3-Year Outcomes of Dolutegravir/Rilpivirine in Virologically Suppressed HIV-Infected PLHIV: Real-world Data From the Prospective German JUNGLE Cohort

P086

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Key Takeaways

- **JUNGLE is a non-interventional, prospective, 3-year, multi-centre cohort study in people living with HIV (PLHIV) on suppressive antiretroviral therapy (ART) switched to co-formulated dolutegravir/rilpivirine (DTG/RPV) in accordance with the label in Germany.**
- **Discontinuations of DTG/RPV were mainly attributed to non–drug-related reasons consistent with a sustained and significant improvement in treatment satisfaction in PLHIV remaining on DTG/RPV for 3 years.**
- **In a real-world setting, DTG/RPV was effective in maintaining virologic suppression with no discontinuations for virologic reasons over 3 years.**

Introduction

- Switching to DTG/RPV for maintenance of viral suppression is supported by large randomized clinical trials, retrospective cohorts and is a recommended switch strategy in European guidelines [1-5].
- The German JUNGLE cohort provides prospective real-world data, focusing on virologic effectiveness, tolerability, and patient-reported outcomes.
- Here we present the 3-year data.

Methods

- JUNGLE is a non-interventional, prospective, 3-year, multi-centre cohort study in people living with HIV (PLHIV) on suppressive antiretroviral therapy (ART) switched to co-formulated DTG/RPV in accordance with the label.

Main Inclusion Criteria

- Adult PLHIV on suppressive ART for ≥6 months switched to DTG/RPV
- No history of virologic failure
- No INSTI or NNRTI resistance mutations
- No hepatitis B coinfection
- No contraindication based on the summary of product characteristics (SmPC)

Outcomes

- Viral suppression at year 3 was defined as HIV-RNA <50 c/mL in the data window 33 to 39 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 study and/or DTG/RPV was estimated using Kaplan-Meier analysis.
- Adverse drug reactions (ADRs) were coded using the Medical Dictionary for Regulatory Activities (MedDRA) by system organ class (SOC) and preferred term (PT).
- Patient-reported symptom burden and treatment satisfaction were assessed using the HIV Symptom Distress Module (HIV-SDM) and the HIV Treatment Satisfaction Questionnaire (10-item status version; HIV-TSQs).

Results

Study Population

- 200 PLHIV were enrolled across 24 study centres in the JUNGLE cohort.
- At data cut (April 2022), 176 participants were eligible for analysis (n=24 excluded due to missing follow-up data/year 3 visit window not yet reached). Baseline characteristics are shown in Table 1.

Table 1. Baseline Characteristics

	Total	N
Sex, male, n (%)	159 (90)	176
Age, median (IQR), years	48 (40-57)	176
Age ≥50 years, n (%)	82 (47)	176
BMI, median (IQR), kg/m^2	24 (22-27)	149
CD4+ T-cell count, median (IQR), cells/mm^3	720 (585-936)	176
History of AIDS (CDC C), n (%)	29 (16)	176
Time since HIV diagnosis, median (IQR), years	11 (6-16)	173
Time on ART, median (IQR), years	8 (5-13)	156
Documented comorbidities, n (%)	110 (63)	176
Most common comorbidities (>10%), n (%)		176
Hypertension	55 (31)	
Depression	32 (18)	
Lipid disorders	29 (16)	
Insomnia	25 (14)	
Chronic kidney disease	23 (13)	

CDC, Centers for Disease Control and Prevention; IQR, interquartile range.

ART Before Switch to DTG/RPV

- The median duration of the previous ART regimen before DTG/RPV was 2.6 years (interquartile range [IQR]: 1.6-4.8 [n=161]).
- Of 176 participants, 11% switched from first-line ART; 41% had a history of ≥3 treatment switches (Table 2A).
- 86% of participants were switched from triple ART; 48% had been on a multi-tablet regimen.

