12-month outcome of Dolutegravir/Rilpivirine in virologically suppressed HIV-infected patients: Real-world data from the German JUNGLE cohort

Sebastian Noe[1], Kevin Ummard-Berger[2], Heribert Hillenbrand[3], Daniel Beer[4], Christoph Wyen[5], Ramona Pauli[6], Nils Postel[7], Kathrin Maria Dymek[8], Bernd Westermayer[9], Jenny Scherzer[8]

[1]MVZ Karlsplatz, Munich, Germany; [2]UBN/Praxis, Berlin, Germany; [3]MVZ PraxisCityOst, Berlin, Germany; [4]Praxis Dr. Knechten Aachen, Germany; [5]Praxis Ebertplatz Cologne, Germany; [6]Isarpraxis Munich, Germany; [7]prinzmed, Munich, Germany; [8]ViiV Healthcare, Munich, Germany; [9]GlaxoSmithKline Munich, Germany

Poster 039

Background

- In the SWORD-1&2 studies, the combination of Dolutegravir (DTG) and Rilpivirine (RPV) maintained viral suppression for 148 weeks with low rates of virologic failure [1].
- The German JUNGLE cohort provides real-word data on DTG/RPV use in a more extensively pre-treated population than in SWORD with a higher prevalence of advanced HIV disease.
- Here we present the 12-month 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
- No prior virologic failure
- No INSTI or NNRTI resistance mutations
- No hepatitis B coinfection
- No contraindication based on the SmPC (summary of product characteristics)

Outcomes

- Month-12 (M12) viral suppression was defined as HIV-RNA<50 cp/mL in data 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 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 outcomes were assessed using validated questionnaires (HIV Symptom Distress Module [HIV-SDM] and Treatment Satisfaction [HIV-TSQ]).

Results

Study population

- 200 patients were enrolled in the JUNGLE cohort.
- At data-cut (5 May 2020), 183 patients were eligible for M12 analysis (90% men, 49 years [median], 18% CDC C, 709 CD4 cells/µL [median]). Baseline characteristics are shown in Table 1.

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

- The median duration of the previous ART regimen before DTG/RPV was 2.6 years (IQR, interquartile range: 1.6 – 5.1 [n=167]).
- Of 183 patients, 11% switched from first-line ART, 42% had a history of ≥3 ART changes (Table 1).
- 86% of patients were switched from triple ART and 48% had been on a multi-tablet regimen.

Table 1. Baseline characteristics

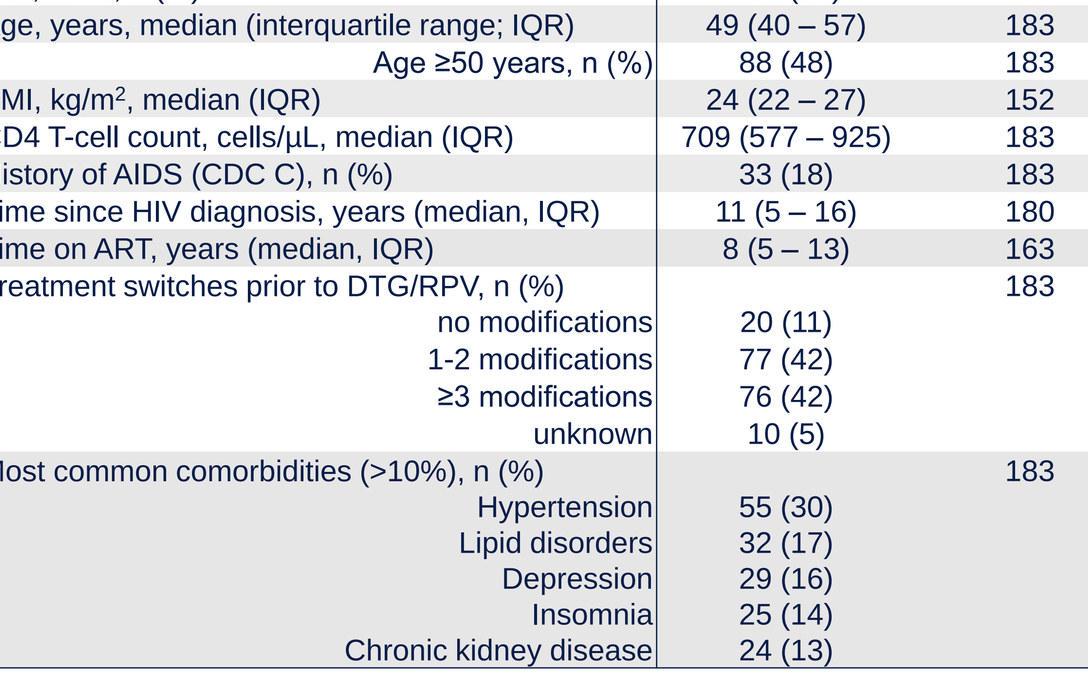
	Total	N
Sex, male, n (%)	164 (90)	183
Age, years, median (interquartile range; IQR)	49 (40 – 57)	183
Age ≥50 years, n (%)	88 (48)	183
BMI, kg/m^2, median (IQR)	24 (22 – 27)	152
CD4 T-cell count, cells/µL, median (IQR)	709 (577 – 925)	183
History of AIDS (CDC C), n (%)	33 (18)	183
Time since HIV diagnosis, years (median, IQR)	11 (5 – 16)	180
Time on ART, years (median, IQR)	8 (5 – 13)	163
Treatment switches prior to DTG/RPV, n (%)		183
no modifications	20 (11)	
1-2 modifications	77 (42)	
≥3 modifications	76 (42)	
unknown	10 (5)	
Most common comorbidities (>10%), n (%)		183
Hypertension	55 (30)	
Lipid disorders	32 (17)	
Depression	29 (16)	
Insomnia	25 (14)	
Chronic kidney disease	24 (13)	

