Real-world data from the prospective URBAN cohort study on the use of Dolutegravir (DTG) + Lamivudine (3TC) in ART-naïve and pre-treated people living with HIV in Germany

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Methods

- URBAN is a prospective, non-interventional, 3-year German cohort study in ART-naïve and pre-treated patients receiving DTG plus 3TC (either as two tablets or – after availability in 7/2019 – as single tablet regimen) in accordance with the label.
- Inclusion criteria for M6 full analysis set (FAS) were a documented M6 follow-up (visit window 4.5-9 months) or premature discontinuation.
- PROs were assessed using validated questionnaires (HIV Symptom Distress Module [HIV-SDM] and Treatment Satisfaction [HIV-TSQ]).
- **Outcomes**
  - Month-6 (M6) viral suppression defined as HIV-RNA level [cp/mL] <50 or 50-200 with subsequent HIV-RNA <50 in the effectiveness set (missing=excluded)
  - Persistence on study and/or DTG/3TC estimated using Kaplan-Meier analysis
  - Adverse drug reactions (ADRs) coded by MedDRA (Medical Dictionary for Regulatory Activities) using system organ class (SOC) and preferred terms (PT)
  - PRO measures at baseline and M3: mean/median total HIV-SDM and HIV-TSQ scores and changes from baseline

