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MUTATION PATTERNS ASSOCIATED WITH RESISTANCE TO TENOFOVIR IN DRUG-NAÏVE PERSONS NEWLY DIAGNOSED WITH HIV

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BACKGROUND: Tenofovir, which has a unique resistance profile that excludes most mutations associated with NRTI resistance, is being evaluated in multiple studies for single-drug pre-exposure HIV prophylaxis. Decreased susceptibility to tenofovir is associated with the RT mutation K65R, and also with at least three of the thymidine analog mutations (TAMS), particularly if these include M41L or L210W, and especially if M184V is absent. We evaluated residual HIV diagnostic sera or plasma from drug-naïve persons newly diagnosed with HIV in diagnostic and clinical centers in eight US states in 2003–2005.

METHODS: Processing of 1682 specimens, each representing one individual newly diagnosed with HIV, took place in the public health laboratories where routine HIV testing takes place or in the CDC Serum Bank. Sequencing was performed at Stanford University, Maryland and Michigan State Health Department laboratories, and University of Washington.

RESULTS: 1621 specimens (96%) were amplifiable for genotyping. Of these, 1096 had available demographic information. Eighty-one percent were male, 78% of whom were exposed to HIV through male to male sex (MSM), 18% by heterosexual sex, 4.0% by drug injection. Nineteen percent were female; of whom 90% were exposed through heterosexual sex and 10% by drug injection. Twenty-eight of the 1621 strains (1.7%) had mutation patterns associated with decreased tenofovir susceptibility. Four strains had K65R; the other 24 had ≥ 3 TAMS in the absence of M184V. Eight of the 24 with multiple TAMS included both M41L and L210W. An additional three, not included among the 28, had three TAMS including M41L, but also had M184V. All those with K65R were MSM; of those with ≥ 3 TAMS without M184V, 19 were MSM, one was a

male heterosexual, and two were female heterosexuals; information was unavailable for the others.

CONCLUSIONS: Mutation patterns associated with tenofovir susceptibility occurred infrequently among this newly diagnosed population, but these data demonstrate that K65R and other relevant combinations of mutations are being transmitted in the US. In areas with a high prevalence of transmission of HIV with mutations associated with reduced tenofovir susceptibility, pre-exposure prophylaxis with tenofovir could be less effective. Studies should evaluate the extent to which resistant HIV could affect prevention of transmission by pre-exposure prophylaxis.

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