

Comparative regimen durability and discontinuation reasons among 3-class experienced patients in a US clinical cohort

James H. Willig¹, Immaculada Aban¹, Christa R. Nevin¹, Jiatuo Ye¹, James L. Raper¹, James McKinnell¹, Lori Delaitsch², Joseph Musz², Guy De La Rosa², Michael J. Mugavero¹, Michael S. Saag¹.

1. University of Alabama at Birmingham (UAB) 1917 Clinic Cohort; 2. Tibotec Therapeutics

BACKGROUND

- The approval of new antiretroviral (ARV) agents after June 2006 has transformed the treatment of experienced patients.
- While clearly efficacious in clinical trials of ARV-experienced patients, few data exist regarding the effectiveness of these new agents in the context of routine clinical care
- We hypothesized that the improved activity and tolerability of these newer agents would translate to greater regimen durability.

METHODS

- Darunavir Outcomes Study (DOS):**
 - Prospective, observational cohort study of 3-class ARV experienced patients at the UAB 1917 HIV/AIDS Clinic (www.uab1917cliniccohort.org)
- Study enrollment:**
 - 1 July 2006 - 30 April 2008
- Key eligibility criteria:**
 - 3-class ARV-experienced pts changing regimen
 - Plasma HIV viral load (VL) >1,000 c/mL
 - No CD4 count inclusion / exclusion criteria
 - Not participating in an ARV clinical trial
- Outcome variables:**
 - Regimen durability/persistence (time to all cause regimen discontinuation)
 - Safety
- Independent variables:**
 - Socio-demographic & clinical characteristics
 - ARV regimen composition and active drugs [based on Genotypic susceptibility score (GSS) using Stanford Database]
- Analyses:**
 - Descriptive analyses (patient characteristics, grade 3-4 adverse events at baseline and 48-wks)
 - Propensity score (for DRV/r receipt) methods to control for socio-demographic factors (age, gender, race, health insurance)
 - Adjusted Cox proportional hazard (PH) model adjusted with propensity score above.

RESULTS

Table 1: Baseline characteristics of 108, 3-class antiretroviral-experienced patients changing regimens by new treatment strategy at the UAB 1917 HIV/AIDS Clinic, July 2006-May 2008.

	Other-PI ^A (n=32)	Darunavir/r (n=51)	PI-Sparing (n=25)	P-value
	Mean±SD or n (%)	Mean±SD or n (%)	Mean±SD or n (%)	
Age	46.1 ± 8.0	46.7 ± 9.1	46.4 ± 8.8	0.94
Gender				0.02
Male	23 (72%)	48 (94%)	20 (80%)	
Female	9 (28%)	3 (6%)	5 (20%)	
Race				0.49
White	15 (47%)	29 (57%)	11 (44%)	
Black	17 (53%)	22 (43%)	14 (56%)	
Insurance				0.37
Private	16 (50%)	21 (41%)	6 (24%)	
Public	12 (38%)	22 (43%)	15 (60%)	
Uninsured	4 (12%)	8 (16%)	4 (16%)	
Baseline HIV VL, log ₁₀ copies/mL	3.81 ± 1.27	4.54 ± 0.88	4.19 ± 1.07	0.01
Baseline CD4, cells/mm ³	233 ± 214	213 ± 173	226 ± 232	0.90
Previous ARVs ^B	9.4 ± 3.5	11.3 ± 4.2	10.3 ± 4.8	0.12
Active drugs ^C				0.25
1 or 2	11 (34%)	22 (43%)	10 (40%)	
3 or 4	14 (44%)	23 (45%)	7 (28%)	
Unknown	7 (22%)	6 (12%)	8 (32%)	
On raltegravir	11 (34%)	35 (69%)	19 (76%)	<0.001
On enfuvirtide	2 (6%)	14 (27%)	0 (0%)	0.002
On etravirine	0 (0%)	8 (16%)	10 (40%)	<0.001

(A) Other-PI group included atazanavir (n=17, 12 ritonavir boosted, 5 not boosted), lopinavir/ritonavir (n=11), fosamprenavir/ritonavir (n=2), nelfinavir (n=1), one regimen both atazanavir and lopinavir/ritonavir.
(B) ARVs = antiretrovirals. (C) GSS per Stanford Genotype Database.

