

Supplementary Appendix

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

Supplement to: Riddler SA, Haubrich R, DiRienzo AG, et al. Class-sparing regimens for initial treatment of HIV-1 infection. *N Engl J Med* 2008;358:2095-106.

Manuscript 07-4609 Additional materials for web-only supplement

Methods

Eligibility criteria: Additional inclusion criteria were: absolute neutrophil count greater than or equal to 750 cells per cubic millimeter (mm^3), hemoglobin greater than or equal to 8.0 g per deciliter (dL), platelet count greater than 50,000 per mm^3 , calculated creatinine clearance greater than or equal to 50 ml per minute (1), serum phosphate greater than or equal to 2.0 mg/dL, serum aminotransferase levels less than or equal to 5 times the upper limit of normal, total bilirubin less than or equal to 2.5 times the upper limit of normal, and lipase less than or equal to 1.5 times the upper limit of normal. Participants were ineligible if they were pregnant or breastfeeding had peripheral neuropathy of Grade 2 or greater; or used any prohibited medications within 30 days prior to randomization.

Study design: At the time the study opened to enrollment, the NRTI choice was zidovudine or stavudine XR. Tenofovir DF was added as an option by protocol modification approximately 3 months after opening of the study.

Definition of virologic failure: Virologic failure before week 32 was met by any of the following three criteria for plasma HIV-1 RNA: less than 1.0 \log_{10} reduction from baseline at or after week 8 and greater than or equal to 200 copies/ml; greater than 1000 copies/ml following confirmed suppression to less than 200

copies/ml; or greater than 1.0 log₁₀ increase from the on study nadir value. At or after week 32, virologic failure was met by either plasma HIV-1 RNA greater than or equal to 200 copies/ml after confirmed suppression to less than 200 copies/ml or failure to suppress HIV-1 RNA to less than 200 copies/ml by 32 weeks.

Author contributions: The initial concept for the study was conceived by Drs. Riddler, Haubrich, DiRienzo, Havlir and Mellors. The final clinical trial protocol was developed by the study team. All data were collected at the study sites of the AIDS Clinical Trials Group and analyzed by Dr. DiRienzo and Ms. Peeples at the Statistical and Data Management Center for the ACTG. Drs. Riddler and Haubrich wrote the first draft of the article with critical review by all authors. All authors, including industry representatives, participated in the development of the study protocol and analysis plan, reviewed the study data reports and approved the final manuscript.

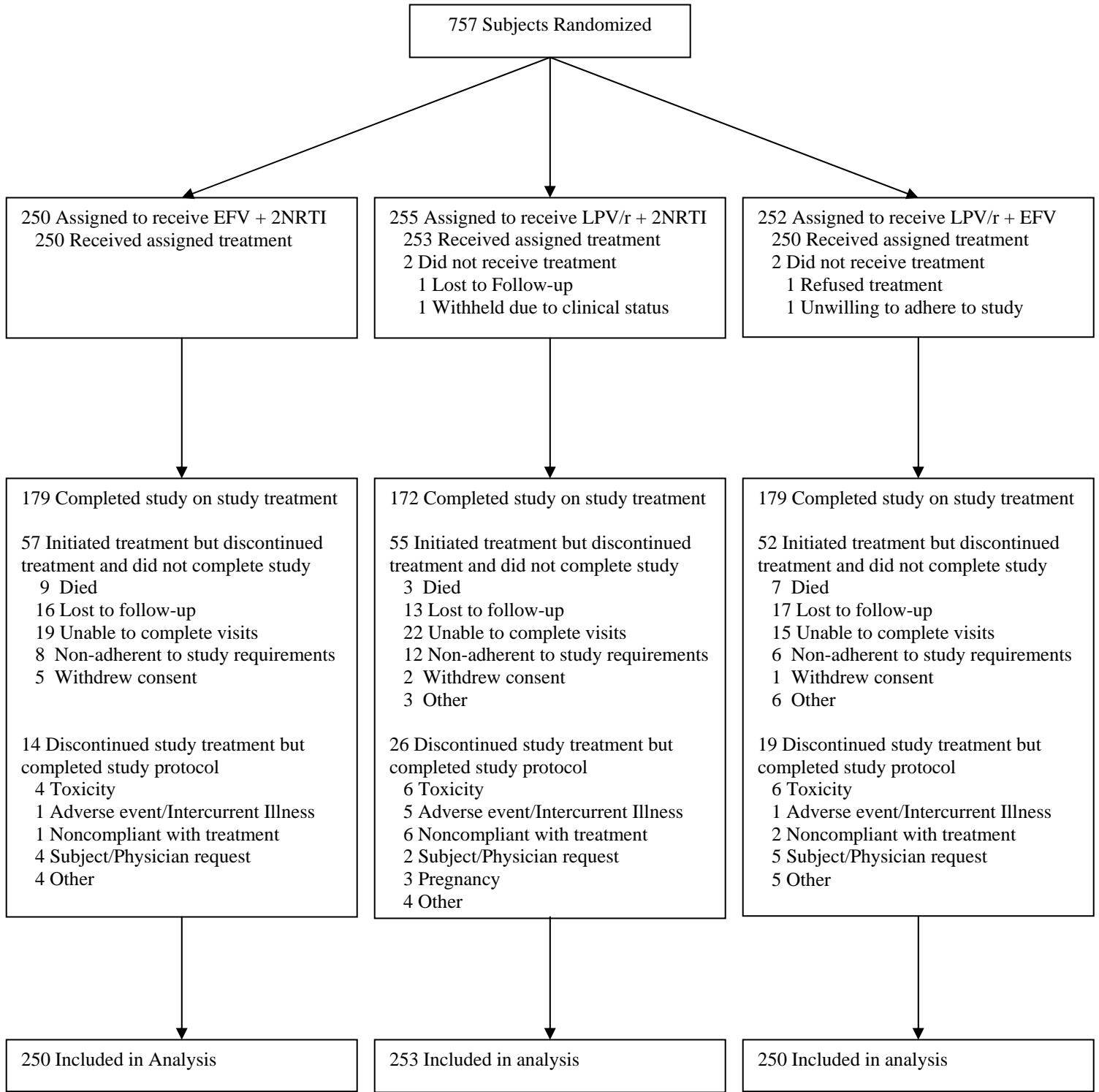
Results:

