

Supplementary Table 3: Resistance-associated aa changes in TK gene of HSV-1 including nt changes, their location, antivirals tested as well as results, methods for phenotypic testing and references.

Amino acid change	Nucleotide change	Domain	Antivirals tested		Drug susceptibility (EC ₅₀ ratio of resistant to sensitive viral isolate or EC ₅₀ value)					Test methods for phenotype	References
			resistant	sensitive	Aciclovir (ACV)	Brivudin (BVDU)	Penciclovir (PCV)	Foscarnet (FOS)	Cidofovir (CDV)		
N23stop	insertion (C) nt 12-15	non-conserved region	ACV	-	EC ₅₀ 12.5 µM	not tested	not tested	not tested	not tested	plaque reduction assay, crystal structure modeling	24055837
R51W	C151T	ATP-binding site	ACV, BVDU, PCV	FOS, CDV	984.0x	500.0x	450.0x	1.1x	1.4x	plaque reduction assay, DNA reduction assay, dye uptake assay, plating efficiency assay	19795980 14670581 10882609 15827202
Y53C	A158G	ATP-binding site	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ 7.9 µM	EC ₅₀ 11.2 µM	EC ₅₀ 94.7 µM	EC ₅₀ 0.7 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
Y53D	T157G	ATP-binding site	ACV	FOS	EC ₅₀ 35.0 µM	not tested	not tested	EC ₅₀ <66.0 µM	not tested	plaque reduction assay, TK functional assay	20733037 23041200
Y53H	T157C	ATP-binding site	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ 9.2 µM	EC ₅₀ 44.2 µM	EC ₅₀ 0.4 µM	modified dye uptake assay including formazan test, TK functional assay	22906425 21178503
Y53stop	T159A	ATP-binding site	ACV	FOS	EC ₅₀ 443.8 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay	14670581
D55N	G163A	ATP-binding site	ACV	CDV	EC ₅₀ 310.8 µM	not tested	not tested	not tested	EC ₅₀ 0.5 µM	plaque reduction assay, cell growth assay, TK functional assay	12406508 11238837
G56S	G166T/ G177C	ATP-binding site	ACV	-	EC ₅₀ 1.9 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
P57H	C170A	AT-binding site	ACV	-	EC ₅₀ 204.2 µM	not tested	not tested	not tested	not tested	DNA hybridization assay, dye uptake assay	9697707

H58N	C172A	ATP-binding site	ACV, PCV, BVDU	FOS, CDV	EC ₅₀ >35.2 µM	EC ₅₀ 1.4 µM	EC ₅₀ >32.0 µM	EC ₅₀ 135.1 µM	EC ₅₀ 3.5 µM	modified dye uptake assay including formazan test	24747042
H58R	A173G	ATP-binding site	ACV	FOS	EC ₅₀ 85.3 µM	not tested	not tested	EC ₅₀ 66.3 µM	not tested	yield reduction assay (enzyme linked virus inhibitory reporter assay - ELVIRA)	15456088
G59R	G175C	ATP-binding site	ACV	-	not given	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
G59W*	G175T	ATP-binding site	ACV, BVDU, PCV	FOS, CDV	605.0x	>2550.0x	73.0x	0.6x	2.0x	plaque reduction assay, TK functional assay	15827202 2833027
G61A	G182C	ATP-binding site	ACV, BVDU, PCV	FOS	EC ₅₀ 46.13 µM	EC ₅₀ 3.06 µM	EC ₅₀ 42.40 µM	not tested	EC ₅₀ 124.75 µM	modified dye-uptake assay including formazan test with recombinant virus	27426251
K62N**	A186C	ATP-binding site	ACV	-	42.0x	not tested	not tested	not tested	not tested	plaque reduction assay, DNA hybridization assay, dye uptake assay, cell growth assay	9697707 16982796 2833027
T63A**	A187G	ATP-binding site	ACV	-	not given	not tested	not tested	not tested	not tested	plaque reduction assay, TK functional assay, crystal structure analysis	12709344 9716390 2833027
