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Discontinuation of Dolutegravir Therapy Due to Any Drug-Related Event Among PLWH in Brazil

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BACKGROUND

Since the Brazilian government introduced Dolutegravir (DTG)-as first-line therapy (2017), some observational studies reported discontinuation rates due to metabolic and central nervous system toxicities. There is a need to determine tolerability and identify adverse outcomes associated with increased use of Integrase inhibitors in low- and middle-income countries, where late presentation and coinfection with opportunistic infections remain common. .

METHODS

We conducted a multicenter, observational study on clinical outcomes of people living with HIV (PLWH), the CODE cohort study , a population-based study on Clinical outcomes of Dolutegravir among ART-recipients in Brazil.

We compared the frequency of any event leading to discontinuation of DTG therapy in participants who initiating DTG or non-DTG-based ART in Brazil. Participants were grouped as:

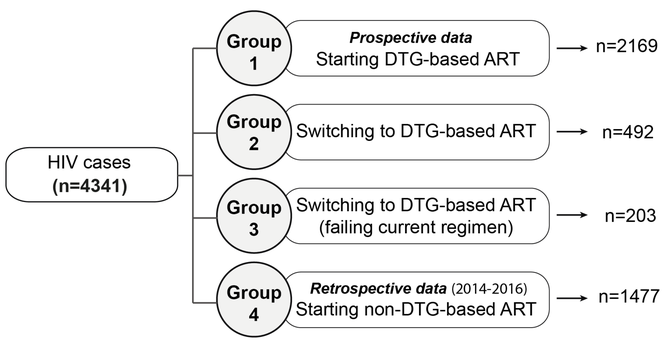


Figure 1. Study groups characteristics

(1) Drug-naïve participants starting DTG-based ART, (2) participants on stable ART switching to DTG-based ART, (3) participants failing current ART and switching to DTG-based ART and (4) participants who started a non-DTG-based ART (data retrospectively collected from 2014 to 2016). Enrolled patients were followed for 36 months. Kaplan–Meier (K-M) analyses with log-rank (L-R) were used to compare cumulative events incidence between groups.

DTG-based regimens **were significantly associated with less treatment discontinuation occurrence** than non-DTG regimens.

RESULTS

Of 4341 PLWHIV included in CODE, 76.5% were male. Mean age was 35 years (27-46), and was higher in groups 2 and 4, as expected (p<0.001). Median viral load was higher in group 1 (68,200 copies/mm3, ,p<0.001), mean CD4+ was lower in group 3 (260 cells/mm3, p<0.001).

The most common discontinuation events were: adverse events (AEs), serious AEs, anti-HIV drug resistance, treatment non-adherence, ART change, and death. (Table 1)

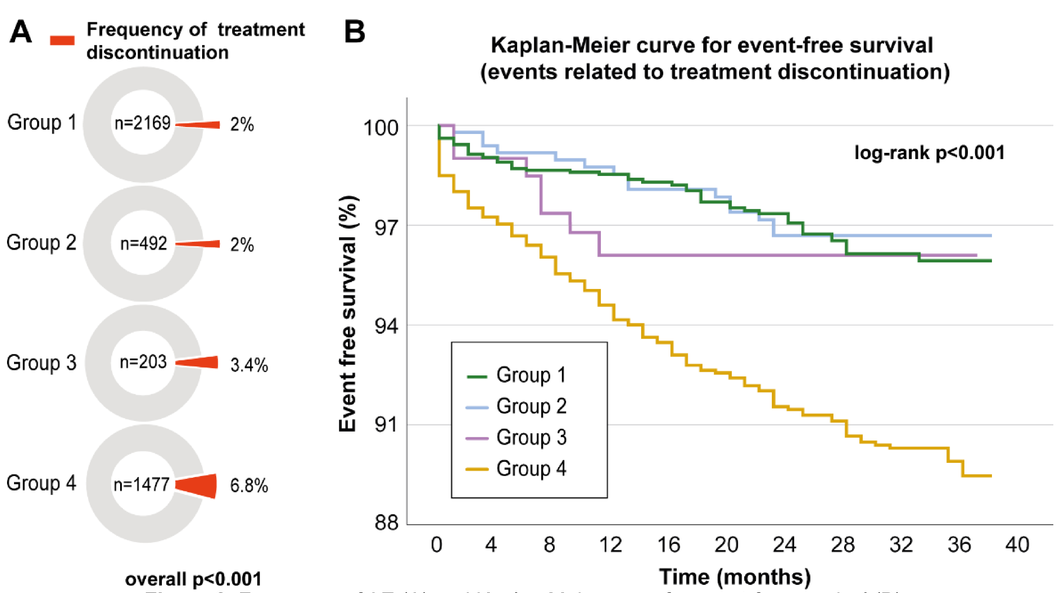


Figure 2. Frequency of AE (A) and Kaplan Meier curve for event-free survival (B).

More treatment discontinuations were observed in group 4 (6.8% vs. <4% in the other groups, p<0.001) (Figure 2A), with AEs being the most common discontinuation event in group 4 (n = 36), while only one AE associated with discontinuation occurred in the others groups. K-M curves shows that the group 4 had significantly lower frequencies for event-free (event related to treatment discontinuation) survival when compared with the other study groups (Figure 2B).`

Table 1. Frequency of discontinuation events

Discontinuation events	Grupo 1 (n=2169)	Grupo 2 (n=492)	Grupo 3 (n=203)	Grupo 4 (n=1477)
No event	2122 (97.8)	477 (97)	196 (96.6)	1340 (90.7)
Death	23 (1.1)	4 (0.8)	4 (2)	11 (0.7)
AE	1 (0.05)	6 (1.2)	0 (0)	72 (4.9)
SAE	3 (0.1)	1 (0.2)	0 (0)	3 (0.2)
Anti-HIV drug resistance	1 (0.05)	1 (0.2)	0 (0)	10 (0.7)
ART change	5 (0.2)	0 (0)	0 (0)	19 (1.3)
Non-adherence	14 (0.6)	3 (0.6)	3 (1.5)	22 (1.5)

CONCLUSIONS

The discontinuation rate for DTG-based regimens was lower than in the group that started a regimen without DTG treatment.

The adverse events associated with dolutegravir were low compared to previous studies.

Generic antiretroviral therapy based on DTG was safe and well tolerated in our cohort.

ADDITIONAL KEY INFORMATION

One of the main limitations is the potential for inaccurate reporting of reasons for discontinuation of DTG (in the retrospective group). Nevertheless, this multicenter study provides real-world, robust evidence on safety and tolerability of DTG in patient starting or switching to DTG-based regimens..

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PLAIN LANGUAGE SUMMARY

People living with HIV in Brazil who used dolutegravir (DTG)-based treatment were less likely to discontinue treatment than those taking non-DTG-based therapies, mainly because DTG caused fewer adverse events.