Four participants (two each in the lopinavir/r and lopinavir/r-efavirenz arms) never started study treatment and were excluded from all analyses. From June 2003 until May 2004, data for 635 screened subjects for A5142 was collected. During this period, 482 of 635 screened subjects were enrolled. The reason for screening failure was reported by the study site to be HIV drug resistance in only 5 subjects.

Reference:

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31-41.

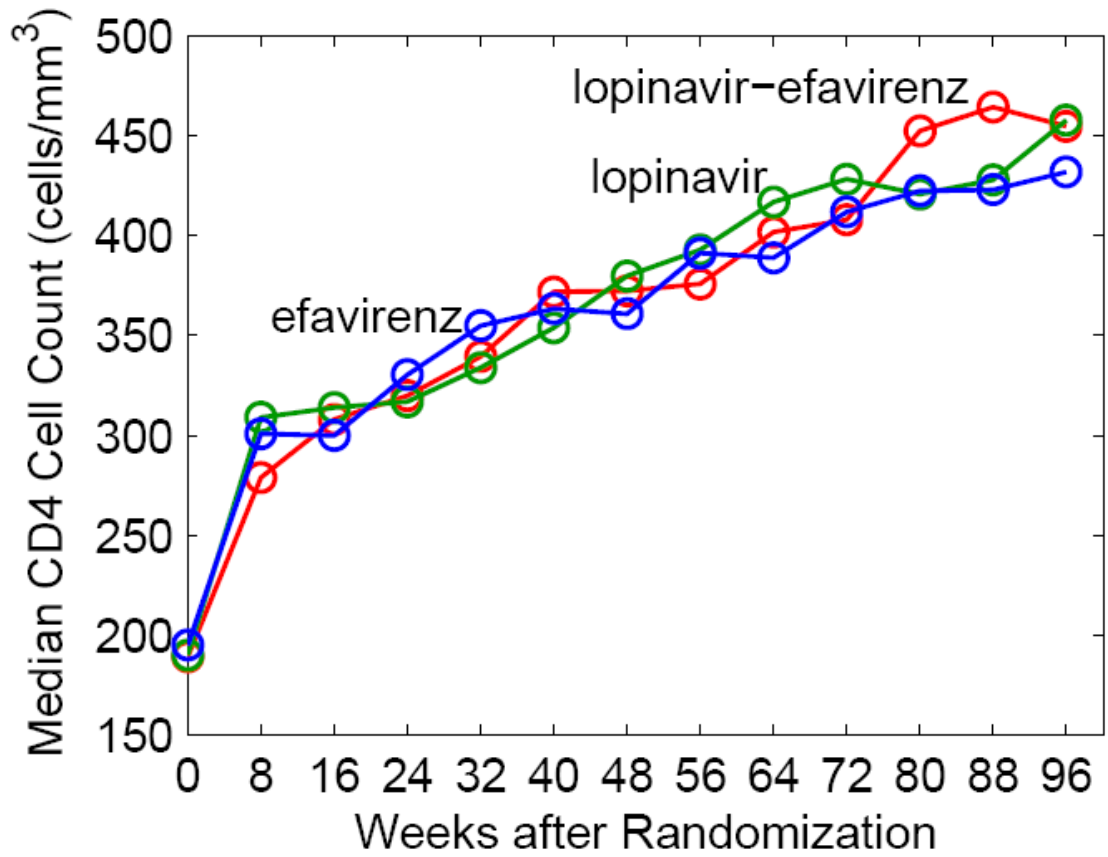
Supplemental Figure: Disposition of Study Participants – A5142



Supplemental Table: AIDS defining conditions

Event	Efavirenz + 2 NRTI N=250	Lopinavir/r + 2 NRTI N=253	Lopinavir/r-efavirenz N=250
Cytomegalovirus esophagitis	1	0	0
Cytomegalovirus retinitis	1	0	2
Central nervous system toxoplasmosis	0	1	0
Cryptococcal meningitis	0	1	1
Cryptococcal pulmonary disease	0	2	0
Esophageal candidiasis	0	1	2
Extrapulmonary tuberculosis	0	1	0
Isosporidiosis	0	1	0
Histoplasmosis pulmonary disease	0	0	2
Lymphoma, non-Hodgkins, large cell	0	1	1
Lymphoma, non-Hodgkins, small non-cleaved	0	1	0
Mucocutaneous Kaposi sarcoma	2	1	3
Mycobacterium avium complex	2	2	2
Pneumocystis pneumonia	2	1	0
Primary central nervous system lymphoma	0	1	0
Pulmonary tuberculosis	2	1	0
Wasting syndrome	0	0	1
Varicella zoster with visceral dissemination	0	1	0

Supplemental Figure. Median CD4 cell count change from baseline for the entire study population



No. at Risk					
efavirenz	250	224	211	201	175
lopinavir	253	224	217	196	175
lopinavir- efavirenz	250	227	214	203	181