AIMS OF THE STUDY

Entry Inhibitors

Integrase

The At M CCR

These HIV NRTI (Nucleoside Reverse Transcriptase Inhibitors) are used to genetically analyse the RAMs (Resistance Associated Mutations) in the treatment of HIV infection.

To genetically analyse the RAMs (Resistance Associated Mutations) within the integrase gene to predict HIV-1 resistance to the integrase strand transfer inhibitors (INSTIs).

To analyse mutations in the V3 loop region of the gp120 of HIV-1 for viral co-receptor tropism alteration to evaluate efficacy of CCR5 inhibitors (e.g. Maraviroc) in Indian HIV-1 patients.

ENTRY INHIBITORS

NRTIs

NNRTIs

PIs

INHIBITORS

INTEGRASE INHIBITORS

PATIENTS AND METHODS

No. of Cases = 56 HIV-1 patients

Males - 43 (10–71 yrs.)

Females - 13 (13–55 yrs.)

Methods:

(Nested RT-PCR)

DNA Extraction

RT-PCR

Sequencing

INTEGRASE RESISTANCE

Table 1: Viral Co-receptor tropism

<table>
<thead>
<tr>
<th>Co-receptor Tropism (NrN)</th>
<th>Frequency (%)</th>
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<tr>
<td>CCR5 (R5)</td>
<td>40 (70.3)</td>
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<tr>
<td>CCR5 (RD)</td>
<td>14 (25)</td>
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<tr>
<td>X4 (RD)</td>
<td>6 (10.7)</td>
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Note: CCR5 includes viruses CCR5 tropic as well as showed dual/mixed tropism.

Out of the 56 specimens analyzed for INI-RAMs, 2 samples (3.5%) showed the presence of Primary RAMs namely, E138A, G140A, Q148R & N155H indicating high-level resistance to the drugs RAL, EVG & DTG in one patient and RAL, EVG resistance in the other patient. Besides these, accessory mutations, L74M and R263K were found in 6 samples (10.7 %) indicating low-level resistance to the same drugs. No particular HIV-1 subtype has been found to influence the presence of INI-RAMs.

For viral tropism, 17 out of 56 (30.35 %) samples indicated the presence of altered co-receptor tropism i.e. CXCR4 co-receptor usage instead of CCR5 by the HIV-1. Therefore, Maraviroc should preferably not be administered to such patients.

CONCLUSIONS

The prevalence of INI-RAMs was found to be low (3.5%) within the studied Indian population. Both the cases showed high resistance to RAL and EVG, of which one case was resistance to DTG as well.

In case of viral tropism, the prevalence of altered co-receptor tropism, i.e. CXCR4 was found to be 30.35 %. Out of these, 16.07 % cases showed dual or mixed tropism.

These novel HIV-1 drug targets viz. Integrase inhibitors and CCR5 antagonists can be included for effective ART regimens in the Indian population after analyzing the genetic profile of the patient with respect to them.

Nested PCR/Sequencing based molecular screening offers accurate detection for mutations within the Integrase gene and the gp120-V3 loop region of the HIV-1, thereby aiding in prediction of HIV-1 Integrase resistance and Viral tropism respectively.