

INSTI Major Mutations: Y143R

INSTI Accessory Mutations: T97A • G163GR

IN Other Mutations: K7R • S17N • V31I • L101I • T112A • S119T • T125A • M154I • V201V

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

IN comments

Major

- Y143C/R/H are non-polymorphic mutations associated with high-level RAL resistance. Alone, they have minimal effects on EVG susceptibility. However, they are associated with intermediate reductions in EVG susceptibility when they occur in combination with one or more accessory INSTI-resistance mutations. Y143 mutations do not reduce susceptibility to DTG, BIC, or CAB.

Accessory

- T97A is a polymorphic INSTI-selected mutation that, depending on subtype, occurs in 1% to 3% of viruses from untreated persons. Alone, it has minimal effects on INSTI susceptibility but in combination with other major resistance mutations, it synergistically reduces susceptibility to each of the INSTIs.
- G163R/K are nonpolymorphic in all subtypes except subtype F. They are accessory resistance mutations as they usually occur in combination with other INSTI-resistance mutations particularly N155H.

- This virus is predicted to have low-level reduced susceptibility to **CAB**. The use of the combination of **CAB**/RPV should be considered to be relatively contraindicated.

Drug resistance mutation scores of INSTI:

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Rule	BIC ÷	CAB ÷	DTG ÷	EVG ÷	RAL ÷
Y143R	5	10	5	10	60
Y143R + G163GR	5	5	5	5	0
T97A + Y143R	0	5	0	5	0
T97A	0	0	0	10	10
G163GR	0	0	0	15	15
Total	10	20	10	45	85