T63I	C188T	ATP-binding site	ACV	-	EC ₅₀ 53.3 µM	not tested	not tested	not tested	not tested	dye uptake assay, DNA hybridization assay	9697707
T65N	C194A	non-conserved region	ACV	CDV	EC ₅₀ 21.3 µM	not tested	not tested	not tested	EC ₅₀ 2.0 µM	plaque reduction assay, TK functional assay	12406508
Q67stop	C199T	non-conserved region	ACV	-	not given	not tested	not tested	not tested	not tested	plaque reduction assay	24075863
S74stop	C221G/ C222A	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 55.1 µM	EC ₅₀ 2.6 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510

Y80N	T238A	non-conserved region	ACV	-	EC ₅₀ 5.3 µM	not tested	not tested	not tested	not tested	DNA reduction assay , plating efficiency assay	19795980
E83K	G247T	conserved region	ACV, PCV	FOS	EC ₅₀ 197.1 µM	not tested	EC ₅₀ 400.0 µM	EC ₅₀ 177.0 µM	not tested	plaque reduction assay, dye uptake assay, DNA reduction assay, plating efficiency assay, TK functional assay	19795980 15728902 10882609 16546268 12709344
P84L	C252T	conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 152.1 µM	EC ₅₀ 3.7 µM	modified dye uptake assay including formazan test, modified dye uptake assay including formazan test with recombinant virus TK functional assay	21178503 22796575 27426251
P84S	C250T	conserved region	ACV	CDV	EC ₅₀ 71.0 µM	not tested	not tested	not tested	EC ₅₀ 1.6 µM	plaque reduction assay, TK functional assay	12406508
M85stop	deletion (A) nt 184-187	ATP-binding site	ACV	-	EC ₅₀ 26.6 µM	not tested	not tested	not tested	not tested	plaque reduction assay, dye uptake assay, DNA hybridization assay	9697707
M85stop	deletion (G) nt 180-183	ATP-binding site	ACV	FOS	EC ₅₀ 148.7 µM	not tested	not tested	EC ₅₀ 45.5 µM	not tested	plaque reduction assay, yield reduction assay (ELVIRA), DNA reduction assay	23026414 23687576
Y87H	T259C	conserved region	ACV	-	EC ₅₀ 1.1 µM	not tested	not tested	not tested	not tested	DNA reduction assay , plating efficiency assay	19795980
W88R	T262C	conserved region	ACV, BVDU	-	>225 .0x	>255.0x	not tested	not tested	not tested	plaque reduction assay	20608173
R89W	C265T	non-conserved region	ACV	-	not given	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
A93V	C278T	non-conserved region	ACV	PCV, FOS, CDV	EC ₅₀ >40.0 µM	not tested	EC ₅₀ 9.7 µM	EC ₅₀ 92.1 µM	EC ₅₀ 2.8 µM	plaque reduction assay	27309375
E95stop	G283A	non-conserved region	ACV	-	EC ₅₀ >444.0 µM	not tested	not tested	not tested	not tested	plaque reduction assay	19770274

T103P	A307C	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 50.2 µM	EC ₅₀ 3.7 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
T103stop	C310T	non-conserved region	ACV	FOS, CDV	EC ₅₀ >443.8 µM	not tested	not tested	EC ₅₀ 33.0 µM	EC ₅₀ 0.5 µM	plaque reduction assay, TK functional assay	12406508
Q104H	A312T	non-conserved region	ACV	-	EC ₅₀ >22.2 µM	not tested	not tested	not tested	not tested	dye uptake assay, DNA hybridization assay	9697707
Q104stop	C310T	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 125.7 µM	EC ₅₀ 8.1 µM	plaque reduction assay, dye uptake assay, DNA reduction assay, TK functional assay	22155911 23026414 21178503 23246510