IQR, interquartile range

Reasons for switching to DTG/RPV

- Primary reasons for switching to DTG/RPV were side effects of previous ART (25%), switch to a single-tablet regimen (23%) and reduction of substance exposure (21%) (see Figure 1).

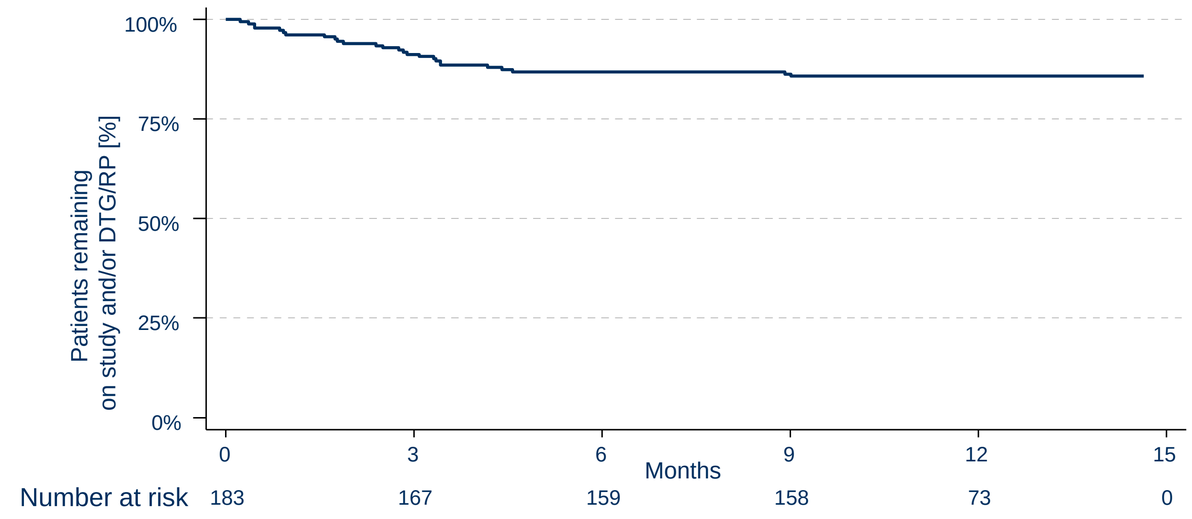
Figure 1. Primary, secondary and tertiary reasons for switch to DTG/RPV



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

- Persistence on study and/or DTG/RPV through M12 was 86% (Figure 2).
- 26 patients (14%) discontinued the study. Reasons were adverse drug reactions (ADRs; n=18 [10%]), patient preference (n=4 [2%]), doctor's decision (n=3 [2%]) and withdrawal of consent (n=1 [<1%]); no discontinuation due to virologic failure.

