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The Impact of Darunavir/ritonavir (DRV/r) & Raltegravir (RAL) in the Clinic: A New Era for Treatment-Experienced Patients?

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Background

- Since June 2006 several new ARVs, including DRV and RAL, approved for treatment-experienced pts
- In 2006, HIV treatment guidelines updated;[1] for the 1sr time, VL<50 c/mL goal for ARV-experienced pts
  - In part due to efficacy of novel ARVs in RCTs[2-5]
- Effectiveness of new ARVs in achieving VL<50 c/mL in clinical practice settings not well studied

Methods

- Prospective cohort study at the UAB 1917 HIV / AIDS Clinic (www.uab1917cliniccohort.org)
- Study enrollment: 1 July 2006 – 30 April 2008
- Eligibility criteria:
  - 3-class ARV-experienced pts changing regimen
  - Plasma HIV viral load (VL) >1,000 c/mL
  - No CD4 count inclusion criteria
  - Not participating in an ARV clinical trial
- Outcome variables:
  - 24-week VL<50 c/mL and change in CD4 count
- Independent variables:
  - Socio-demographic & clinical characteristics
  - ARV regimen composition and active drugs (based on GSS using Stanford Database)
- Statistical analysis:
  - Univariate analyses: T-test, ANOVA, chi square
  - Multivariate analyses: logistic regression (VL) and linear regression (CD4)
  - Propensity score method to control for socio-demographics (age, sex, race, health insurance) in models; propensity for DRV/r receipt

Results

- ARV regimen composition (n=109, Table 1) :
  - DRV/r 51 pts (47%), other PI 33 pts (30%), PI-sparing 25 pts (23%)
  - RAL 65 pts (60%)
- Among 99 pts with available 24-week VL, 54 pts (55%) achieved VL<50 c/mL
- 24-week VL<50 c/mL by regimen factors (Figure):
  - PI-sparing regimen 41%
  - DRV/r containing regimen 65%
  - Other PI containing regimen 48%
  - No RAL in regimen 38%
  - RAL containing regimen 65%
  - 1 or 2 active drugs 41%
  - 3 or 4 active drugs 66%
- HIV VL <50 c/mL at week 24 (Table 2)
- Unadjusted analyses: 24-week VL<50 c/mL (OR, 95% CI)
  - 3 or 4 active drugs (2.83, 1.14-7.03)
  - RAL containing regimen (2.97, 1.29-6.85)
- MV logistic regression: 24-week VL<50 c/mL (OR, 95%CI)
  - DRV/r containing regimen (4.24, 1.28-14.06)
  - RAL containing regimen (3.10, 1.12-8.62)
- 24-week change in CD4 count (mean ± SD) not statistically significantly different across ARV regimen factors:
  - PI-sparing 62 ± 127 cells/mm^3
  - DRV/r 62 ± 104 cells/mm^3
  - Other PI 53 ± 169 cells/mm^3
  - No RAL 39 ± 126 cells/mm^3
  - RAL 71 ± 135 cells/mm^3

Table 1. Characteristics

	DRV/r (n=51)	Other PI[1] (n=33)	PI-sparing (n=25)	P-Value
Socio-demographic & clinical characteristics, mean ± SD or n (column%)				
Age, years	46.8 ± 9.1	45.9 ± 8.0	46.4 ± 8.8	0.91
Male	48 (94.1)	23 (69.7)	20 (80)	0.01
Minority race/ethnicity	22 (43.1)	18 (54.5)	14 (56.0)	0.45
Health insurance				0.43
Private	21 (41.2)	16 (48.5)	6 (24.0)	
Public	22 (43.1)	13 (39.4)	15 (60.0)	
Uninsured	8 (15.7)	4 (12.1)	4 (16.0)	
Baseline HIV $\log_{10}$ VL	4.5 ± 0.9	3.8 ± 1.3	4.2 ± 1.1	0.01
Baseline CD4 count	213 ± 173	235 ± 211	226 ± 232	0.48
Previous ARVs	11.3 ± 4.2	9.4 ± 3.4	10.3 ± 4.8	0.11
ARV regimen characteristics, mean ± SD or n (column%)				
Active drugs in regimen				0.24
1 or 2	22 (43.1)	11 (33.3)	10 (40.0)	
3 or 4	23 (45.1)	15 (45.5)	7 (28.0)	
Unknown (No genotype)	6 (11.8)	7 (21.2)	8 (32.0)	
Raltegravir in regimen	35 (68.6)	11 (33.3)	19 (76.0)	<0.01
Enfuvirtide in regimen	14 (27.5)	3 (9.1)	0 (0.0)	<0.01
Etravirine in regimen	8 (15.7)	0 (0.0)	10 (40.0)	<0.01

