Durability of dual antiretroviral regimens and factors associated with discontinuation in the clinical practice

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Background

Dual antiretroviral regimens (DR) may be a suitable option to reduce the toxicity, complexity and costs associated with antiretroviral therapy. However, long-term data about DR are scarce.

Objective

- **To assessed the durability of switching to DR in people living with HIV (PLWH)**.

Methods

✓ We prospectively analyzed a cohort of consecutive PLWH with HIV-RNA switching to dual regimens during 2015-2019.

DR initiation

HIV-RNA viral load ≤50 copies/mL

Outcome of interest = treatment discontinuation:

- ✓ Treatment failure
  - ✓ Non-adherence/loss of follow-up
  - ✓ Virological failure: HIV-RNA ≥200 copies/mL, or 2 consecutive HIV-RNA >50 copies/mL
- ✓ Toxicity/intolerance
- ✓ Simplification
- ✓ Drug-drug interactions.

✓ A Kaplan-Meier curve with log-rank test was used to assess the cumulative probability of occurrence of the outcome of interest by DR.

✓ Multivariate logistic regression model was created to explore the factors associated with DR treatment discontinuation.

Results

- Overall, 352 dual regimens were initiated in 292 individuals.
- The main dual regimens were dolutegravir plus rilpivirine (33%), boosted darunavir plus lamivudine (29%), and boosted darunavir plus dolutegravir (16%, Figure 1).
- The initial DR was discontinued in 102 (29%) cases during a median follow-up of 52 months (interquartile range 41-68, 1688 person-years).
- The main causes of treatment discontinuation were drug-drug interactions (11%), simplification (7%), toxicity/intolerance (5%; 3% gastrointestinal, 2% neurological), and treatment failure [5%; 4.7% due to non-adherence, and only 0.3% (1 case) due to virological failure, Figure 3].
- **The probabilities of all-cause treatment discontinuation at 1, 3 and 5 years were 3%, 7%, and 12%, respectively.**
- Furthermore, the probabilities of treatment failure excluding non-virological reasons at 1, 3 and 5 years were 1%, 2%, and 4%, respectively.
- After discontinuing the DR, 22% switched to a single-tablet regimen.

Results

Table 1. Baseline Characteristics of the cohort population by dual antiretroviral regimen

	Total (n=352)	Dolutegravir + rilpivirine (n=117)	Boosted darunavir + lamivudine (n=102)	Boosted darunavir + dolutegravir (n=55)	Boosted protease inhibitors + raltegravir (n=41)	Boosted darunavir + NNRTI (n=23)	Etravirine + raltegravir (n=14)
Age [years], mean (range)	53 (31-85)	55 (31-85)	52 (31-76)†	52 (33-66)†	53 (36-73)*	53 (35-73)*	55 (46-78)*
Female gender, n (%)	104 (29.5)	31 (27)	32 (31)*	15 (27)*	15 (36)*	8 (35)*	3 (21)*
Intravenous drug use, n (%)	212 (60)	65 (56)	64 (63)*	33 (60)*	24 (58)*	15 (65)*	11 (79)†
Men who have sex with men, n (%)	71 (20)	26 (22)	19 (19)*	11 (20)*	7 (17)*	4 (17)*	2 (14)†
History of AIDS, n (%)	153 (43)	40 (34)	42 (41)*	34 (62)†	23 (56)†	7 (30)*	7 (50)*
Nadir CD4+ T-cell count [cells/mm^3], median (IQR)	193 (79-300)	213 (74-303)	200 (90-312)*	150 (63-295)*	109 (61-261)*	202 (136-312)*	191 (103-251)*
CD4+ T-cell count at inclusion [cells/mm^3], median (IQR)	557 (370-776)	610 (443-833)	563 (394-785)*	551 (284-680)*	425 (204-590)‡	669 (388-883)*	476 (282-896)*
Duration of HIV infection [months], median (IQR)	247 (177-298)	254 (175-298)	211 (160-279)*	279 (223-323)*	259 (204-298)*	251 (159-317)*	258 (207-346)*
Duration of cART [months], median (IQR)	185 (138-235)	211 (152-241)	177 (117-211)‡	221 (155-262)*	201 (127-252)*	217 (125-252)*	215 (176-250)*

*= non-significant, †= *P*-value <0.05, and ‡ *P*-value <0.001 compared with dolutegravir + rilpivirine.
AIDS, acquired immunodeficiency syndrome; cART, combined antiretroviral therapy; IQR, interquartile range; NNRTI, non-nucleoside reverse transcriptase inhibitor

