3-Year Outcomes for Dolutegravir (DTG) + Lamivudine (3TC) in ART-Naive and Pre-treated People Living With HIV-1 (PLHIV) in Germany: Real-world Data From the German URBAN Cohort

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Sebastian Noe,[1] Stefan Scholten,[2] Christoph Wyen,[3] Michael Sabranski,[4] Nils Postel,[5] Olaf Degen,[6] Daniel Beer,[7] Kevin Ummard-Berger,[8] Bernd Westermayer,[9] Kathrin M. Dymek,[10] Jenny Scherzer[10]

[1]MVZ München am Goetheplatz, Munich, Germany; [2]Praxis Hohenstaufenring, Cologne, Germany; [3]Praxis Ebertplatz, Cologne, Germany; [4]ICH Study Center, Hamburg, Germany; [5]prinzmed, Munich, Germany; [6]Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; [7]Praxis Dr. H. Knechten, Aachen, Germany; [8]UBN/Praxis, Berlin, Germany; [9]GSK, Munich, Germany; [10]ViiV Healthcare, Munich, Germany

Key Takeaways

- **URBAN is a prospective, non-interventional, 3-year cohort study in antiretroviral therapy (ART)-naive and pre-treated people living with HIV-1 (PLHIV) receiving dolutegravir and lamivudine (DTG + 3TC) in Germany**
- **DTG + 3TC maintained high rates of virologic suppression after 3 years in both pre-treated and ART-naive PLHIV in a real-world setting**
- **Through 3 years of DTG + 3TC treatment, changes in lipid and liver parameters from baseline were minimal**
- **Significant improvements in treatment satisfaction were observed in pre-treated individuals through 3 years**

Introduction

- Although clinical trials have assessed DTG + 3TC for first-line therapy and maintenance of virologic suppression,[1-3] clinical practice observations can complement these data in more diverse populations
- The URBAN study provides real-world data on effectiveness, tolerability, metabolic parameters, and patient-reported outcomes (PROs) in PLHIV using DTG + 3TC
- Here we present Year 3 results

Methods

- URBAN is a prospective, non-interventional, multi-center, 3-year German cohort study (initiated 11/2018) in ART-naive and pre-treated PLHIV receiving DTG + 3TC in accordance with the label
  - DTG + 3TC was used as a 2-pill regimen and/or a 1-pill regimen (after availability in 7/2019)
- Inclusion criteria for the Year 3 full analysis set were a documented Year 3 follow-up or treatment discontinuation

Outcomes

- The primary endpoint was proportion of individuals with virologic suppression (HIV-1 RNA <50 or 50-200 c/mL with subsequent HIV-1 RNA <50 c/mL within 120 days; discontinuation = failure) at 3-year follow-up
- A key exploratory endpoint was proportion of individuals with virologic suppression (HIV-1 RNA <50 c/mL) through 3 years based on missing = excluded (M = E) and discontinuation = failure (D = F; individuals discontinuing DTG + 3TC before the visit window had viral load imputed as ≥50 c/mL) analyses
- Virologic failure was not protocol-defined in this real-world study; however, investigators could discontinue a person at any time for "virologic reasons" at their discretion
- Tolerability, lipids, and liver parameter changes were evaluated at 3-year follow-up
- PROs were assessed via the HIV Treatment Satisfaction Questionnaire, status version (HIV-TSQs)[4] and the HIV Symptom Distress Module (HIV-SDM)[5]

Results

Study Population

- Among 366 individuals, median baseline age was 47 years; 93.2% were male (Table 1)
- Overall, 332/366 (90.7%) individuals were eligible for the primary analysis; those with missing data (n=8) or lost to follow-up (n=26) were excluded
- In pre-treated individuals, median time on ART before switch to DTG + 3TC was 7 years (IQR, 4-13; n=303), and 32.8% had a history of ≥3 ART switches

