

Supplemental Table 1

A	WT	Y143R (RAL)	N155H (RAL)	G140S/Q148H (RAL)	T66I (EVG)	E92Q (EVG)	H51Y (DTG)	G118R (DTG)	R263K (DTG)	H51Y/R263K (DTG)	E138K/R263K (DTG)
RAL	4.0 ± 2.0	162.4 ± 16.2	153.6 ± 32.8	1900.0 ± 300.0	2.8 ± 0.4	29.8 ± 10.2	3.4 ± 0.2	35.5 ± 5.0	5.7 ± 2.3	6.0 ± 2.3	8.0 ± 1.6
EVG	6.4 ± 0.8	7.9 ± 2.3	90.0 ± 17.8	5700.0 ± 1100.0	66.2 ± 0.7	153.7 ± 34.0	4.5 ± 2.1	21.0 ± 9.5	5.4 ± 0.1	52.6 ± 18.2	11.4 ± 0.2
DTG	1.6 ± 0.9	4.3 ± 1.2	3.6 ± 1.3	5.8 ± 0.5	0.9 ± 0.8	2.3 ± 0.4	3.2 ± 0.2	13.0 ± 5.0	11.3 ± 3.4	16.0 ± 1.9	3.2 ± 0.5
CAB	2.4 ± 0.2	2.7 ± 0.6	2.2 ± 0.3	36.3 ± 6.5	0.9 ± 0.3	4.2 ± 0.1	9.8 ± 1.8	12.1 ± 1.9	13.4 ± 1.3	10.4 ± 1.5	4.2 ± 0.8
BIC	1.9 ± 0.3	2.6 ± 0.1	2.7 ± 0.8	5.5 ± 0.7	0.2 ± 0.1	2.0 ± 0.1	2.2 ± 0.4	5.4 ± 0.6	4.1 ± 1.1	3.5 ± 1.0	3.5 ± 0.6

B	<i>p</i> -Value	
WT	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
Y143R	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
N155H	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
G140S/Q148H	DTG > CAB	0.002
	DTG – BIC	NS
	BIC > CAB	0.002
T66I	DTG – CAB	NS
	DTG – BIC	NS
	BIC > CAB	0.01
E92Q	DTG > CAB	0.002
	DTG – BIC	NS
	BIC > CAB	< 0.001
H51Y	DTG > CAB	0.005
	BIC > DTG	0.009
	BIC > CAB	0.003
G118R	DTG – CAB	NS
	BIC > DTG	NS
	BIC > CAB	0.004
R263K	DTG – CAB	NS
	BIC > DTG	0.02
	BIC > CAB	< 0.001
H51Y/R263K	CAB > DTG	0.004
	BIC > DTG	< 0.001
	BIC > CAB	< 0.001
E138K/R263K	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS

Supplementary Tables 1A/B-7A/B. A. The EC50 values, with the standard deviations following the plus-minus sign (nM), were determined for RAL, EVG, DTG, BIC, and CAB against the INSTI-resistant mutants using single round infection assays (n=4). B. P values indicating statistically significant differences in the antiviral activities of the INSTIs for the various INSTI-resistant mutants. Dashes between the two INSTIs represent no significance differences in the data, whereas the ">" sign indicates a significant difference in the antiviral activity of one INSTI over the other.

