2-Year Outcomes of Dolutegravir (DTG) and Lamivudine (3TC) in Art-Naive and Pre-treated People Living With HIV in Germany: Real-world Data From the German URBAN Cohort

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Key Takeaways

- **URBAN is a prospective, non-interventional, 3-year German cohort study in antiretroviral therapy (ART)-naive and pre-treated people living with HIV (PLHIV) receiving dolutegravir and lamivudine (DTG/3TC) in accordance with the label in Germany.**
- **After 2 years in a real-world setting, DTG/3TC maintained high rates of virologic suppression with improved treatment satisfaction in pre-treated participants.**
- **Discontinuations of DTG/3TC were mainly attributed to non–drug-related reasons consistent with a sustained and significant improvement in treatment satisfaction in PLHIV remaining on DTG/3TC for 2 years.**

Introduction

- Although evidence from clinical trials with DTG+3TC for first-line therapy or maintenance of viral suppression has increased remarkably during recent years, experience from routine clinical care is needed to complement the findings for diverse populations in various real-world settings.
- The URBAN cohort study (initiated in 11/2018) provides prospective real-world data on effectiveness, tolerability, weight, and patient-reported outcomes (PROs) in PLHIV using DTG and 3TC either as a two-pill regimen, and after availability in 7/2019 as a one-pill regimen.
- Here we present the 2-year results.

Methods

- URBAN is a prospective, non-interventional, 3-year German cohort study in ART-naive and pre-treated PLHIV receiving DTG/3TC in accordance with the label.
- Inclusion criteria for the year 2 full analysis set were a documented year 2 follow-up (visit window 21-27 months) or premature discontinuation.

Outcomes

- 2-year viral suppression was defined as HIV-RNA <50 c/mL in the visit window (21-27 months) or 50 to 200 c/mL with subsequent HIV-RNA <50 c/mL (discontinuation = failure; excluding missing data/lost to follow-up).
- Virologic failure is not defined within this study, but investigators may discontinue a person at any time for “virologic reasons” at their discretions.
- Persistence on DTG/3TC was estimated using Kaplan-Meier analysis.
- Treatment satisfaction and symptom burden were assessed by the HIV Treatment Satisfaction Questionnaire (status version; HIV-TSQs) and the HIV Symptom Distress Module (HIV-SDM).

Results

Study Population

- Overall, 367 PLHIV were enrolled in the URBAN cohort.
- At data cut, 352 PLHIV were eligible for full analysis dataset (91% pre-treated, 93% men, and median age at baseline 47 years; Table 1).

Table 1. Baseline (BL) Characteristics

	Pre-treated	ART-naive
Sex, male, n (%) [N]	297 (93%) [321]	30 (97%) [31]
Age, median (IQR), years [N]	48 (39-55) [321]	35 (26-42) [31]
Age ≥50 years, n (%) [N]	147 (46%) [321]	5 (16%) [31]
Body weight, median (IQR), kg [N]	80 (71-91) [230]	68 (65-82) [30]
BMI, median (IQR), kg/m^2 [N]	25 (23-28) [230]	23 (21-25) [30]
Treatment start with fixed-dose DTG/3TC, n (%) [N]	162 (50%) [321]	10 (32%) [31]
HIV-RNA, median (IQR), c/mL [N]	<50 [319]	37,200 (5100-70,700) [31]
HIV-RNA >100,000 c/mL, n (%)	1 (<1%)	3 (10%)
HIV-RNA <50 c/mL, n (%)	310 (97%)	0 (0%)
CD4+ T-cell count, median (IQR), cells/mm^3 [N]	748 (549-940) [319]	456 (328-664) [31]
History of AIDS (CDC C), n (%) [N]	42 (13) [321]	0 (0) [31]
Time since HIV diagnosis, median (IQR), years [N]	10 (5-16) [319]	0 (0-0) [31]
Time on ART, median (IQR), years [N]	7 (4-13) [290]	NA
Pre-treatment, n (%) [N]	[320]	
INSTI-based	267 (83%)	
NNRTI-based	26 (8%)	NA
PI-based	21 (7%)	
PI/INSTI-based	6 (2%)	
Most common comorbidities (≥10%), n (%) [N]	[321]	[31]
Hypertension	79 (25%)	1 (3%)
Depression	59 (18%)	3 (10%)
Chronic kidney disease	40 (12%)	0 (0%)
Insomnia	32 (10%)	2 (6%)
Lipid disorders	38 (12%)	1 (3%)

CDC, Centers for Disease Control and Prevention; IQR, interquartile range; NA, not applicable.

