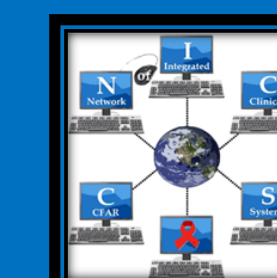


# Relative Effectiveness of Preferred Initial Antiretroviral Regimens in the CNICS Cohort

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## ABSTRACT

**Background:** Data on antiretroviral (ARV) regimen effectiveness in routine care settings complement clinical trial findings and inform clinical practice. ARV regimen durability (i.e., time to change or discontinuation) and viral load (VL) suppression are commonly used to compare regimen effectiveness, and are simultaneously evaluated by the adverse benefit ratio (ABR). This novel, previously published metric was used to assess the relative effectiveness of preferred initial ARV regimens in the CNICS cohort.

**Methods:** ARV-naive patients (pts) with VL>400 c/mL upon starting ART with EFV, LPV/r or ATV/r and TDF/FTC or ABC/3TC between 08/2004-12/2008 at 7 CNICS sites were included. Survival methods were used to separately evaluate regimen durability and time to VL suppression (<400 c/mL) up to 48 weeks. Next, these outcomes were simultaneously analyzed using a competing risks framework to generate the ABR for each 3rd drug. The ABR (range 0, infinity) represents the ratio of the cumulative incidence of regimen change or discontinuation compared to that of VL suppression. The lower the ABR (approaching zero) the more effective the regimen; an ABR<1 indicates a greater probability of achieving VL<400 c/mL prior to a change in regimen. Multivariate models control for sociodemographic and clinical factors.

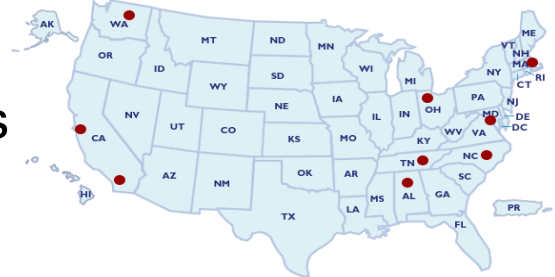
**Results:** Among 1048 pts (median age=38, 15% female, 29% African American (AA), 13% IDU, 42% CD4 count<200, 49% VL>100K), 3rd drugs were EFV 56%, LPV/r 8%, ATV/r 36%; 94% received TDF/FTC. At 48 weeks, 54% had a regimen change or discontinuation; VL<400 c/mL was achieved by 73%. Measuring time to the first of these events, the ABR for EFV, LPV/r, and ATV/r were 0.37 (95%CI=0.29-0.45), 0.39 (0.18-0.60), and 0.42 (0.31-0.53) respectively at 48 weeks, and were not significantly different. Relative to other racial/ethnic groups (ABR=0.35, 0.28-0.41), a significantly higher ABR (p=0.002) was observed for AAs (ABR=0.52, 0.37-0.66) indicating inferior ART effectiveness.

**Conclusions:** When simultaneously analyzing regimen durability and VL suppression among naive pts starting ART in a large US HIV cohort, the relative effectiveness of 3rd drugs was similar and highly effective; pts were roughly 2.7 times more likely to first achieve VL suppression than a regimen change at 48 weeks. As observed in other studies, racial disparities in HIV outcomes were observed with less favorable ABRs among AA pts.

## BACKGROUND

- Data on comparative ART regimen effectiveness from cohort studies complement RCT findings and inform policy and practice
- Cohort studies commonly use viral load suppression and/or regimen durability (i.e., time to ART change or discontinuation) to evaluate the relative between regimen effectiveness of initial ART regimens<sup>1,2</sup>
- In contrast to RCTs, short-term ART change or D/C is considerably more common in cohort studies,<sup>3</sup> and often not accounted for when comparing b/t regimen differences in VL suppression
- The adverse benefit ratio (ABR) uses a competing risks framework to simultaneously evaluate regimen durability and VL suppression<sup>4</sup>

## METHODS

- CFAR Network of Integrated Clinical Systems (CNICS) is a 9-site US clinical cohort study<sup>5</sup>

