

## **Antiretroviral Regimen Durability in HIV-Infected Adults**

Birgitt Dau and Nancy Nguyen, Co-Principal Investigators

Mark Holodniy, Senior Investigator

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### **1. Abstract**

**Background:** The first antiretroviral (ARV) regimen that a treatment-naïve HIV-infected individual takes tends to be the longest-lived regimen. Subsequent regimens, on average, last significantly shorter periods of time, and are less likely to result in virologic suppression (1, 2). A minority of patients with HIV within the VA stay on any one antiretroviral regimen for more than 12 months (Dau and Holodniy, unpublished observations). Factors that impact regimen durability include toxicity or side effects and adherence or virologic failure. It is unknown whether there are differences in durability between current ARV regimens, and what impact initial ARV regimen durability has on clinical outcomes. The impact of frequent regimen switching and gaps in treatment upon clinical outcomes is also unknown.

**Study Aims:** The goal of this study is to define antiretroviral regimen durability within the national VA system. The results of the study will aid HIV providers in choosing initial ARV regimens which provide excellent long-term clinical outcomes for HIV-infected patients. This study will perform a retrospective review of the over 17,000 patients receiving antiretroviral therapy through the VA. The overall goals of the study are to determine if certain regimens have greater longevity than others and if the length of time on a regimen or the frequency of switching regimens is predictive of clinical outcomes. Objective 1 is to determine which initial 3-drug antiretroviral regimens are most durable. Protease inhibitor (PI), ritonavir boosted PI, and non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimens will be compared. Each PI and NNRTI-based regimen evaluated will include 2 nucleoside reverse transcriptase inhibitors (NRTIs). NRTI combinations will also be compared to see if they influence regimen durability independently of the PI or NNRTI they are combined with. Objective 2 will evaluate the influence of the length of persistence of the patient's initial regimen on clinical outcomes of death, CD4 response to therapy (increase in CD4 from baseline, and proportion with CD4 counts above 200 cells/ml), and virologic success (proportion with an undetectable HIV-1 viral load). Objective 3 is to assess whether the frequency of regimen switching affects the clinical outcomes in Objective 2.

**Methods:** This will be a retrospective, observational, cohort study. Patient data and antiretroviral therapy will be analyzed using data from the Veterans Health Administration's HIV Clinical Case Registry (CCR) which houses data on over 50,000 HIV-infected veterans. Patients will be included if they were registered in the CCR before June 30<sup>th</sup>, 2009, utilized at least 2 outpatient Veterans Affairs (VA) medical services between January 1<sup>st</sup>, 2000 and June 30<sup>th</sup>, 2009, and had at least 1 follow-up CD4 count or HIV viral load after starting combination antiretroviral therapy. All eligible patients will be included in the study, estimated to be approximately 10,000 patients. The primary endpoints will be duration of the initial ARV regimen, rates of death, increase in CD4 from baseline and proportion of patients with a CD4 greater than 200, the proportion with an undetectable viral load, and the frequency of regimen changes per year. Durability will be compared using Kaplan-Meier Method. There is a 100% probability of detecting a difference in regimen durability with our dataset. Factors contributing to durability and outcomes will be determined by logistic regression.

**Anticipated Significance:** The primary goal of this study is to address the question of which initial ARV therapies patients are able to continue taking for the longest period of time, and whether improved durability of the initial regimen is associated with better long-term clinical outcomes. Identifying which regimens are most durable in actual clinical practice, regardless of the underlying cause of durability, is important in aiding HIV providers in selecting the optimal ARV regimen for their patients.