Lamivudine plus either Atazanavir/ritonavir, Darunavir/ritonavir or Dolutegravir as switch strategies in HIV-positive, virologically-suppressed patients: a comparison

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Background

- In selected HIV-positive, virologically-suppressed patients, dual therapies with lamivudine and boosted-PI represent effective simplification strategies.
- Recent observational studies have underlined the potential role of lamivudine with dolutegravir in this clinical setting.
- Comparison studies among lamivudine-based dual therapies in simplification strategies are lacking.

Matherials and Methods

Retrospective, observational, monocentric study

Inclusion criteria

- Adults (>18 years-old)
- HIV-RNA<50 cp/mL
- Starting Lamivudine plus either: DRV/r, ATV/r or DTG

Exclusion criteria

- HBsAg-positive serostatus

Study outcomes

Main Objective

- Comparing the incidence of treatment failure (TF, the composite outcome of treatment discontinuation and/or virological failure, as defined by single HIV-RNA>1000 cp/ml or two consecutive HIV-RNA>50 cp/mL) at week 24 and 48 in the 3 study arms.

Secondary objective

- Comparing immunological and laboratory changes at week 24 and 48 among different groups.

Patients characteristics at baseline (1)

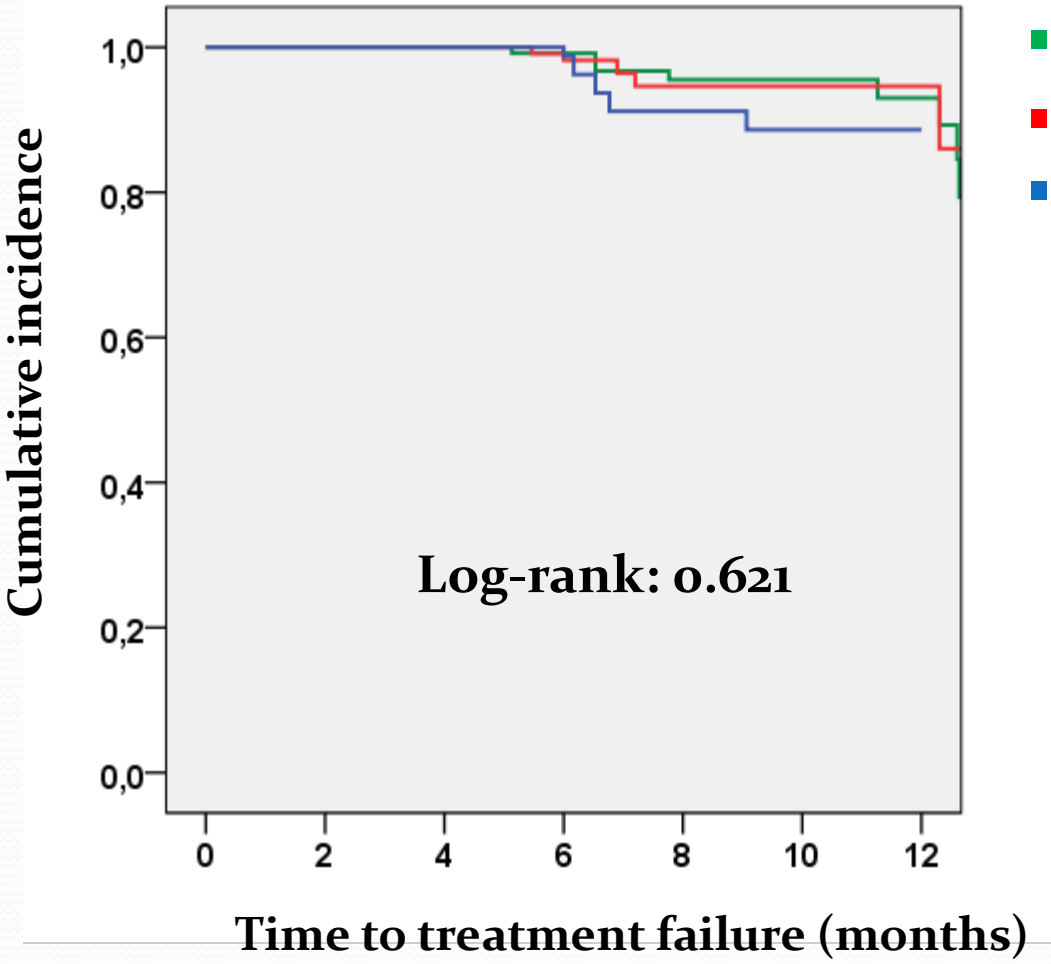
Variables	DRV/r n= 120	ATV/r n= 111	DTG n= 82	*p*
Age, years*	48 (38-54)	47 (42-53)	49 (41-58)	0.278
Male sex	94 (78.3)	75 (67.6)	62 (75.6)	0.162
Caucasians	104 (86.7)	105 (94.6)	78 (95.1)	0.314
Risk factor for HIV: - **Heterosexual** - **MSM** - **IDUs** - **Other**	 40 (33.3) 50 (41.7) 5 (4.2) 25 (20.8)	 46 (41.4) 26 (23.4) 18 (16.2) 21 (18.9)	 29 (35.4) 32 (39.0) 3 (3.7) 18 (22.0)	**0.002**
Time since HIV diagnosis, years*	8 (4-16)	11 (5-17)	13 (7-20)	**0.018**
Time on ART, years*	7 (3-14)	8 (3-13)	10 (5-18)	**<0.001**
Anti-HCV positive	15 (12.5)	23 (20.7)	10 (12.2)	0.146
CDC stage C	32 (26.7)	25 (22.5)	21 (25.6)	0.757
Zenith HIV-RNA (log_{10} cp/mL)*	4.77 (4.15-5.36)	4.96 (4.46-5.29)	4.86 (4.34-5.36)	0.491
Nadir CD4 count (cells/mmc)*	224 (62-323)	199 (62-294)	194 (62-283)	0.659
Viral suppression before switch, yrs*	2 (1-3)	2 (1-4)	8 (4-10)	**<0.001**

