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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PE2/52

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%)*

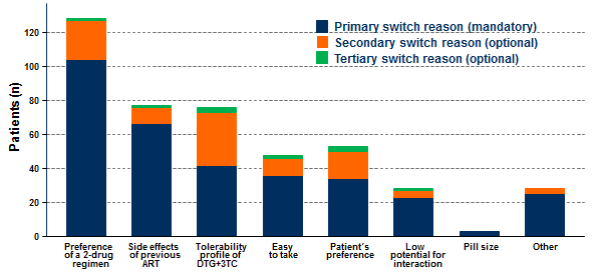
	n (%); N=333
DTG/3TC/ABC	148 (44.4)
DTG + FTC/TAF	42 (12.6)
BIC/FTC/TAF	24 (7.2)
DTG + FTC/TDF	20 (6.0)
EVG/COBI/FTC/TAF	17 (5.1)

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.

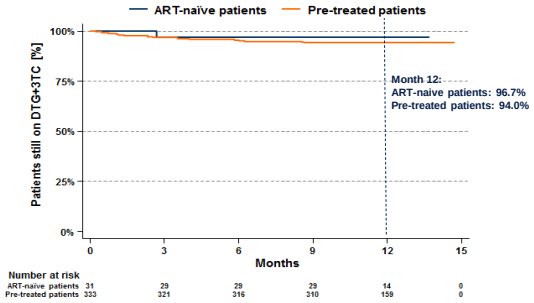
Figure 1. Primary, secondary and tertiary reasons for switch to DTG+3TC



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)



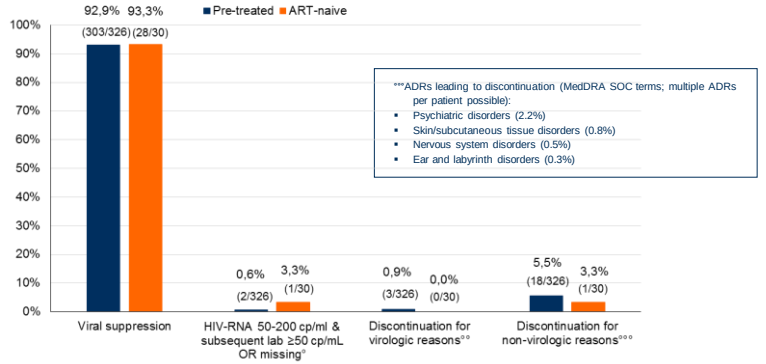
Safety

- 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.

Acknowledgments

Special thanks to the participating patients and investigators of the URBAN study centers: MVZ am Isartor/Munich; ICH/Hamburg; IZ Steglitz/Berlin; Klinikum Osnabrueck/Osnabrueck; MEDCENTER/Weimar; MVZ München am Goetheplatz/Munich; Onkologie Mannheim/Mannheim; Praxis City Ost/Berlin; Praxis Cordes/Berlin; Praxis Ebertplatz/Cologne; Praxis Hohenstaufenring/Cologne; Praxis Jessen/Berlin; Praxis Kaiserdamm/Berlin; Praxis Knechten/Aachen; Praxis UBN/Berlin; Praxis Wuensche/Berlin; PRINZMED/Munich; UNI Hamburg/Hamburg; WIR/Bochum.

Statistical analysis and support in medical writing were provided by MUC Research. The study is sponsored by ViiV Healthcare, Germany.

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