H105P	A314C	non-conserved region	ACV	FOS	EC ₅₀ 46.8 µM	not tested	not tested	EC ₅₀ 51.2 µM	not tested	plaque reduction assay, DNA reduction assay, TK functional assay	1846499 23026414 16970995
E111stop	insertion (G) nt 182-185	ATP-binding site	ACV	-	EC ₅₀ 10.0 µM	not tested	not tested	not tested	not tested	plaque reduction assay, crystal structure modeling	24055837
E111stop	insertion (G) nt 273-277	non-conserved region	ACV	FOS	EC ₅₀ 53.0 µM	not tested	not tested	EC ₅₀ 142.0 µM	not tested	dye uptake assay	10882609
D116N*	G346A	non-conserved region	ACV, PCV	-	EC ₅₀ 225.1 µM	not tested	EC ₅₀ 369.6 µM	not tested	not tested	plaque reduction assay	16546268
V120stop	deletion (G) nt 277	non-conserved region	ACV	-	not tested	not tested	not tested	not tested	not tested	not phenotypically tested	24075863
M121R	T362G	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 48.5 µM	EC ₅₀ 1.9 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
S123R	C369G/A	non-conserved region	ACV	-	not given	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980

Q125H	G375C	non-conserved region	ACV	PCV, BVDU	not given	not given	not given	not tested	not tested	modified dye-uptake assay including formazan test with recombinant virus	23100343
M128L	A382C	non-conserved region	ACV	-	EC ₅₀ 5.3 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
G129D	G386A	non-conserved region	ACV	FOS	EC ₅₀ 196.3 µM	not tested	not tested	EC ₅₀ 82.2 µM	not tested	yield reduction assay (ELVIRA)	15456088
P131S*	C391T	non-conserved region	ACV	-	EC ₅₀ >44.4 µM	not tested	not tested	not tested	not tested	plaque reduction assay, TK functional assay	12709344
I143V	A427G	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 108.0 µM	EC ₅₀ 3.7 µM	modified dye uptake assay including formazan test, TK functional assay	21178503 23246510
D162A	A485C	conserved region	ACV	FOS	EC ₅₀ 443.8 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay, TK functional assay	14670581 16970995
D162H	G484C	non-conserved region	ACV	-	>3.5x	not tested	not tested	not tested	not tested	yield reduction assay (ELVIRA)	15572000
D162N	G484A	non-conserved region	ACV	FOS	EC ₅₀ 11.0 µM	not tested	not tested	EC ₅₀ 89.4 µM	not tested	plaque reduction assay, DNA reduction assay, TK functional assay	24075863 23582986
R163H**	G488A	conserved region	ACV	FOS	EC ₅₀ 27.3 µM	not tested	not tested	EC ₅₀ 71.3 µM	not tested	plaque reduction assay, yield reduction assay (ELVIRA), DNA reduction assay, TK functional assay	8218229 16410361 23026414 15456088 22796575
A167V*	G500T	non-conserved region	ACV	-	EC ₅₀ >44.3 µM	not tested	not tested	not tested	not tested	plaque reduction assay, TK functional assay	12709344
A168T	G502A	nucleoside-binding site	BVDU	ACV, PCV, FOS, CDV	1.0x	>2260.0x	0.7x	1.2x	0.8x	plaque reduction assay, TK functional assay, crystal structure analysis	15827202 8021603 9716390

L170P	T509C	nucleoside-binding site	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >35.2 µM	EC ₅₀ >24.0 µM	EC ₅₀ >31.6 µM	EC ₅₀ 52.7 µM	EC ₅₀ 3.7 µM	plaque reduction assay, modified dye uptake assay including formazan test, TK functional assay	24075863 24747042 23041200
Y172C	A515G	nucleoside-binding site	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 30.7 µM	EC ₅₀ 0.4 µM	modified dye uptake assay including formazan test, TK functional assay	21178503 23246510
