
We read with interest the work by Badulli et al., in which further evidence that HLA-B*57:01 and HCP5 rs2395029(G) are in high, but not complete, linkage disequilibrium (LD) ($r^2 = 0.89$) in a HLA-B*5701-enriched sample of 185 Caucasian individuals from Italy [1]. They found that two out of 119 individuals who were HLA-B*57:01-positive and HCP5 rs2395029(G) negative, would be at risk of abacavir hypersensitivity reaction (HSR) if exposed to the drug. The authors also identified that three out of the 120 individuals who were HCP5 rs2395029(G)-positive and HLA-B*57:01-negative, would be unnecessarily excluded from receiving abacavir treatment. The authors are mainly concerned about the risk of exposing individuals to abacavir who would be mistakenly identified by HCP5 rs2395029(G) as HLA-B*57:01-negative, and thus caution against the use of HCP5 rs2395029(G) as a marker for HLA-B*57:01 carriage. They recommend that clinical laboratories keep performing HLA-B*5701 allelotyping to screen for the risk of abacavir HSR in HIV patients starting therapy with abacavir.

In their study, the authors cite our work published in Pharmacogenomics [2], and state that we “endorse the original suggestion by Colombo et al. to rely on the HCP5 SNP test alone to determine individual susceptibility to abacavir HSR in HIV-positive patients before starting therapy”.

We would like to point out that although we identified a complete LD ($r^2 = 1$) in our study on 300 samples of well characterized Mexican Mestizos, we advised caution when interpreting the results due to previous reports by Nolan et al. [3], Colombo et al. [4] and Rodríguez-Nóvoa et al. [5], which demonstrated that LD is high but not complete. We did not however observe individuals that were HCP5 rs2395029(G)-positive and HLA-B*5701-negative; this may be due to the relatively low (2%) HLA-B*57:01 allele frequency observed and the small number of individuals included in our study.

In addition, we suggested that it would be of clinical relevance to have a pharmacogenetic program for Mexican patients initiating abacavir therapy, using HCP5 rs2395029(G) as a screening tool and confirmation of HLA-B*57:01 carriage by either sequencing or PCR sequence-specific primer assay methods; and furthermore, that the clinical utility of such a program must be confirmed by a clinical trial in Mexican Mestizo HIV patients initiating treatment with abacavir.

Another consideration is that our study may be relevant in Mexico and other Latin American countries that share both our European, Amerindian, African and east Asian ancestry contribution, as well as having a limited access for sequencing-based HLA typing or limited resources. Limitation of resources may be aggravated in the actual circumstances of health expenditure constraints.

We agree with the authors that if HCP5 rs2395029(G) is used as a screening tool for HLA-B*57:01 carriage, a low number of individuals susceptible to abacavir HSR may be mistakenly identified by HCP5 rs2395029(G) as tolerant, and subsequently be exposed to abacavir. Their conclusion against using HCP5 rs2395029(G) as a screening tool for abacavir HSR in Caucasians may be true for countries with resources and an economy like Italy; however, we believe that in developing countries, a pharmacogenetic program for patients who will initiate abacavir therapy, using HCP5 rs2395029(G) as a screening tool and confirmation of HLA-B*5701 carriage by either sequencing or PCR sequence-specific primer assay methods, although imperfect, would be preferable to no screening at all, as is the actual clinical practice in Mexico and other Latin American countries. Finally, as we stated in

our article, genetic screening to prevent abacavir HSR should never act as a substitute for clinical vigilance in patients starting abacavir treatment.

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