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Patient profile characteristics when choosing different dolutegravir-based dual therapies: impact on long term efficacy and durability

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Introduction

- Dolutegravir (DTG)-based dual therapies (2DR) has demonstrated non-inferior efficacy compared to standard three-drug regimens in several clinical trials. Indeed, they are increasingly used in routine clinical practice.
- In our study, we aimed to evaluate patient profile characteristics associated with choosing different DTG-based 2DR, and evaluate their impact on long-term efficacy and durability of regimens.

Methods

- Retrospective, single-centre study.
- **Inclusion criteria:** people living with HIV (PLWH) with HIV-RNA <50 copies/mL, undergoing switch to DTG-based 2DR.
- **Exclusion criteria:** Age <18 years, no available follow-up.
- Variables of interest were collected at **baseline (BL, time of switch)** and every 6 months during follow-up, until discontinuation of 2DR or last available visit.
- **Main outcomes:**
  - **virological failure:** defined as a single HIV RNA > 1000 copies/mL or two consecutive HIV RNA > 50 copies/mL.
  - **Discontinuation of 2DR:** defined as any modification, intensification or discontinuation of the regimen.
- Using Kaplan-Meier curves and Cox regression analysis, we estimated incidence and predictors of virological failure and treatment discontinuation.

Results - 1

Figure 1. **2DR tipe: absolute number and percentage**

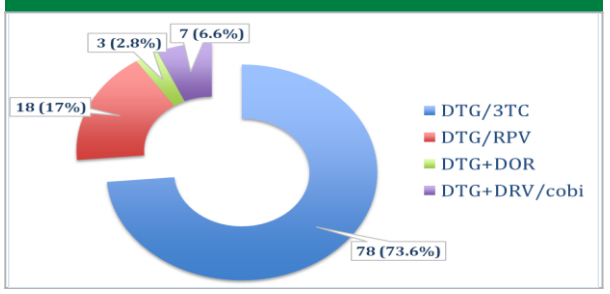

Table.1. **Comparison of baseline characteristics of the DTG/3TC group versus other 2DR (n=106)**

	DTG/3TC N=78	Other 2DR N=28	p
Age, years	52 (47-59)	57 (49-63)	0.172
Male sex	63 (80.8)	18 (64.3)	0.133
Risk factors:			0.103
- Heterosexual	31 (39.7)	17 (60.7)	
- homo/bisexual	35 (44.9)	8 (28.6)	
-Intravenous drug use	2 (2.6)	2 (7.1)	
-Other	10 (12.8)	1 (3.6)	
Not italians	20 (25.6)	6 (21.4)	0.851
Previous HBV	34 (43.6)	6 (21.4)	0.065
Ab HCV+	4 (5.1)	4 (14.3)	0.203
Previous AIDS	12 (15.4)	9 (32.1)	0.103
Years since HIV diagnosis	11.4 (5.3-16.2)	18.2 (10.7-24.3)	**0.001**
Nadir CD4, cell/mmc	197 (100-397)	187 (73-252)	0.437
Zenith HIV-RNA, log cp/mL	5.07 (4.52-5.67)	5.20 (4.67-5.89)	0.585
Years since first ART beginning	9.6 (5.1-15.3)	16.2 (9.7-22.2)	**0.005**
Number of therapeutic lines	3 (2-5)	5 (3-7)	**0.016**
Pre dual therapy:			
-InSTI-based	48 (61.5)	6 (21.4)	**<0.001**
-NNRTI-based	16 (20.5)	6 (21.4)	
-PI-containing	14 (17.9)	16 (57.1)	
Pre dual cause of stopping therapy:			.
-simplification	61 (78.2)	12 (42.9)	
-toxicity	9 (11.5)	6 (21.4)	**0.001**
-proactive switch	4 (5.1)	1 (3.6)	
-other	4 (5.1)	9 (32.1)	
CD4, cell/mmc	815 (520-1098)	703 (441-1047)	0.534
CD4%	35 (28-42)	34 (26-43)	0.600
CD8, cell/mmc	812 (581-1010)	729 (491-1003)	0.293
CD4/CD8 ratio	1.00 (0.65-1.30)	0.84 (0.70-1.38)	0.913

Results - 2

- In a median follow-up of 39.6 months (IQR 17.5-101), only 3 (2.8%) patients experienced virological failure.
- The incidence of virological failure was 0.52 per 100 PYFU in the DTG/3TC group versus 0.43 per 100 PYFU in the other 2DR group.