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RESULTS

Figure 1: Kaplan-Meier plot of comparative regimen durability for Darunavir/r. Other-PI and PI-Sparing regimens.

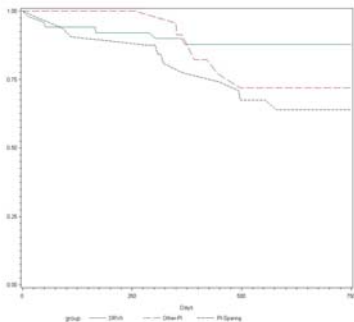


Table 2: Cox PH model of comparative regimen durability/persistence^A in the DOS study (n=108)

	Unadjusted HR	Adjusted HR
Propensity score ^A (HR per 10% increment)	0.90 (0.69-1.17)	1.18 (0.85-1.64)
Baseline HIV VL, log ₁₀ copies/mL	0.94 (0.65-1.35)	0.89 (0.60-1.32)
Baseline CD4 (per 50 cells/mm ³)	0.82 (0.70-0.96)	0.77 (0.65-0.92)
Active drugs ^B		
1 or 2	1.0	1.0
3 or 4	1.14 (0.48-2.70)	1.77 (0.66-4.75)
Unknown	0.76 (0.24-2.44)	1.18 (0.33-4.24)
Treatment strategy		
Darunavir/r	1.0	1.0
Other-PI	3.26 (1.22-8.71)	3.27 (0.97-10.96)
PI-sparing	2.21 (0.71-6.88)	3.43 (0.95-12.32)
Raltegravir		
No	1.0	1.0
Yes	0.44 (0.20-1.00)	0.35 (0.12-1.03)

- A. Durability/persistence hazard ratios greater than 1 denote an increased risk for regimen discontinuation. Propensity score (modeling likelihood of DRV/r use) included: age, gender, insurance status.
B. GSS (genotypic susceptibility score) per Stanford Genotype Database

Table 3: Laboratory grade 3-4 adverse events^A at baseline and 48-weeks in DOS Study patients with available values collected as part of routine care.

Laboratory value	Other-PI		Darunavir/r		PI-Sparing	
	Baseline (n=32)	Week 48 (n=32)	Baseline (n=48)	Week 48 (n=50)	Baseline (n=25)	Week 48 (n=25)
Hb ^B	0	0	0	0	0	0
LDL ^B	0	2 (6%)	0	0	1 (4%)	0
Glucose	0	1 (3%)	0	0	0	2 (8%)
Creatinine	3 (9%)	5 (16%)	0	0	0	0
T. bilirubin ^B	0	1 (3%)	0	0	1 (4%)	0
Alk Phos ^B	0	0	0	0	0	0
AST ^B	0	1 (3%)	0	0	0	0
ALT ^B	1 (3%)	0	0	1 (2%)	0	0

- A. Per AIDS Clinical Trial Group (ACTG) laboratory adverse event scoring.
B. Hb = hemoglobin; LDL = low density lipoprotein cholesterol; T. bilirubin = total bilirubin; Alk Phos = alkaline phosphatase; AST = aspartate aminotransferase and ALT = alanine aminotransferase.

- Overall 26 patients (24%) discontinued their regimens: 6 DRV/r (12%), 15 Other-PI (47%) and 5 PI-Sparing (20%). Discontinuation reasons included: non-adherence/virologic failure (n=18; 4 DRV/r, 11 Other-PI and 3 PI-sparing); toxicity (n=4; 2 DRV/r - hyperglycemia, rash, 2 Other-PI - nausea, diarrhea); other [n=4; 2 medication interaction (e.g. proton pump inhibitor and atazanavir), 1 study enrollment and 1 needed liquid agents]

CONCLUSIONS

- A trend towards increased risk of regimen discontinuation for Other-PI and PI-Sparing strategies when compared to DRV/r was observed, as was a trend towards prolonged regimen durability for regimens containing RAL.
- The lower prevalence observed for grade 3-4 laboratory adverse events at 48 weeks in the DRV/r and PI-Sparing treatment strategies echo the favorable safety profiles for post-2006 treatment options reported in recent clinical trials.
- Though future study into optimal combinations of novel antiretroviral agents released post-2006 are needed, the previously reported increased efficacy, effectiveness and trend towards enhanced durability/persistence and safety of these agents are indicative of important advancements in the care of treatment experienced patients.