Pre-treated PLHIV: ART Before Switch to DTG/3TC

- The median duration of the previous ART regimen before DTG/3TC was 7 years (interquartile range [IQR]: 4-13 [n=290]).
- Of pre-treated participants, 34% had a history of >3 ART switches (Table 2A).
- Previous regimens are shown in Table 2B.

Table 2. (A) Treatment Switches Before DTG/3TC and (B) Previous ART Before DTG/3TC (in >5%)

	n (%); N=321
Participants still on first-line ART	49 (15)
1-2 switches	139 (43)
3-5 switches	82 (26)
>5 switches	26 (8)
Unknown	25 (8)

	n (%); N=321
DTG/3TC/ABC	140 (44)
DTG + FTC/TAF	42 (13)
BIC/FTC/TAF	22 (7)
DTG + FTC/TDF	19 (6)
EVG/COBI/FTC/TAF	17 (5)

ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; TAF, tenofovir alafenamide; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.

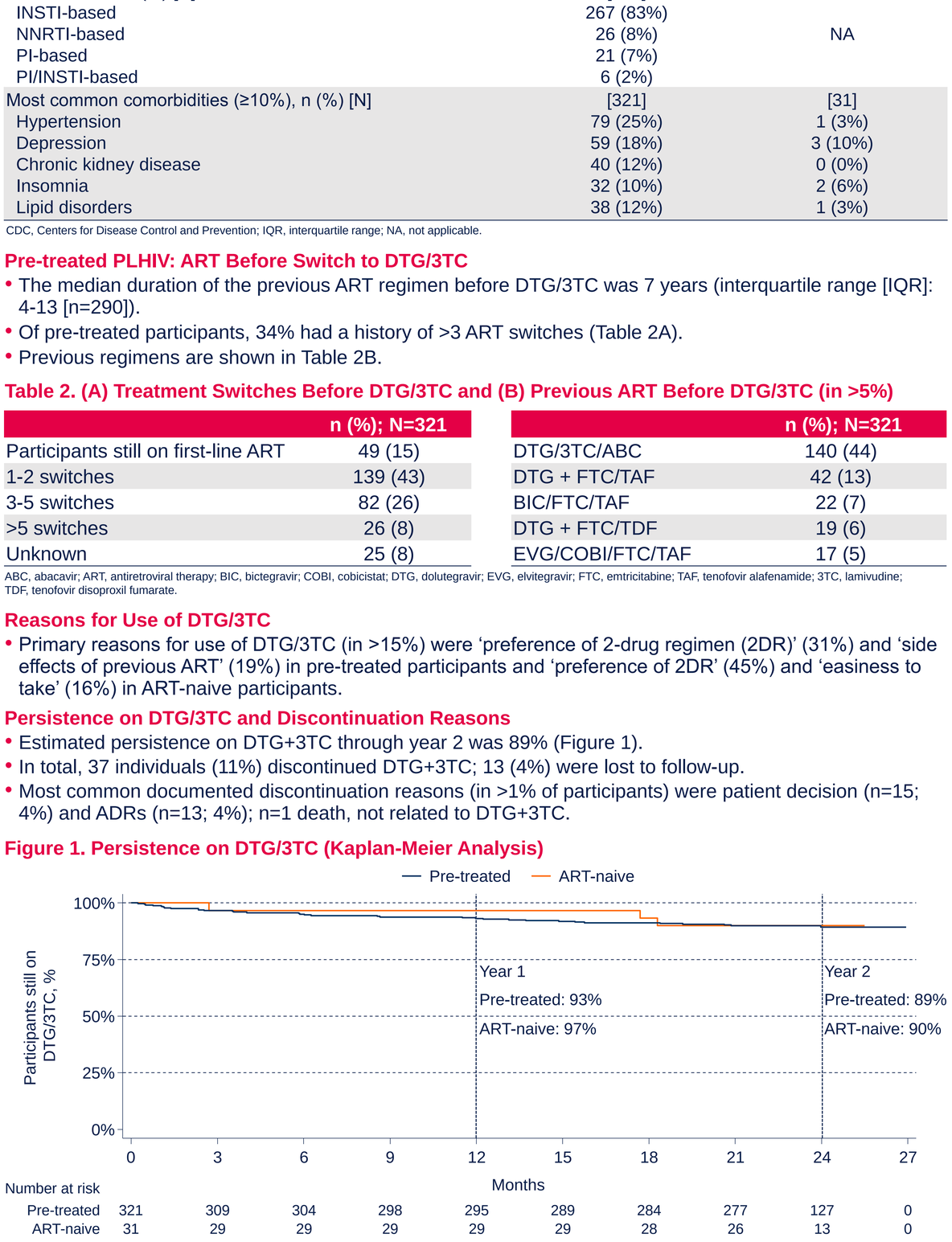
Reasons for Use of DTG/3TC

- Primary reasons for use of DTG/3TC (in >15%) were ‘preference of 2-drug regimen (2DR)’ (31%) and ‘side effects of previous ART’ (19%) in pre-treated participants and ‘preference of 2DR’ (45%) and ‘easiness to take’ (16%) in ART-naive participants.

Persistence on DTG/3TC and Discontinuation Reasons

- Estimated persistence on DTG+3TC through year 2 was 89% (Figure 1).
- In total, 37 individuals (11%) discontinued DTG+3TC; 13 (4%) were lost to follow-up.
- Most common documented discontinuation reasons (in >1% of participants) were patient decision (n=15; 4%) and ADRs (n=13; 4%); n=1 death, not related to DTG+3TC.

Figure 1. Persistence on DTG/3TC (Kaplan-Meier Analysis)