- The current study included 7 CNICS sites:
  - Case Western Reserve University; University of Alabama at Birmingham; University of California, San Francisco; University of California, San Diego; Fenway Community Health Center of Harvard University; Johns Hopkins University; and University of Washington
- Study eligibility criteria:
  - Antiretroviral therapy naïve
  - Initiated ART between August 2004-December 2008 with:
    - EFV or LPV/r or ATV/r and
    - TDF/FTC or ABC/3TC
  - Pre-ART viral load >400 c/mL
- Survival methods were used to separately evaluate time to regimen change or discontinuation (regimen durability) and time to VL suppression (<400 c/mL) up to 48 weeks post ART start
- Next, these outcomes were simultaneously analyzed using a competing risks framework to generate the ABR for each 3rd drug (EFV, LPV/r and ATV/r) and for race (African American and Other)
  - ABR represents the ratio of cumulative incidence of regimen change or discontinuation (durability) compared to that of VL suppression
  - The lower the ABR (range=0, infinity) the more effective the regimen
  - ABR<1.0 indicates a greater probability of achieving VL suppression (<400 c/mL) prior to a change or discontinuation of regimen
- Multivariable models control for sociodemographic & clinical factors

## RESULTS

- Of 1048 pts 3rd drugs were EFV 56%, LPV/r 8% & ATV/r 36%; at 48 weeks, 54% had regimen change & 73% VL<400 c/mL (Table 1)
- Measuring time to first of these events, no differences were observed between 3rd drugs and a significantly higher ABR was observed for African Americans (Figures 1, 2 & Tables 2, 3)

