Deep insights in two-drug antiretroviral regimen

SC 26 # Effectiveness of first-line lamivudine-dolutegravir antiretroviral therapy in persons with HIV: real-life data from the ICONA Foundation cohort

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ABSTRACT

Background: Dolutegravir plus lamivudine (DTG/3TC) is as effective as standard triple therapy for first-line antiretroviral therapy (ART) in persons with HIV (PWH), but its long-term effectiveness, the impact of pre-ART CD4 count, viral load, and in vulnerable populations need further exploration.

This analysis aimed to evaluate the rate of failure of 3TC/DTG in a real-world data population of PWH starting the combination when ART-naïve.

Methods: The study included PWH from the ICONA Foundation cohort who started first-line 3TC/DTG between 2016 and 2024. The primary objective was to assess time to treatment failure (TF), defined by treatment discontinuation for toxicity/non-adherence, virological failure (2 viral load >50 copies/mL after six months) or death. Secondary objectives included time to treatment discontinuation for any reasons (TD) and virological failure (VF). Main exposures of interest were CD4 count, age, sex, HIV-RNA, and geographic location. Survival analysis was conducted using Kaplan-Meier curves and Cox regression.

Results: This analysis included 446 PWH, all HBsAg-negative: 20% started 3TC/DTG with HIV-RNA >100,000 copies/mL. The median age was 37 years, 15% were female, and 57% MSM, the median CD4 count was 478 cells/mm³, with 6% with CD4 ≤200 cells/mm³ and <1% with an AIDS diagnosis. After a median follow-up of 22 months, 19 PWH (4.3%) experienced TF. The cumulative probability of TF for all exposure of interests are shown in Figure 1. Baseline CD4 count was associated to a 3-fold higher risk of TF, which decreased after adjustments (aHR=2.67; 95%CI 0.75-9.49); higher viral loads (>100,000 copies/mL) and foreign-born status were associated with an increased risk of treatment failure, older participants also had a higher risk (Table 1). Overall, a total of 42 participants (9.4%) discontinued 3TC/DTG over follow-up, mainly for simplification to the long-acting injecting regimen (47.6%), detailed reasons for discontinuation are showed in Table2. The cumulative probability of experiencing 3TC/DTG discontinuation regardless of the reason was 4.6% (95% CI: 2.5-6.8) at 1 year, 10.1% (95% CI: 6.6-13.6) at 2 years and 13.4% (95% CI: 9.1-17.6) at 3 years; n=5 (1.1%) participants experienced pure virological failure, by 3 years the risk of pure VF by Kaplan-Meier was 2.3% (95%CI 0.2-4.4).

Conclusions: In our real-world setting, the TF rate for first-line 3TC/DTG was below 20% at 3 years, lower than in randomized trials. Our data suggest that PWH starting 3TC/DTG with CD4 ≤200 cells/mm³, HIV RNA >100,000 cps/mL, older age and foreign-born status may be at higher risk of TF, though larger studies are needed to confirm these findings.

Figure 1. Kaplan–Meier curves and estimated probabilities of treatment failure (TF) at 1, 2, 3 years among PWH initiating 3TC/DTG as first-line ART; overall (A), according to CD4 strata (B), HIV-RNA strata (C), age strata (D), nation of birth (E) and sex at birth (F)
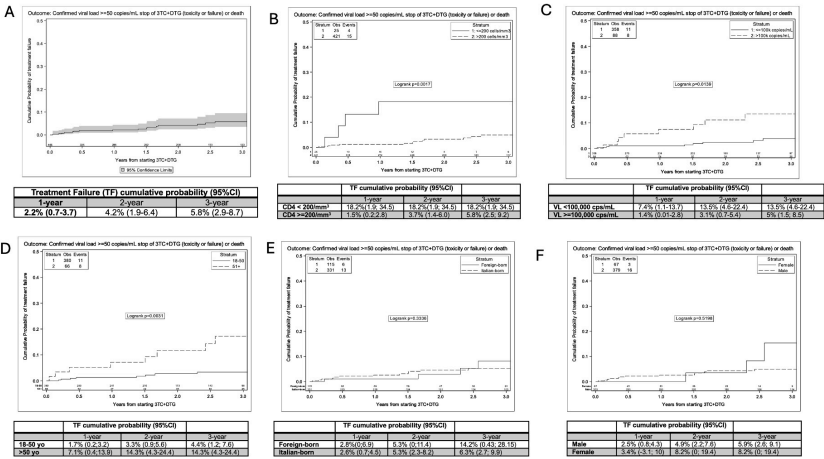

