

Mutations in the Protease Gene Associated with Resistance to Protease Inhibitors

Atazanavir +/- ritonavir	L 10	G 16	K 20	L 24	V 32	L 33	E 34	M 36	M 46	G 48	I 50	F 53	I 54	D 60	I 62	I 64	A 71	G 73	V 82	I 84	I 85	N 88	L 90	I 93
	I	E	R	I	I	I	Q	I	I	V	L	L	L	E	V	L	V	C	A	V	V	S	M	L
	F	M	I		F			L	L		Y	V				M	I	S	T				M	L
	V				V			V				V				V	T	T	F					M
	C											M					L	A	I					M
												A												
Darunavir/ ritonavir	V 11				V 32	L 33			I 47	I 50	I 54						T 74	L 76		I 84			L 89	
	I				I	F			V	V	M						P	V		V			V	
											L													
Fosamprenavir/ ritonavir	L 10				V 32				M 46	I 47	I 50	I 54					G 73	L 76	V 82	I 84			L 90	
	F				I				I	V	V	L					S	V	A	V			M	
	I								L			V							F					
	R											M							S					
	V																		T					
Indinavir/ ritonavir	L 10	K 20	L 24		V 32			M 36	M 46		I 54						A 71	G 73	L 76	V 77	V 82	I 84	L 90	
	I	M	I		I			I	I		V						V	S	V	I	A	V	M	
	R	R						L									T	A			F			
	V																				T			
Lopinavir/ ritonavir	L 10	K 20	L 24		V 32	L 33			M 46	I 47	I 50	F 53	I 54			L 63	A 71	G 73	L 76	V 82	I 84		L 90	
	F	M	I		I	F			I	V	V	L	V			P	V	S	V	V	A	V	M	
	I	R							L	A		L									F			
	R											L									T			
	V											A									S			
Nelfinavir	L 10				D 30			M 36	M 46								A 71		V 77	V 82	I 84	N 88	L 90	
	F				N			I	I								V		I	A	V	D	M	
	I								L								T			F		S		
																				T				
Saquinavir/ ritonavir	L 10		L 24						G 48		I 54			I 62			A 71	G 73	V 77	V 82	I 84		L 90	
	I		I						V		V			V			V	S	I	A	V		M	
	R										L						T			F				
	V																			T				
Tipranavir ritonavir	L 10				L 33			M 36	K 43	M 46	I 47	I 54	Q 58			H 69	T 74		V 82	N 83	I 84		L 89	
	V				F			L	T	L	V	A	E		K		P		L	D	V		M	
								V				M			R				T				I	
												V											M	
																							V	

Mutations in the Envelope Gene Associated with Resistance to Entry Inhibitors

Enfuvirtide	G 36	I 37	V 38	Q 39	Q 40	N 42	N 43
	D	V	A	R	H	T	D
	S		M				
			E				
Maraviroc	Activity limited to patients with R5 viruses						

Mutations in the Integrase Gene Associated with Resistance to Integrase Strand Transfer Inhibitors

Dolutegravir					F 121	E 138	G 140	Q 148
					Y	A	S	H
						K	A	
Elvitegravir		T 66			E 92	T 97	F 121	S 147
		I			Q	A	Y	H
		A			G			H
		K						K
Raltegravir			L 74		E 92	T 97	F 121	G 138
			M		Q	A	Y	A
								S
								K
								C
								R
								H
								K
								R

FIGURE 226-46 (Continued)

increased levels of calcium channel blockers, macrolide antibiotics, HMG-CoA reductase inhibitors, and sildenafil. Levels of atazanavir are lower in the presence of tenofovir or efavirenz. In these settings, levels of atazanavir should be boosted with the use of low-dose ritonavir. In a head-to-head comparison, more patients discontinued atazanavir than either darunavir or raltegravir. The

main reasons for discontinuation were bilirubin elevations and gastrointestinal side effects.

Darunavir is a nonpeptidic HIV protease inhibitor initially licensed in 2006. It is indicated for coadministration with 100 mg of ritonavir and other antiretroviral agents for the treatment of HIV infection. In initial studies in treatment-experienced subjects, 46% of