Patients characteristics at baseline (2)

Variables	DRV/r n= 120	ATV/r n= 111	DTG n= 82	*p*
Previous virological failures	63 (52.5)	69 (62.2)	45 (54.9)	0.314
Previous resistance mutation to 3TC	17 (14.2)	13 (11.7)	7 (8.5)	0.476
CD4+ count at BL (cells/mmc) *	592 (484-769)	621 (526-778)	633 (500-805)	0.502
Therapy before switch:				**<0.001**
- 2NRTIs+PI/r	60 (50.0)	101 (91.0)	9 (11.0)	
- 2NRTIs+other 3rd agent	31 (25.8)	3 (2.7)	24 (29.3)	
- Other two-drug regimen	19 (15.8)	4 (3.6)	49 (59.8)	
- Other regimen	10 (8.3)	3 (2.7)	0 (0)	
Reasons for switching to dual regimen:				**<0.001**
- Simplification	67 (55.8)	86 (77.5)	21 (25.6)	
- Dyslipidemia	5 (4.2)	4 (3.6)	34 (41.5)	
- GI toxicity	4 (3.3)	2 (1.8)	7 (8.5)	
- Liver toxicity	6 (5.0)	0 (0)	2 (2.4)	
- Renal toxicity	19 (15.8)	9 (8.1)	6 (7.3)	
- Nervous system toxicity	0 (0)	0 (0)	3 (3.7)	
- Other toxicity	14 (11.7)	2 (1.8)	0 (0)	
- Other/unknown	5 (4.2)	8 (7.2)	9 (11.0)	

Values within brackets are expressed in percentage, except for *median values (interquartile range)

