Real-world Experience of DTG + 3TC Regimen: Results From the French Dat'AIDS Cohort (2015-2022)

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Key Takeaways

- **Observations from the Dat'AIDS cohort were analyzed to provide real-world data for people living with HIV-1 using dolutegravir (DTG) + lamivudine (3TC) in France**
- **At database lock (December 31, 2022), most (93%-97%) people using DTG + 3TC were virologically suppressed, with few confirmed virologic failures (VFs; <1%) and rare instances of emergent resistance-associated mutations**
- **Over a median 1.4 years of follow-up, 14% of people discontinued DTG + 3TC, with 38% to 44% of discontinuations attributed to adverse events (AEs)**
- **These data from the French Dat'AIDS cohort reinforce the effectiveness and tolerability of DTG + 3TC in people living with HIV-1 who are either naive to antiretroviral therapy (ART) or virologically suppressed in a real-world setting**

Introduction

- Compared with 3-drug ART regimens, 2-drug regimens (2DRs) may reduce side effects, drug–drug interactions, and treatment costs for people living with HIV-1[1]
- Multiple randomized clinical trials (GEMINI-1/-2, TANGO, and SALSA) have demonstrated that the 2DR DTG + 3TC provides durable efficacy, a good safety and tolerability profile, and a high barrier to resistance[2-4]
- DTG + 3TC is recommended as a first-line treatment option for people living with HIV-1 by the European AIDS Clinical Society[5]; however, supplementing clinical trial results with observational data is important for evaluating effectiveness in real-world settings
- This analysis of data from the Dat'AIDS cohort evaluated real-world VF and reasons for treatment discontinuation in people living with HIV-1 using DTG + 3TC in France

Methods

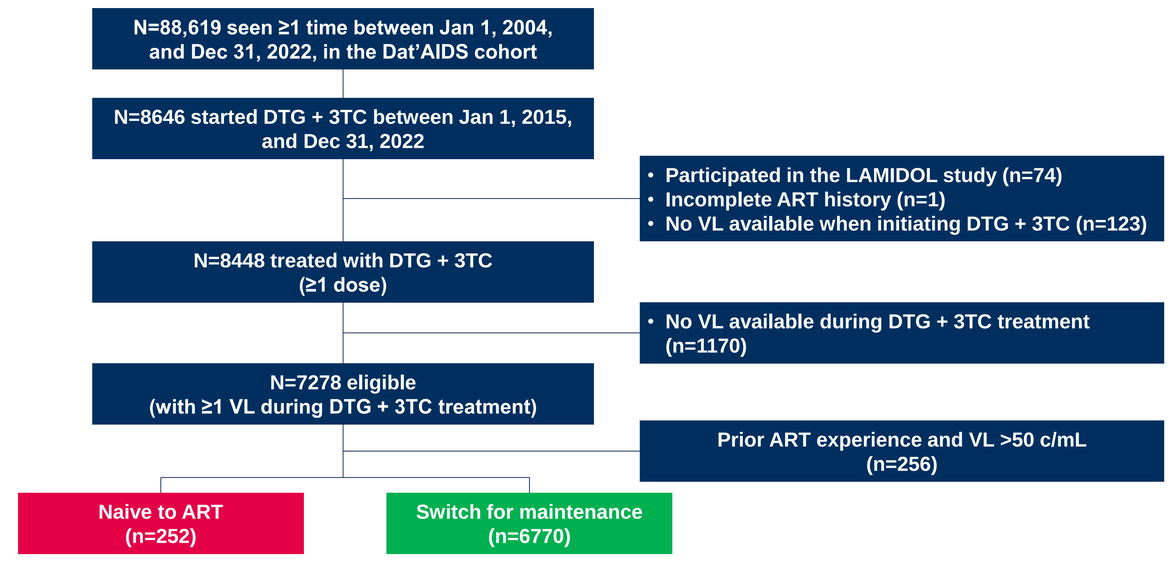
- The Dat'AIDS cohort includes 33 French HIV centers (in metropolitan France, Guadeloupe, and Martinique) using the Nadis® electronic medical records system for the management and follow-up of people living with HIV-1
  - Inclusion into the Dat'AIDS cohort is proposed to each individual during consultations at participating centers
- This analysis included adults aged ≥18 years who initiated DTG + 3TC as of January 1, 2015, with at least 1 available viral load (VL) during follow-up
- Individuals who had previously participated in clinical trials evaluating DTG + 3TC or in the LAMIDOL study were excluded
- People living with HIV-1 were divided into 3 groups according to the reason for DTG + 3TC initiation: naive to ART, switch for failure on prior ART (VL >50 c/mL), or switch for maintenance of virologic suppression (VL ≤50 c/mL)
- In the current analysis, we present data for people who were naive to ART and those who switched to DTG + 3TC for maintenance of suppression
- VF (defined as 2 consecutive VL >50 c/mL or 1 VL >200 c/mL) and discontinuations from DTG + 3TC were analyzed at database lock (December 31, 2022)

