Assessing the Paradox Between Transmitted and Acquired HIV Type 1 Drug Resistance Mutations in the Swiss HIV Cohort Study From 1998 to 2012

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BACKGROUND: Transmitted human immunodeficiency virus type 1 (HIV) drug resistance (TDR) mutations are transmitted from nonresponding patients (defined as patients with no initial response to treatment and those with an initial response for whom treatment later failed) or from patients who are naive to treatment. Although the prevalence of drug resistance in patients who are not responding to treatment has declined in developed countries, the prevalence of TDR mutations has not. Mechanisms causing this paradox are poorly explored. METHODS: We included recently infected, treatment-naive patients with genotypic resistance tests performed >/= 1 year after infection and before 2013. Potential risk factors for TDR mutations were analyzed using logistic regression. The association between the prevalence of TDR mutations and population viral load (PVL) among treated patients during 1997-2011 was estimated with Poisson regression for all TDR mutations and individually for the most frequent resistance mutations against each drug class (ie, M184V/L90M/K103N). RESULTS: We included 2421 recently infected, treatment-naive patients and 5399 patients with no response to treatment. The prevalence of TDR mutations fluctuated considerably over time. Two opposing developments could explain these fluctuations: generally continuous increases in the prevalence of TDR mutations (odds ratio, 1.13; P = .010), punctuated by sharp decreases in the prevalence when new drug classes were introduced. Overall, the prevalence of TDR mutations increased with decreasing PVL (rate ratio [RR], 0.91 per 1000 decrease in PVL; P = .033). Additionally, we observed that the transmitted high-fitness-cost mutation M184V was positively associated with the PVL of nonresponding patients carrying M184V (RR, 1.50 per 100 increase in PVL; P > .001). Such association was absent for K103N (RR, 1.00 per 100 increase in PVL; P = .99) and negative for L90M (RR, 0.75 per 100 increase in PVL; P = .022). CONCLUSIONS: Trans-

mission of antiretroviral drug resistance is temporarily reduced by the introduction of new drug classes and driven by nonresponding and treatment-naive patients. These findings suggest a continuous need for new drugs, early detection/treatment of HIV-1 infection.
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