Treatment failures



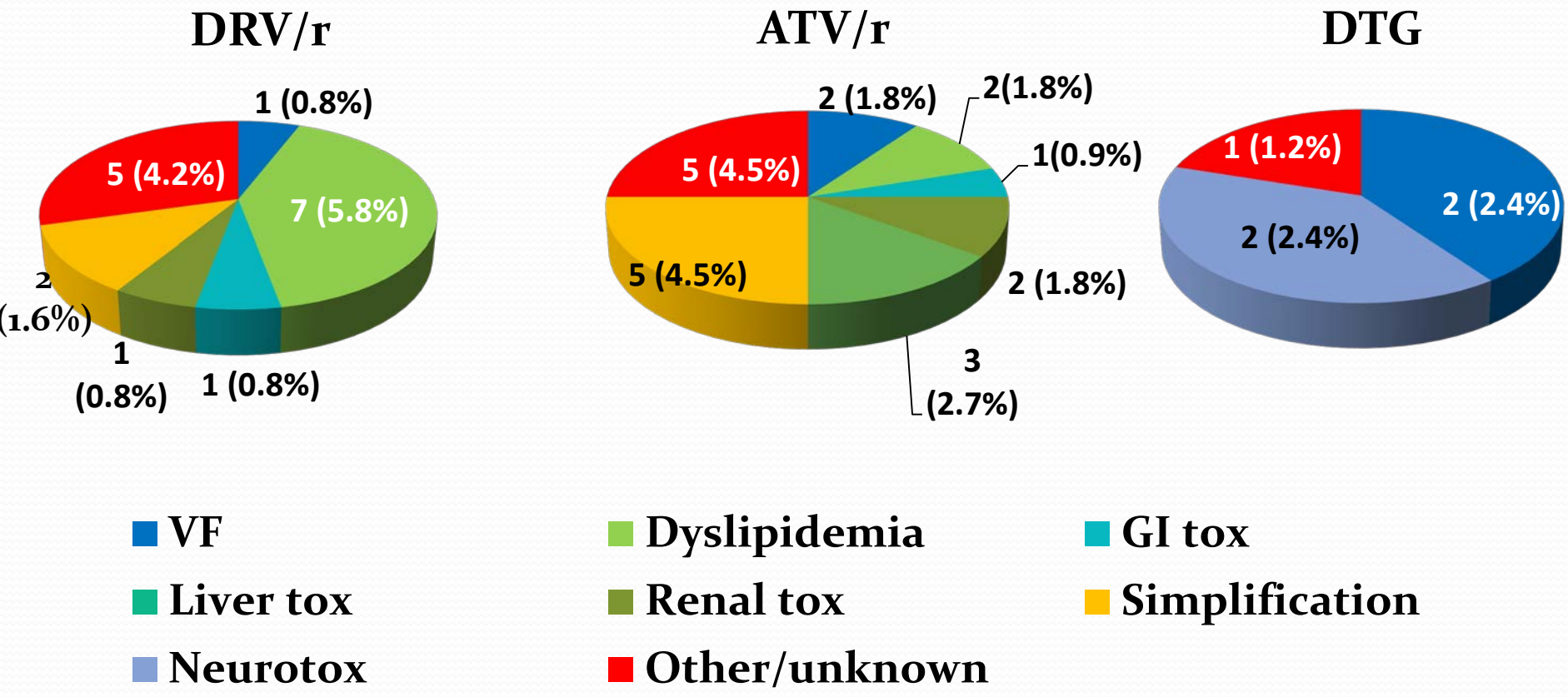
Estimated probability of remaining free from treatment failure at week 48

DRV/r: 93.0% (87.6-98.4)
ATV/r: 94.6% (91.8-100.0)
DTG: 88.6% (79.0-98.2)