Table 1. Demographics and Baseline Characteristics

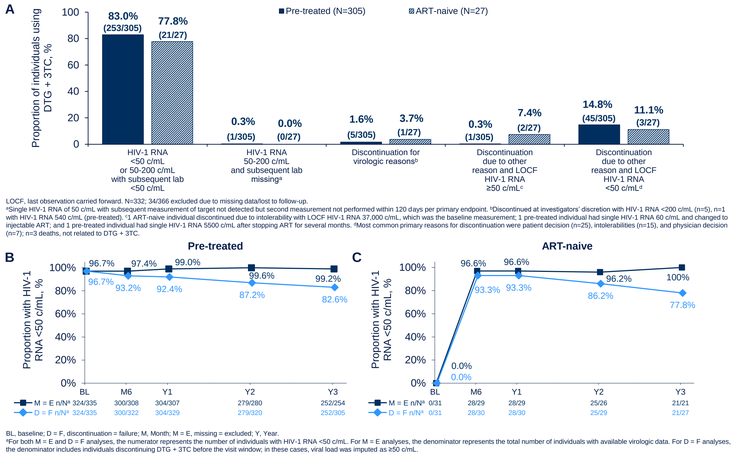
Parameter	ART-naive (N=31)	Pre-treated (N=335)
Age, median (range), y	35 (21-55)	49 (22-82)
<50 y, n (%)	26 (83.9)	180 (53.7)
50-65 y, n (%)	5 (16.1)	135 (40.3)
>65 y, n (%)	0	20 (6.0)
Sex, male, n (%)	30 (96.8)	311 (92.8)
BMI, median (IQR), kg/m²	23 (21-25)	25 (23-28)
HIV-1 RNA, median (IQR), c/mL	37,200 (5100-70,700)	19 (0-39)
<50 c/mL, n (%)	0	324 (96.7)
50 to <200 c/mL, n (%)	2 (6.5)	7 (2.1)
200 to 100,000 c/mL, n (%)	26 (83.9)	3 (0.9)
>100,000 c/mL, n (%)	3 (9.7)	1 (0.3)
CD4+ cell count, median (IQR), cells/mm³	456 (328-664)	748 (549-940)
<200 cells/mm³, n (%)	4 (12.9)	2 (0.6)
Time on ART, median (IQR), y	NA	7 (4-13)
No. of treatment switches, n (%)		
Still on first-line ART	NA	56 (16.7)
1-2		143 (42.7)
≥3		110 (32.8)
Unknown		26 (7.8)
Most common (≥5%) prior ART regimens, n (%)		
DTG/ABC/3TC	NA	148 (44.2)
DTG + FTC/TAF		42 (12.5)
BIC/FTC/TAF		25 (7.5)
DTG + FTC/TDF		20 (6.0)
EVG/COBI/FTC/TAF		17 (5.1)
Most common comorbidities (>10%), n (%)[a]		
Depression (acute or status post)	3 (9.7)	114 (34.0)
Hypertension	1 (3.2)	85 (25.4)
Lipidemia disorder	1 (3.2)	45 (13.4)
Chronic kidney insufficiency	0	40 (11.9)
Insomnia	2 (6.5)	35 (10.4)

ABC, abacavir; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; NA, not applicable; TAF, tenofovir alafenamide; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate. [a]Relevant concomitant diseases according to ICD-10 chapter (per participant total, multiple answers possible).

Virologic Suppression

- Year 3 virologic suppression rates were 83.0% (253/305) for pre-treated and 77.8% (21/27) for ART-naive individuals (Figure 1A)
- Rates of virologic suppression through 3 years were high in both M = E and D = F analyses in pre-treated and ART-naive individuals (Figure 1B-C)
- Overall, 1.8% (6/332) of individuals discontinued DTG + 3TC for virologic reasons at investigator's discretion with HIV-1 RNA ≥50 c/mL (n=5 pre-treated, n=1 ART-naive)
  - HIV-1 RNA at discontinuation was 138, 89, 540, 83, and 128 c/mL (pre-treated) and 95 c/mL (ART-naive)
- In 1 pre-treated individual without a historical resistance test, integrase mutations T97A, E138K, and N155H were detected at Month 24 (HIV-1 RNA 540 c/mL), which in combination confer low-level resistance to DTG.[6] Viral load was re-suppressed (<40 c/mL) at treatment discontinuation at Month 25. HIV history other than immediate prior ART (DTG + TAF/FTC) is unknown. Participant switched to DRV/c/FTC/TAF + DTG

Figure 1. (A) Primary Endpoint: Virologic Suppression at Year 3 and Exploratory Endpoint: Virologic Suppression Using M = E and D = F Analyses in (B) Pre-Treated and (C) ART-Naive Individuals



BL, baseline; D = F, discontinuation = failure; M, Month; M = E, missing = excluded; Y, Year.
[a]For both M = E and D = F analyses, the numerator represents the number of individuals with HIV-1 RNA <50 c/mL. For M = E analyses, the denominator represents the total number of individuals with available virologic data. For D = F analyses, the denominator includes individuals discontinuing DTG + 3TC before the visit window; in these cases, viral load was imputed as ≥50 c/mL.

Tolerability

- Through Year 3, 21 adverse drug reactions (ADRs; grade 1-2, n=20; grade 3, n=1) were documented in 20 individuals (5.5%)
  - The most common ADRs (Medical Dictionary for Regulatory Activities [MedDRA] preferred term; n >1) were depression (n=5), sleep disorder (n=2), and headache (n=2)
- 2 serious ADRs were reported in 2 individuals (MedDRA preferred term: anemia, fall, brachial plexus injury, concussion, and hyponatremia)
- 59 non–treatment-related serious adverse events were documented in 39 individuals (10.7%)
- 15 individuals discontinued due to intolerability (4.1%; n=12 pre-treated, n=3 ART-naive)
  - The most common ADRs (MedDRA system organ class) leading to discontinuation were psychiatric disorders (n=10), skin and subcutaneous tissue disorders (n=3), and nervous system disorders (n=2)