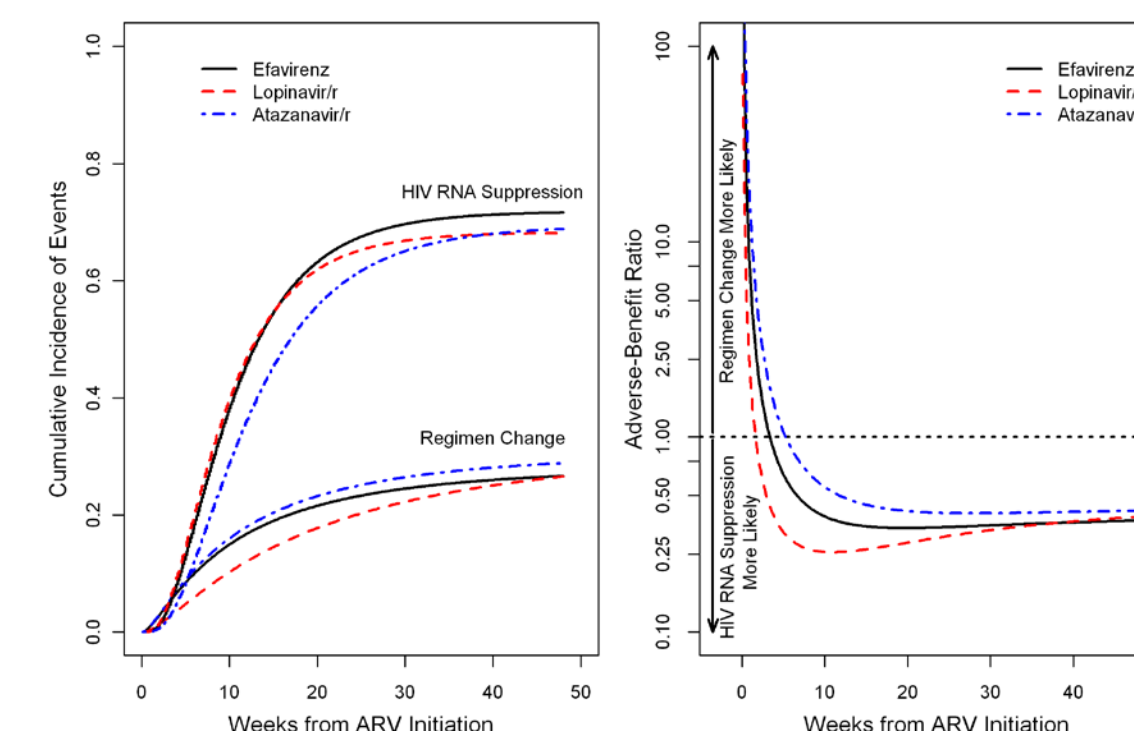
## TABLE 1

Pt characteristics overall and by 48 week outcomes

	Overall (N=1086)	Regimen change or D/C by 48 weeks (N=567)	No Regimen change or D/C by 48 weeks (N=481)	HIV VL suppression <400 c/mL (N=766)	Did not suppress HIV VL<400 c/mL (N=282)
<b>Third Drug</b>					
Efavirenz	592 (56%)	335 (59%)	257 (53%)	436 (57%)	156 (55%)
Lopinavir/r	84 (8%)	46 (8%)	38 (8%)	60 (8%)	24 (9%)
Atazanavir/r	372 (36%)	186 (33%)	186 (39%)	270 (35%)	102 (36%)
<b>NRTI Backbone</b>					
Tenofovir/FTC	980 (94%)	529 (93%)	451 (94%)	721 (94%)	259 (92%)
Abacavir/3TC	68 (6%)	38 (7%)	30 (6%)	45 (6%)	23 (8%)
<b>Baseline CD4</b>					
CD4<200	440 (42%)	228 (40%)	212 (44%)	318 (42%)	122 (43%)
200<CD4<350	372 (36%)	198 (35%)	174 (36%)	278 (36%)	94 (33%)
CD4≥350	236 (23%)	141 (25%)	95 (20%)	170 (22%)	66 (23%)
<b>Baseline HIV RNA</b>					
<10K c/mL	97 (9%)	59 (10%)	38 (8%)	73 (10%)	24 (9%)
10K - <50K c/mL	253 (24%)	143 (25%)	110 (23%)	200 (26%)	53 (19%)
50K - <100K c/mL	184 (18%)	94 (17%)	90 (19%)	138 (18%)	46 (16%)
≥100K c/mL	514 (49%)	271 (48%)	243 (51%)	355 (46%)	159 (56%)
<b>Female</b>	160 (15%)	90 (16%)	70 (15%)	112 (15%)	48 (17%)
<b>African-American</b>	309 (29%)	176 (31%)	133 (28%)	206 (27%)	103 (37%)
<b>Prior AIDS Dx</b>	269 (26%)	122 (22%)	147 (31%)	206 (27%)	63 (22%)
<b>IDU risk group</b>	136 (13%)	67 (12%)	69 (14%)	102 (13%)	34 (12%)
<b>Median Age (IQR)</b>	38 (32-45)	38 (32-44)	38 (32-45)	38 (32-45)	37 (31-44)

