Impact of routine integrase genotyping on HIV drug resistance surveillance

Chibo D[1,2], Gooey M[1], D'Costa J[1], Sameer R[1], Richards N[1], Macksabo L[1], Bonanzinga S[1], Li X, Williams E[1,2].

[1]Victorian Infectious Diseases Reference Laboratory, Doherty Institute.

[2]Department of Infectious Diseases, University of Melbourne, Australia

Background:
Introduction of routine integrase strand transfer inhibitor (INSTI) genotyping has enhanced the laboratory capacity to detect emerging HIV drug resistance patterns. As INSTI antiretrovirals are included in all first-line antiretroviral therapy (ART) regimen recommendations, the Victorian Infectious Diseases Reference Laboratory (VIDRL) has incorporated integrase genotyping in all HIV resistance testing requests since 2024. We describe resistance patterns identified over the first two years of this integrated protease (PR), reverse transcriptase (RT), and integrase genotyping approach.

Methods:
We analysed 905 HIV-1 sequences with PR, RT, and integrase genotypes generated by routine PCR and Sanger sequencing between January 2024 and March 2026. Drug resistance mutations were identified using the Stanford HIV drug resistance database and classified by drug class. Mutations were further categorised as major or accessory. Resistance prevalence and mutation patterns were assessed.

Results:
NNRTI resistance was most frequently detected (17.5%), followed by NRTI (10.4%) and INSTI resistance (9.6%). PI resistance was uncommon (2.9%). Integrase mutations were identified in 87 sequences. Of these, major INSTI resistance was identified in 19/87 (21.8%) genotypes, representing less than 3% of the overall cohort, while 68/87 (78.2%) harboured accessory mutations only. These mutations frequently occurred with NRTI and/or NNRTI resistance, consistent with selection during treatment rather than widespread transmitted resistance. Multi-class drug resistance was uncommon (7.3%) and largely restricted to treatment-experienced individuals. Most sequences showed no resistance (67.3%) or resistance to a single drug class (25.4%). Dual-class resistance occurred in 6.5% of samples, most often involving NRTI + NNRTI mutations, while triple-class resistance was rare (0.8%). No four-class resistance was observed.

Conclusions:
Routine inclusion of integrase genotyping since 2024 revealed that while major INSTI resistance remains uncommon, integrase-associated mutations are now detected at frequencies comparable to NRTI resistance. These findings underscore the value of routine integrase sequencing for resistance surveillance and support its role in guiding investigation of virological failure.

Disclosure of interest: N/A