



# Consistency of Initial ART with HIV Treatment Guidelines: U.S. HIV-infected Women Report Use of Suboptimal Therapies

Cocohoba JM<sup>1</sup>, Wang OJ<sup>2</sup>, Cox C<sup>2</sup>, Gange SJ<sup>2</sup>, Cohen M<sup>3</sup>, Glesby M<sup>4</sup>, DeHovitz JA<sup>5</sup>, Greenblatt RM<sup>6</sup>.

<sup>1</sup>University of California San Francisco School of Pharmacy, San Francisco, CA, USA; <sup>2</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>3</sup>Cook County Hospital, University of Illinois at Chicago, Chicago, IL, USA; <sup>4</sup>Weill Medical College of Cornell University, New York, NY, USA; <sup>5</sup>State University of New York Downstate Medical Center, Brooklyn, NY, USA; <sup>6</sup>University of California San Francisco School of Medicine, San Francisco, CA, USA

## BACKGROUND

- Female sex may influence antiretroviral therapy (ART). In previous studies women were less likely to receive zidovudine, start ART early or start any ART, or use potent ART (defined by PI use).
- Successful response to initial ART is a predictor of successful long-term virologic and immunologic outcomes therefore initial regimens must be selected carefully
- To assist clinicians' choice of initial ART, the U.S. Department of Health and Human Services issues treatment guidelines that define initial regimens which are preferred, alternative, or contraindicated based on information from clinical trials.
- Different factors influence whether women receive treatment by HIV guidelines. It is unknown whether women are at higher risk for receiving a contraindicated initial ART.

## METHODS

**Data Collection**

- WIHS participants interviewed approximately every 6 months
- Medical and behavioral questionnaires administered
- Medication use data collected routinely at every WIHS study visit via interviewer-assisted self-report of ART use with photo-ID cards.
- CD4+ cell counts and HIV-1 plasma RNA viral load (VL) levels obtained at each WIHS study visit at laboratories participating in NIAID quality assurance programs

**Classification of regimens**

- DHHS guidelines from 4/98 – 10/04 obtained from Internet
- Initial ART grouped into 3 categories for each guideline period: Preferred/alternate (P/A), Contraindicated (C), Unlisted (U)
- Reported WIHS regimens date-matched to DHHS guideline in effect at that time and regimen categorized as above. "Contraindicated" ART described in detail in table below

Dates guideline effective	Not generally recommended	Not recommended
4/24/98 – 6/16/98	2-NRTI+ combinations - zidovudine + didanosine - stavudine + didanosine - zidovudine + zalcitabine - zidovudine + lamivudine - stavudine + lamivudine	All monotherapies Stavudine + zidovudine Zalcitabine + didanosine Zalcitabine + stavudine Zalcitabine + lamivudine
6/17/98 – 5/4/99*	<i>Addition:</i> saquinavir hard-gel capsules + 2NRTIs	No changes
5/5/99 – 1/27/00	<i>Addition:</i> didanosine + lamivudine as 2 NRTI combination	No changes
1/28/00 – 2/4/01*	<i>Category not in guidelines</i>	<i>Addition:</i> saquinavir hard-gel capsules as sole protease inhibitor
2/5/01 – 7/13/03*	<i>Category not in guidelines</i>	No changes
7/14/03 – 11/9/03	<i>Category not in guidelines</i>	<i>Additions:</i> All 2-agent drug combinations Stavudine + didanosine use during pregnancy Efavirenz use during pregnancy Amprenavir oral solution use in pregnancy, children < 4 years old, renal/hepatic failure or by those taking metronidazole or disulfiram Hydroxyurea <i>Deletions:</i> zalcitabine + lamivudine removed from list
11/10/03 – 10/28/04*	<i>Category not in guidelines</i>	<i>Additions:</i> Abacavir + tenofovir + lamivudine as a 3 NRTI regimen Tenofovir + didanosine + lamivudine as a 3 NRTI regimen Atazanavir + indinavir Emtricitabine + lamivudine <i>Changes:</i> stavudine + didanosine not recommended for use in all patients
10/29/04 – 4/6/05	<i>Category not in guidelines</i>	<i>Additions:</i> For initial therapy: amprenavir, delavirdine, enfuvirtide, indinavir or ritonavir or saquinavir SOC as sole protease inhibitor, and zalcitabine + zidovudine Fosamprenavir + amprenavir Amprenavir oral solution + ritonavir oral solution Lamivudine + zalcitabine (returns to list) <i>Changes:</i> efavirenz restriction changed to 1 <sup>st</sup> trimester pregnancy and/or all women of child-bearing potential

## OBJECTIVES

- Characterize initial ART used by women in the Womens' Interagency HIV Study (WIHS) according to DHHS guidelines applicable to estimated use dates.
- Determine whether there are patient characteristics associated with use of a contraindicated first ART regimen.
- Compare short-term immunologic and virologic outcomes for women receiving preferred/alternate (P/A) versus unlisted (U) or contraindicated (C) ART

## METHODS

**Study Design**

The WIHS is a prospective, longitudinal, multicenter, observational cohort study of HIV infection in U.S. women at six study sites and a data coordinating center in Los Angeles, San Francisco, Chicago, Bronx, Brooklyn, Washington D.C., and Baltimore.

