Quick Reference Guide to Antiretrovirals

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Guide to Antiretroviral Agents

Nucleoside Analogue Reverse Transcriptase Inhibitors (Nucleoside Analogues, NRTIs)

Generic	Brand	Dose	Comments and Common Side Effects
Abacavir (ABC)	*Ziagen*	300 mg twice daily	About 4% hypersensitivity reaction: fever, malaise, possible rash, GI, respiratory. Resolves within 2 days after discontinuation. DO NOT RECHALLENGE. Also: rash alone without hypersensitivity.
Didanosine (ddI)	*Videx EC*	400-mg capsule once daily on empty stomach (>60 kg body weight)	Peripheral neuropathy in 15%, rare pancreatitis; avoid alcohol. OK to take *Videx EC* at same time as other antiretrovirals that can be taken on an empty stomach. Older chewable tablet formulation has additional restrictions.
Lamivudine (3TC)	*Epivir*	150 mg twice daily	Generally well tolerated. Active against HBV.
Stavudine (d4T)	*Zerit*	40 mg twice daily (>60 kg body weight)	Peripheral neuropathy (1%-4% in early studies; 24% in expanded access patients with CD4+ counts <50).
Zalcitabine (ddC)	*Hivid*	0.375-0.75 mg 3 times daily	Peripheral neuropathy in 17%-31% of trial participants; oral ulcers.
Zidovudine (ZDV, AZT)	*Retrovir*	300 mg twice daily	Initial nausea, headache, fatigue, anemia, neutropenia, neuropathy, myopathy.
Zidovudine + Lamivudine	*Combivir*	1 tablet twice daily	Combination tablet containing 300 mg of ZDV and 150 mg of 3TC.
Zidovudine + Lamivudine + Abacavir	*Trizivir*	1 tablet twice daily	Combination tablet containing 300 mg of ZDV, 150 mg of 3TC, and 300 mg of abacavir.

Protease Inhibitors (PIs)

Generic	Brand	Dose	Comments and Common Side Effects
Amprenavir	*Agenerase*	1200 mg (8 cap) twice daily *	Rash (20%), diarrhea, nausea
Indinavir	*Crixivan*	800 mg (2 cap) every 8 hours on empty stomach or with snack containing <2 g of fat *	Kidney stones in 6%-8%: good hydration essential. Occasional nausea and GI upset. Store in original container which contains desiccant; without this, IDV is stable for only about 3 days.
Lopinavir/ Ritonavir	*Kaletra*	Coformulated lopinavir 400 mg + ritonavir 100 mg (3 cap) twice daily with food	GI side effects common but mild.
Nelfinavir	*Viracept*	1250 mg (5 tab) twice daily or 750 mg (3 tab) 3 times daily with food	Diarrhea common; occasional nausea
Ritonavir	*Norvir*	600 mg (6 cap) twice daily; start with 300 mg twice daily and increase to full dose over 14 days	Nausea, diarrhea, numb lips for up to 5 weeks or longer; occasional hepatitis. Store capsules in refrigerator. Stable at room temperature for up to 1 month. Used at lower dosages as pharmacokinetic enhancer of other protease inhibitors.
Saquinavir soft gel cap	*Fortovase*	1600 mg (8 cap) twice daily or 1200 mg (6 cap) 3 times daily with fat-containing food (>28 g) *	Soft gel formulation with improved absorption, essentially replacing previous hard gel formulation (*Invirase*). Long-term storage in refrigerator. Stable at room temperature for 3 months.

* Frequently dosed with ritonavir to simplify administration and raise drug levels. See Drug-Drug Combinations section for details.

Guide to Antiretroviral Agents (Cont.)