Table 2. (A) Treatment Switches Before DTG/RPV and (B) Last ART Before DTG/RPV (in >5%)

	n (%); N=176
Participants still on first-line ART	19 (11)
1-2 switches	75 (43)
≥3 switches	73 (41)
Unknown	9 (5)

	n (%); N=176
DTG/3TC/ABC	26 (15)
RPV/FTC/TAF	21 (12)
DTG + RPV	14 (8)
EFV/FTC/TDF	13 (7)
EVG/COBI/FTC/TAF	13 (7)
DTG + FTC/TAF	10 (6)

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

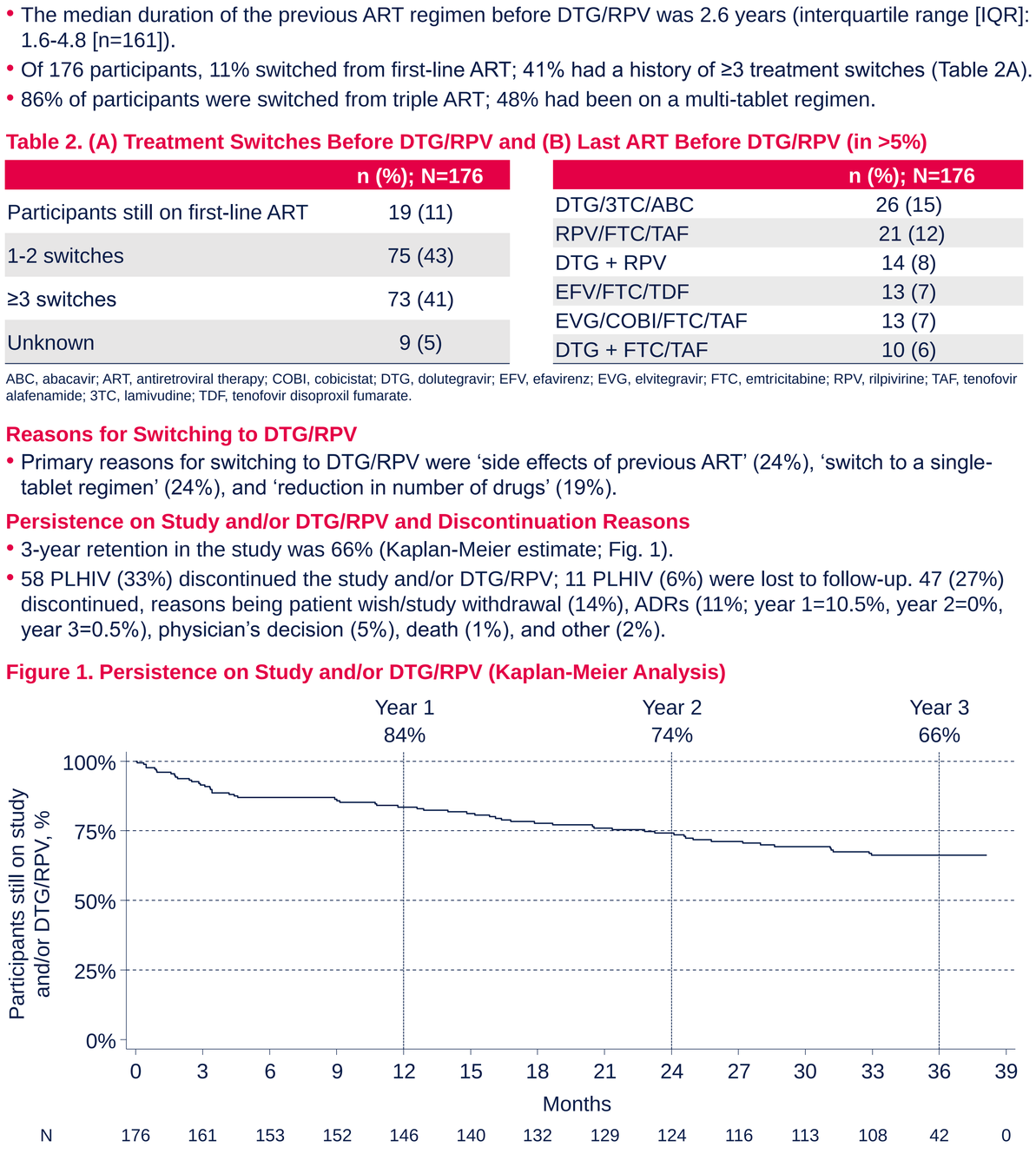
Reasons for Switching to DTG/RPV

- Primary reasons for switching to DTG/RPV were ‘side effects of previous ART’ (24%), ‘switch to a single-tablet regimen’ (24%), and ‘reduction in number of drugs’ (19%).

Persistence on Study and/or DTG/RPV and Discontinuation Reasons

- 3-year retention in the study was 66% (Kaplan-Meier estimate; Fig. 1).