**Inclusion Criteria**

- HIV+ WIHS participants reporting use of first ART between 4/98-10/04
- CD4/VL analyses – WIHS participants with available baseline data (within 1 year of reported ART start)

- Exclusion Criteria**
- HIV(-) WIHS participants
  - WIHS participants starting ART < 4/98
  - WIHS participants starting ART due to pregnancy

## RESULTS

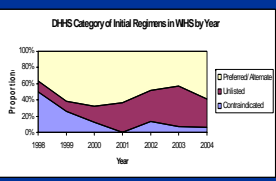
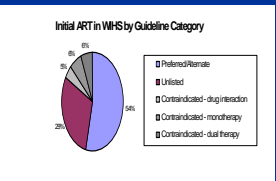
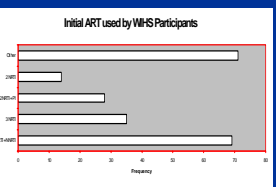
HIV positive women in WIHS (2793)

No prior antiretroviral therapy  
 (ART naive at baseline: 1572, ART incidence: 1062)

Initiated antiretroviral therapy after April 24<sup>th</sup>, 1998 (256)

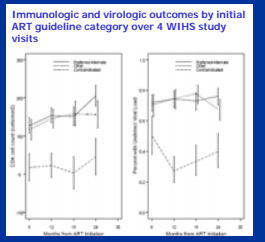
Not pregnant at ART initiation: (217)

Characteristic	Preferred/ Alternate Regimen n=116 (53%)	Unlisted Regimen n=64 (30%)	Contraindicated Regimen n=37 (17%)	P value
Mean age in years (range)	37.7 (20.2-65.3)	37.7 (23.2-61.9)	39.5 (21.6-60.2)	0.58
Median CD4+ nadir (IQR)	251 (121-416)	254 (126-334)	267 (122-433)	0.35
Median pre-initiation CD4+ (IQR)	291.5 (139.5-421.5)	286.0 (126-389)	324.5 (176.0-559.5)	0.054
Median pre-initiation log <sub>10</sub> HIV RNA (IQR)	4.43 (3.85-4.97)	4.43 (4.11-5.23)	3.60 (3.08-4.46)	<0.0001
Clinical AIDS (%)	31	30	34	0.90



Characteristic	p-value
Race Hispanic Non-Hispanic Black Other	0.54
Center Bronx Brooklyn Washington D.C. Los Angeles San Francisco Chicago	0.02
Education < 12 grade Completed high school ≥ High school	0.34
Employed (%)	0.10
Annual Income < \$4000 \$4001-\$12000 \$12001 - \$18000 > \$18001	0.56
Insurance Government Private/Other No insurance	0.97
CESD <sup>a</sup> Depression Score ≥ 16 (%)	0.11
Alcohol Abstain Light/moderate Heavy	0.96
Smoking Current Former Never	0.42
Current Non-IV Illicit Drug Use	0.73
Current IDVU	1.00
Ever IDVU	0.51
Initial antiretroviral regimen after 2001 (%)	<0.0001

Effect	Odds Ratio (95% CI)
Age per 10 years	1.10 (0.66 – 1.84)
CD4+ nadir per 100 cells	1.07 (0.86 – 1.34)
Pre-initiation HIV-1 viral load (per log <sub>10</sub> copies)	0.43 (0.26 – 0.71)
Race	
Non-Hispanic Black vs. Other	1.06 (0.32 – 3.48)
Hispanic vs. Other	0.88 (0.20 – 3.90)
Initial antiretroviral regimen after 2001	0.24 (0.09 – 0.62)



## CONCLUSIONS

- A disturbing number of women in WIHS reported using inappropriate initial ART as classified by U.S. Department of Health and Human Services guidelines
- This practice was more prevalent during early stages of ART (1998-2001)
- Inappropriate ART was associated with suboptimal short term immunologic and virologic outcomes
- Patient characteristics that may be associated with reporting use of contraindicated ART include regimen date, pre-initiation CD4+, VL, and U.S. location
- This study is limited by reliance on self-reported ART. Regimens reported by WIHS participants do not necessarily reflect prescriber's intent.
- Although the proportion of women reporting use of suboptimal initial ART appears to be diminishing over time, it will be important to understand this in the larger context of ART prescribed to both men and women.

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