Table 237.3. Pharmacokinetic variables of delavirdine when co-administered with other drugs.

Co-administered drug	Dose of co-administered drug	Dose of delavirdine	No. of subjects	% Change in variables pharmacokinetic variables (90% CI)		
				C_{max}	AUC	C_{min}
HIV protease inhibitors						
Indinavir	400 or 600 mg tid ± 7 days	400 mg tid ± 7 days	81	No apparent changes based on a comparison with historical data		
Nelfinavir	750 mg tid ± 7 days	400 mg tid ± 14 days	7	↓ 27 (↓ 49–↓ 4)	↓ 31 (↓ 57–↑ 10)	↓ 33 (↓ 70–↑ 49)
Saquinavir	Soft gel capsule 1000 mg tid × 28 days	400 mg tid for 7–28 days	23	No apparent changes based on a comparison with historical data		
Nucleoside reverse transcriptase inhibitors						
Didanosine (buffered tablets)	125 or 200 mg bid × 28 days	400 mg tid × 28 days	9	↓ 32[a] (↓ 48–↓ 11)	↓ 19[a] (↓ 37–↓ 6)	↔[a]
Zidovudine	200 mg tid for ≥ 7 days	400 mg tid for 7–14 days	42	No apparent changes based on a comparison with historical data		
Anti-infective agents						
Clarithromycin	500 mg bid × 15 days	300 mg tid × 30 days	6	↔	↔	↔
Fluconazole	400 mg qd × 15 days	300 mg tid × 30 days	8	↔	↔	↔
Ketoconazole	Various	200–400 mg tid	26	—	—	↑ 50[b]
Rifabutin	300 mg qd × 14 days	400 mg tid × 28 days	7	↓ 72 (↓ 61–↓ 80)	↓ 82 (↓ 74–↓ 88)	↓ 94 (↓ 90–↓ 96)
Rifampin	600 mg qd × 15 days	400 mg tid × 30days	7	↓ 90 (↓ 94–↓ 83)	↓ 97 (↓ 98–↓ 95)	↓ 100
Sulfamethoxazole or trimethoprim and sulfamethoxazole	Various	200–400 mg tid	311	—	—	↔[b]
Other						
Antacid (Maalox TC)	20 ml	300 mg single dose	12	↓ 52 (↓ 68–↓ 29)	↓ 44 (↓ 58–↓ 27)	—
Fluoxetine	Various	200–400 mg tid	36	—	—	↑ 50[b]
Phenytoin, phenobarbital, carbamazepine	Various	300–400 mg × 3 days	8	—	—	↓ by 90%

[a]Delavirdine taken with didanosine (buffered tablets) relative to doses of delavirdine and didanosine (buffered tablets) separated by at least 1 hour.
[b]Population pharmacokinetic data from efficacy studies.
Abbreviations: CI: confidence interval; C_{max}: maximum concentration; AUC: area-under-the-concentration-time curve; C_{min}: minimum concentration; ↑: increase; ↓: decrease; ↔: no significant change; —: no available data.

transcriptase inhibitors, usually zidovudine and lamivudine) improved virologic control and immune recovery, although in this study the investigator attributed the efficacy chiefly to the antiviral effects of delavirdine rather than its effect on plasma concentrations of indinavir (Bellman *et al.*, 1998). This study enrolled 47 HIV-1-infected patients with peripheral blood CD4 lymphocyte counts < 300 cells/μl (median 127), in whom antiretroviral therapy had failed or whose condition was deteriorating (median prestudy HIV viral load was 5.0 $\log_{10}$ RNA copies/ml). Delavirdine was added to the current therapy, and in approximately half of the patients zidovudine was replaced with stavudine. The study showed that addition of delavirdine to the therapeutic regimen produced a rapid and sustained decrease in HIV viral load of 1.1 $\log_{10}$ RNA copies/ml over 6 months; 18–21% of patients showed decreases of 2–3 $\log_{10}$ copies/ml and in 33% viral load became undetectable (< 2.6 $\log_{10}$ copies/ml). CD4 lymphocyte counts increased by 66–90% between 1 and 9 months (mean increase ~ 60 cells/μl after 6 months). The fact that 9% of the subjects developed kidney stones while on delavirdine could be taken as evidence for rather high indinavir levels in the study subjects.

Delavirdine increased systemic exposure to ritonavir by 50–80% when the drugs were co-administered, but ritonavir had no apparent effect on the pharmacokinetic variables of delavirdine (Shelton *et al.*, 2003b). Delavirdine co-administered with saquinavir increased the AUC of saquinavir fivefold and appeared to modestly increase that of delavirdine (by about 15%) (ViiV Healthcare, product information, 2012). A study by Justesen *et al.* (2003) showed that co-administration of delavirdine with amprenavir (1000 and 450 mg, respectively) to healthy volunteers markedly increased the median plasma concentration of delavirdine at 12 hours by over 450% (from 835 to 3944 ng/ml) when compared with a combination with a slightly lower dose of delavirdine (600 mg delavirdine and 600 mg amprenavir) (Justesen *et al.*, 2004). Only small differences in the amprenavir pharmacokinetic variables (< 25%) were seen, although in a previous study this same group had