Table 2. **Virological failure and causes of discontinuation**

	Total population (n=106)	DTG/3TC (n=78)	Other 2DR (n=28)
Total virological failure	3 (2.8)	2 (2.6)	1 (3.6)
Total discontinuations	12 (11.3)	5 (6.4)	7 (25.0)
Discontinuation for:			
-Virological failure	1 (0.9)	1 (1.3)	0
-Blip	1 (0.9)	1 (1.3)	0
-Toxicity	3 (2.8)	1 (1.3)	2 (7.1)
-Immunological failure	2 (1.9)	0	2 (7.1)
-Other	5 (4.7)	2 (2.6)	3 (10.7)

- Twelve (11.3%) patients discontinued 2DR with an incidence of 2.26 per 100 PYFU.

Figure 2. **Kaplan Meier estimates of time to treatment discontinuation in patients treated with Dolutegravir/lamivudine versus Other Dolutegravir-based dual therapies (2DR).**

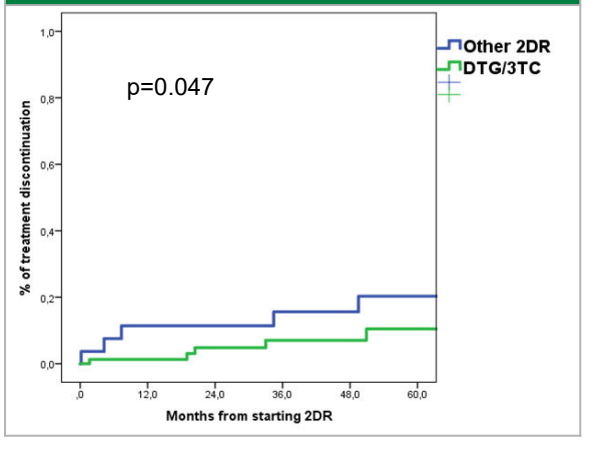

Fig.2

- At 5 years, the estimated incidence of discontinuation was lower for DTG/3TC (10.5%, 95% CI 1.3-19.7) when compared to other 2DR (20.3%, 95% CI 4.2-36.4)(p=0.047).

Results - 3

Table 3

- Only past AIDS events were independently associated to discontinuation (aHR 4.70, p=0.013).
- No difference in time to treatment discontinuation was observed between DTG/3TC versus other 2DR in the adjusted analysis.

Table 3. **Predictors of discontinuation (multivariate Cox analysis)**

	Multivariate analysis	
	aHR 95% CI	p
Previous AIDS	4.70 (1.39-15.97)	**0.013**
Pre dual cause of stopping therapy:	Ref	.
-semplification	1.30 (0.26-6.49)	0.753
-toxicity	0.00 (0.00-nc)	0.990
-proactive switch	3.59 (0.91-14.13)	0.067
-other		
DTG/3TC versus other Dual	0.59 (0.17-1.99)	0.392

Evolution of Laboratiory parameters

- After 1 year of follow-up, a significant increase in median CD4 count versus baseline was observed for DTG/3TC but not for other 2DR
  - DTG/3TC: +102 cells/mmc (p<0.01 versus BL)
  - Other 2DR: +88 cells/mmc (p>0.05 versus BL)
- No significant modifications in other laboratory parameters were observed (CD4/CD8 ratio, creatinine, liver function, total cholesterol, LDL cholesterol, HDL cholesterol, tryglicerides).

Conclusions

- Dolutegravir-based 2DR demonstrated high long-term efficacy in a real-life setting, with rare virological failures and limited rates of discontinuation.
- Despite the “other 2DR” group consisted of patients with more advanced HIV infection, adjusted rates of discontinuation and virological failures were similar to patients treated with DTG/3TC.
- This demonstrated that tailored switch to 2DR is a feasible strategy in routine clinical practice.