Origin of minority drug-resistant HIV-1 variants in primary HIV-1 infection

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BACKGROUND
Drug-resistant human immunodeficiency virus type 1 (HIV-1) minority variants (MVs) are present in some antiretroviral therapy (ART)-naive patients. They may result from de novo mutagenesis or transmission. To date, the latter has not been proven.

METHODS
MVs were quantified by allele-specific polymerase chain reaction in 204 acute or recent seroconverters from the Zurich Primary HIV Infection study and 382 ART-naive, chronically infected patients. Phylogenetic analyses identified transmission clusters.

RESULTS
Three lines of evidence were observed in support of transmission of MVs. First, potential transmitters were identified for 12 of 16 acute or recent seroconverters harboring M184V MVs. These variants were also detected in plasma and/or peripheral blood mononuclear cells at the estimated time of transmission in 3 of 4 potential transmitters who experienced virological failure accompanied by the selection of the M184V mutation before transmission. Second, prevalence between MVs harboring the frequent mutation M184V and the particularly uncommon integrase mutation N155H differed highly significantly in acute or recent seroconverters (8.2% vs 0.5%; \( P < .001 \)). Third, the prevalence of less-fit M184V MVs is significantly higher in acutely or recently than in chronically HIV-1-infected patients (8.2% vs 2.5%; \( P = .004 \)).

CONCLUSIONS
Drug-resistant HIV-1 MVs can be transmitted. To what extent the origin-transmission vs sporadic appearance of these variants determines their impact on ART needs to be further explored.
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