Supplemental Table 2

A

	M50I	L74M	T97A	S119R	E138K	G140S	Q146L	Q146P	Q148H	Q148K	Q148R	S153Y
RAL	30.7 ± 6.9	7.4 ± 2.1	2.9 ± 0.2	25.9 ± 0.1	6.5 ± 0.9	10.0 ± 3.7	24.1 ± 2.3	6.0 ± 0.8	142.2 ± 4.1	1450.0 ± 242.5	272.7 ± 7.0	18.0 ± 2.4
EVG	2.8 ± 0.4	6.0 ± 0.4	5.3 ± 0.4	7.6 ± 0.2	2.7 ± 0.4	12.6 ± 2.6	43.2 ± 5.4	4.7 ± 0.6	23.7 ± 4.2	309.8 ± 12.4	296.1 ± 24.2	4.2 ± 0.9
DTG	2.1 ± 0.9	2.2 ± 0.4	1.1 ± 0.5	2.3 ± 0.6	1.8 ± 0.4	2.7 ± 0.7	2.1 ± 0.8	0.5 ± 0.04	0.6 ± 0.1	1.0 ± 0.01	1.3 ± 0.2	2.0 ± 0.7
CAB	0.8 ± 0.1	0.9 ± 0.2	2.7 ± 0.7	2.3 ± 1.0	12.9 ± 1.0	5.1 ± 1.5	3.4 ± 0.6	10.3 ± 2.1	6.8 ± 1.5	2.9 ± 0.6	4.5 ± 1.3	3.2 ± 0.6
BIC	2.5 ± 0.3	1.4 ± 0.4	1.5 ± 0.3	3.3 ± 0.1	4.0 ± 0.2	3.5 ± 0.4	5.2 ± 1.3	0.8 ± 0.01	0.9 ± 0.1	1.2 ± 0.3	1.2 ± 0.3	2.8 ± 0.4

B

p-Value		
M50I	DTG – CAB	NS
	DTG – BIC	NS
	CAB > BIC	< 0.001
L74M	DTG – CAB	0.003
	DTG – BIC	NS
	CAB – BIC	NS
T97A	DTG > CAB	0.01
	DTG – BIC	NS
	CAB – BIC	NS
S119R	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
E138K	DTG > CAB	< 0.001
	DTG > BIC	< 0.001
	BIC > CAB	< 0.001
G140S	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
Q146L	DTG – CAB	NS
	DTG > BIC	0.01
	CAB – BIC	NS
Q146P	DTG – CAB	0.003
	DTG – BIC	< 0.001
	CAB – BIC	0.003
Q148H	DTG > CAB	0.004
	DTG > BIC	0.01
	BIC – CAB	0.004
Q148K	DTG > CAB	0.02
	DTG – BIC	NS
	BIC > CAB	0.01
Q148R	DTG > CAB	0.02
	DTG – BIC	NS
	BIC > CAB	0.01
S153Y	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS

Supplemental Table 3

A

	G140A/ Q148H	Y143R/ Q148H	Q148H/ N155H	E138K/ Q148K	G140A/ Q148K	G140S/ Q148K	E138A/ Q148R	E138K/ Q148R	G140A/ Q148R	G140C/ Q148R	G140S/ Q148R	Q148R/ N155H
RAL	476.3 ± 22.0	2040.0 ± 99.0	337.5 ± 69.0	2885.0 ± 49.5	>5000	113.3 ± 1.4	3150.0 ± 210.0	3240.0 ± 876.8	>5000	>5000	>5000	>5000
EVG	250.8 ± 4.9	23.2 ± 5.7	620.9 ± 90.6	1890.0 ± 42.4	2053.3 ± 45.1	543.1 ± 89.2	293.2 ± 35.6	801.6 ± 67.7	575.0 ± 19.8	>5000	1326.3 ± 32.7	285.8 ± 18.2
DTG	3.9 ± 0.7	0.8 ± 0.2	4.0 ± 0.6	25.0 ± 2.1	450.7 ± 58.8	2.3 ± 0.2	4.4 ± 0.8	3.9 ± 0.1	4.1 ± 0.3	2.9 ± 0.6	26.2 ± 6.8	7.1 ± 2.0
CAB	3.9 ± 0.8	6.0 ± 0.4	13.3 ± 2.9	772.1 ± 72.2	393.1 ± 51.1	87.3 ± 7.6	25.6 ± 0.8	24.1 ± 0.1	13.7 ± 2.7	66.6 ± 8.1	414.6 ± 14.5	50.5 ± 6.5
BIC	1.1 ± 0.3	0.4 ± 0.1	4.0 ± 0.7	59.3 ± 4.9	137.1 ± 5.0	4.5 ± 0.4	4.1 ± 0.6	3.5 ± 0.4	10.0 ± 2.5	6.4 ± 1.4	6.1 ± 1.3	2.0 ± 0.4