Y172S	A515C	nucleoside-binding site	ACV, PCV	FOS, CDV	EC ₅₀ >40.0 µM	EC ₅₀ >160.0 µM	not tested	EC ₅₀ 110.8 µM	EC ₅₀ 3.0 µM	plaque reduction assay	27309375
P173L**	C518T	nucleoside-binding site	ACV	-	not given	not tested	not tested	not tested	not tested	plaque reduction assay, DNA reduction assay, TK functional assay	23582986 12709344
P173R	C518G	nucleoside-binding site	ACV	CDV	EC ₅₀ >443.8 µM	not tested	not tested	not tested	EC ₅₀ 0.2 µM	plaque reduction assay, TK functional assay	12406508
A174P	G520C	nucleoside-binding site	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 137.9 µM	EC ₅₀ 9.3 µM	modified dye uptake assay including formazan test, TK functional assay	21178503 23246510
A175V	C524T	nucleoside-binding site	ACV	FOS	EC ₅₀ 42.0 µM	not tested	not tested	EC ₅₀ 167.0 µM	not tested	dye uptake assay, TK functional assay	15728902 10882609 22796575
R176Q	G527A	nucleoside-binding site	ACV	FOS	EC ₅₀ 443.8 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay, DNA hybridization assay, cell growth assay, dye uptake assay, TK functional assay, crystal structure analysis	14670581 11238837 9716390
R176stop	C526T	nucleoside-binding site	ACV	-	not given	not tested	not tested	not tested	not tested	not tested	24075863
R176W	C526T/ A528G	nucleoside-binding site	ACV	-	EC ₅₀ >50.0 µM	not tested	not tested	not tested	not tested	plaque reduction assay, TK functional assay	23041200
L178R	T533G	non-conserved region	ACV	-	EC ₅₀ 2.6 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980

S181N	G542A	non-conserved region	ACV	FOS	EC ₅₀ 21.5 µM	not tested	not tested	EC ₅₀ 46.0 µM	not tested	plaque reduction assay	18627246
M182stop	deletion (C) nt 455-458	non-conserved region	ACV	FOS	EC ₅₀ 154.5 µM	not tested	not tested	EC ₅₀ 57.1 µM	not tested	yield reduction assay (ELVIRA)	15456088
M182stop	deletion (C) nt 460-464	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 75.6 µM	EC ₅₀ 1.1 µM	plaque reduction assay, modified dye uptake assay including formazan test, DNA reduction assay, dye uptake assay, DNA hybridization assay, yield reduction assay (ELVIRA), TK functional assay	22155911 9697707 23026414 23246510 15456088
M182stop	deletion (G) nt 430-436	non-conserved region	ACV	FOS	EC ₅₀ <887.5 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay, plating efficiency assay, dye uptake assay, DNA hybridization assay, yield reduction assay (ELVIRA), DNA reduction assay, TK functional assay	19795980 24075863 23582986 14670581 9697707 23246510 15572000
T183stop	insertion (GG) nt 430-437	non-conserved region	ACV	-	EC ₅₀ 126.1 µM	not tested	not tested	not tested	not tested	plaque reduction assay, DNA hybridization assay	9697707
Q185R*	C553A/A554G	non-conserved region	ACV, PCV	-	EC ₅₀ 135.9 µM	not tested	EC ₅₀ 392.8 µM	not tested	not tested	plaque reduction assay, TK functional assay	16546268
V187M	G559A	non-conserved region	ACV	-	EC ₅₀ >40.0 µM	not tested	not tested	not tested	not tested	plaque reduction assay, in vivo test in mice	9728528
A189V	C566T	non-conserved region	ACV, PCV	FOS	EC ₅₀ 255.3 µM	not tested	EC ₅₀ 38.0 µM	EC ₅₀ 74.9 µM	not tested	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), DNA reduction assay, TK functional assay	19795980 14670581 16546268 23687576 15456088 22796575
