

RESISTANCE TO PIs

Mutations of at least twenty-five different codons have been implicated in the development of HIV resistance to PIs. There is also a significant degree of cross-resistance among the members of the PI class.

SQV: Reduced sensitivity to SQV is most often associated with three mutations in the protease gene at codons 48 (G48V), 84 (I84V), and 90 (L90M). Additional mutations at codons 54, 71, 73, 77, and 82 have also been observed in patients receiving SQV. When SQV is administered with RTV, mutations at codons 24, 62, and 90 have been reported in patients failing treatment.

RTV: Resistance to RTV involves multiple mutations, usually at greater than three sites and up to eleven. Resistant viruses generally show mutation at codons 46, 82, 84, and 90, with the mutation at codon 82 appearing first in most patients. Other mutations have been observed in patients at codons 20, 24, 32, 36, 54, 71, 73, and 77.

IDV: Resistance to IDV is very similar to RTV resistance, with multiple mutations required usually at greater than three sites and up to eleven. Mutations at codon 82 or codon 46 (M46I or M46L) are the most commonly seen (with or without other mutations).

NFV: The most common mutations observed *in vivo* are D30N and L90M. D30N occurs more commonly and does not induce cross-resistance with other PIs. Reduction in susceptibility is also displayed by isolates harbouring a mutation at codon 82 in association with other mutations.

APV: A specific mutation at codon 50 induces resistance to APV. Otherwise, up to three mutations at codons 10, 32, 46, 47, 54, 73, 82, 84, and 90 are required to induce resistance to APV. When APV is administered with RTV, up to five of these mutations are needed.

LPV: LPV is co-formulated with RTV, which boosts the serum drug levels of LPV. Multiple mutations in the protease gene are required to generate significant resistance to LPV/RTV, making this a useful agent for initial as well as salvage therapy.