B

	<i>p</i> -Value	
G140A/Q148H	DTG – CAB	NS
	BIC > DTG	0.002
	BIC > CAB	0.002
Y143R/Q148H	DTG > CAB	< 0.001
	BIC > DTG	0.02
	BIC > CAB	< 0.001
Q148H/N155H	DTG > CAB	0.006
	DTG – BIC	NS
	BIC > CAB	0.006
E138K/Q148K	DTG > CAB	< 0.001
	DTG > BIC	< 0.001
	BIC > CAB	< 0.001
G140A/Q148K	DTG – CAB	NS
	BIC > DTG	0.002
	BIC > CAB	0.002
G140S/Q148K	DTG > CAB	< 0.001
	DTG > BIC	< 0.001
	BIC > CAB	< 0.001
E138A/Q148R	DTG > CAB	< 0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
E138K/Q148R	DTG > CAB	< 0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
G140A/Q148R	DTG > CAB	0.005
	DTG > BIC	0.02
	CAB – BIC	NS
G140C/Q148R	DTG > CAB	< 0.001
	DTG > BIC	0.01
	BIC > CAB	< 0.001
G140S/Q148R	DTG > CAB	< 0.001
	BIC > DTG	0.008
	BIC > CAB	< 0.001
Q148R/N155H	DTG > CAB	< 0.001
	BIC > DTG	0.01
	BIC > CAB	< 0.001

Supplemental Table 4

A

	T66I/E157Q	E92Q/N155H	G140S/N155H	Y143H/N155H	Y143R/N155H	N155H/G163R
RAL	98.7 ± 20.2	>5000	477.8 ± 66.6	1205.0 ± 77.8	>5000	245.5 ± 43.8
EVG	67.5 ± 10.6	1601.0 ± 77.8	51.9 ± 10.8	70.0 ± 13.3	170.1 ± 34.0	72.6 ± 6.8
DTG	0.5 ± 0.1	1.8 ± 0.2	2.0 ± 1.0	1.7 ± 0.7	2.5 ± 0.8	1.6 ± 0.4
CAB	0.3 ± 0.1	4.6 ± 1.7	4.4 ± 0.6	1.2 ± 0.1	3.7 ± 0.2	2.2 ± 0.4
BIC	1.1 ± 0.2	3.3 ± 0.9	2.2 ± 0.5	2.7 ± 0.6	4.0 ± 0.8	2.1 ± 0.1

B

<i>p</i> -Value		
T66I/E157Q	DTG – CAB	NS
	DTG > BIC	0.004
	CAB > BIC	0.001
E92Q/N155H	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
G140S/N155H	DTG > CAB	0.01
	DTG – BIC	NS
	BIC > CAB	0.001
Y143H/N155H	DTG – CAB	NS
	DTG – BIC	NS
	CAB > BIC	0.01
Y143R/N155H	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
N155H/G163R	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS

Supplemental Table 5

A

	T97A/Y143R/Q148H	T97A/Q148H/N155H	E138K/G140A/Q148K	L74M/G140A/Q148R	L74M/G140C/Q148R	E138K/G140C/Q148R	E138A/S147G/Q148R
RAL	>5000	4455.0 ± 388.9	>5000	>5000	>5000	>5000	1410.0 ± 183.8
EVG	41.6 ± 3.0	224.5 ± 24.8	4090.0 ± 641.0	747.4 ± 78.5	>5000	945.3 ± 176.4	774.9 ± 17.2
DTG	1.5 ± 0.1	2.4 ± 0.7	212.1 ± 46.0	12.0 ± 2.1	10.2 ± 1.3	5.3 ± 1.0	5.5 ± 1.3
CAB	5.3 ± 0.7	1.8 ± 0.6	610.3 ± 8.6	53.2 ± 14.8	220.3 ± 41.2	134.2 ± 0.3	4.0 ± 0.2
BIC	1.2 ± 0.7	1.8 ± 0.3	223.0 ± 30.7	11.7 ± 1.3	6.1 ± 0.9	8.2 ± 1.1	2.3 ± 0.0