I194 deletion	deletion (CCC) nt 582-584	non-conserved region	ACV	-	EC ₅₀ 6.9 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
G200C	G598T	non-conserved region	ACV	CDV	EC ₅₀ 44.4 µM	not tested	not tested	not tested	EC ₅₀ 4.8 µM	plaque reduction assay, yield reduction assay (ELVIRA), TK functional assay	12406508 23246510
G200D	G599A	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.2 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 49.8 µM	EC ₅₀ 2.8 µM	plaque reduction assay, modified dye uptake assay including formazan test, DNA reduction assay, plating efficiency assay,	22155911 19795980

G200S	G598T/ G599C	non-conserved region	ACV	-	EC ₅₀ 35.0 µM	not tested	not tested	EC ₅₀ 334.0 µM (intermediate resistance level)	not tested	dye uptake assay, TK functional assay	18336925 22796575
T201P	A601C	non-conserved region	ACV	-	EC ₅₀ 106.6 µM	not tested	not tested	not tested	not tested	dye uptake assay, DNA hybridization assay	9697707
V204G	T611G	non-conserved region	ACV, PCV	FOS, CDV	EC ₅₀ 25.0 µM	not tested	EC ₅₀ >160.0 µM	EC ₅₀ 220.0 µM	EC ₅₀ 8.8 µM	plaque reduction assay, TK functional assay	23945375 27309375
G206R*	G616A	non-conserved region	ACV, BVDU, PCV	FOS, CDV	>979.0x	>3230x	>769.0x	1.2x	1.1x	plaque reduction assay	15827202
A207P	G619C	non-conserved region	ACV	FOS	EC ₅₀ >50.0 µM	not tested	not tested	EC ₅₀ <66.0 µM	not tested	plaque reduction assay, TK functional assay	20733037 23041200
L208F	C622T	non-conserved region	ACV	-	EC ₅₀ 12.5 µM	not tested	not tested	not tested	not tested	plaque reduction assay, crystal structure modeling	24055837
L208H	T623A	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ 7.9 µM	EC ₅₀ 11.2 µM	EC ₅₀ 296.0 µM	EC ₅₀ 1.9 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
R216C	C646T	conserved region	ACV, PCV	-	EC ₅₀ 197.1 µM	not tested	EC ₅₀ 116.8 µM	not tested	not tested	plaque reduction assay, DNA hybridization assay, dye uptake assay, TK functional assay	9697707 16546268
R216H	G647A	conserved region	ACV	FOS	EC ₅₀ 116.8 µM	not tested	not tested	EC ₅₀ 74.6 µM	not tested	yield reduction assay (ELVIRA), DNA reduction assay, TK functional assay	23582986 15456088
R216S*	C646T/ G647C	conserved region	ACV	CDV	EC ₅₀ >88.8 µM	not tested	not tested	not tested	EC ₅₀ >0.04 µM	plaque reduction assay, TK functional assay	12709344
R220C	C658T	conserved region	ACV	FOS	EC ₅₀ 887.5 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay, yield reduction assay (ELVIRA)	14670581 15572000

R220H**	G659A	conserved region	ACV, PCV, BVDU	CDV, FOS	147.0x	>3230.0x	5.4x	0.7x	0.7x	plaque reduction assay, plating efficiency assay DNA reduction assay, TK functional assay	19795980 23582986 15827202 12709344
R222C	C664T	conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ 23.7 µM	EC ₅₀ 20.6 µM	EC ₅₀ 8.2 µM	EC ₅₀ 44.3 µM	EC ₅₀ 1.0 µM	modified dye uptake assay including formazan test, DNA hybridization assay, dye uptake assay, cell growth assay	24747042 9697707 11238837