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Generic	Brand	Dose	Comments and Common Side Effects
Delavirdine	*Rescriptor*	400 mg (2 tab) 3 times daily	Transient rash. P450 3A4 inhibitor. 600 mg twice daily dosing being studied. Coadministration with agents that lower gastric acid decreases absorption.
Efavirenz	*Sustiva*	600 mg (3 cap) once daily initially at bedtime	Initial dizziness, insomnia, transient rash, P450 3A4 inducer; avoid clarithromycin.
Nevirapine	*Viramune*	200 mg (1 tab) once daily for 2 weeks, then 200 mg twice daily or 400 mg once daily	Transient rash, hepatitis. P450 3A4 inducer. Once-daily dosing recommendation based on limited clinical data.

Nucleotide Reverse Transcriptase Inhibitors

Generic	Dose	Comments and Common Side Effects
Tenofovir (not FDA-approved)	300 mg once daily	Chemically related to adefovir. No significant renal toxicity reported. In limited expanded access.

Ribonucleotide Reductase Inhibitors

Generic	Brand	Dose	Comments and Common Side Effects
Hydroxyurea (not FDA-approved for HIV therapy)	*Hydrea*	500 mg twice daily	Bone marrow suppression, aphthous ulcers, hair loss, neuropathy, hepatotoxicity. Augments ddI and d4T and their toxicities. No direct antiviral effect.

Drug-Drug Combinations

This table gives an overview of current knowledge of drug-drug combinations. The NRTIs are not listed since they do not require dose adjustments when combined. In contrast, PIs and NNRTIs tend to have complex metabolism and in combinations affect each other's drug levels and potency. The knowledge on these combinations is still evolving, and few formal dose modification recommendations are available. Caution and close monitoring are advised. Treating physicians should verify all information with an AIDS specialist and check any dose adjustments with a pharmacist.
** Comments on each combination are given below.*

	Amprenavir	Indinavir	Lopinavir/ Ritonavir	Nelfinavir	Ritonavir	Saquinavir	Delavirdine	Efavirenz
Nevirapine	No data	↓ IDV [1]	↓ LPV [2]	No significant interaction [3]	No significant interaction [4]	↓ SQV [5]	No data	↓ EFV [6]
Efavirenz	↓ APV [7]	↓ IDV [8]	↓ LPV [9]	No significant interaction [10]	Modest ↑ in both [11]	↓ SQV level; do not combine [12]	No data	
Delavirdine	APV [13]	↑ IDV [14]	No data	↑ NFV [15]	↑ RTV [16]	↑ SQV [17]		
Saquinavir	↓ APV; ↓ SQV [18]	Antagonistic in vitro (in 1 lab)	↑ SQV-S [19]	↑ SQV-S [12]	↑ SQV [21]			
Ritonavir	↑ APV; ↓ RTV [22]	↑ IDV [23]	↓ RTV [24]	↑ NFV [25]				
Nelfinavir	↑ APV [26]	↑ IDV [27]	↑ NFV [28]					
Lopinavir/ Ritonavir	↓ APV; ↓ LPV [29]	↑ IDV [30]						
Indinavir	↑ APV; ↓ IDV [31]							

Contraindicated Combinations

- ZDV + d4T combination is antagonistic in vivo
- ddI and ddC should not be combined due to increased risk of peripheral neuropathy
- IDV + SQV combination is antagonistic in vitro and in practice extremely difficult to dose

