

REPLY TO AMBROSIONI ET AL

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In reply: We read with interest the letter by Ambrosioni, Mosquera and Miro.¹ They raise the issue that polymorphisms, eg, E157Q and T97A, that can potentially reduce integrase strand transfer inhibitor (InSTI) activity are not infrequently detected in HIV-1 infected drug-naïve individuals, particularly with subtype B infection.²⁻⁴ They point out that E157Q at baseline has been associated with raltegravir- and elvitegravir/cobicistat-based regimens in some cases,^{5,6} and thus baseline InSTI resistance testing for might be considered if treatments with raltegravir or elvitegravir/cobicistat are planned. We await evidence that these polymorphisms increase the risk of failure with INSTI-based regimens, especially with the newer recommended regimens containing dolutegravir or bictegravir.^{7,8}

The reason we have not recommended routinely performing baseline InSTI-associated resistance testing is that so far there have been only very limited reports of transmitted major InSTI resistance, and the large phase III trials with raltegravir and elvitegravir/cobicistat failures were not associated with polymorphisms potentially associated with InSTI resistance mutations.⁹⁻¹² Therefore, these tests are not yet cost effective. In addition, current recommendations for initial antiretroviral therapy include those InSTIs with a higher resistance barrier (dolutegravir or bictegravir).^{8,13,14} For these drugs, integrase polymorphisms have not yet been shown to result in any impact on treatment responses.

As we have stated in our recommendations, surveillance for the emergence of transmitted InSTI resistance in all geographic regions is important because we do not know the future consequences of expanded use of InSTIs occurring in resource rich and in low and middle income countries. With the introduction of next-generation

sequencing for routine genotypic testing instead of Sanger sequencing, the costs may decrease in the future to allow general recommendations for routine baseline resistance testing covering a larger portion of the HIV genome.

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