R222H	G665A	conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >35.2 µM	EC ₅₀ >24.0 µM	EC ₅₀ >31.6 µM	EC ₅₀ 36.7 µM	EC ₅₀ 1.6 µM	plaque reduction assay, modified dye uptake assay including formazan test, DNA reduction assay, plating efficiency assay, cell growth assay	19795980 24747042 11238837
G224 frameshift	deletion (C) nt 666-669	conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 82.8 µM	EC ₅₀ 4.4 µM	modified dye uptake assay including formazan test, dye uptake assay, DNA hybridization assay, TK functional assay	9697707 21178503 23246510
L227F	C679T	non-conserved region	ACV	FOS	EC ₅₀ 887.5 µM	not tested	not tested	EC ₅₀ <660.0 µM	not tested	plaque reduction assay, TK functional assay	14670581 22796575
L227stop	insertion (A) nt 438	non-conserved region	ACV (intermediate resistance), PCV	FOS, CDV	EC ₅₀ 27.37 µM	not tested	EC ₅₀ >160.0 µM	EC ₅₀ 100.0 µM	EC ₅₀ 3.6 µM	plaque reduction assay	27309375
D228stop*	insertion (T) nt 364	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >444.0 µM	EC ₅₀ 123.2 µM	EC ₅₀ >400.0 µM	EC ₅₀ 83.2 µM	EC ₅₀ 1.9 µM	plaque reduction assay, TK functional assay	11160674
D228stop**	insertion (G) nt 430-436	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 136.3 µM	EC ₅₀ 7.0 µM	plaque reduction assay, modified dye uptake assay including formazan test, DNA reduction assay, dye uptake assay, yield reduction assay (ELVIRA), plating efficiency assay, cell growth assay, TK functional assay	19795980 14670581 9311864 12709344 11238837 21178503 23246510 15456088
D228stop	insertion (C) nt 460-464	non-conserved region	ACV	FOS	EC ₅₀ 31.0 µM	not tested	not tested	EC ₅₀ <66.0 µM	not tested	plaque reduction assay	20733037
D228stop	insertion (C) nt 548-553	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ 222.0 µM	not tested	not tested	EC ₅₀ 27.4 µM	not tested	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, DNA reduction assay, TK functional assay	18336925 14670581 23246510 15572000
D228stop	insertion (T) nt 651	conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 104.0 µM	EC ₅₀ 4.4 µM	modified dye uptake assay including formazan test, TK functional assay	21178503 23246510

Y239S*	A716C	non-conserved region	ACV, BVDU, PCV	FOS, CDV	186.5x	79.5x	22.0x	1.1x	0.9x	plaque reduction assay	15827202
T245M	C245T	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 104.0 µM	EC ₅₀ 4.4 µM	plaque reduction assay, modified dye uptake assay including formazan test, TK functional assay	22155911 12406508 12709344 23246510
T245P	A733C	non-conserved region	ACV	-	EC ₅₀ 5.4 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
L249P	T746C	non-conserved region	ACV	-	EC ₅₀ 53.0 µM	not tested	not tested	not tested	not tested	dye uptake assay	25218782
Q250stop	C748T	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 77.9 µM	EC ₅₀ 0.4 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
R215827202 W	C766T	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 107.9 µM	EC ₅₀ 3.7 µM	modified dye uptake assay including formazan test, TK functional assay	21178503 23246510
E257K	G769A	non-conserved region	ACV	FOS	EC ₅₀ >35.5 µM	not tested	not tested	not given	not tested	modified dye uptake assay including formazan test	26055375
Q261R	A782G	non-conserved region	ACV	FOS	EC ₅₀ 106.6 µM	not tested	not tested	EC ₅₀ 306.9 µM	not tested	plaque reduction assay, plating efficiency assay, TK functional assay	23687576
