Table 237.5. Comparison of the efficacy of nevirapine and delavirdine for treatment of HIV-I infection.[a]

Study name	No of subjects	Comparator drug[b]	Outcome measures at 52 weeks		
			Mean decrease in HIV viral load[c]	No (%) with undetectable HIV viral load	Mean increase in CD4 count[d]
INCAS	50	Nevirapine	2.2	18 (45%)	139
Protocol 0021	34	Delavirdine	2.1	20 (59%)	88

[a]Studies were separate open-label trials and were not randomized; subjects were antiretroviral naive (from Conway, 2000).
[b]Both drugs were combined with zidovudine and lamivudine.
[c]Mean decrease in HIV viral load (as $\log_{10}$ RNA copies/ml) from baseline to 52 weeks.
[d]Mean increase in CD4 count (cells/μl) from baseline to 52 weeks.

Another phase I/II study evaluated the safety, toxicity, pharmacokinetics, and antiretroviral activities of two-drug and three-drug combinations of delavirdine and conventional doses of nucleoside analogs compared with either delavirdine monotherapy or two-drug nucleoside analog therapy (Davey *et al.*, 1996). A total of 85 HIV-infected patients with CD4 counts of 100–300 cells/μl were enrolled in two periods. In the first period patients were randomized to receive either zidovudine plus didanosine (group 1) or zidovudine plus didanosine plus escalating doses (400–1200 mg/day) of delavirdine (group 2). In the second period, patients were randomized to receive either 1200 mg of delavirdine alone per day (group 3) or zidovudine plus 1200 mg of delavirdine per day (group 4). Overall, group 2 patients (two nucleosides plus delavirdine) demonstrated more sustained increases in CD4 counts and decreases in HIV viral load (assessed by concentrations of both plasma RNA and p24 antigen and titer of infectious virus) than group 1, 3, or 4 patients.

In the randomized, double-blind study Protocol 0021, 718 patients with a mean baseline CD4 count of 334 cells/μl and a mean baseline HIV viral load of 5.25 $\log_{10}$ RNA copies/ml who had received < 6 months of prior zidovudine therapy were randomized to receive either zidovudine alone or zidovudine plus delavirdine (200, 300, or 400 mg three times daily). There was no significant difference in CD4 count in dual therapy versus monotherapy recipients at week 24 of therapy. Recipients of delavirdine and zidovudine had a greater decline in HIV RNA than zidovudine monotherapy recipients (1.0 $\log_{10}$ vs. 0.5 $\log_{10}$ RNA copies/ml plasma) at week 4, but there was little difference observed at 24 weeks, with those randomized to receive combination therapy having approximately a 0.6 $\log_{10}$ level below baseline and the monotherapy group being about 0.5 $\log_{10}$ below baseline (ViiV Healthcare, product information, 2012).

In study Protocol 0017, delavirdine and didanosine combination therapy was compared with didanosine monotherapy in a randomized double-blind trial that enrolled 1190 HIV-infected patients who had a mean baseline CD4 count of 142 cells/μl and a mean baseline HIV viral load of 5.77 $\log_{10}$ RNA copies/ml. After 6 months of treatment, there was no significant difference between the two arms in terms of survival or progression to AIDS (ViiV Healthcare, product information, 2008).

The activity of delavirdine mesylate was evaluated in the AIDS Clinical Trials Group study, ACTG261 (Friedland *et al.*, 1999). This was a phase II, randomized, double-blind, multicenter trial comparing the three-drug combination of delavirdine with zidovudine and didanosine with two-drug combinations of these drugs. A total of 544 patients with CD4 counts between 100 and 500 cells/μl with either no prior or < 6 months of monotherapy with zidovudine or didanosine were randomized to one of four arms and observed on a followup basis for 48 weeks. In those assigned to the three-drug regimen, mean short-term (weeks 4–12) and long-term (weeks 40–48) changes in CD4 counts from baseline were 49.3 ± 8.1 and 65.4 ± 13.4 cells/μl, respectively; mean short-term and long-term HIV-1 RNA changes from baseline were –1.13 log10 ± 0.12 and – 0.73 ± 0.12 copies/ml, respectively. These responses in CD4 cell counts and HIV-1 RNA levels were better than observed in each of the two-drug arms at all study points; however, differences were not consistently significant. In this study, therapy with delavirdine, zidovudine, and didanosine was safe and showed modest, but not always significant, antiviral activity and CD4 cell count benefit compared with two-drug regimens with these agents.

Analysis of the 1-year data from two separate trials comparing protease-sparing regimens with either delavirdine (Protocol 0021, Part II) or nevirapine (INCAS study) combined with dual nucleoside analog therapy appeared to show that the two drugs had equivalent efficacy based on decreases in HIV viral load and rises in CD4 lymphocyte counts (Conway, 2000; Table 237.5).

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