Increased Persistence Of Initial Art With INSTI-containing Regimens

Thibaut Davy, Sonia Napravnik, Oksana Zakharova, Joseph J. Eron

Department of Medicine, University of North Carolina, Chapel Hill, North Carolina

465

Background

- Initiating antiretroviral therapy for HIV infection irrespective of CD4 cell count improves clinical outcomes and prevents transmission.
- Current U.S. treatment guidelines recommend starting ART with a combination of two nucleoside reverse transcriptase inhibitors (NRTI), and an integrase strand transfer inhibitor (INSTI), or a boosted protease inhibitor (bPI).
- Previous studies have estimated the durability (persistence) of initial antiretroviral therapy to be between 1 and 3 years.

Objective

- To estimate and compare the persistence and virologic response to the first combination ART regimen received by antiretroviral-naïve patients

Methods

Study population

- HIV-infected adults initiating ART at UNC between 1996 and 2014.

Regimen categories

- NRTIs + bPI (LPV/r, DRV/r, ATV/r)
- NRTIs + NNRTI (EFV or RPV)
- NRTIs + INSTI (any)
- Other combinations (includes unboosted and other bPI)
- NRTI agents only

Analysis

- Outcome 1: first regimen discontinuation, defined as a change in anchor agent or stopping ART for longer than 2 weeks.
- Outcome 2: virologic failure, defined as having any single HIV RNA level ≥ 400 copies/mL after 24 weeks of therapy.
- Kaplan-Meier curves: time from ART initiation to outcome.
- Censored at loss to follow-up, death, or November 2015, whichever occurred first
- Cox proportional hazards models, adjusted for age, sex, race, baseline CD4, baseline HIV RNA, and calendar period

Results

1624 patients included in analysis
- 28% women
- 60% African Americans
- Median age of 37 years (IQR 29, 46)
- Baseline median CD4 count was 277 (IQR 104, 463)

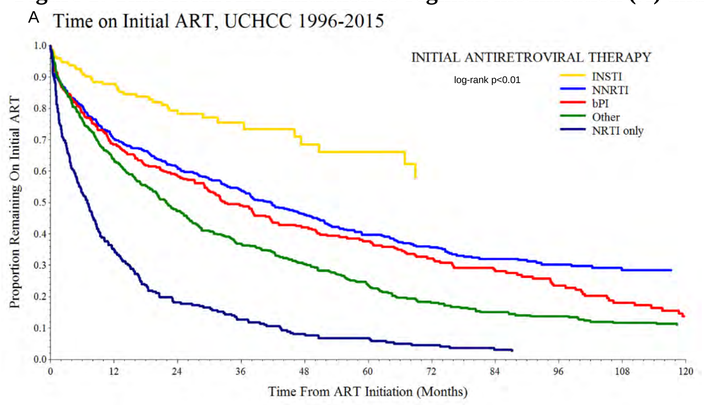
Over the study period,
- age at start of treatment decreased by 4 years,
- baseline median HIV VL decreased by 0.5 log copies/mL,
- baseline median CD4 count increased by 180 cells/mm^3,
- and male proportion increased by 9 percentage points.

(all p<0.01)

Table 1: Patient demographic and clinical characteristics at ART initiation by regimen

	INSTI (n = 173)	NNRTI (n = 536)	bPI (n = 331)	Other (n = 434)	NRTI only(n = 150)	P value
Age, median years (IQR)	38 (26, 48)	37 (29, 46)	37 (29, 47)	37 (29, 45)	37 (31, 45)	0.90
Women, N (%)	30 (17%)	124 (23%)	107 (32%)	146 (34%)	53 (35%)	<0.01
Race, N (%)						<0.01
African-American	109 (63%)	328 (61%)	174 (53%)	268 (62%)	100 (67%)	
White	52 (30%)	129 (24%)	112 (34%)	122 (28%)	38 (25%)	
Other	12 (7%)	79 (15%)	45 (14%)	44 (10%)	12 (8%)	
CD4 Count, median cells/mm^3 (IQR)	403 (246, 579)	279 (116, 468)	230 (78, 401)	237 (69, 442)	341 (127, 475)	<0.01
HIV RNA level, median log10 copies/mL (IQR)	4.4 (3.9, 5.0)	4.8 (4.2, 5.4)	4.9 (4.3, 5.5)	4.9 (4.2, 5.4)	4.6 (3.9, 5.1)	<0.01
ART Year, median (IQR)	2013 (2012, 2014)	2007 (2002, 2010)	2007 (2005, 2010)	1999 (1998, 2003)	1998 (1997, 2001)	<0.01

Figure 1: Time from ART initiation to regimen modification (A) and virologic failure (B) by ART, 1996-2014



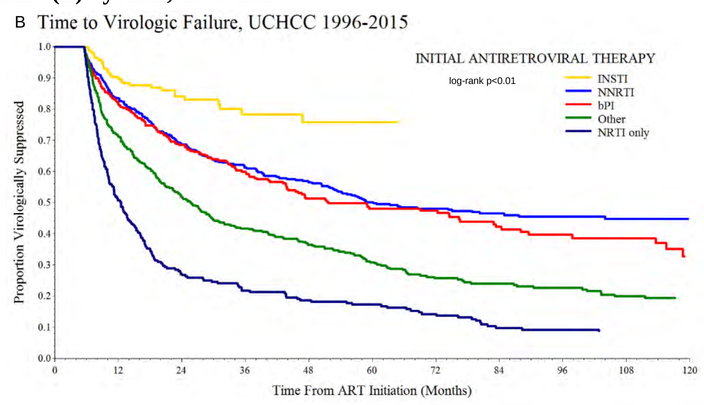


Figure 2: Changes in initial ART regimen by year

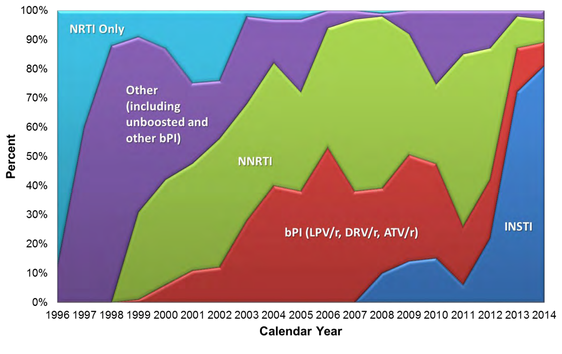


Table 2: Hazard ratios (HR) and 95% confidence intervals (CI), adjusted for age, sex, race, CD4, HIV RNA, and calendar period

	Discontinuation	Virologic failure
	HR (95% CI)	HR (95% CI)
INSTI	0.49 (0.35, 0.69)	0.70 (0.46, 1.06)
bPI	1.24 (1.05, 1.47)	1.24 (1.01, 1.53)
Other	1.47 (1.24, 1.75)	1.21 (0.99, 1.46)
NRTI	2.98 (2.38, 3.74)	1.72 (1.35, 2.19)
NNRTI	Ref.	Ref.

Conclusion

- There is a substantial increase in the durability (persistence) of initial antiretroviral regimens that include an INSTI inhibitor and virologic failure is uncommon.
- This likely captures the contributions of favorable safety, efficacy and tolerability profiles of INSTI regimens.

Contact

Thibaut Davy-Méndez
tdavy@med.unc.edu +1 919 843 0010

Acknowledgements

University of North Carolina Center for AIDS Research P30 AI50410