Q261stop*	A782T	non-conserved region	ACV, BVDU, PCV	FOS, CDV	468.0x	>3230.0x	>769.0x	1.5x	1.8x	plaque reduction assay, DNA reduction assay, plating efficiency assay	19795980 15827202
S263stop	deletion (CAGCTTTC GGGGG) nt 781-793	non-conserved region	ACV	FOS	EC ₅₀ >35.5 µM	not tested	not tested	not given	not tested	modified dye uptake assay including formazan test	26055375
V267 frameshift	deletion (C) nt 548-553	non-conserved region	ACV	CDV	EC ₅₀ >444.0 µM	not tested	not tested	not tested	EC ₅₀ 0.5 µM	plaque reduction assay, plating efficiency assay, dye uptake assay, DNA reduction assay, TK functional assay	19795980 12406508 12709344

R281stop*	C841T	non-conserved region	ACV, BVDU, PCV	CDV, FOS	316.0x	>1770.0x	>438.0x	1.1x	0.9x	plaque reduction assay, plating efficiency assay, yield reduction assay, DNA reduction assay, in vivo test in mice, TK functional assay	19795980 15827202 197959804
D286 frameshift	deletion (G) nt 853-815827202	conserved region	ACV	FOS	EC ₅₀ 16.0 µM	not tested	not tested	EC ₅₀ <66.0 µM	not tested	plaque reduction assay	20733037
T287M	C860T	conserved region	ACV, BVDU, PCV	CDV, FOS	>1050.0x	>3230.0x	>769.0x	1.0x	1.3x	plaque reduction assay, plating efficiency assay, DNA hybridization assay, dye uptake assay, DNA reduction assay, TK functional assay	19795980 9697707 15827202 12406508 23246510
L288stop	T862A	conserved region	ACV	-	EC ₅₀ 16.0 µM	not tested	not tested	not tested	not tested	plaque reduction assay, crystal structure modeling	24055837
L291R	T872G	non-conserved region	ACV	-	EC ₅₀ 1.0 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
A294 frameshift	deletion (G) nt 878-880	non-conserved region	ACV	FOS	EC ₉₀ 443.8 µM	not tested	not tested	EC ₉₀ <660.0 µM	not tested	plaque reduction assay	14670581
L297S	T890C	non-conserved region	ACV	-	EC ₅₀ >22.2	not tested	not tested	not tested	not tested	dye uptake assay, DNA hybridization assay	9697707
N301 frameshift	deletion (C) nt 896-900	non-conserved region	ACV	FOS	EC ₉₀ 443.8 µM	not tested	not tested	EC ₉₀ <660.0 µM	not tested	plaque reduction assay	14670581
A301 insertion*	insertion (GCC) nt 896	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₉₀ 233.1 µM	EC ₉₀ >44.0 µM	EC ₉₀ >400.0 µM	EC ₉₀ 48.8 µM	EC ₉₀ 1.5 µM	plaque reduction assay, TK functional assay	11160674
N306stop*	insertion (C) nt 698-699	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >444.0 µM	EC ₅₀ 146.1 µM	EC ₅₀ >400.0 µM	EC ₅₀ 38.3 µM	EC ₅₀ 1.9 µM	plaque reduction assay, TK functional assay	11160674
N306stop**	insertion (C) nt 883-887	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₉₀ 233.1 µM	EC ₉₀ >44.0 µM	EC ₉₀ 151.2 µM	EC ₉₀ 22.8 µM	EC ₉₀ 2.2 µM	plaque reduction assay, crystal structure modeling, TK functional assay	24055837 11160674

N306stop*	insertion (A) nt 901-902	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ 233.1 µM	EC ₅₀ >44.0 µM	EC ₅₀ >44.0 µM	EC ₅₀ 22.8 µM	EC ₅₀ 2.2 µM	plaque reduction assay, TK functional assay	11160674
N306stop*	insertion (G) nt 904-905	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ 233.1 µM	EC ₅₀ >44.0 µM	EC ₅₀ >44.0 µM	EC ₅₀ 22.8 µM	EC ₅₀ 2.2 µM	plaque reduction assay	11160674