Results

Disposition and Baseline Characteristics

- Among the 88,619 people living with HIV-1 followed in the Dat'AIDS cohort, 252 were naive to ART and 6770 were virologically suppressed and switched to DTG + 3TC for maintenance of suppression (Figure 1)

Figure 1. Disposition



- Mean age was 39.6 years in people naive to ART and 52.1 years in those who switched for maintenance; the majority of people were male in both groups (71%-74%; Table 1)
  - 10% of people naive to ART had comorbidities; the corresponding value for those who switched for maintenance was 26%
- Among those who switched for maintenance, 88% were using a 3-drug regimen before switching to DTG + 3TC, with therapeutic optimization (75%) as the most common reason for switch

Table 1. Baseline Characteristics

Parameter	Naive to ART (N=252)	Switch for maintenance (N=6770)
Age, mean (SD), y	39.6 (13.2)	52.1 (12.5)
Sex, male, n (%)	186 (74)	4800 (71)
BMI, mean (SD), kg/m^2	24.2 (3.7)	23.4 (3.8)
Weight, mean (SD), kg	74.5 (13.6)	75.1 (15.3)
Comorbidities, n (%)[a]	24 (10)	1783 (26)
Hypertension	11 (4)	1054 (16)
Dyslipidemia	5 (2)	1053 (16)
Depression	8 (3)	957 (14)
Neoplasms	4 (2)	639 (9)
Cardiovascular disease	7 (3)	581 (9)
Diabetes	4 (2)	380 (6)
Duration of HIV-1, median (IQR), y	0.1 (0.0-1.6)	15.3 (7.7-24.1)
CDC stage A or B, n (%)	247 (98)	5587 (83)
CD4+ cell count, mean (SD), cells/mm^3	534 (263)	755 (313)
CD8+ cell count, mean (SD), cells/mm^3	873 (413)	768 (360)
CD4+/CD8+ ratio, mean (SD)	0.7 (0.4)	1.2 (6.6)
HIV-1 RNA, median (IQR), $\log_{10}$ c/mL	3.9 (3.0-4.5)	1.3 (1.3-1.5)
Duration with undetectable VL, mean (SD), y	—	9.3 (5.7)
Number of prior ART regimens, mean (SD)	—	5.2 (4.2)
ART before DTG + 3TC, n (%)	—	
Monotherapy	—	195 (3)
2-drug regimen	—	570 (8)
3-drug regimen	—	5960 (88)
2 NRTIs + 1 INSTI	—	4158 (61)
2 NRTIs + 1 NNRTI	—	1344 (20)
2 NRTIs + 1 boosted PI	—	362 (5)
≥4-drug regimen	—	45 (<1)
Reason for switch to DTG + 3TC, n (%)	—	
Therapeutic optimization	—	5098 (75)
Adverse events	—	733 (11)
Toxicity prevention	—	367 (5)
Pharmacologic reason	—	212 (3)
Participant decision	—	51 (<1)
Immunovirologic failure	—	17 (<1)
People with ≥1 available genotype, n (%)	153 (61)	4031 (60)
M184V/I mutation	0 (0)	521 (13)
≥1 integrase mutation[b]	26 (17)	514 (13)

[a]In ≥5% of people in either group. [b]People could have more than 1 mutation.

Virologic Outcomes

- After a median (IQR) follow-up of 1.4 (0.8-2.1) years, among those with available data, 93% (234/251) of people naive to ART and 97% (6586/6758) of those who switched for maintenance of suppression had VL ≤50 c/mL (Table 2)

Table 2. Virologic and Immunologic Outcomes at Database Lock[a]