- 58 PLHIV (33%) discontinued the study and/or DTG/RPV; 11 PLHIV (6%) were lost to follow-up. 47 (27%) discontinued, reasons being patient wish/study withdrawal (14%), ADRs (11%; year 1=10.5%, year 2=0%, year 3=0.5%), physician’s decision (5%), death (1%), and other (2%).

Figure 1. Persistence on Study and/or DTG/RPV (Kaplan-Meier Analysis)



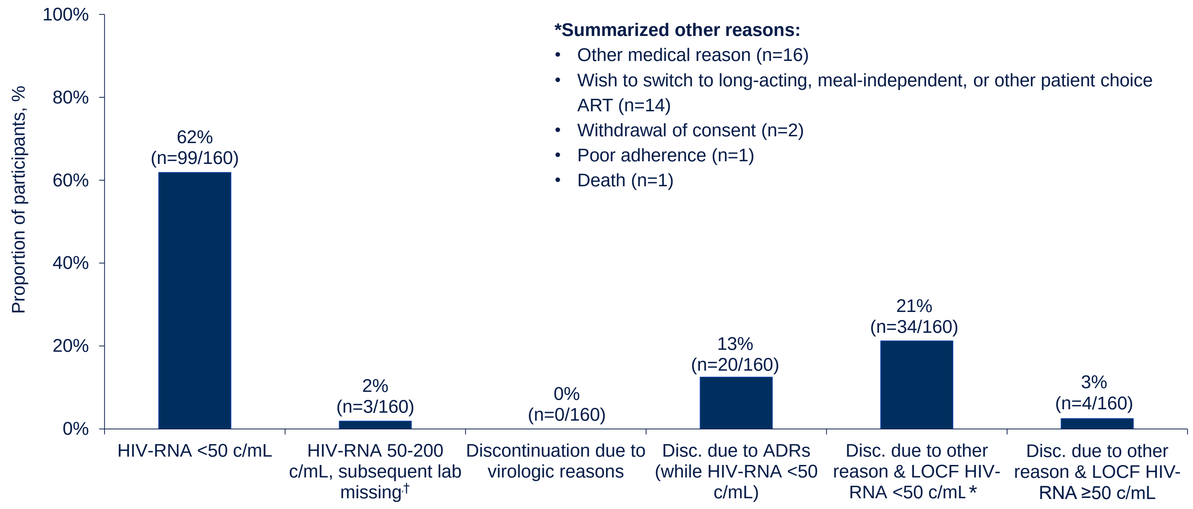
Tolerability

- Until data cut, 32 ADR events have been reported, yielding 37 ADRs using MedDRA coded terms (grades 1-2 [n=34], grade 3 [n=1], grade unknown [n=2]) in 27 participants (15%).
- No serious ADRs were reported.
- In 20 participants (11%), ADRs led to discontinuation of DTG/RPV, most common among them (>1) sleep disorder (n=6), depression (n=4), and nervous system disorder (n=2).
- At year 3, the median (IQR) weight change from baseline was +0.6 kg (−1.0, +6.0; n=58).