B

<i>p</i> -Value		
T97A/Y143R/ Q148H	DTG > CAB	0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
T97A/Q148H/ N155H	DTG – CAB	NS
	DTG – BIC	NS
	CAB – BIC	NS
E138K/G140A/ Q148K	DTG > CAB	< 0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
L74M/G140A/ Q148R	DTG > CAB	0.01
	DTG – BIC	NS
	BIC > CAB	0.01
L74M/G140C/ Q148R	DTG > CAB	0.002
	BIC > DTG	0.003
	BIC > CAB	0.002
E138K/G140C/ Q148R	DTG > CAB	< 0.001
	DTG > BIC	0.008
	BIC > CAB	< 0.001
E138A/S147G/ Q148R	DTG – CAB	NS
	BIC > DTG	0.02
	BIC > CAB	< 0.001

Supplemental Table 6

A

	T66I/T97A/E157Q	T97A/Y143R/N155H	G140S/Y143R/N155H	E92Q/N155H/G163R
RAL	33.5 ± 8.7	>5000	>5000	>5000
EVG	69.4 ± 11.8	642.7 ± 16.5	93.1 ± 16.1	677.9 ± 45.8
DTG	0.5 ± 0.1	8.5 ± 1.5	2.6 ± 0.3	3.8 ± 0.7
CAB	0.8 ± 0.1	142.2 ± 8.3	20.0 ± 3.5	4.2 ± 1.5
BIC	0.4 ± 0.2	8.2 ± 1.7	2.1 ± 0.1	2.0 ± 0.4

B

p-Value		
T66I/T97A/ E157Q	DTG > CAB	0.005
	DTG – BIC	NS
	BIC > CAB	0.02
T97A/Y143R/ N155H	DTG > CAB	< 0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
G140S/Y143R/ N155H	DTG > CAB	0.002
	DTG – BIC	NS
	BIC > CAB	0.002
E92Q/N155H/ G163R	DTG – CAB	NS
	BIC > DTG	0.007
	CAB – BIC	NS

Supplemental Table 7

A

	T97A/G140S/Q148H	E138A/G140S/Q148H	E138K/G140S/Q148H	G140S/Y143R/Q148H	G140S/Q148H/N155H	G140S/Q148H/G163K
RAL	>5000	>5000	>5000	>5000	>5000	>5000
EVG	>5000	>5000	>5000	>5000	>5000	>5000
DTG	55.9 ± 3.0	13.8 ± 4.8	68.2 ± 2.0	7.7 ± 2.0	77.9 ± 15.9	24.3 ± 1.1
CAB	43.7 ± 4.2	70.2 ± 9.0	93.0 ± 6.1	113.8 ± 23.1	2423.3 ± 453.9	32.4 ± 3.1
BIC	29.5 ± 4.4	5.1 ± 0.5	4.9 ± 0.3	9.4 ± 0.3	57.5 ± 5.0	8.8 ± 1.9

B

<i>p</i> -Value		
T97A/G140S/ Q148H	CAB > DTG	0.004
	BIC > DTG	< 0.001
	BIC > CAB	0.003
E138A/G140S/ Q148H	DTG > CAB	< 0.001
	DTG – BIC	NS
	BIC > CAB	< 0.001
E138K/G140S/ Q148H	DTG > CAB	0.002
	BIC > DTG	< 0.001
	BIC > CAB	< 0.001
G140S/Y143R/ Q148H	DTG > CAB	0.003
	DTG – BIC	NS
	BIC > CAB	0.003
G140S/Q148H/ N155H	DTG > CAB	0.002
	DTG – BIC	NS
	BIC > CAB	0.002
G140S/Q148H/ G163K	DTG > CAB	0.009
	BIC > DTG	< 0.001
	BIC > CAB	< 0.001