Comments on Drug-Drug Combinations

1	**IDV & NVP**	NVP decreases IDV levels by 30%. (Indinavir decrease is most pronounced in patients with a high IDV level within the interpatient variability of IDV levels). Consider IDV dosage increase, eg, 1000 mg every 8 hours (5th CROI, 1998).
2	**LPV/RTV & NVP**	Decrease in LPV Cmin by 35% -40% and AUC by 20%-25%; considered not significant in patients naive to PIs. If PI resistance suspected, consider LPV dose increase to 533/133 mg (4 cap) 2x/d (Abbott data, 2000).
3	**NFV & NVP**	Steady-state studies indicate no significant changes in NVP or NVP levels, suggesting standard doses of each (5th CROI, 1998).
4	**RTV & NVP**	NVP decreases RTV levels by 11%, not requiring dose adjustment.
5	**SQV & NVP**	SQV-hard gel AUC decreased by 27%, which is of concern as SQV-hard gel by itself reaches marginal levels only. No effect on NVP level. No data on nevirapine and SQV-soft gel formulation.
6	**NVP & EFV**	Decrease in EFV AUC by 22% and EFV Cmin by 36%; NVP levels unchanged; dose increase of EFV to 800 mg daily being discussed, but no safety data are available for this dose (7th CROI, 2000).
7	**APV & EFV**	Decrease in APV Cmax by 36%, AUC by 39%, and Cmin by 43% (5th CROI, 1998). See comments 22 and 25 below for dosing options.
8	**IDV & EFV**	EFV decreases IDV AUC by 31% and Cmax by 16%; consider dose increase to IDV 1000 mg every 8 hours (ICAAC, 1998).
9	**LPV/RTV & EFV**	Decrease in LPV Cmin by 35%-40% and AUC by 20%-25%; considered not significant in patients naive to PIs. If PI resistance suspected, consider LPV dose increase to 533/133 mg (4 cap) 2x/d (Abbott data, 2000).
10	**NFV & EFV**	EFV increases NFV level by 20%. No change in EFV level. Clinical efficacy documented in several studies with standard dose of both drugs (6th CROI, 1999) .
11	**RTV & EFV**	EFV increases RTV AUC by 18% and Cmax by 24%. No dose adjustment for EFV necessary. Consider dose reduction of RTV. Monitor LFTs (ICAAC, 1998). See comment 21 for further dosing options.
12	**SQV & EFV**	EFV decreases SQV-S AUC by 62% and Cmax by 50%. Avoid combination with SQV as sole PI (ICAAC 1998). See comment 21 for further dosing options.
13	**APV & DLV**	DLV increases APV Cmax/AUC/Cmin by 1.3-fold/4-fold/6-fold, respectively (Glasgow, 2000). Effect of APV on DLV under evaluation.
14	**IDV & DLV**	Compared with IDV 800 mg 3x/d alone, IDV 400 or 600 mg with DLV 400 mg 3x/d leads to increase in IDV Cmin of 140% and 400% respectively. IDV 1200 mg with DLV 600 mg 2x/d with food increases IDV Cmin/AUC/Cmax by 0%/+40%/+70%. Consider dosing IDV 600 mg with DLV 400 mg 3x/d, or IDV 1200 mg with DLV 600 mg 2x/d with or without food (ICAAC, 1999, Glasgow, 2000).
15	**NFV & DLV**	Increase in NFV levels by 113%. 40% decrease in DLV AUC (Pharmacia & Upjohn data 8/98).
16	**RTV & DLV**	DLV increases RTV levels by 70%. May merit RTV dose reduction, eg, 400 mg 2x/d. Limited data (5th CROI, 1998, P&U data 8/98).
17	**SQV & DLV**	DLV dosed 400 mg 3x/d or 600 mg 2x/d decreases SQV clearance by 63%, resulting in increase in SQV AUC/Cmin/Cmax. Dose of SQV 1400 mg 2x/d or 1000 mg 3x/d with DLV 600 mg 2x/d or 400 mg 3x/d being evaluated (7th CROI, 2000).
18	**APV & SQV**	Decrease in APV Cmax/AUC/Cmin by 37%/32%/14%, respectively, and increase in SQV Cmax by +21%, but decrease of SQV AUC by 19% and Cmin by 48% (Geneva, 1998). SQV 800 mg + RTV 100 mg + APV 600 mg 2x/d suggested (Salvage Workshop, 2000).
19	**LPV/RTV & SQV**	Single-dose PK suggests increase in SQV AUC and Cmin; SQV 800 mg 2x/d with standard-dose LPV suggested (Abbott data).
20	**NFV & SQV**	NFV increases SQV-S levels 3-fold or higher. Consider dosage of NFV 750 mg + SQV-S 800 mg 3x/d, or NFV 1250 mg + SQV-S 1200 mg 2x/d (under study) (6th CROI, 1999).
21	**RTV, SQV & EFV**	RTV increases SQV levels 3-fold or higher. No food effect on SQV level in this combination. RTV level not affected, but generally same clinical efficacy with reduced RTV dose with considerably fewer GI side effects. Good results from studies of 400 mg 2x/d for each drug. Once-daily dosing of SQV with low-dose RTV as pharmacokinetic enhancer being studied. The addition of EFV to RTV/SQV 400 mg 2x/d does not significantly change levels (7th CROI, 2000).
22	**APV, RTV & EFV**	RTV increases APV levels significantly, ie, APV 1200 mg with RTV 200 mg 2x/d increases APV Cmax/AUC/Cmin by +33%/+131%/+680%. The addition of EFV 600 mg qd to this combination results in Cmax -9%, AUC +8% and Cmin +27% (Falloon, 1999; Lamotte, 2000). APV decreases RTV Cmin 3-fold compared with RTV Cmin in RTV/IDV or RTV/SQV, which may affect levels of other PIs added to APV/RTV. (PK Workshop, 2001). Most commonly used dose: APV 600 mg + RTV 100 mg 2x/d. Once-daily dosing with APV 1200 mg + RTV 200 mg being evaluated.
23	**IDV & RTV**	RTV increases IDV AUC up to 480%. Compared with IDV alone, 400 mg of both drugs 2x/d leads to same IDV peak and higher trough levels and acts as true dual-PI combo. No reports of nephrolithiasis in this combination. IDV/RTV 800/100 mg or 800/200 mg 2x/d augments IDV to higher peak and trough levels without antiviral activity of RTV. No significant food effect on IDV absorption with either dose combination. Other dose combinations under study (6th CROI, 1999).