Effectiveness

- At year 3, there were no confirmed HIV-RNA >200 c/mL and no discontinuations for virologic reasons over the entire study period.
- Year 3 viral suppression rate was 62% (n=99/160; effectiveness set, n=16 excluded due to missing data), primarily driven by discontinuations for non–treatment-related reasons with HIV-RNA <50 c/mL* (Fig. 2).
- Of note, in 82% of PLHIV with any virologic data during follow-up, HIV-RNA was continuously <50 c/mL (n=137/168; with a median [range] of 11 [7-12] HIV-RNA measurements per individual).

Figure 2. Virologic Outcomes at Year 3

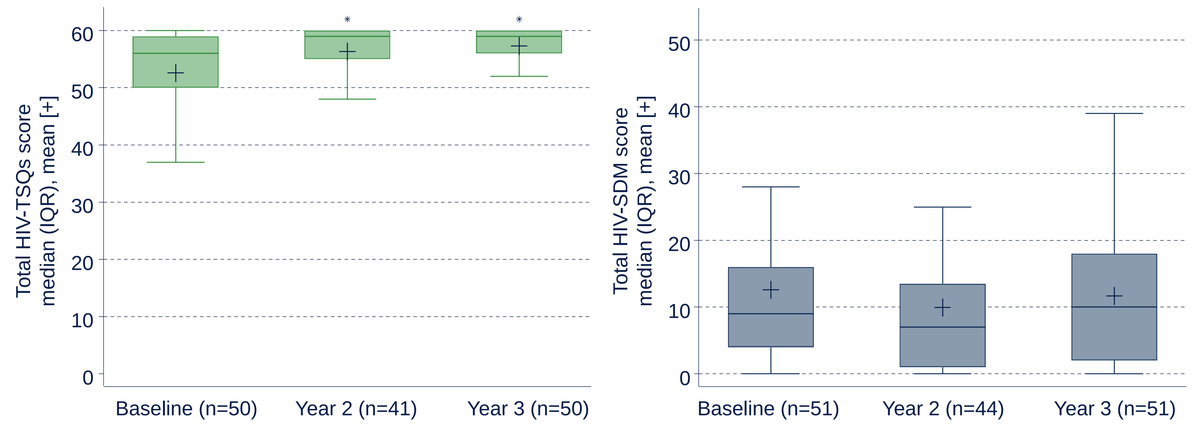


Effectiveness set: N=160; n=16/176 excluded due to missing data. †3 PLHIV with HIV-RNA 50-200 c/mL have no follow-up yet (subsequent lab missing). LOCF, last observation carried forward.

Patient-Reported Outcomes

- The statistically significant increase in treatment satisfaction score already observed at year 2 was maintained at year 3 (mean change +4.2 [*P*<0.001] at year 2 and +4.7 [*P*<0.001] at year 3; Fig. 3).
- Symptom Distress Module scores remained consistent (mean change −1.6 [*P*=0.085] and −0.9 [*P*=0.163], respectively).

Figure 3. Treatment Satisfaction (HIV-TSQs) and HIV Symptom Distress Module (HIV-SDM) in PLHIV Completing Questionnaires at Baseline and Year 3



*P<0.05 for comparison of baseline and years 2 and 3. HIV-SDM: 20 items, range of total score 0-80; negative changes indicate improvement. HIV-TSQs: 10 items, range of total score 0-60; positive changes indicate improvement.
Median (horizontal line in the box) and interquartile range (IQR) are shown as box plot; mean is displayed as a plus sign (+).

Conclusions

- In the prospective real-world setting of the JUNGLE cohort, DTG/RPV maintained viral suppression over 3 years with no discontinuations for virologic reasons.
- Discontinuations of DTG/RPV were mainly attributed to non–drug-related reasons consistent with a sustained and significant improvement in treatment satisfaction in PLHIV remaining on DTG/RPV for 3 years.

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