2 year outcomes of dolutegravir/rilpivirine in virologically suppressed HIV-infected PLHIV: Real-world data from the German JUNGLE cohort

Kevin Ummard-Berger[1], Christoph Wyen[2], Farhad Schabaz[3], Heribert Hillenbrand[4], Daniel Beer[5], Stephan Schneeweiss[6], Gordon Weinberg[7], Nils Postel[8], Bernd Westermayer[9], Kathrin Maria Dymek[10], Jenny Scherzer[10]

[1]UBN/Praxis, Berlin, Germany; [2]Praxis Ebertplatz Cologne, Germany; [3]MVZ München am Goetheplatz, Munich, Germany; [4]MVZ PraxisCityOst, Berlin, Germany; [5]Praxis Dr. Knechten Aachen, Germany; [6]Praxis Hohenstaufenring, Cologne, Germany; [7]Infektiologisches Zentrum Steglitz, Berlin, Germany; [8]prinzmed, Munich, Germany; [9]GlaxoSmithKline Munich, Germany; [10]ViiV Healthcare, Munich, Germany

PE2/2

Background

- In the SWORD-1&2 studies, switch to dolutegravir (DTG) and rilpivirine (RPV) maintained viral suppression for 148 weeks with low rates of virologic failure [1].
- The German JUNGLE cohort provides prospective real-world data (RWD) on DTG/RPV effectiveness, tolerability, symptom distress and patient reported treatment satisfaction in pre-treated people living with HIV (PLHIV).
- Of note, JUNGLE participants were more extensively pre-treated than SWORD participants and had a higher prevalence of advanced HIV disease at baseline.
- Here we present the 2 year outcomes.

Methods

JUNGLE is an ongoing non-interventional, 3 year, prospective, multi-center cohort study in Germany

Main inclusion criteria

- Adult HIV-1 infected patients on suppressive ART for ≥6 months switched to DTG/RPV in routine clinical care
- No history of virologic failure
- No INSTI or NNRTI resistance mutations
- No hepatitis B coinfection
- No contraindication based on the SmPC (summary of product characteristics)

Outcomes

- Year 2 viral suppression was defined as HIV-RNA<50 cp/mL in data window (21-27 months) or 50-200 cp/mL with subsequent HIV-RNA<50 cp/mL (excluding missing data/loss-to-follow-up).
- Persistence on study and/or DTG/RPV 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).
- Patient-reported symptom burden and treatment satisfaction were assessed using validated instruments: HIV Symptom Distress Module [HIV-SDM], and HIV Treatment Satisfaction Questionnaire [status version; HIV-TSQs].

Results

Study population

- Overall, 200 patients were enrolled across 24 study centers in the JUNGLE cohort.
- At data-cut, 188 PLHIV were eligible for analysis (n=12 excluded due to missing follow-up data/M12 visit window not yet reached). Baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics	Total	N (Observed data)
Sex, male, n (%)	170 (90.4)	188
Age, years, median (interquartile range; IQR)	49 (40 – 57)	188
Age ≥50 years, n (%)	90 (47.9)	188
Body weight, kg, median (IQR)	78 (68 – 89)	155
BMI, kg/m^2, median (IQR)	24 (22 – 27)	155
CD4 T-cell count, cells/µL, median (IQR)	712 (575 – 934)	188
History of AIDS (CDC C), n (%)	33 (17.6)	188
Time since HIV diagnosis, years, median (IQR)	11 (6 – 16)	185
Time on ART, years, median (IQR)	8 (4 – 14)	167

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

Comorbidities at baseline

- Comorbidities were documented in 117 patients (62.2%).
- The most common comorbidities (in >10% of patients) were hypertension (n=58, 30.9%), acute depression (n=32, 17.0%), lipid disorders (n=32, 17.0%), chronic kidney disease (n=27, 14.4%), insomnia (n=25, 13.3%), and pulmonary disease (n=19, 10.1%).

Antiretroviral treatment (ART) prior to switch to DTG/RPV

- The median duration on ART before DTG/RPV was 8.0 years (IQR: 4.0 – 14.0).
- Of 188 patients, 10.6% switched from first-line ART, 41.5% had a history of ≥3 ART changes (Table 2a).
- 86.6% of patients were switched from triple ART and 47.6% had been on a multi-tablet regimen. Previous antiretroviral regimens are shown in Table 2b.

Table 2a. Treatment switches prior to DTG/RPV	n (%); N=188
No modifications	20 (10.6)
1-2 modifications	77 (41.0)
≥3 modifications	78 (41.5)
unknown	13 (6.9)

Table 2b. Previous ART prior to DTG/RPV (in >5%)	n (%); N=188
DTG/3TC/ABC	26 (13.8)
RPV/FTC/TAF	25 (13.3)
EVG/COBI/FTC/TAF	15 (8.0)
EFV/FTC/TDF	13 (6.9)
DTG + RPV	13 (6.9)
DTG + FTC/TAF	11 (5.9)

3TC, lamivudine; ABC, abacavir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; RPV, rilpivirine;