Comments on Drug-Drug Combinations (Cont.)

24	**LPV/RTV & RTV**	Addition of RTV to LPV/RTV increases LPV concentration. Studies in progress. LPV/RTV produces RTV Cmin that is 3-fold lower than RTV Cmin when RTV 100 mg 2x/d is combined with IDV or SQV (PK Workshop, 2001).
25	**NFV & RTV**	RTV increases level of NFV and NFV M8 metabolite. Once-daily NFV 2000 mg + RTV 200 mg increases combined NFV + M8 Cmin/AUC/Cmax by 50% compared with NFV 1250 mg 2x/d in HIV-negative volunteers. Rashes noted (PK Workshop, 2001). RTV 400 mg with NFV 500 mg or 750 mg (all 2x/d) results in NFV AUC equivalent to standard dose. Higher dose results in higher AUC of M8, but also lower RTV level. Limited clinical data (6th CROI, 1999).
26	**APV, NFV & EFV**	Full dose of APV+NFV results in decrease in APV Cmax by -14%, but increase in AUC by +46% and Cmin by +235%. No significant effect on NFV levels. The addition of EFV 600 mg qd resulted in same APV Cmax and AUC and mild reduction of Cmin by -14%. Consider dosing APV/NFV or APV/NFV/EFV at full dose of each drug (7th CROI, 2000).
27	**IDV & NFV**	NFV increases IDV level by 51%; IDV does not affect NFV level. NFV 1250 mg with IDV 1200 mg 2x/d with a low-fat snack on empty stomach shows good drug levels and clinical efficacy (6th CROI, 1999).
28	**LPV/RTV & NFV**	Limited data from single-dose PK suggests unchanged NFV AUC, but increase in NFV Cmin and M8 metabolite.
29	**LPV/RTV & APV**	APV 450-750 mg + LPV/RTV 2x/d leads to significant decrease of APV Cmin by 220-420% and trend to lower LPV Cmin, compared with APV + RTV 100 mg or LPV/RTV alone (historical controls). Additional RTV 100 mg 2x/d did not compensate for this interaction (PK Workshop, 2001).
30	**LPV/RTV & IDV**	Single-dose PK show increase in IDV level; IDV dose reduction suggested (Abbott data, 2000).
31	**APV & IDV**	Increase in APV Cmax/AUC/Cmin by 18%/32%/25%, respectively, and decrease in IDV Cmax by 22%, AUC by 38% and Cmin by 27% (GlaxoWellcome data, 1999).