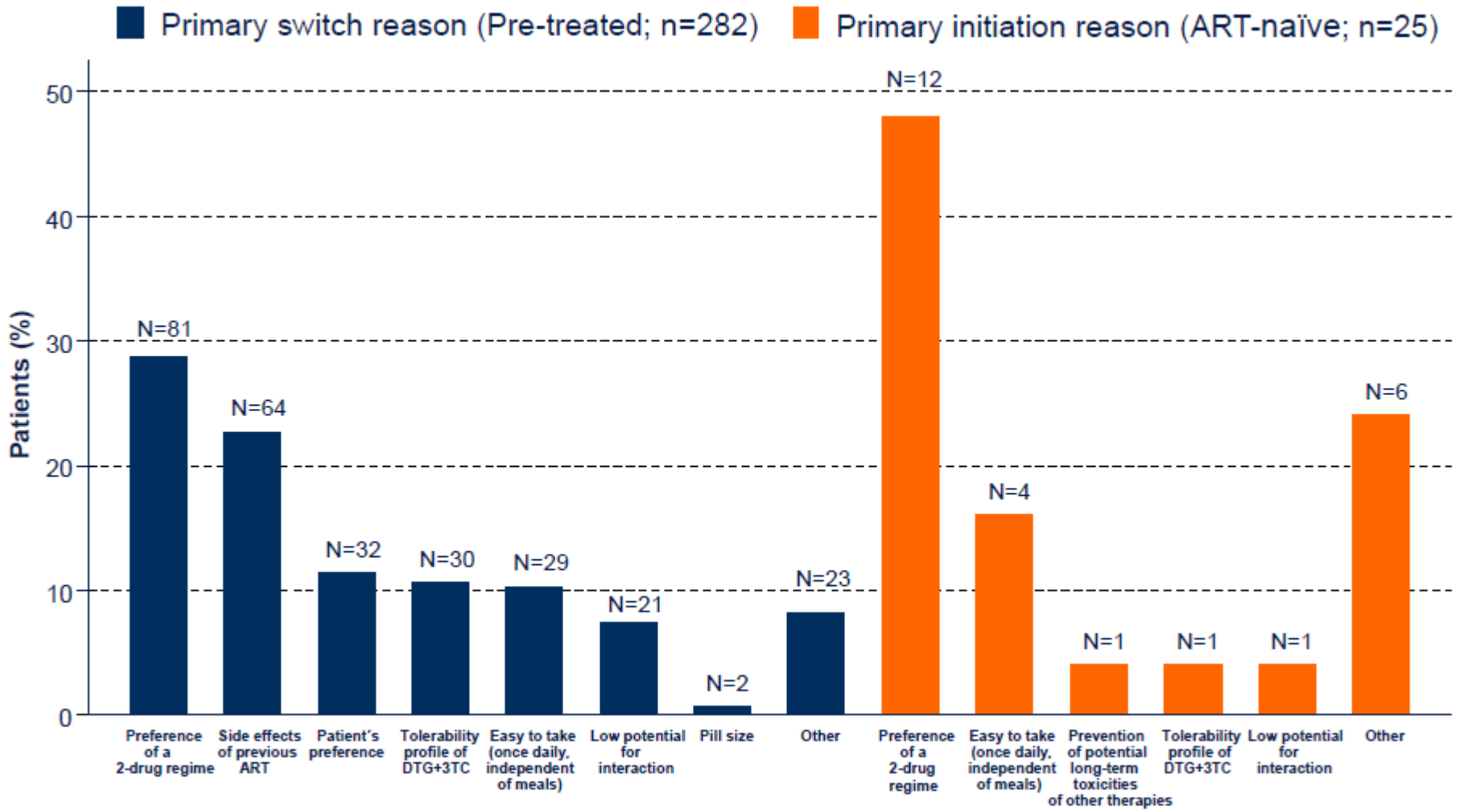
Baseline characteristics

- Overall, 367 patients were enrolled
- M6 FAS included 307 patients (92% pre-treated, 93% men, median age 48 years).
- Of pre-treated participants, 33% had a history of >3 ART regimens. Baseline HIV-RNA was <50 cp/mL in 96% of pre-treated patients; median HIV-RNA in ART-naïves was 37,100 copies/mL. Baseline characteristics are shown in Table 1.

	Pre-treated	ART-naïve
Sex, male, n (%) [N]	262 (93) [282]	24 (96) [25]
Age, years, median (IQR) [N]	49 (39 – 55) [282]	35 (26 – 46) [25]
Age ≥50 years, n (%) [N]	132 (47) [282]	5 (20) [25]
Body weight, kg, median (IQR) [N]	79 (70 – 90) [219]	68 (65-83) [25]
BMI, kg/m^2, median (IQR) [N]	25 (23 – 28) [217]	23 (21 – 25) [25]
Treatment start with fix-dose DTG/3TC, n (%) [N]	123 (44) [282]	5 (20) [25]
