

Amino acid substitutions in the NAs of variants in clinical samples or isolates causing reduced antiviral susceptibility

Amino Acid substitution¹	Type/ Subtype	<i>In vivo/in vitro</i>²	Oseltamivir³	Zanamivir	Peramivir
V116A	H5N1	in vivo	M	M	L
I117V+I131V	H5N1	in vivo	M	S	S
E119V	H3N2	in vivo/in vitro	M/H	S	S
E119I	H3N2	in vivo/in vitro	H	M	L
E119G	B	in vitro	M	M/H	H
E119A	B	in vivo	?	?	?
Q136L	H5N1	in vivo	M	H	?
Q136K	H1N1	in vivo	S	H	H
Q136K	H3N2	in vivo	S	M	?
V149A	H5N1	in vivo	L	L	?
K150N+I222L+S246N	H5N1	in vivo	H	S	?
D151V/D	H3N2	in vivo	L	H	?
R152K	B	in vivo	H	H	H
Y155H	H1N1	in vivo	M	H	H
D198Y	B	in vivo	M	M	?
D198N	B	in vivo	L	L	L
D198G	H5N1	in vitro	M	M	L
D198E	B	in vivo	M	L	M
I222V/I	B	in vivo	L	S	L
I222V	H1N1	in vitro	L	S	S
I222V	H5N1	in vitro	L	S	S
I222T	B	in vivo	L	S	?
I222R	H1N1pdm	in vivo	M	L	?
I222M	H1N1	in vitro	L	S	S
I222M	H5N1	in vitro	M	S	S
I222K	H1N1pdm	in vivo	M	L	S
S246N	H1N1pdm	in vivo	L	L	S
S246N	H5N1	in vivo	M	S	?
S246G	H1N1	in vivo	L	S	?
H274Y	B	in vivo	L	S	S
H274Y	H1N1	in vivo	H	S	H
H274Y	H5N1	in vivo	H	S	H
H274Y	H1N1pdm	in vivo	H	S	H
R292K	H3N2	in vivo/in vitro	H	M	H
N294S	H3N2	in vivo	H	L/M	M/H
N294S	H5N1	in vivo	M/H	L/H	L/H
N294S	B	in vivo	M	S	?
Q313K+I427T	H1N1pdm	in vivo	M	M	L
R371K	B	in vivo	H	M	?
G402S	B	in vivo	L	L	?

¹ N2 numbering

² *In vivo*, detected in surveillance or during antiviral treatment; *in vitro*, selected in cell culture in presence of antiviral.

³ L <10-fold change from wild type; M <50-fold change from wild type; H >50-fold change from wild type; S sensitive

Adapted from Nguyen *et al. Antiviral Therapy*, **17**, 159-173 2012

Differential susceptibility of mutants, e.g. H274Y and Q136K, to the antivirals, especially oseltamivir and zanamivir, reflects the complementary activities of the antivirals against viruses with certain mutations.