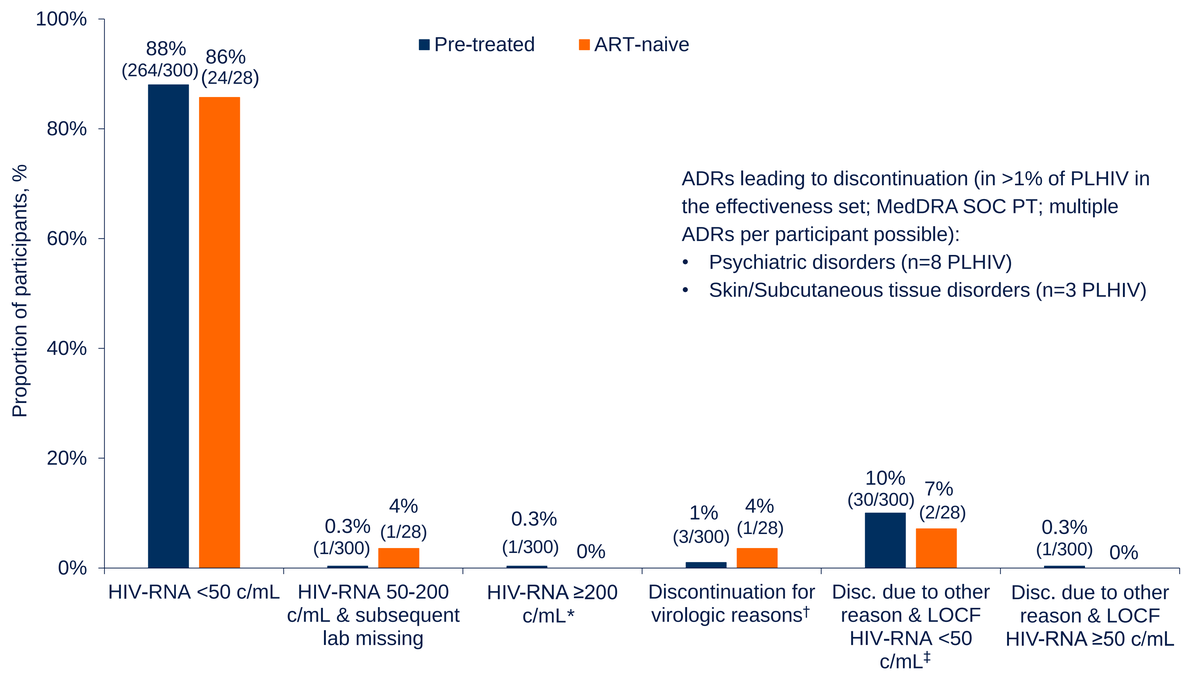
Tolerability

- Median weight change from baseline at year 2 was +2.0 kg (IQR, −1.0 to +4.0; n=127) in pre-treated PLHIV and +5.0 kg (IQR, +2.0 to +10.0; n=17) in ART-naive PLHIV.
- Until year 2, 24 non-serious ADRs (grades 1-2 [n=23]; grade 3 [n=1]) were documented in 19 PLHIV (5%); in addition, one SADR report (hospitalization; grade 3) was submitted, including 4 ADRs using Medical Dictionary for Regulatory Activities (MedDRA) PT terms (fall, brachial plexus injury, concussion, and hyponatraemia); the SADR led to discontinuation of DTG/3TC.
- Most common ADRs (MedDRA PT; n >1) were depression (n=4), sleep disorders (n=2), and headache (n=2).

Effectiveness

- 2-year viral suppression rate was 88% for pre-treated PLHIV and 86% for ART-naive PLHIV (Figure 2).
- Overall, 4 PLHIV (1%; n=3 pre-treated, n=1 ART-naive) discontinued DTG/3TC for virologic reasons at investigator’s discretion with HIV-RNA <200 c/mL.
- No emergent resistance was reported.

Figure 2. Virologic Outcomes at Year 2

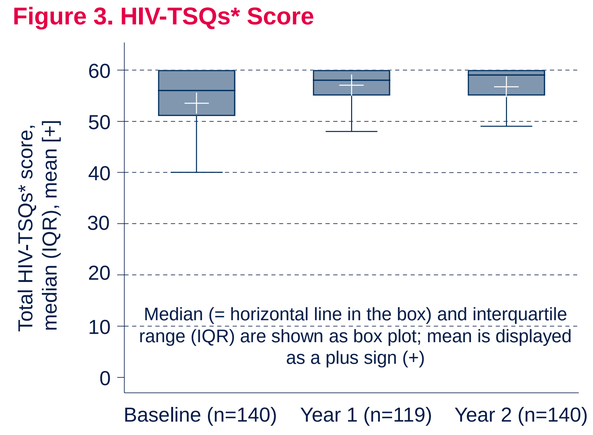


Effectiveness set: N=328; n=24/352 excluded due to missing data. *Confirmed HIV-RNA >200 c/mL (129 and 540 c/mL). †At investigator’s discretion with HIV-RNA <200 c/mL (83, 89, 95, and 128 c/mL). ‡Most common reasons (in >1% of participants) were patient decision (n=15) and ADRs (n=13); n=1 death, not related to DTG/3TC.
