

Background: Tenofovir, a reverse transcriptase inhibitor (RTI), is increasingly used in salvage regimens among patients with prior multidrug exposure and evidence of NRTI resistance.

Objective: To evaluate the virologic and immunologic responses to TDF-containing regimens, and where there was virologic failure (VF), to assess RT sequences for the selection of new RT mutations.

Methods: A clinical database was reviewed to identify all patients in the San Mateo County AIDS program who initiated TDF. Among those with VF defined as >500 copies/ml of HIV RNA after 8 weeks, baseline (BL) and VF pol sequences were compared to identify thymidine analog mutations (TAMS) and other RT changes associated with drug resistance.

Results: 82 patients initiated TDF from October 2001 through June 2003, of whom 58 remained on drug for >8 weeks; 13 had <8 weeks of follow-up, 8 were lost to follow-up, 6 discontinued, and 2 died. Mean age was 43, 26% were female, 38% were Black, 34% were Hispanic and 26% were White. Baseline median log HIV RNA and CD4 were 3.7 log copies/ml and 241 per mm³. TDF was included in an initial regimen in 7/58 and after initial HAART failure or multi-drug failure patients in 51/58. CD4 increased by a mean of 38.6 per mm³. VF in 17 patients was identified after a median of 3 months. There was no apparent difference in VF between NRTI (29%), NNRTI (21%) and PI (33%) regimens. Before TDF 7/14 had TAMS (5/14 TAMS only, 2/14 TAMS+M184V), and 2/14 M184V only. At follow-up, 8/14 had a change in RT mutations; 5/14 increased TAMS from median of 1 to median of 4 and 5/14 acquired M184V. The most frequent TAMS were 41 and 215 in 6/7. The K65R mutation was not observed.

Conclusions: In highly treatment experienced patients, VF with TDF were similar across NRTI, NNRTI, and PI regimens. VF analysis demonstrated a high frequency of M184V, T215, and M41L. The K65R mutation was not seen among sequences despite evolution of TAMS and selection of M184V.