

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Laessig KA, Lewis LL, Hammerstrom TS. Tenofovir DF and emtricitabine vs. zidovudine and lamivudine. *N Engl J Med* 2006;354:2506-7.

Web-supplement

Sensitivity analyses examining effect of press release

There were 51 patients who switched therapy despite having HIV RNA<400 at the time of their last observation after the press release. Eighteen of these subjects were on TDF+FTC and the other 33 were on AZT+3TC. Of these, 9 TDF+FTC and 27 control subjects had HIV RNA that was still suppressed to <400 at the time of their last measurement, had their last recorded HIV RNA between 1 and 30 days prior to the announcement, and were not observed to rebound but were considered failures because they never had an observation of HIV RNA after day 310 (Days 310-379 are the window for the week 48 visit).

The FDA statistical reviewer used five ways to explore the sensitivity of the conclusion of TDF+FTC superiority to the influence of the public announcement on the behavior of these 36 subjects. Methods 1-5 leave the ultimate status of the TDF+FTC subjects unchanged, since they had no incentive to discontinue their assigned treatment. The 27 control subjects were 1) reclassified from failure to success, 2) left as failures if they discontinued due to AE and otherwise reclassified to success, 3) deleted from the analysis entirely, 4) reclassified from failure to censored or 5) left as failures if discontinued due to AE and otherwise reclassified from failure to censored. Methods 4 and 5 impute some fraction of these 27 subjects as successes and the remaining fraction as

failures, using the Kaplan-Meier curve to impute success or failure. Methods 6-8 apply methods 1, 3, and 4 to both arms rather than to the AZT arm only. In all the analyses in this section, only those patients who received at least one dose of drug and did not have prior ART experience or baseline NRTI mutations are included.

Sensitivity analyses to adjust for open label

The AZT+3TC arm had 75 withdrawals as opposed to only 50 in the TDF+FTC. Of these, 33 discontinuations in the AZT+3TC arm still had viral suppression at the time of discontinuation as opposed to only 18 discontinuations while still suppressed in the TDF+FTC arm. The same five methods noted above were used for these 33 discontinuations.