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ORAL COMMUNICATION

Tailored approaches to antiretroviral therapy

OC 35 Cumulative risk of discontinuation of modern first-line ART by reason for stopping and type of ART initiated: findings from the ICONA cohort

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ABSTRACT

Background: Higher long-term antiretroviral treatment (ART) success is reported in People living with HIV (PLWH) remaining on their first-line ART over an extended period. This study estimates the current incidence and the leading causes for first-line ART discontinuation among ART-naive PWH after the advent of Integrase Strand Transfer Inhibitors (INSTI), a more effective, less toxic, and better-tolerated ART option.

Materials and Methods: The analysis included all >18 years ART-naive PLWH enrolled in the ICONA Foundation study cohort, who started their initial ART over January 1, 2012, to December 31, 2022. ART discontinuation was defined as either discontinuing or modifying ≥1 drug in the initial regimen (excluding backbone and booster). All PLWH were followed up until either discontinuation or their last follow-up visit or death before December 31, 2023. The cumulative incidence of first-line ART discontinuation due to simplification, failure, or toxicity, was calculated separately for each of the reasons for discontinuation treating the other reasons as competing events and stratified by regimen type (2DR vs 3DR) and the class of the anchor drug included in the initial regimen (NNRTI, PI, INSTIs). Gray's Test was employed to compare the cumulative incidence curves over time. Multivariable competing risk Cox regression analysis was performed to compare the risk of discontinuation according to initial regimens after controlling for potential confounding factors (the full list is shown in Table 1 footnote).

Results: Out of 10,462 ART-naive PLWH, a total of 5,261 (50%) discontinued their first ART by December 31, 2023. The median (95% Confidence Interval, CI) persistence in the first ART by Kaplan-Meier estimates was 6.52 (6.37-6.64) years. There was strong evidence for a difference in the cumulative incidence of discontinuations due to simplification and toxicity by type of initial regimen (p-value<.0001) but not for discontinuing due to treatment failure (p-value=0.12), Figure 1. By 4 years the cumulative risk of discontinuation for simplification was 2.7% for PLWH starting 3TC+DTG, 6.3% for PLWH on INSTI-based,8.5% on NNRTI-based, and 16.4% on PI-based regimens, respectively; for toxicity the same risks were 7.3% for 3TC+DTG, 9.5% for INSTI-based, 14.4%for NNRTI-based, and 16.6% for PI-based regimens, respectively. Table 1 shows the results of the multivariable competing risk Cox regression model comparing 3TC/DTG with all other types of regimens initiated and separately for each of the reasons for discontinuation.

Conclusions: In the INSTI era, a non-negligible proportion of ART-naive patients within the ICONA cohort still discontinue their first-line ART, mainly for simplification or toxicity. INSTI 2DR showed a lower rate of discontinuation for simplification/toxicity than PI- and NNRTI-based regimens. However, INSTI 3DR were also more frequently discontinued because of toxicity than NNRTI-based regimens.

Figure 1. Kaplan Maier curves illustrate the cumulative incidence of first-line ART discontinuation over the study period (2012-2022) due to simplification (A), failure (B) or toxicity (C) stratified in accordance to first anchor drug class: Dolutegravir + Lamivudine (3TC+DTG), Integrase Strand Transfer Inhibitors (INSTI), Non Nucleoside Reverse Transcriptase Inhibitors (NNRTI), Protease Inhibitors (PI).

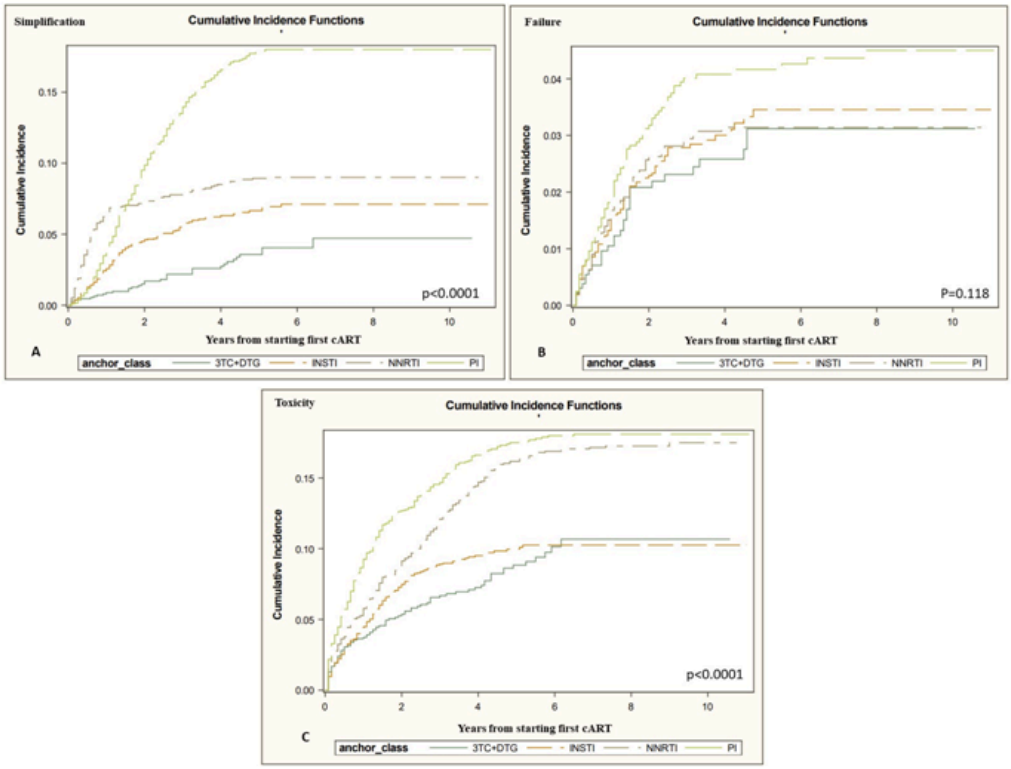

Table 1. Hazard ratio (HR) with 95% Confidence Interval (CI) of discontinuation by reason and according to initial regimens from fitting a Cox multivariable regression model after controlling for potential confounding factors.

	Failure	Simplification	Toxicity
	aHR*[95% CI]	aHR*[95% CI]	aHR*[95% CI]
3TC+DTG vs INSTI	1.30[0.76-2.13]	0.59[0.40-0.88]	0.86[0.65-1.16]
3TC+DTG vs NNRTI	1.00[0.58-1.74]	0.57[0.38-0.85]	0.58[0.43-0.77]
3TC+DTG vs PI	1.17[0.69-1.98]	0.29[0.20-0.42]	0.54[0.40-0.72]
INSTI vs NNRTI	0.79[0.50-1.26]	0.96[0.72-1.28]	1.49[1.21-1.85]
INSTI vs PI	0.92[0.61-1.37]	0.49[0.39-0.61]	0.62[0.51-0.76]
NNRTI vs PI	1.16[0.55-1.36]	0.51[0.39-0.66]	0.93[0.76-1.13]

*adjusted for: age, sex, nationality, route of HIV transmission, baseline AIDS diagnosis, Hepatitis Virus co-infection, smoking habit, alcohol consumption, education level and for baseline CD4+ cells, Total Cholesterol and eGFR values.
3TC: Lamivudine; DTG: Dolutegravir; INSTI: Integrase Strand Transfer Inhibitors; NNRTI: Non Nucleos(t)ide Reverse Transcriptase Inihibitors; PI: Protease Inhibitors