HIV-1 Subtype and Virological Response to Antiretroviral Therapy: A Confirmatory Analysis

TO THE EDITOR—In an analysis of data from the Swiss HIV Cohort Study, Scherrer et al intriguingly reported significantly better virological outcomes in white patients infected with human immunodeficiency virus type 1 (HIV-1) non-B subtypes compared with subtype B[1]. However, the authors pointed out the need for confirmatory analyses in other cohort studies. We previously published a similar analysis using merged data from the UK HIV Drug Resistance Database and UK Collaborative HIV Cohort studies but including all patients regardless of ethnicity[2]. We have modified and updated this analysis using the same methods employed in the Swiss study (analysis A) with 2 modifications: patients who received mono/dual nucleoside reverse transcriptase inhibitors (NRTIs) before initiation of combination antiretroviral therapy (≥3 drugs from ≥2 classes) were excluded, as were patients with intermediate/high-level resistance to any drug in the initial regimen[3].

Overall, 3471 patients were included in the analysis, of whom 3213 were infected with subtype B virus and 258 with a non-B subtype. Of the non-B subtypes, 110 (43%) were subtype C, 45 (17%) subtype CRF_AE, 39 (15%) subtype A, 22 (9%) subtype CRF_AG, and 42 (16%) other non-B subtypes. The subtype B group was comprised mainly of homosexual men (93%), whereas exposure group in the non-B subtype group was more diverse (44% homosexual men, 27% heterosexual men, 22% heterosexual women). Mean CD4 count (236 cells/mm³) and viral load (4.88 log₁₀ copies/mL) at baseline were similar in the 2 groups, as was the class of non-NRTI drug in the initial regimen (67% nonnucleoside reverse transcriptase inhibitor, 25% boosted protease inhibitor [PI], 4% unboosted PI).

Figure 1 shows the cumulative proportion of patients who experienced virological failure over a total 11 117 person-years of follow-up. The 2 curves appear to separate after approximately 1 year, with a lower rate of failure observed in the non-B subtype group. Note that the definition of virological failure encompasses both failure to achieve initial suppression and viral rebound following suppression; Figure 1 suggests that the subtype difference is related to the latter rather than the former. The unadjusted and adjusted (for age, sex, exposure group, baseline viral load, baseline CD4 count, non-NRTI drug class) hazard ratios (HRs) were 0.72 (95% confidence interval [CI], .49–1.06) and 0.78 (95% CI, .51–1.20; P = .26), respectively.

Given the infrequent use of regimens that included an unboosted PI, it is most relevant to compare our results with the Swiss analysis that excluded this drug class. The adjusted HR was 0.78 (95% CI, .43–1.40), identical to that found in our analysis though also not reaching statistical significance. It is noted that the distribution of non-B subtypes were very different in the 2 studies, the most common in the Swiss study being CRF_AG. The
combined evidence from the 2 studies supports the hypothesis of a lower virological failure rate associated with non-B subtype infection, although this is not statistically conclusive and plausible biological mechanisms remain to be identified [4]. Also, we cannot exclude the possibility that white patients who become infected with a non-B subtype virus may have characteristics, unrelated to the viral genotype, that make them intrinsically more likely to achieve prolonged virological suppression.

Note

Potential conflicts of interest. All authors: 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.

References


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