LOCF, last observation carried forward.

Patient-Reported Outcomes

- In pre-treated PLHIV completing questionnaires at baseline (BL) and year 2, mean (standard deviation [SD]) total HIV-TSQs score increased significantly, from 53.5 (8.4) to 56.7 (5.1), with a change of +3.2 (8.1; *P*<0.001; Figure 3).
- The total HIV-SDM score was relatively stable in pre-treated and ART-naive PLHIV completing both questionnaires (at BL and year 2; Table 3).

Figure 3. HIV-TSQs* Score



*HIV-TSQs: 10 items; range of total score 0-60; positive changes indicate improvement.

Table 3. HIV-SDM for Participants Completing Both Questionnaires (at BL and Year 2)

HIV-SDM total score*	N	Baseline	Year 1	Year 2	Change†	*P* value
Pre-treated, mean (SD)	144	14.0 (11.5)	12.5‡ (11.0)	13.0 (11.9)	−1.0 (11.4)	0.258
ART-naive, mean (SD)	11	12.1 (14.1)	10.1§ (16.7)	12.2 (12.6)	+0.1 (12.7)	0.964

BL, baseline; SD, standard deviation.
*HIV-SDM: 20 items, range of total score 0-80; negative changes indicate improvement. †Change from BL until year 2. ‡N=125. §N=10.

Conclusions

- Prospective real-world data from the URBAN cohort showed high virologic suppression rates after 2 years on DTG/3TC with low numbers of discontinuations for virologic reasons.
- In pre-treated PLHIV, a statistically significant improvement in treatment satisfaction was observed after 2 years of DTG/3TC use.

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