed resistance to other members of the class.[1] When combined with other antiretroviral agents selected with the help of a genotypic resistance test, it proved to be more effective in suppressing HIV than a comparator protease inhibitor in two large trials involving patients with extensive prior antiretroviral experience. Patients who also received at least one other active drug (most often the fusion inhibitor enfuvirtide) had particularly excellent responses, underscoring the importance of combination therapy for HIV whenever possible. Patients receiving tipranavir had higher rates of liver inflammation and lipid elevations, but in general the drug was well tolerated. Tipranavir is a welcome addition to currently available antiretroviral agents and represents an important option for patients with protease inhibitor-resistant viruses. To maximize its impact, it should preferentially be used when at least one other active drug is still available. ▲

Reference

1. Larder BA, Hertogs K, Bloor S, et al. Tipranavir inhibits broadly protease inhibitor-resistant HIV-1 clinical samples. AIDS 2000 Sep 8; 14 (13): 1943-8