[1] Atazanavir 18, Lopinavir/r 11, Fosamprenavir 2, Nelfinavir 1, Atazanavir and Lopinavir/r 1

Figure. ARV regimen factors associated with 24-week VL<50 c/mL

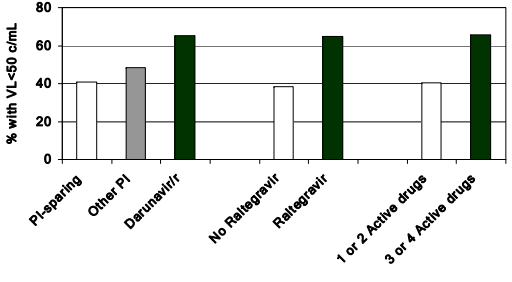

Table 2. Factors associated with HIV viral load <50 c/mL at week 24

	VL<50 c/mL (n=54)	VL≥50 c/mL (n=45)	Unadjusted OR (95%CI)[1]	Adjusted OR (95%CI)[1]
Clinical characteristics, mean ± SD				
Baseline VL, $\log_{10}$ c/mL	4.0 ± 1.2	4.4 ± 1.0	0.68 (0.46-1.01)	0.64 (0.39-1.06)
Baseline CD4 count (OR per 50 cells/mm^3)	245 ± 180	195 ± 206	1.07 (0.96-1.19)	1.06 (0.93-1.20)
Regimen characteristics[3], n (row%)				
Active drugs (GSS)				
1 or 2	17 (40.5)	25 (59.5)	1.0 (Referent)	1.0 (Referent)
3 or 4	25 (65.8)	13 (34.2)	2.83 (1.14-7.03)	2.20 (0.79-6.11)
Unknown (no genotype)	12 (63.2)	7 (36.8)	2.52 (0.83-7.71)	2.05 (0.55-7.65)
Protease Inhibitor (PI)				
None	9 (40.9)	13 (59.1)	1.0 (Referent)	1.0 (Referent)
Darunavir/r	30 (65.2)	16 (34.8)	2.71 (0.95-7.70)	4.24 (1.28-14.06)
Other PI[3]	15 (48.4)	16 (51.6)	1.35 (0.45-4.08)	1.93 (0.51-7.30)
Raltegravir				
No	15 (38.4)	24 (61.5)	1.0 (Referent)	1.0 (Referent)
Yes	39 (65.0)	21 (35.0)	2.97 (1.29-6.85)	3.10 (1.12-8.62)

[1] MV model controls for age, sex, race, insurance as propensity score for DRV receipt [Adjusted OR (95%CI)= 1.06 (0.75-1.50)]
[2] Enfuvirtide, Etravirine and Maraviroc perscribed in n<20; excluded from analyses
[3] Atazanavir 18, Lopinavir/r 11, Fosamprenavir 2, Nelfinavir 1, Atazanavir and Lopinavir/r 1

Conclusions

- Among 3-class ARV-experienced patients changing regimens, those treated with DRV/r and/or RAL were more likely to achieve VL<50 c/mL at week 24
- These ARV agents appear to perform similarly in the clinic as they have in clinical trials, ushering in a new era for treatment-experienced patients

Citations: [1] *JAMA* 2006;296:827-43 [2] *Lancet* 2007;369:1169-78 [3] *N Engl J Med* 2008;359:339- 54 [4] *Clin Infect Dis* 2008;47:969-78 [5] *N Engl J Med* 2008;359:1429-41

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