Figure 1. Percentage of dual antiretroviral regimens initiated during 2015-2019

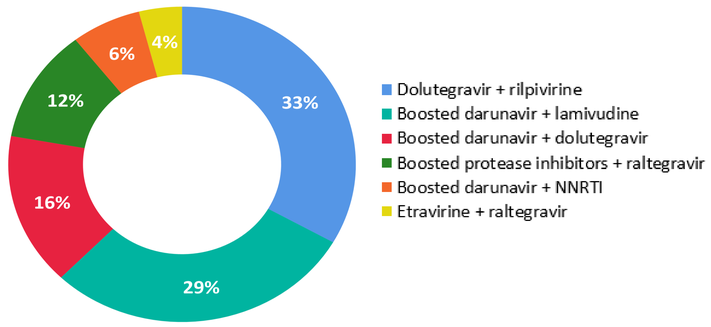


Table 2. Factors associated with dual antiretroviral treatment discontinuation

	Adjusted* Hazard Ratio	95% confidence interval
Male gender	0.5	0.3-0.9
DR based on dolutegravir + rilpivirine	0.4	0.2-0.8
Lower number of pills	0.6	0.4-0.8

*Adjusted for age, duration of HIV diagnosis, total duration of antiretroviral therapy, history of AIDS, CD4<200/mm^3 at DR initiation, CD4/CD8 ratio at DR initiation, and HCV coinfection.

Figure 2. Time to treatment discontinuation by dual regimen

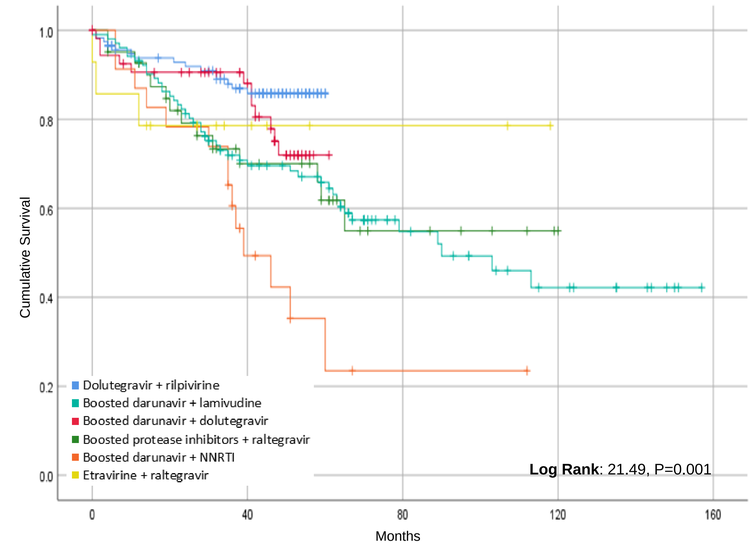
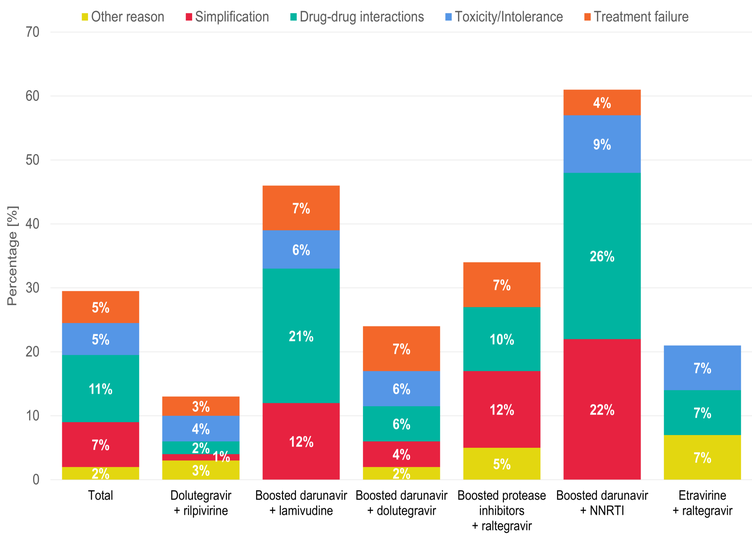


Figure 3. Percentage and causes of treatment discontinuation by dual regimen



Conclusions

Dual regimens were highly effective in the long term with only one case of virological failure.
88% of PLHIV maintained the same dual regimen over 5 years of follow-up.
The vast majority of treatment **discontinuations** were related to **non-virological reasons**, mainly due to drug-drug interactions or simplification.

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