

INSTI Major Mutations:

E138K • S147G • Q148R

INSTI Accessory Mutations:

None

IN Other Mutations:

K7KR • E35EK • V54I • I72V • V79I • V88I • K111Q • I113V • T124A • T125A • G163E • I203M • I208L • L234I

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

- E138K/A/T are common nonpolymorphic accessory resistance mutations selected in patients receiving RAL, EVG, CAB, and DTG. Alone they do not reduce INSTI susceptibility. However, they contribute to reduced susceptibility in combination with other mutations particularly those at position 148.
- S147G is a nonpolymorphic mutation selected in patients receiving RAL, EVG, and DTG. Alone it reduces EVG susceptibility about 3-fold.
- 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.

- 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 ÷
E138K	10	10	10	15	15
E138K + Q148R	10	20	10	0	0
S147G	10	10	10	60	10
S147G + Q148R	15	20	15	0	0
Q148R	25	40	25	60	60
Total	70	100	70	135	85