HIV-1 RNA, cp/mL, median (IQR) [N]	<50 [277]	37,100 (5,100-66,550) [25]
HIV-1 RNA >100,000 cp/mL, n (%)	1(<1)	1 (4)
HIV-1 RNA <50 cp/mL, n (%)	267 (96)	0 (0)
CD4 T-cell count, cells/µL, median (IQR) [N]	738 (544 – 942) [277]	475 (386 – 664) [25]
History of AIDS (CDC C), n (%) [N]	36 (13) [282]	0 (0) [25]
Time since HIV diagnosis, years (median, IQR) [N]	10 (5 – 16) [279]	0 (0 – 0) [25]
Time on ART, years (median, IQR) [N]	7 (4 – 12) [253]	n.a.
Pretreatment, n (%)		
INSTI-based	231 (83)	n.a.
NNRTI-based	23 (8)	
PI-based	20 (7)	
PI/INSTI-based	6 (2)	
Most common comorbidities (>10%), n (%) [N]	[282]	[25]
Hypertension	67 (24)	0 (0)
Depression	54 (19)	3 (12)
Chronic kidney disease	39 (14)	0 (0)
Insomnia	31 (11)	1 (4)
Lipid disorders	31 (11)	0 (0)

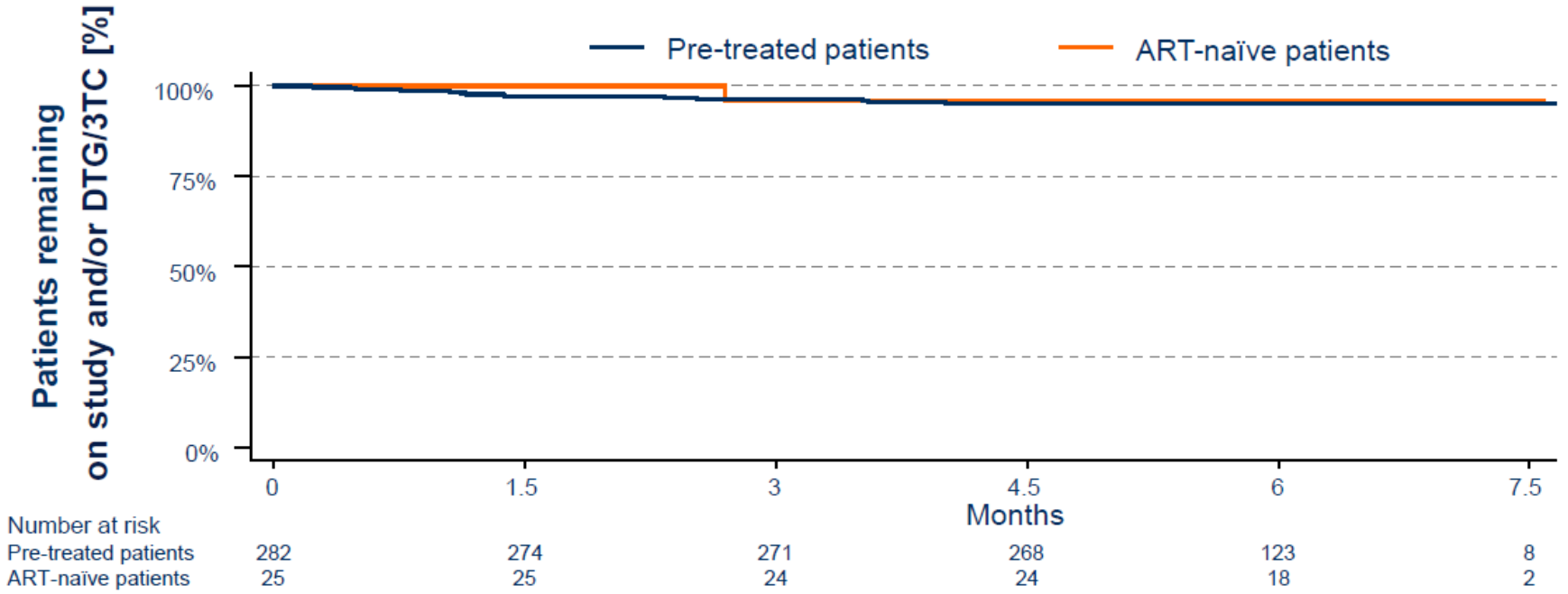
IQR: interquartile range; n.a.: not applicable