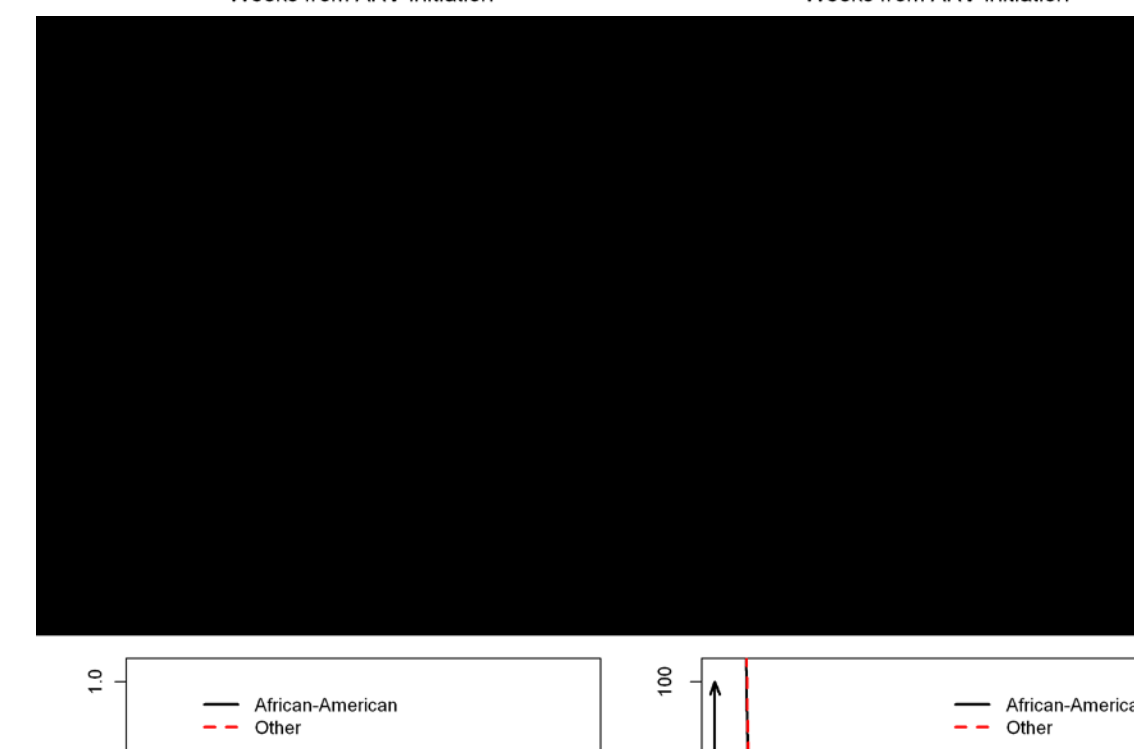
## FIGURE 1

Cumulative event incidence & ABR by 3rd Drug



## FIGURE 2

Cumulative event incidence & ABR by race



## TABLE 2

Adverse Benefit Ratio (ABR) by 3rd Drug\*

	12 Weeks (95% CI)	24 Weeks (95% CI)	36 Weeks (95% CI)	48 Weeks (95% CI)
EFV	0.37 (0.27, 0.45)	0.34 (0.27, 0.42)	0.36 (0.28, 0.44)	0.37 (0.29, 0.45)
LPV/r	0.26 (0.08, 0.43)	0.31 (0.13, 0.48)	0.36 (0.16, 0.55)	0.39 (0.18, 0.60)
ATV/r	0.50 (0.34, 0.65)	0.41 (0.30, 0.52)	0.41 (0.30, 0.52)	0.42 (0.31, 0.53)

\*There is NO significant difference in ABR estimates by 3rd drug

## TABLE 3

Adverse Benefit Ratio (ABR) by Race\*

	12 Weeks (95% CI)	24 Weeks (95% CI)	36 Weeks (95% CI)	48 Weeks (95% CI)
Other	0.37 (0.29, 0.47)	0.33 (0.36, 0.40)	0.34 (0.27, 0.40)	0.35 (0.28, 0.41)
African-American	0.45 (0.30, 0.59)	0.45 (0.32, 0.58)	0.49 (0.35, 0.63)	0.52 (0.37, 0.66)

\*There is a significant difference in ABR estimates by race (P=0.002)

## LIMITATIONS

- As with all observational studies there is potential for unmeasured confounding and ART regimen selection bias
  - On-going analyses use propensity score methods to address ART regimen selection bias
- Data regarding reason for ART regimen change or discontinuation were not systematically available

## CONCLUSIONS

- The relative effectiveness of 3rd drugs among patients initiating contemporary ART regimens was similar and highly effective
  - Pts on EFV, LPV/r or ATV/r were roughly 2.7 times more likely to first achieve VL<400 c/mL than regimen change at 48 wks
- Racial disparities in HIV outcomes were observed with worse ART effectiveness in African Americans (AA)
  - AA pts were roughly 1.9 times more likely to first achieve VL<400 c/mL than regimen change vs. 2.9 in other groups (P=0.002)
- The ABR provides an analytic tool that is well suited for comparative effectiveness research in HIV cohort studies

<sup>1</sup> *AIDS* 2008;22:1951-60    <sup>4</sup> *Stat Med* 2008;27:4313-27  
<sup>2</sup> *AIDS* 2008;22:2481-92    <sup>5</sup> *Int J Epi* 2008;37:948-55  
<sup>3</sup> *JAIDS* 2008;197:1685-94

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