Metabolic Parameters

- Overall, 4 treatment discontinuations due to weight gain were reported (pre-treated; 1 investigator decision, 3 patient wish)
- Among individuals with weight data at both time points, median (IQR) weight change from baseline at Year 3 was 2.0 kg (−1.0, 6.0; n=131) in pre-treated and 5.0 kg (1.0-10.0; n=13) in ART-naive individuals
- Lipid and liver parameter changes from baseline were minimal (Figure 2)

Patient-Reported Outcomes

- Pre-treated individuals who completed baseline and Year 3 questionnaires had statistically significantly increased HIV-TSQs scores at Year 3 (Figure 3), consistent with the significant improvements observed at Years 1 and 2[7,8]
- HIV-SDM scores remained stable (Table 2)

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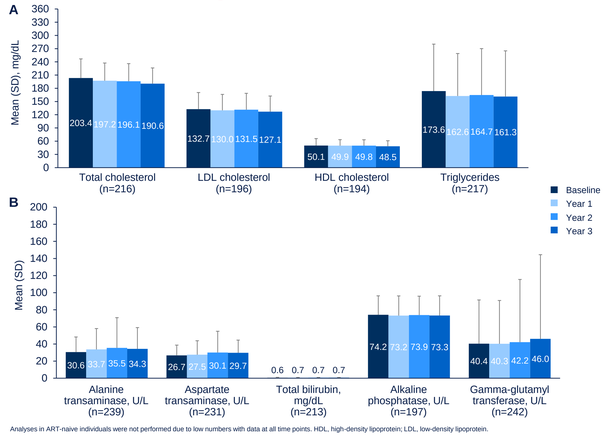
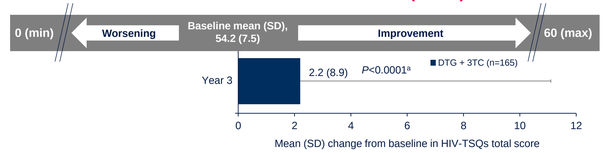
References: 1. Cahn et al. *AIDS.* 2022;36:39-48. **2.** Osiyemi et al. *Clin Infect Dis.* 2022;75:975-986. **3.** Llibre et al. *Clin Infect Dis.* 2023;76:720-729. **4.** Woodcock and Bradley. *Qual Life Res.* 2001;10:517-531. **5.** Justice et al. *J Clin Epidemiol.* 2001;54(suppl 1):S77-S90. **6.** Stanford University HIV Drug Resistance Database. https://hivdb.stanford.edu/. Accessed September 25, 2023. **7.** Scholten et al. EACS 2021; London, UK. Poster PE2/52. **8.** Beer et al. HIV Drug Therapy Glasgow 2022; Glasgow, Scotland. Poster P117.

Figure 2. Change in (A) Lipid and (B) Liver Laboratory Parameters by Year in Pre-treated Individuals Using DTG + 3TC Who Had Data at All Time Points



Analyses in ART-naive individuals were not performed due to low numbers with data at all time points. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Figure 3. Mean Change From Baseline to Year 3 in HIV-TSQs Among Pre-treated Individuals With Data at Both Time Points (n=165)



HIV-TSQs: 10-item version. Range per item is 0-6: 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of items 1-10; range for total score is 0-60; positive changes indicate improvement.[4] HIV-TSQs scores were not assessed at baseline in ART-naive individuals; mean (SD) HIV-TSQs score at Year 3 was 58.9 (2.0; n=12). [a]Wilcoxon signed rank test.

Table 2. HIV-SDM Scores for Individuals Completing Both Baseline and Year 3 Questionnaires

HIV-SDM total score[a]	n	Baseline	Year 3	Change from baseline at Year 3	*P* value
Pre-treated, mean (SD)	165	14.2 (12.2)	14.3 (12.4)	0.1 (9.6)	0.7607[b]
ART-naive, mean (SD)	10	10.8 (10.1)	7.6 (8.7)	−3.2 (8.0)	—[c]

HIV-SDM, HIV Symptom Distress Module. [a]20-item questionnaire with total score ranging from 0-80; decreases indicate improvement.[5] [b]Wilcoxon signed rank test. [c]Due to small sample size, HIV-SDM scores in ART-naive individuals were not analyzed for statistically significant differences from baseline.

Limitations

- Fewer than half of the total population had available data at baseline and Year 3 for the weight and PRO analyses

Conclusions

- Over 3 years, high virologic suppression rates with DTG + 3TC were observed
- Few discontinuations for virologic reasons were reported; integrase resistance-associated mutations conferring low-level resistance to DTG were detected in 1 participant at Month 24
- Treatment was well tolerated, with minimal changes in lipid and liver parameters
- Pre-treated individuals maintained statistically significant improvements in treatment satisfaction at Year 3, consistent with findings from Years 1 and 2 and supporting stable improvements in treatment satisfaction[7,8]

Corresponding author: Jenny Scherzer; jenny.x.scherzer@viivhealthcare.com

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