12-month outcomes of Dolutegravir (DTG) + Lamivudine (3TC) in ART-naïve and pre-treated PLHIV in Germany: Real-world data from the German URBAN cohort

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Background

- The URBAN cohort study (initiated in 11/2018) provides prospective real-world data regarding the effectiveness, safety, metabolic outcomes, and patient-reported outcomes (PROs) associated with dolutegravir (DTG) plus lamivudine (3TC) in people living with HIV (PLHIV) either as two-pill or – after availability in 7/2019 – as one-pill regimen.
- Here we present the month-12 (M12) outcomes.

Methods

- URBAN is a prospective, non-interventional, 3-year German cohort study in adult ART-naïve and pre-treated PLHIV receiving DTG/3TC in accordance with the label.
- Inclusion criteria for the M12 analysis set were a documented M12 follow-up (visit window 9-15 months) or discontinuation prior to M12.
- M12 viral suppression was defined as HIV-RNA<50 cp/mL in visit window (9-15 months) or 50-200 cp/mL with subsequent HIV-RNA <50 cp/mL (excluding missing data/loss-to-follow-up).
- Persistence on DTG/3TC was estimated using Kaplan-Meier analysis.
- Adverse drug reactions (ADRs) were coded by MedDRA (Medical Dictionary for Regulatory Activities) using system organ class (SOC) and preferred terms (PT).
- PRO measures included the HIV Symptom Distress Module [HIV-SDM] and the HIV Treatment Satisfaction Questionnaire [status version; HIV-TSQs].

Results

Study population

- Overall, 367 patients were enrolled across 19 study centers in the URBAN cohort.
- At data-cut, 364 PLHIV were eligible for M12 analysis, 91.5% pre-treated, 93.4% men, median age 47.0 years. Baseline characteristics are shown in Table 1.
- 181 patients (49.7%) started on the two-pill regimen; 165/181 patients (91.2%) were switched to the one-pill regimen by M12.

Table 1. Baseline characteristics

	ART-naïve (N=31)	Pre-treated (N=333)
Sex, male, n (%) [N]	30 (96.8) [31]	310 (93.1) [333]
Age, years, median (interquartile range; IQR) [N]	35 (26 – 42) [31]	49 (39 – 55) [333]
Age ≥50 years, n (%)	5 (16.1)	155 (46.5)
Body weight, kg, median (IQR) [N]	68 (65 – 82) [30]	79 (70 – 90) [236]
BMI, kg/m², median (IQR) [N]	23 (21 – 25) [30]	25 (23 – 28) [236]
HIV-1 RNA, cp/mL, median (IQR) [N]	37,200 (5,100-70,700) [31]	19 (0 – 39) [330]
HIV-1 RNA >100,000 cp/mL, n (%)	3 (9.7)	1 (0.3)
HIV-1 RNA <50 cp/mL, n (%)	0 (0.0)	319 (96.7)
CD4 T-cell count, cells/µL, median (IQR) [N]	456 (328 – 664) [31]	748 (550 – 940) [329]
History of AIDS (CDC C), n (%) [N]	0 (0) [31]	42 (12.6) [333]
Time since HIV diagnosis, years (median, IQR) [N]	0 (0 – 0) [31]	10 (5 – 16) [330]
Time on ART, years (median, IQR) [N]	n.a.	7 (4 – 13) [301]
Prevalence of comorbidities (as defined by disease categories in the eCRF), n (%) [N]	10 (32.3) [31]	189 (56.8) [333]
Most common comorbidities (>10%), n (%)		
Hypertension	1 (3.2)	82 (24.6)
Depression	3 (9.7)	62 (18.6)
Lipid disorders	1 (3.2)	41 (12.3)
Chronic kidney disease	0 (0.0)	40 (12.0)

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

ART prior to switch to DTG+3TC in pre-treated patients

- The median duration on ART before DTG+3TC was 7.0 years (IQR: 4.0 – 13.0).
- 32.7% had a history of ≥3 ART changes (Table 2a).
- Previous regimens are shown in Table 2b.

Table 2a. Treatment switches prior to DTG/3TC

	n (%); N=333
No modifications	56 (16.8)
1-2 modifications	142 (42.6)
3-5 modifications	83 (24.9)
>5 modifications	26 (7.8)
unknown	26 (7.8)

Table 2b. Previous ART prior to DTG+3TC (in >5%)*

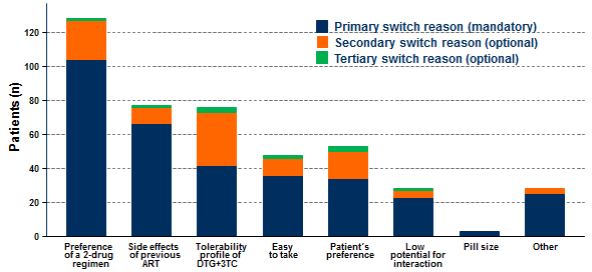
	n (%); N=333
DTG/3TC/ABC	148 (44.4)
DTG + FTC/TAF	42 (12.6)
BIC/FTC/TAF	24 (7.2)
DTG + FTC/TDF	20 (6.0)
EVG/COBI/FTC/TAF	17 (5.1)

3TC, lamivudine; ABC, abacavir; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; RPV, rilpivirine; * in pre-treated PLHIV

Reasons for use of DTG+3TC

- Primary reasons for use of DTG plus 3TC (in >15%) were 'preference of 2-drug regimen (2DR)' (31.2%) and 'side effects of previous ART' (19.8%) in pre-treated patients (Figure 1), and 'preference of 2DR' (45.2%) and 'easiness to take' (16.1%) in ART-naïve patients.

