HIV-1 Subtype and Virological Response to Antiretroviral Therapy: Acquired Drug Resistance

To the Editor—In a recent article published in Clinical Infectious Diseases, Scherrer and colleagues [1] have described the most comprehensive study analyzing the impact of the infecting human immunodeficiency virus type 1 (HIV-1) subtype (B or non-B) on virological outcome in the Swiss HIV Cohort Study. Unlike previous studies, the authors were able to eliminate important confounding factors of the analysis, such as ethnicity and cultural characteristics, as all subjects analyzed were white and living in Switzerland. The authors found that patients infected by non-B subtypes had improved virological response over an 8-year period of treatment follow-up, particularly those treated with unboosted protease inhibitors (PIs) [1]. Despite the fact that this study suffered from important limitations, such as being an unplanned analysis, having infecting HIV-1 subtypes assigned from partial genome fragments and deriving data from older drugs and currently obsolete therapeutic schemes [2], it comprised the largest cohort analyzed to date and addressed additional factors such as adherence and transmitted (primary) drug resistance. Moreover, the study succeeded in showing a proof of principle (even with some obsolete drugs), and used viral genomic information (protease and reverse transcriptase) relevant for the antiretroviral drugs analyzed in the study.

An important issue not addressed by the above-mentioned study is the acquired (secondary) drug resistance developed during antiretroviral treatment. This feature, which may also differ between infecting HIV-1 subtypes, can impact profoundly on treatment response over time and consequently on virological outcome. Our group has previously shown that HIV-1 subtype C (HIV-1C) acquires fewer drug resistance mutations in the viral protease and reverse transcriptase genomic regions compared with subtype B counterparts under identical therapeutic schemes and extent of drug exposure, in a population with homogeneous demographic, clinical, and genetic characteristics [3]. Southern Brazil has experienced the introduction of HIV-1C in the late 1980s, nearly 2 decades after subtype B [4–6], but attempts to associate these infecting subtypes to particular characteristics have failed [7, 8]. In our study, we evaluated the rates of acquired drug resistance to each of the major 3 antiretroviral classes (PIs, nucleoside reverse-transcriptase inhibitors [NRTIs], and nonnucleoside reverse-transcriptase inhibitors [NNRTIs]). Our data suggested that HIV-1C is less prone to select for NRTI- and PI-related mutations compared with HIV-1B, but no difference was observed for the development of NNRTI-related mutations [3]. Our analysis was conducted with follow-up data over a 10-year time span, at a time when most PI-based highly active antiretroviral therapy schemes were composed of unboosted PIs, except for lopinavir/ritonavir. Our data on PI-related resistance mutations over time is consistent with the study by Scherrer and colleagues, where unboosted PI shows the largest differences between HIV-1B and a non-B subtype (HIV-1C in our scenario). It is conceivable that the better virological outcome seen by Scherrer and colleagues may be explained at least in part by the lower acquisition of drug-resistance mutations in the non–B subtype group. Prospective longitudinal follow-up with large numbers of patients will provide definitive conclusions to the impact of antiretroviral therapy on the ever-increasing numbers of HIV-1 non–B subtype infections worldwide.

Notes

Financial support. The authors have received institutional grant support from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), and the Brazilian Ministry of Health.

Potential conflicts of interest. No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Esmeralda A. Soares,1 Andre F. Santos,2 and Marcelo A. Soares1,2
1Programa de Genética, Instituto Nacional de Câncer; and 2Departamento de Genética, Universidade Federal do Rio de Janeiro, Brazil

References


Correspondence: Marcelo A. Soares, PhD, Programa de Genética, Instituto Nacional de Câncer, Rua André Cavalcanti, 37 - 4o andar Bairro de Fátima 20231-050 - Rio de Janeiro, RJ, Brazil (masoares@inca.gov.br).

Clinical Infectious Diseases 2012;54(5):738–9

© The Author 2011. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

DOI: 10.1093/cid/cir906