Impact of baseline HIV-1 integrase polymorphisms with virological outcome in patients starting a Raltegravir-containing regimen

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Background: Raltegravir is a very potent and effective strand-transfer integrase-inhibitor (INSTI), recently FDA-approved for use also in first-line HAART regimen. Previous, analysis in a small cohort of HAART multi-experienced patients, suggests that some integrase polymorphisms at baseline were associated with different virologic response to Raltegravir. Therefore, the aim of this study is to evaluate the impact of baseline HIV-1 integrase polymorphisms with virological outcome in a larger cohort of patients starting a Raltegravir-containing regimen.

Methods: We analyzed 206 multi-experienced patients that received Raltegravir plus optimized-background-therapy (OBT) from seven clinical centres within Italy and France. HIV-1 RNA and integrase HIV-genotypes were assessed at baseline and at failure. For subtyping Maximum-Likelihood phylogenetic analyses (PAUP*4.0b10) were performed. For 177 patients, viremia values at 24-week HIV-genotypes were assessed at baseline and at failure. For subtyping Maximum-Likelihood Methods:

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Results: Overall, 186 (90.3%) patients were infected by HIV-1 subtype B versus 20 (9.7%) infected by non-B viruses (4A, 1C, 2D, 5F, 2G, 5CRF_02AG, 1CRF_12BF2). At week 24, 70% of patients achieved VS (71.3% [114/160] and 58.8% [10/17] infected by B and non-B viruses, respectively, p=NS). At baseline, all major Raltegravir resistance mutations were completely absent, and secondary mutations (L74M, T97A, G140A, V151I, N155S, G163R) were present at very low frequency (<5%). Among all integrase polymorphisms, the codon usage of mutated amino acids were also considered. Logistic regression analyses (uni- and multivariate) were performed to investigate if baseline integrase polymorphisms and other variables (such as: baseline HIV-1 RNA, drugs in co-usage and/or subtype) were independent predictors of VS.

Conclusion: At baseline, all major Raltegravir resistance mutations were completely absent, and secondary mutations were present at very low frequency (≤1%). Among all integrase polymorphisms, only T125A (specific GCA codon) at baseline was associated with poorer virologic response to Raltegravir. This finding in non-B subtypes is intriguing and further research is warranted. The clinical implications and relevance of this polymorphism is still to be determined.

No conflict of interest