

PREVALENCE OF INTEGRASE STRAND TRANSFER INHIBITOR GENOTYPIC RESISTANCE IN CLINICAL SPECIMENS IN NSW FOLLOWING INTRODUCTION OF INTEGRASE INHIBITORS, 2012-2015.

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Background: There has been a rapid uptake of integrase strand transfer inhibitors (INSTIs) in Australia. Due to the inclusion of INSTIs in four of five recommended first line regimens in current guidelines, usage is likely to increase. Unlike other antiretroviral classes, genotypic antiretroviral resistance testing (GART) has most often been performed in the setting of treatment failures. We evaluated all specimens referred for INSTI genotypic resistance testing in NSW between Jan 2012 to December 2015.

Methods: For this analysis, samples referred for integrase testing were identified retrospectively from a single laboratory databass. The ViroSeq™ HIV-1 Integrase Genotyping Kit was used for RNA isolation, RT-PCR and integrase gene sequencing. A 1.1kb amplicon is generated, sequenced and assembled into a 0.9kb consensus sequence. Analysis was performed with the Stanford HIV Drug resistance database version 7.0. Major and minor mutations to three commonly used INSTIs are reported.

Results: There were 177 specimens tested, 147 (83%) subtype B. Integrase testing was requested in 24/805 (3%) of all GART in 2012 vs 68/635 (11%) in 2015 ($p < 0.001$). There were major INSTI mutations found in 25 (14.1%) of all referred specimens, whereas 21% of all GART contained at least one major reverse transcriptase or protease mutations. The most frequent major mutations were N155H (5.1%), Q148H (4.5%) and Y143 (2.3%). More samples were genotypically sensitive to elvitegravir 155/177 (87.6%) than raltegravir and dolutegravir 141/177 (79.7%). There was no increase in frequency of mutations over time.

Conclusion: 14.1% of specimens referred for INSTI resistance testing had major mutations. Although the frequency of INSTI resistance testing has increased, the prevalence of mutations has remained stable. Ongoing surveillance of INSTI resistance is required as treatment uptake increases.