Antiretroviral Drug Interactions

The following tables summarize current knowledge of drug interactions between antiretrovirals and selected classes of medications. The information available is limited and the following categories explain the source of information provided. Treating physicians should verify all information with an AIDS specialist and check any dose adjustments with a pharmacist.

① Case reports/abstracted data; ② Pharmacokinetic study; ③ Clinical study; ④ Manufacturer's information; ⑤ Expert opinion

1. TB Medication/Antiretroviral Drug Interactions

The information in this table is based on pharmacokinetic data. Most problematic drug interactions occur between rifampin and PIs or NNRTIs. Since rifabutin interactions are less pronounced, it can be considered as an alternative to rifampin when coadministered with PIs or NNRTIs. Clinical judgment is advised, especially in view of decreased anti-TB activity of rifabutin when compared with rifampin. No significant drug interactions are noted between TB medications and NRTIs, with the exception of ddI which should be dosed 1 hour apart due to its antacid buffer. There may be an increased risk of neuropathy if ddC and isoniazid are coadministered. Rifampin reduces the AUC of AZT by 47%, but this is not clinically significant as intracellular levels of AZT triphosphate are not significantly affected. Ethambutol, pyrazinamide, and the fluoroquinolones have no known CYP3A4 effect, and hence no known interactions with antiretrovirals. If PIs and NNRTIs are used in combination, inhibition and induction of CYP3A4 can occur; dose adjustments for rifamycins and antiretrovirals remain unknown at this time.

	Isoniazid Mild inhibitor of CYP3A4	**Rifampin** Potent inducer of CYP3A4	**Rifabutin** Moderate inducer of CYP3A4
DLV	No known interaction	DO NOT COMBINE. 96% ↓ in DLV, no change in rifampin.	DO NOT COMBINE. 80% ↓ in DLV AUC, 342% ↑ in rifabutin AUC.
EFV	No known interaction	13%-26% ↓ EFV AUC, no change in rifampin. Unclear significance, no dose change recommended, limited data. ②	No change in EFV, 38% ↓ in rifabutin AUC, consider ↑ rifabutin to 450-600 mg 1x/d or 600 mg 3x/wk. ②
NVP	No known interaction	37% ↓ in NVP AUC. No change in rifampin. Insufficient data to recommend dose change.	16% ↓ in NVP AUC, moderate ↓ in rifabutin. Use standard-dose rifabutin. ②
APV	No known interaction	DO NOT COMBINE. 81% ↓ in APV AUC.	↓ rifabutin to 150 mg qd or 300 mg 3x/wk (200% ↑ in rifabutin AUC, 14% ↓ in APV AUC. ①
IDV	13%↑ in INH AUC after 1 week	DO NOT COMBINE. 92% ↓ in IDV AUC.	↓ rifabutin to 150 mg qd and ↑ IDV to 1000 mg 3x/d (173%↑ in rifabutin AUC, 34% ↓ in IDV AUC). ②
LPV/RTV	No known interaction	DO NOT COMBINE.	↓ rifabutin to 150 mg 3x/week (↑↑ in rifabutin AUC).
NFV	No known interaction	DO NOT COMBINE. 82% ↓ in NFV AUC.	↓ rifabutin to 150 mg qd or 300 mg 3x/wk (207% ↑ in rifabutin AUC, 32% ↓ in NFV AUC). ③
RTV	No known interaction	35% ↓ in RTV AUC and 25% ↓ in Cmax. 80% ↓ in SQV AUC and Cmax. Avoid dosing RTV or SQV alone with rifampin. With RTV/SQV 400/400 mg 2x/d combination, consider standard-dose rifampin.①	293% ↑ in rifabutin AUC. ↓ rifabutin to 150 mg qod if dosed with RTV alone. 45% ↓ in SQV AUC. Standard-dose rifabutin may be ok with SQV-SGC alone, but limited data. ②③ With RTV/SQV 400/400 mg 2x/d combination consider ↓ rifabutin to 150 mg 3x/wk or 300 mg 1x/wk. ②
SQV	No known interaction		