Primary reasons for use of DTG/3TC

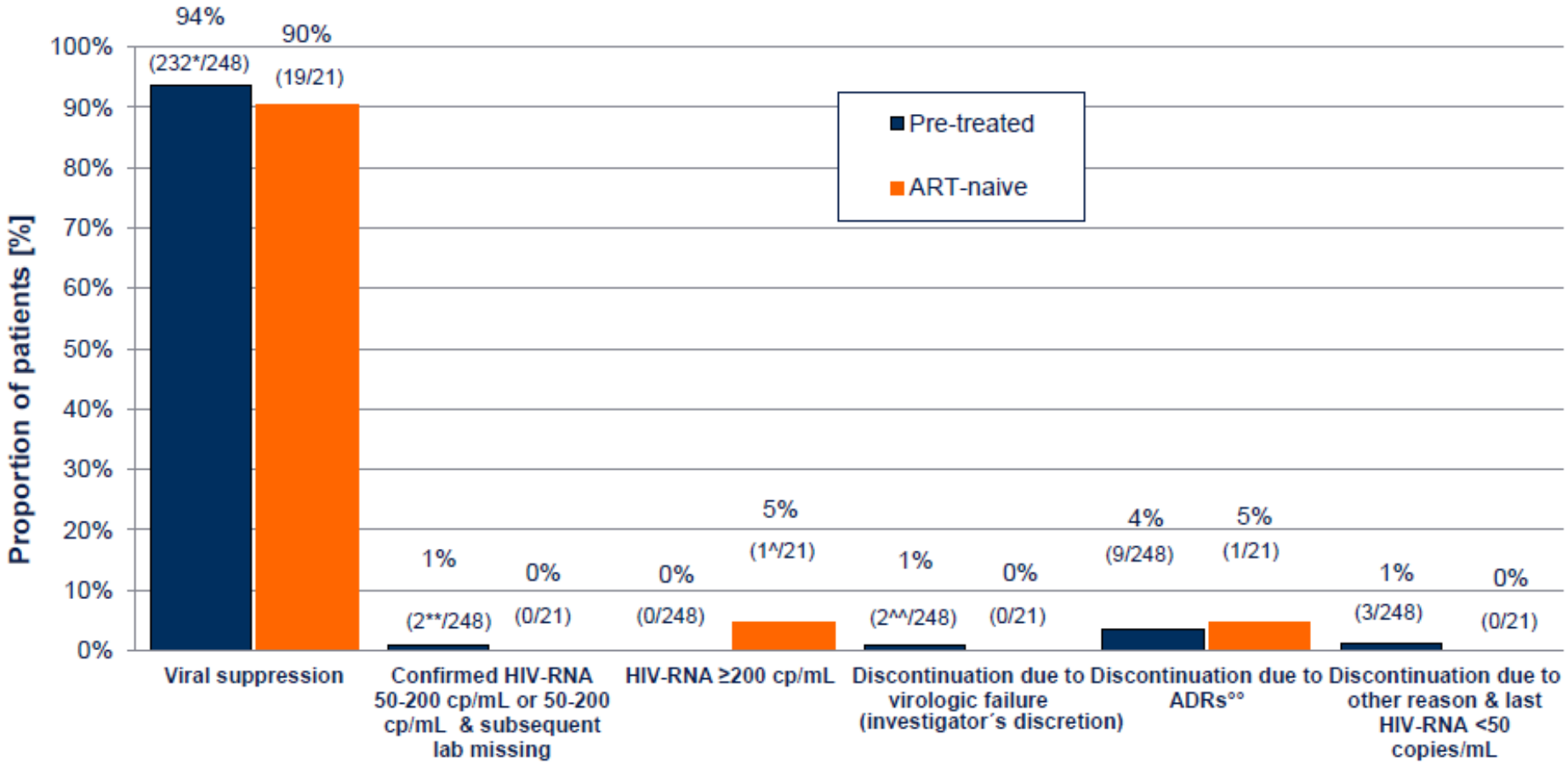


Persistence on study and/or DTG/3TC (Kaplan-Meier analysis)

- Estimated persistence on study and/or DTG/3TC through M6 was 95%
- 5% of patients (n=15/307) discontinued the study; reasons were adverse drug reactions (ADRs; 3.3%), virologic failure (investigator´s discretion) (0.7%; n=2 with <200 copies/mL [without new resistance mutations, in one patient INI resistance test was not available]), patient wish (0.3%), withdrawal of consent (0.3%) and doctor's decision (0.3%).



Virologic outcomes at M6 (effectiveness set: N=269; n=38/307 with missing data)



*including n=4 with 50-200 cp/mL & subsequent HIV-RNA level <50 cp/mL; **n=1 with confirmed 50-200 cp/mL; ^n=1 with 360 cp/mL at M6 and 1,100,000 cp/mL at baseline; ^^n=2 with a single HIV-RNA measurement of 128 and 89 cp/mL, respectively; °°ADRs (adverse drug reactions) (MedDRA SOC terms; multiple ADRs per patient possible) leading to discontinuation in >1% of the analysis set (N=269): psychiatric disorders (3%), skin and subcutaneous tissue disorders (1%).

Safety

- Until M6, 22 ADRs (grades 1-2) were documented in 17 patients (6%).
- No serious ADR was reported.
- In 10 patients (3%), ADRs led to DTG/3TC discontinuation (n=13; several ADRs per patient possible; most common ADR (MedDRA PT) was depression (n=3 [1%]).
- The following body weight changes through M6 were reported:
  - Median weight changes were +2.0 kg (IQR: -3.0 kg - +8.0 kg; n=7) in ART-naïve patients and +1.0 kg (-1.0 kg – +3.3 kg; n=104) in pre-treated patients.
  - No ADR or discontinuation due to weight gain were reported

Patient Reported Outcomes

- In pre-treated patients completing PRO questionnaires at both time-points, mean changes in HIV-SDM and HIVTSQ were -3.1 (p<0.001) and +2.5 (p<0.001), respectively

Table 2. Patient-reported outcomes in patients completing baseline and month-3 (M3) questionnaires

	Pre-treated patients	ART-naïve patients
HIV Symptom Distress Module (HIV-SDM)^, N	194 of 282	13 of 25
Baseline total score; mean/median (IQR)	14.5/12.0 (5.0 - 22.0)	12.2/9.0 (3.0 - 15.0)
M3 total score; mean/median (IQR)	11.4/8.0 (2.0 - 17.0)	7.6/3.0 (1.0 - 7.0)
Change from baseline mean/median (IQR)^^	-3.1/-3.0 (-8.0 - +1.0)	-4.6/-3.0 (-9.0 - ± 0.0)
p-value (Wilcoxon signed-rank test)	<0.001	0.068
HIV Treatment Satisfaction (HIV-TSQ)*, N	193	17
Baseline total score; mean/median (IQR)	53.4/56.0 (50.0 - 60.0)	n.a.
M3 total score; mean/median (IQR)	56.0/58.0 (53.0 - 60.0)	54.6/56.0 (54.0 - 58.0)
Change from baseline mean/median (IQR)**	+2.5/±0.0 (±0.0 – +4.0)	n.a.
p-value (Wilcoxon signed-rank test)	<0.001	n.a.

^HIV-SDM: 20 items, range of total score 0-80; ^^negative changes indicate improvement;
*HIVTSQ: range of total score 0-60; **positive changes indicate improvement; IQR: interquartile range

Conclusions

- DTG/3TC showed a high acceptance in ART-naïve and pre-treated patients with a persistence of 95% until month 6 and a viral suppression rate of 93%.
- Patients reported significant improvements in symptom distress and treatment satisfaction after the first months of treatment

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