A Review of the Virological Efficacy of the Four Tenofovir-Containing WHO-Recommended Regimens for Initial HIV Therapy

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INTRODUCTION

The 2010 WHO ARV Treatment guidelines recommend phasing out d4T and adding four new options for first-line therapy: TDF/3TC/NVP, TDF/FTC/NVP, TDF/3TC/EFV, and TDF/FTC/EFV. TDF is more potent and less toxic than AZT and d4T. It is not known whether the four WHO-recommended, TDF-containing regimens are equally efficacious or even whether each offers an improvement over the older dual NRTI / NNRTI regimens. Therefore, we reviewed published studies of the virological efficacy of each of these regimens for first-line therapy.

METHODS

• To identify studies assessing the efficacy of WHO-recommended, TDF-containing first-line ARV regimens, we searched for papers and meeting abstracts that included prospective or retrospective studies of these four treatment regimens. We excluded (i) studies comprising ARV-experienced patients (ii) studies lacking virological efficacy results (iii) studies for which the % of individuals receiving each regimen was unknown (iv) studies containing ten or fewer subjects.

• Results for treatment failure, virological failure and genotypic resistance (if available) were extracted. Treatment failure is generally defined as those subjects who did not achieve the predefined virological endpoint for any reason. Virological failure (VF) is defined as those who failed due to poor virological response.

RESULTS

• We screened 330 publications and 1,233 conference abstracts. 29 publications met study criteria: TDF/3TC/NVP (3 studies), TDF/FTC/NVP (8 studies), TDF/3TC/EFV (6 studies), TDF/FTC/EFV (14 studies). Tables 1-4 describe all evaluable studies. Figure 1 presents RR and 95CI for treatment failure and VF for comparative studies.

• TDF/3TC/NVP was associated with a higher risk of virological failure in comparison to AZT/3TC/NVP in two studies (Figure 1), and was prematurely discontinued in a pilot study due to high rates of VF and drug resistance (Table 1).

• TDF/FTC/EFV had a risk ratio similar to that of the comparator arm with the exception of two retrospective studies and one very small prospective study.

• TDF/3TC/EFV, and TDF/FTC/EFV were equivalent or superior to their comparators.

• Of studies with resistance testing results, 9% had TDF samples compared to 65% for TDF/3TC/EFV and 31% for TDF/FTC/EFV. Of those receiving TDF/3TC/EFV, 36% (36/100) of those receiving TDF/FTC/EFV, and 41/114 (11%) of those receiving TDF/3TC/EFV.