2. Oral Contraceptive/Antiretroviral Drug Interactions

Although pharmacokinetic studies have been performed with some of the NNRTIs and PIs combined with oral contraceptives (OC) to define the changes in AUC and/or Cmax, *the overall consensus by all manufacturers of these agents is to use additional or alternative forms of contraception* since the interactions are either unpredictable or their clinical significance is unclear. In clinical studies, ethinyl estradiol was the most commonly used estrogen and the progesterone was norethindrone. There is no known significant OC effect on levels of antiretrovirals at this time.

	Estrogen	Progesterone	Comment
DLV	Not felt to be a significant interaction, but possible ↑ estrogen levels	Possibly significant interaction; possible ↑ progesterone levels.	No clinical data available.
NVP	AUC↓ 29%, no change in Cmax	AUC ↓ 18%	Probably through NVP induction.
EFV	↑ AUC of uncertain significance. No significant change in Cmax	AUC↑ 37%, Cmax ↑ 8%	
APV	No data	No data	Unknown interaction at this time.
IDV	AUC↑ 24%	AUC ↑ 26%	
LPV/RTV	0.58↓ in AUC ratio, 0.59↓ in Cmax ratio	0.83↓ in AUC ratio, 0.84↓ in Cmax ratio	Ratio of 1.00 equals no effect.
NFV	AUC ↓ 47% No change in Cmax	AUC↓ 18%	Probably due to increased glucuronidation.
RTV	AUC↓ 40%, Cmax ↓ 32%	No data	Probably due to increased glucuronidation.
SQV	No clinically significant interaction	No data	Durban study TuPeB3226 did not look at OC levels.

3. Methadone/Antiretroviral Drug Interactions

Like many medications, methadone is primarily metabolized by cytochrome P450 CYP3A4. Minor metabolic pathways exist through CYP 2D6, 2C9, and 2C19. Drug interactions are to be expected, especially with NNRTIs and PIs.

	Dose Change	Comment
ZDV	None	↑ ZDV AUC by 40% not clinically significant. ④Consider monitoring for ↑ ZDV toxicity. ②
ddI	Consider ↑ ddI tablet form	Methadone causes delayed ddI tablet absorption: ↓ ddI Cmax by 64% and AUC by 41-60. No data on other ddI formulations. ②
ddC	No data	
d4T	None	↓ d4T Cmax by 39% and AUC by 18%-27%. Not clinically significant. ②
3TC	None	No drug interaction expected. ④
ABC	None	ABC is metabolized by 2 primary routes: glucuronyl transferase (like ZDV) and alcohol dehydrogenase. Consider monitoring for possible ↑ ABC toxicity. Leads to ↑ in methadone clearance by 22%. ⑤
DLV	No data	As DLV inhibits P450 CYP3A4, methadone levels are predicted to increase. Not formally studied. ⑤
EFV	Consider ↑ methadone	Levels of methadone have been reported to decrease by 25%-50%. Consider ↑ methadone dose or monitor closely for withdrawal symptoms. ①
NVP	Consider ↑ methadone	↓ methadone levels by 46%-60% have been reported. Consider ↑ methadone dose or monitor closely for withdrawal symptoms. ① ②
APV	Consider ↑ methadone	In vitro studies predict ↓ methadone AUC; monitor for withdrawal and consider ↑ methadone dose if needed. ⑤
IDV	None	Methadone slows IDV absorption without significant effect on IDV AUC. In vitro PK study predicts ↑ methadone AUC by 30%. Probably no need for dose adjustment. ②
LPV/RTV	Consider ↑ methadone ④	Study in healthy volunteers showed ↓ methadone by 53%. ②
NFV	Consider small ↑ methadone	Clinical study reported 34%-47% ↓ methadone and metabolite levels. Only 2/75 patients required 10 mg/day ↑ of methadone after started on standard dose NFV. ①③
RTV	Consider small ↑ methadone	Conflicting results of in vitro vs in vivo RTV PK studies. In vivo ↓ methadone Cmax by 38% and AUC by 36%. ② In vitro SQV study predicted no drug interaction. Combination study of RTV/SQV combination with methadone showed ↓ methadone of 19.9%-24.6% after correction for protein binding. No withdrawal symptoms observed in this study (Gerber et al, 2000) .③
SQV	No data	