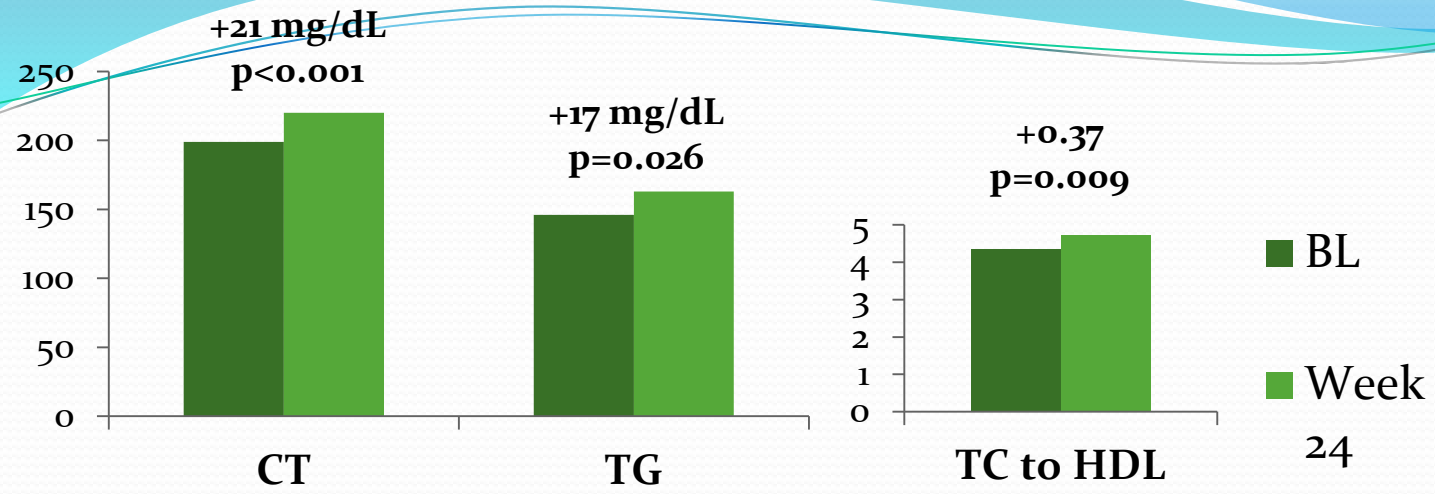
Predictors of treatment failure

Variables	OR (95% CI)	p	OR (95% CI)	p
Time since HIV diagnosis	1.09 (1.02-1.15)	0.008	1.06 (0.99-1.14)	0.113
Switch from TDF	0.42 (0.18-0.98)	0.045	0.35 (0.12-0.96)	0.041
Time on ARV	1.12 (1.04-1.21)	0.002	0.92 (0.75-1.13)	0.435
Previous treatment with NNRTI	3.33 (1.23-9.06)	0.018	2.48 (0.79-7.82)	0.120
Treatment arm:				
- **DRV/r**	Ref	Ref	Ref	Ref
- **ATV/r**	0.97 (0.35-2.66)	0.952	1.13 (0.36-3.55)	0.834
- **DTG**	1.67 (0.53-5.31)	0.383	0.74 (0.22-2.49)	0.621