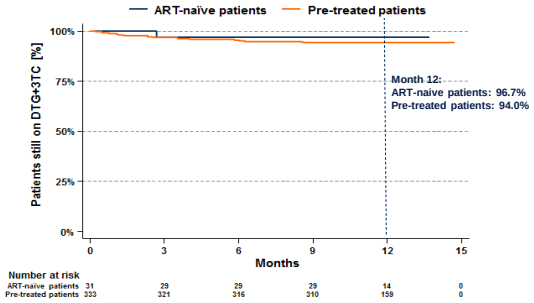
Figure 1. Primary, secondary and tertiary reasons for switch to DTG+3TC



Persistence on DTG+3TC discontinuation reasons

- Persistence on DTG+3TC through M12 was 94.2% (Figure 2).
- 21 patients discontinued DTG+3TC (5.8%), 3 patients were lost-to-follow-up and one patient withdrew consent.
- Reasons for discontinuation were ADRs (n=11 patients [3.0%]), patient wish (n=6 [1.6%]), virologic reasons (n=3 [0.8] all pre-treated) and doctor's decision (n=1 [0.3%]).

Figure 2. Persistence on DTG+3TC (Kaplan-Meier analysis)



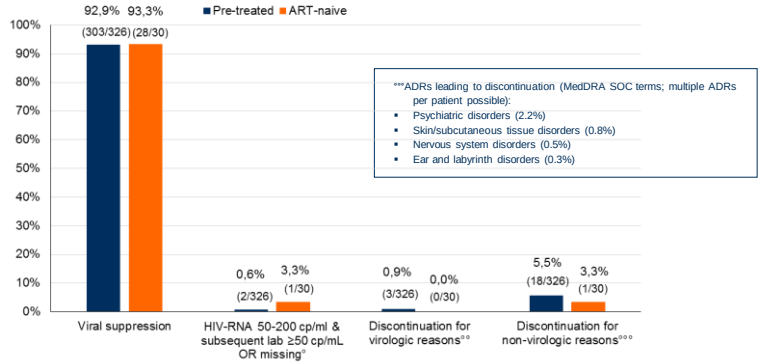
Safety

- Median weight change from baseline was +1.4 kg (IQR, -1.0–4.0; n=122) in pre-treated, and +2.0 kg (IQR, 1.0 – 6.0; n=15) in ART-naive PLHIV.
- Until data-cut, 23 ADRs (grades 1-2, none serious) were reported in 18 PLHIV (4.9%).
- Most common ADRs (>1 event) were depression (n=3), sleep disorders (n=2) and headache (n=2).

Effectiveness

- Viral suppression rate at M12 was 92.9% for pre-treated and 93.3% for ART-naïve PLHIV (Figure 3).
- Overall, 3 patients were discontinued due to virologic reasons (at investigator's discretion, while HIV-RNA was <200 copies/mL).
- No treatment-emergent resistance was reported (resistance testing was available in 7 participants).

Figure 3. Virologic outcomes at month 12



Effectiveness set: N=356; n=8/364 with missing data; °incl. n=1 with subsequent lab (57 and 50 cp/mL), n=2 with missing subsequent lab; °° at investigator's discretion with HIV-RNA<200 cp/mL; °°°Most common reasons (in >1% of patients) were adverse drug reactions (ADRs): 3.0%, n=11), and patient decision (1.9%, n=7).

Patient reported outcomes

- For pre-treated PLHIV completing questionnaires at baseline and M12, PROs changed statistically significantly: the median total HIV-SDM score decreased from 12.0 (IQR, 4.0–22.0) to 8.0 (3.0–18.0; p<0.001); HIV-TSQs score increased from 56.0 (51.0–60.0) to 59.0 (56.0–60.0; p<0.001) (Table 3).

Table 3. Patient reported outcomes

Pre-treated N	Baseline Total score; median (IQR)	Month 12 Total score; median (IQR)	Month 12 Change from baseline median (IQR)	p-value (Wilcoxon-sign-rank test)
HIV-SDM^ 211	12.0 (4.0 – 22.0)	8.0 (3.0 – 18.0)	-2.0 (-7.0 – +2.0)	<0.001
HIV-TSQs* 202	56.0 (51.0 – 60.0)	59.0 (56.0 – 60.0)	+1.0 (0.0 – +6.0)	<0.001

^HIV-SDM: 20 items, range of total score 0-80; negative changes indicate score improvement;

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

Due to small sample size, PROs in ART-naïve PLHIV were not analyzed for statistically significant differences from baseline; the median total HIV-SDM score decreased from 8.5 (IQR, 1.0–22.0) to 7.0 (1.0–16.0; n=14). The median HIV-TSQs at month 12 was 58.0 (55.0–60.0; n=15).

Conclusions

- DTG+3TC use in a real-world setting showed high virologic suppression rates after one year with low numbers of discontinuations for virologic reasons (0.8%) and 0 cases of resistance development.
- In pretreated PLHIV, who made up the majority of the URBAN cohort, symptom distress and treatment satisfaction improved significantly.

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