Guide to Antiretroviral Resistance Mutations

These tables give an overview of mutations associated with resistance to antiretrovirals. While the interaction between mutations is complex and cannot be fully represented in a concise table format, these tables may still aid in the interpretation of genotypic analysis results. The tables list mutations seen frequently and/or considered significant. Results of genotypic testing always indicate mutations in the majority virus population only (>20%). Mutations caused by previous antiretrovirals may only be present in minority virus populations and may thus not be detected, but will re-emerge if the drug(s) in question is resumed. Any mutations reported on previous genotypic testing of a given patient should be taken into account when deciding on future treatment.

How to read these tables:

Bold underlined: Major mutation frequently associated with high-level resistance
Bold: Common mutation that can be associated with resistance
Italicized: Not always associated with resistance; possible polymorphism

Nucleosides and Nucleotides

ZDV	**41**			**67**		**69***	**70**				**151**			**210**	**215**	**219**	**333**	184 restores ZDV sensitivity in presence of 41+215. 333 likely resistant to ZDV + 3TC
ddI			**65**			**69***		**74**			**151**		*184*					
ddC			**65**		**69**	**69***		**74**			**151**		**184**					Incomplete data
d4T		*50*				**69***	**70**		*75*		**151**	**178**			**215**			Multiple ZDV mutations also led to d4T resistance
3TC						**69***					**151**		**184**				**333**	
ABC			**65**			**69***		**74**		**115**	**151**		**184**					Multiple mutations required
ADV			**65**		**69**	**69***	**70**											184 increases ADV sensitivity
TNV			**65**				**70**											Limited data

69* = 69SS insertion, which along with other RT-mutations leads to cross resistance for the class and is difficult to identify in genotypic testing.
151 = leads to cross-resistance to NRTI class when present along with ≥3 mutations.

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

DLV		**103**				**181**				**236**	NNRTI resistance occurs quickly if viral suppression is incomplete. K103N and Y181C are the most common mutations and lead to cross-resistance. Y181C alone may not lead to EFV resistance.
EFV	**100**	**103**		**108**	**179**	**181**	**188**	**190**	**225**		
NVP	**100**	**103**	**106**	**108**		**181**	**188**	**190**			

Protease Inhibitors (PIs)

APV	*10*						*36*	*46*	**47**	**48**	**50**	**54**	*63*	*71*			**82**	**84**			1° mutn: I50V; 88 increases APV sensitivity
IDV	*10*	**20**	**24**		**32**		*36*	**46**		*48*		**54**	*63*	*71*	**73**	*77*	**82**	**84**		**90**	≥3 mutns needed for high-level resistance
LPV	*10*	20	**24**		*32*			*46*	*47*		**50**	**54**	*63*	*71*	**73**		**82**	**84**		**90**	Resistance with multiple mutations only
NFV	*10*			**30**			*36*	*46*		*48*				*71*		*77*	**82**	**84**	**88**	**90**	Primary mutation: D30N, occ. L90M
RTV	*10*	**20**			**32**	**33**	*36*	*46*				**54**	*63*	*71*		77	**82**	**84**		**90**	Multiple mutations required
SQV	*10*	**20**	**24**	**30**			*36*	*46*		**48**		**54**	*63*	*71*	**73**	77	**82**	**84**		**90**	Primary mutations: G48V & L90M

Primary mutations are 30, 48, 54, 82, 84, 90. Resistance to all PIs is likely if 2 or more of these mutations are present