Outcome	Naive to ART (N=252)	Switch for maintenance (N=6770)
HIV-1 RNA, median (IQR), $\log_{10}$ c/mL [n]	1.3 (1.3-1.5) [251]	1.3 (1.3-1.5) [6758]
HIV-1 RNA, c/mL, n/N (%)		
≤50	234/251 (93)	6586/6758 (97)
>50	17/251 (7)	172/6758 (3)
Discontinued DTG + 3TC with VL >50 c/mL, n/N (%)	9/251 (4)	89/6758 (1)
Confirmed VF, n/N (%)	4/251 (2)	28/6758 (<1)
CD4+ cell count, mean (SD), cells/mm^3 [n]	719 (313) [237]	773 (319) [6261]
Change from DTG + 3TC initiation	189 (228) [228]	18 (203) [6091]
CD8+ cell count, mean (SD), cells/mm^3 [n]	838 (460) [232]	778 (382) [6190]
Change from DTG + 3TC initiation	−38 (392) [221]	7 (258) [5974]
CD4+/CD8+ ratio, mean (SD) [n]	1.0 (0.5) [232]	1.2 (0.6) [6186]
Change from DTG + 3TC initiation	0.3 (0.3) [221]	0.0 (0.3) [5970]

[a]N = total number of people included in study; n = number of people with available data at database lock.

- Of the 7009 people with available data in both groups, 98 (1%) discontinued DTG + 3TC with a VL >50 c/mL and 32 (<1%) had confirmed VF at the end of database lock
- At VF, 4 of the 26 available genotypes harbored resistance-associated mutations (naive to ART, n=1; switch for maintenance, n=3)
  - M184V on reverse transcriptase was observed in all cases and was associated with N155H on integrase in 1 person naive to ART (VL 5162 c/mL, 11.2 months after DTG + 3TC initiation; no genotype available at baseline); of the 3 people who switched for maintenance, 1 had M184V at baseline, 1 had no mutations at baseline, and 1 had no genotype available at baseline
  - No INSTI-associated mutations were observed in the switch for maintenance group at VF

Tolerability

- Across groups, 14% (964/7022) of people discontinued DTG + 3TC (naive to ART, n=45; switch for maintenance, n=919; Table 3)
  - Among people who discontinued, median (min-max) duration of DTG + 3TC use was 12.8 (0.7-56.1) months for those naive to ART and 10.2 (0.1-92.2) months for those who switched for maintenance
  - Median (IQR) HIV-1 RNA at time of discontinuation was 1.4 (1.3-1.6) $\log_{10}$ c/mL in those naive to ART and 1.3 (1.3-1.5) $\log_{10}$ c/mL in those who switched for maintenance
  - The most common reason for discontinuation was AEs in both groups

Table 3. Reasons for Discontinuation in People Who Stopped Using DTG + 3TC

n (%)	Naive to ART (N=45)	Switch for maintenance (N=919)
Adverse events[a]	20 (44)	353 (38)
Neuropsychiatric	11 (24)	136 (15)
Other	5 (11)	79 (9)
Intolerance to treatment	1 (2)	32 (3)
Gastrointestinal	1 (2)	29 (3)
Osteoarticular	0 (0)	21 (2)
Skin	0 (0)	20 (2)
Liver toxicity	1 (2)	4 (<1)
Hematologic toxicity	1 (2)	3 (<1)
Therapeutic optimization	8 (18)	219 (24)
Relief/Simplification	5 (11)	149 (16)
Intensification/Other	3 (7)	70 (8)
Non-adherence/Participant decision	3 (7)	86 (9)
Immunologic failure	4 (9)	78 (8)
Death	4 (9)	59 (6)
Other reason	2 (4)	37 (4)
Desire for pregnancy	2 (4)	24 (3)
Pharmacologic motive (adaptation/interaction)	0 (0)	25 (3)
Current pregnancy	1 (2)	18 (2)
Toxicity prevention	0 (0)	8 (<1)
Unknown	1 (2)	1 (<1)

[a]In ≥2% of people in either group.

- Since DTG + 3TC initiation, median (IQR) weight gain was 3.0 (0.0 to 5.2) kg in people naive to ART and 1.0 (−1.0 to 3.0) kg in those who switched for maintenance

Conclusions

- Real-world data for DTG + 3TC in France demonstrate high rates of virologic suppression among people living with HIV-1 who are naive to ART or virologically suppressed, reinforcing results from randomized clinical trials
- DTG + 3TC was primarily prescribed for people with prior ART experience who were virologically suppressed
- Discontinuations occurred in 14% of people using DTG + 3TC, with the most common reason being AEs
- VF was infrequent, with rare instances of emergent resistance-associated mutations and no INSTI-associated mutations observed in the switch for maintenance group, confirming the effectiveness of DTG + 3TC in real-world settings

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