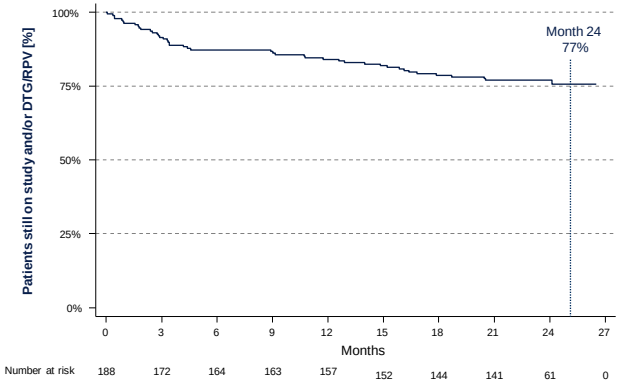
Reasons for switch

- Primary reasons for switching to DTG/RPV were side effects of previous ART (26.6%), switch to a single-tablet regimen (22.3%) and reduction of substance exposure (20.2%).

Persistence on study and/or DTG/RPV and discontinuation reasons

- Persistence on study and/or DTG/RPV through 2 years was 77% (Figure 1).
- 43 PLHIV discontinued the study (23%); 4 PLHIV (2%) were lost to follow-up.
- Reasons for discontinuation were adverse drug reactions (ADRs; total 10.6%; year 1 10.0%; year 2 0.6%), patient wish (6.4%), doctor's decision (2.7%), and other (3.2%); no discontinuation due to virologic reasons.

Figure 1. Persistence on study and/or DTG/RPV (Kaplan-Meier analysis)



Safety

- Until data-cut, 40 ADRs (grades 1-2, 1x grade 3) were reported for 28 PLHIV (15%).
- No serious ADR was reported.
- Most common ADRs were (>1 event): Sleep disorder (n=9), depression (n=4), diarrhoea (n=3), vomiting (n=2), myalgia (n=2) and nervous system disorder (n=2)
- In 20 patients (10.6%), ADRs led to discontinuation of DTG/RPV (n=29 ADRs; multiple ADRs per patient possible, see Figure 2).

References

[1] Llibre JM, Hung CC, Brinson C, et al. Lancet. 2018 Mar 3;391(10123):839-849.

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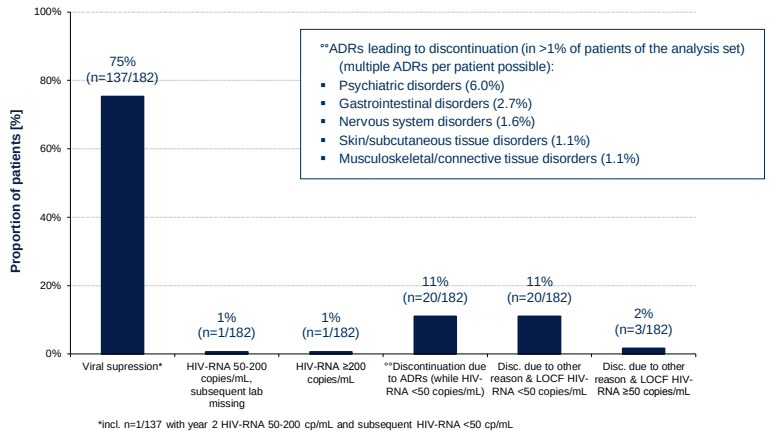
Effectiveness

- Year 2 viral suppression rate was 75% (n=137/182; n=6 excluded due to missing data) (Figure 2). No patient was discontinued for virologic reasons, and no resistance test during follow-up was performed.

Figure 2. Virologic outcomes at year 2



*incl. n=1/137 with year 2 HIV-RNA 50-200 cp/mL and subsequent HIV-RNA <50 cp/mL

Patient reported outcomes (PROs)

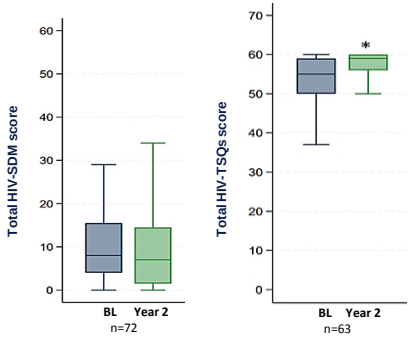
- In PLHIV completing questionnaires at baseline and year 2, median changes in HIV-SDM and HIV-TSQs were -1.0 (p=0.089) and +3.0 (p<0.001), respectively (Figure 3).

Figure 3. PROs. HIV Symptom Distress Module (HIV-SDM) and HIV Treatment Satisfaction status Questionnaire (HIV-TSQs) in patients completing baseline and year 2; box plot presentation (with median and IQR)

*p<0.05 for comparison of year 2 vs. baseline (BL);

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



Conclusions

- DTG/RPV demonstrated high virologic effectiveness with no discontinuations attributed to virologic reasons over two years of observation in a real world setting.
- Overall, 11% of individuals discontinued DTG/RPV due to ADRs, with only 1% in the 2nd year.
- This was consistent with a statistically significant improved treatment satisfaction score in patients remaining on DTG/RPV for two years.

Presenting author: Jenny Scherzer, Jenny.x.scherzer@viivhealthcare.com

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