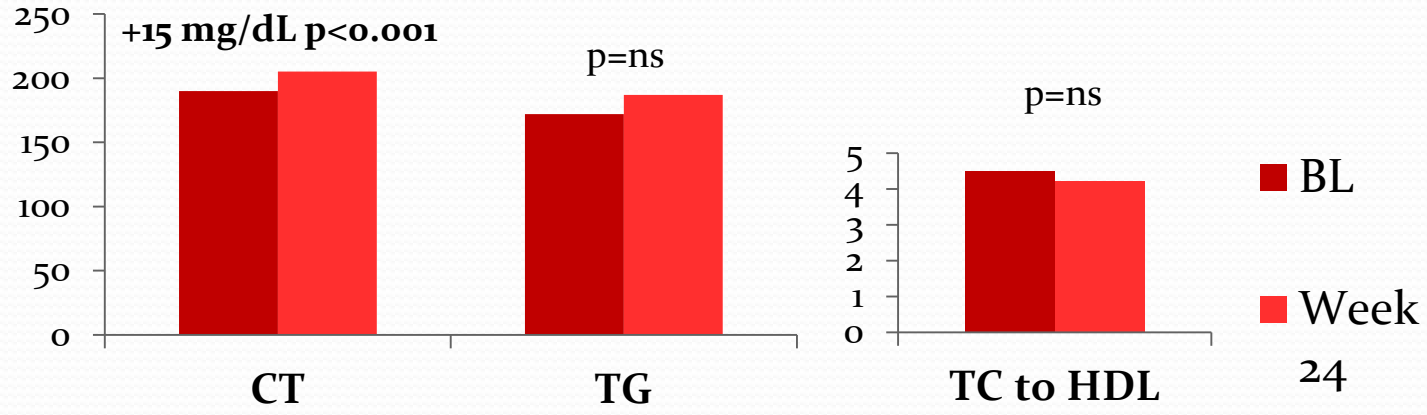
Causes of treatment failures



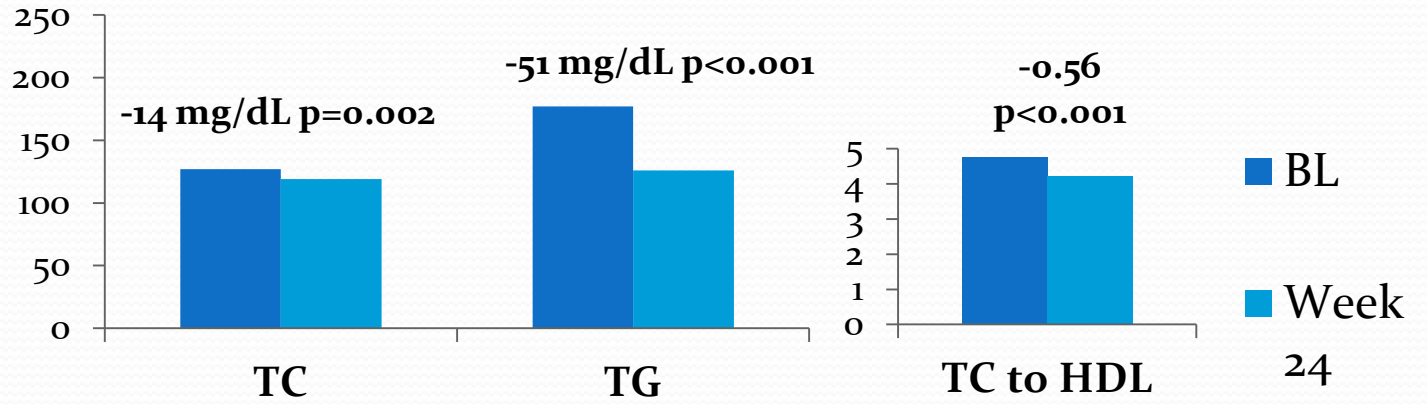
Changes in lipid profile



Darunavir/r



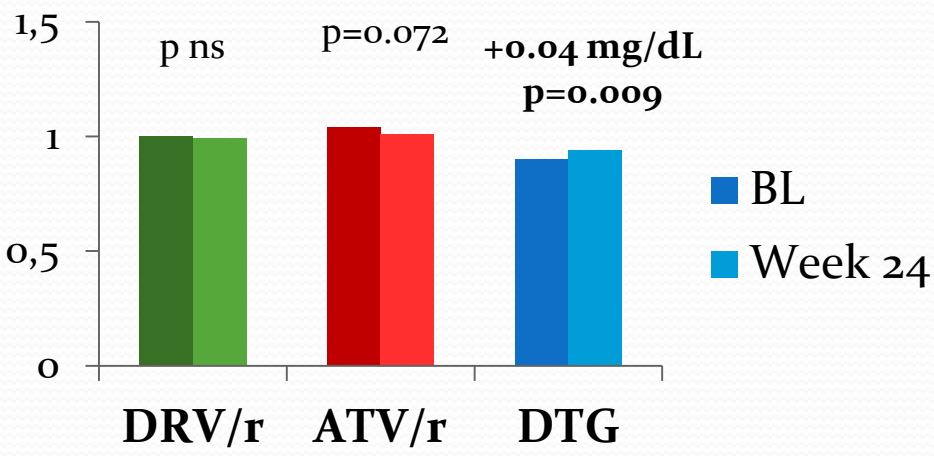
Atazanavir/r



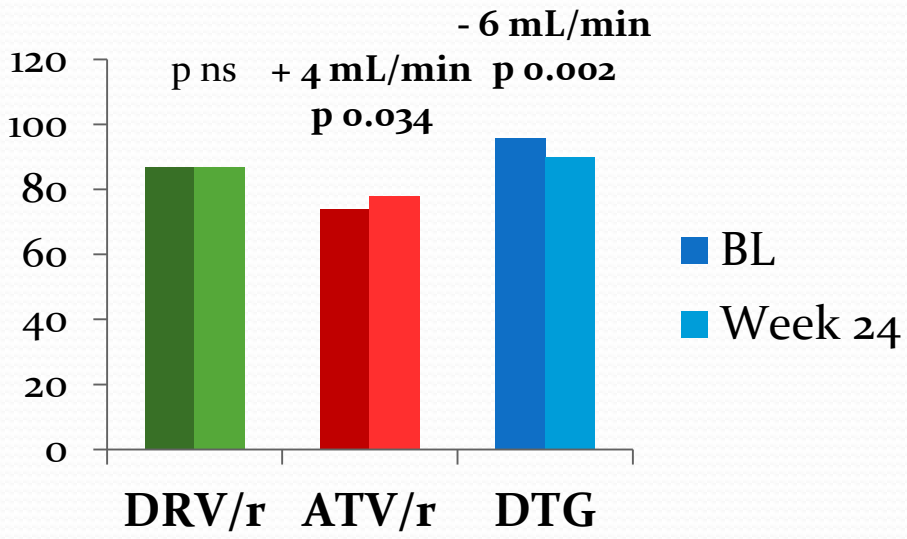
Dolutegravir

Changes in renal and liver functions

Serum creatinine



eGFR (MDRD)



No clinically relevant changes in CD4+ cell count and liver function tests (GPT: + 7 IU/mL in DTG group; p=0.008)

Conclusions

- NRTI-sparing simplification strategies with lamivudine are a safe and tolerable option in treatment-experienced patients;
- Rate of treatment failures are similar between PI/r-based and DTG-based dual therapies after 48 weeks; few virological failures emerged (despite M184V);
- Among PIs, ATV/r confirms to have a more favorable effect on lipids than DRV/r, and represents a better option in pts with reduced eGFR;
- DTG plus lamivudine is a promising treatment option in simplification strategies, especially among pts with issues of dyslipidemia.

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Thanks for the attention!