

INSTI Major Mutations:

G140S • Q148H

INSTI Accessory Mutations:

None

IN Other Mutations:

L63I • I73V • L74I • E96D • L101I • T112I • I208L • D232E

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	High-Level Resistance
cabotegravir (CAB)	High-Level Resistance
dolutegravir (DTG)	High-Level Resistance
elvitegravir (EVG)	High-Level Resistance
raltegravir (RAL)	High-Level Resistance

IN comments

Major

- G140S(A/C are non-polymorphic mutations that usually occur with Q148 mutations. Alone, they have minimal effects on INSTI susceptibility. However, in combination with Q148 mutations they are associated with high-level resistance to RAL and EVG and intermediate reductions in DTG and BIC susceptibility.
- Q148H(K/R are nonpolymorphic mutations reported in persons receiving RAL, EVG, CAB, and DTG. They nearly always occur in combination with G140A/S or E138K. In this setting they are associated with near complete resistance to RAL and EVG, high-levels of reduction in CAB susceptibility, and low-to-intermediate reductions in DTG and BIC susceptibility.

Other

- L74I is a highly polymorphic mutation with a prevalence of 3% to 30% depending on subtype. It is the consensus amino acid in subtype A viruses belonging to the A6 clade. It does not appear to be selected by any of the INSTIs or to reduce their susceptibility.
- There is evidence for high-level DTG resistance. If DTG is used, it should be administered twice daily.

Drug resistance mutation scores of INSTI:

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Rule	BIC ⚡	CAB ⚡	DTG ⚡	EVG ⚡	RAL ⚡
L74I + Q148H	15	15	15	15	15
G140S	10	10	10	30	30
G140S + Q148H	10	20	10	0	0
Q148H	25	30	25	60	60
Total	60	75	60	105	105