V307 frameshift*	deletion (G) nt 919	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >444.0 µM	EC ₅₀ 55.4 µM	EC ₅₀ >40.0 µM	EC ₅₀ 104.9 µM	EC ₅₀ 2.2 µM	plaque reduction assay	11160674
L315S	T944C	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 50.5 µM	EC ₅₀ 6.7 µM	plaque reduction assay, modified dye uptake assay including formazan test, TK functional assay	14670581 22906425 21178503
M322K*	T965A	non-conserved region	ACV, PCV	-	EC ₅₀ 197.1 µM	not tested	EC ₅₀ >400.0 µM	not tested	not tested	plaque reduction assay	16546268
P334 frameshift	deletion (G) nt 996	non-conserved region	ACV	FOS	EC ₅₀ 20.0 µM	not tested	not tested	EC ₅₀ 96.0 µM	not tested	plaque reduction assay	18336925
C336Y	G1007A	conserved region	ACV	-	EC ₅₀ 55.5 µM	not tested	not tested	not tested	not tested	plaque reduction assay, DNA reduction assay, cell growth assay, dye uptake assay, DNA hybridization assay, TK functional assay, crystal structure analysis	23582986 9697707 11238837 3015009 9716390
Q342stop	C1024T/ A1025G	non-conserved region	ACV	FOS	EC ₅₀ 443.8 µM	not tested	not tested	EC ₉₀ <660.0 µM	not tested	plaque reduction assay, plating efficiency assay DNA reduction assay	19795980 14670581
T354P	A1060C	non-conserved region	ACV	-	EC ₅₀ 1.5 µM	not tested	not tested	not tested	not tested	DNA reduction assay, plating efficiency assay	19795980
P355 frameshift	deletion (C) nt 1061-1065	non-conserved region	ACV	CDV	EC ₅₀ >443.8 µM	not tested	not tested	not tested	EC ₅₀ 0.03 µM	plaque reduction assay, TK functional assay	12406508
G315827202 frameshift	deletion (A) nt 1065	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ >32.0 µM	EC ₅₀ 120.1 µM	EC ₅₀ 1.9 µM	plaque reduction assay, modified dye uptake assay including formazan test, cell growth assay, TK functional assay	22155911 11238837 23246510

A365T	G1039A	non-conserved region	ACV	-	112.8x	not tested	not tested	not tested	not tested	plaque reduction assay, modified Vero-ICP10-Luciferase assay	21778105
E374 frameshift	deletion (G) nt 1117-1121	non-conserved region	ACV, BVDU, PCV	CDV, FOS	EC ₅₀ >35.5 µM	EC ₅₀ >35.2 µM	EC ₅₀ 5.2 µM	EC ₅₀ 200.3 µM	EC ₅₀ 0.4 µM	modified dye uptake assay including formazan test, TK functional assay	22155911 23246510
N376stop	deletion (969 nt) nt 363	non-conserved region	ACV	FOS	EC ₅₀ >887.5 µM	not tested	not tested	EC ₉₀ <660.0 µM	not tested	plaque reduction assay	12367650
N376stop	insertion (C) nt 666-669	conserved region	ACV	-	EC ₅₀ 12.5 µM	not tested	not tested	not tested	not tested	plaque reduction assay, crystal structure modeling	24055837
N376stop*	insertion (G) nt 919	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ 233.1 µM	EC ₅₀ >44.0 µM	EC ₅₀ 151.2 µM	EC ₅₀ 22.8 µM	EC ₅₀ 2.2 µM	plaque reduction assay, TK functional assay	11160674
N376stop*	insertion (T) nt 929	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >443.8 µM	EC ₅₀ 112.2 µM	EC ₅₀ >400.0 µM	EC ₅₀ 171.9 µM	EC ₅₀ 0.3 µM	plaque reduction assay, TK functional assay	11160674
N376stop	insertion (C) nt 1061-1065	non-conserved region	ACV, BVDU, PCV	FOS, CDV	EC ₅₀ >35.2 µM	EC ₅₀ 16.8 µM	EC ₅₀ >31.6µM	EC ₅₀ 84.0 µM	EC ₅₀ 0.9 µM	modified dye uptake assay including formazan test	24747042