Panel A

Treatment Failure (TF) cumulative probability (95%CI)		
1-year	2-year	3-year
2.2% (0.7-3.7)	4.2% (1.9-6.4)	5.8% (2.9-8.7)

Panel B

TF cumulative probability (95%CI)		
1-year	2-year	3-year
CD4 < 200/mm³	18.2%(1.9, 34.5)	18.2%(1.9, 34.5)	18.2%(1.9, 34.5)
CD4 >=200/mm³	1.5% (0.2,2.8)	3.7% (1.4-6.0)	5.8% (2.5, 9.2)

Panel C

TF cumulative probability (95%CI)		
1-year	2-year	3-year
VL <100,000 cps/mL	7.4% (1.1-13.7)	13.5% (4.6-22.4)	13.5% (4.6-22.4)
VL >=100,000 cps/mL	1.4% (0.01-2.8)	3.1% (0.7-5.4)	5% (1.5, 8.5)

Panel D

TF cumulative probability (95%CI)		
1-year	2-year	3-year
18-50 yo	1.7% (0.2,3.2)	3.3% (0.9,5.6)	4.4% (1.2, 7.6)
>50 yo	7.1% (0.4,13.9)	14.3% (4.3-24.4)	14.3% (4.3-24.4)

Panel E

TF cumulative probability (95%CI)		
1-year	2-year	3-year
Foreign-born	2.8%(0,6.9)	5.3% (0,11.4)	14.2% (0.43, 28.15)
Italian-born	2.6% (0.7,4.5)	5.3% (2.3-8.2)	6.3% (2.7, 9.9)

Panel F

TF cumulative probability (95%CI)		
1-year	2-year	3-year
Male	2.5% (0.8,4.3)	4.9% (2,2,7.8)	5.9% (2.8, 9.1)
Female	3.4% (-3.1; 10)	8.2% (0, 19.4)	8.2% (0, 19.4)

Table 1. Hazard Ratio and adjusted Hazard Ratio of TF from fitting a Cox regression model

	Unadjusted		Adjusted[1]		Adjusted[2]	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
CD4 count, cells/mm³						
<=200 vs >200	4.93 (1.63, 14.90)	0.005	3.73 (1.15, 12.09)	0.028	2.67 (0.75, 9.49)	0.130
HIV-RNA, copies/mL						
>100k vs. <=100k	2.97 (1.19, 7.38)	0.019	2.52 (1.01, 6.33)	0.049		
Nationality						
Foreign vs. Italian	1.61 (0.61, 4.25)	0.338	2.83 (0.98, 8.18)	0.055		
Age						
50+ vs. 18-50	3.62 (1.45, 9.01)	0.006				
Year of ART initiation						
per more recent	0.87 (0.65, 1.16)	0.330				
Sex at birth						
Female vs. Male	1.50 (0.43, 5.17)	0.523				

[1] adjusted for year of ART initiation, age and sex
[2] adjusted for year of ART initiation, age, sex, geographical location of attending site and HIV-RNA

Figure 2. Reasons for 3TC/DTGdiscontinuation

Toxicity/Intolerance 11.9%
Simplification less pills 7.1%
Adherence/patients' choice 16.7%
Lack virological control 4.8%
Other/Unknown 11.9%
Simplification Long Acting 47.6%