Figure 2. Persistence on study and/or DTG/RPV (Kaplan-Meier analysis)



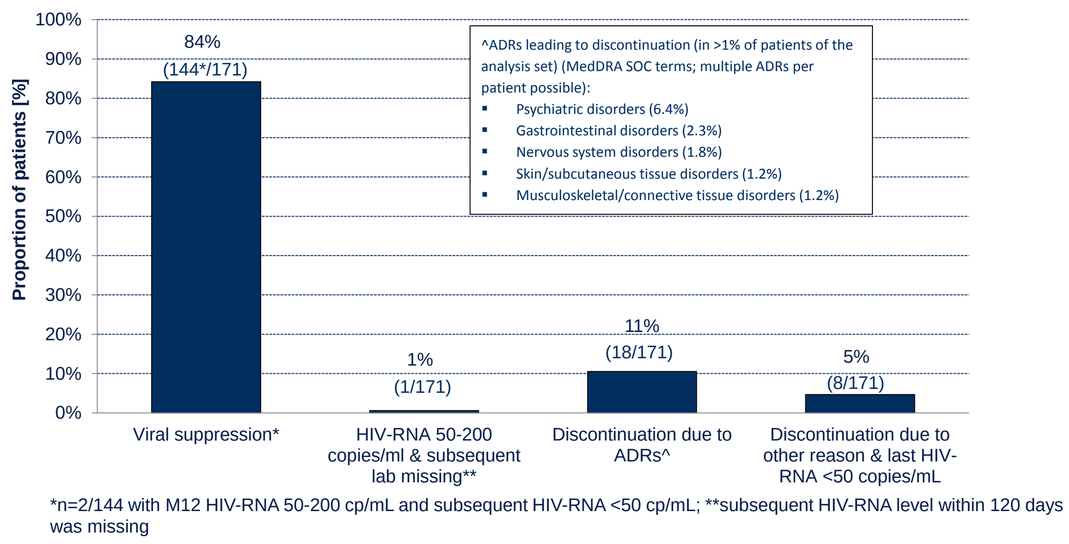
Safety

- Until data-cut, 31 ADRs (grades 1-2 [n=30], grade 3 [n=1]) had been documented in 22 patients (12%). No serious ADR was reported.
- In 18 patients (10%), ADRs led to discontinuation of DTG/RPV (n=27 ADRs; multiple ADRs per patient possible). Most common ADRs (MedDRA PT terms) were (>1 event):
  - Sleep disorder (n=7 [4%])
  - Depression (n=4 [2%])
  - Nervous system disorder (n=2 [1%])

Effectiveness

- M12 viral suppression rate was 84% (n=144/171; n=12 excluded due to missing data) (Figure 3).
- Of note, in 94% of patients with virologic data during follow-up, HIV-RNA measurements were continuously <50 cp/mL (n=165/175; with a median of 4 HIV-RNA measurements per individual, range 1-7).

Figure 3. Virologic outcomes at month 12 (M12)



*n=2/144 with M12 HIV-RNA 50-200 cp/mL and subsequent HIV-RNA <50 cp/mL; **subsequent HIV-RNA level within 120 days was missing

Patient reported outcomes

- In patients completing questionnaires at both time points (baseline, M12), mean changes in HIV-SDM and TSQ were +1.1 (p=0.479) and +2.7 (p<0.001), respectively (Table 2).

Table 2. HIV Symptom Distress Module (HIV-SDM) and Treatment Satisfaction (HIV-TSQ) in patients completing baseline and month-12 (M12) questionnaires

	N	Baseline Total score; mean/median (IQR)	M12 Total score; mean/median (IQR)	Change from baseline mean/median (IQR)	p-value (Wilcoxon-sign-rank test)
HIV-SDM^	81	12.4/8.0 (4.0 - 18.0)	13.5/9.0 (4.0 - 21.0)	+1.1/±0.0 (-5.0 - +6.0)	0.4793
HIV-TSQ*	76	53.4/55.5 (51.0 - 59.0)	56.1/58.0 (55.0 - 60.0)	+2.7/+1.0 (-0.5 - +4.5)	<0.001

^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;

Conclusion

- Real-world DTG/RPV use showed a high virologic suppression rate over one year with no discontinuation attributed to virologic failure.
- Although 10% discontinued DTG/RPV due to ADRs, Treatment Satisfaction (HIV-TSQ) increased in patients remaining on DTG/RPV for one year.

Acknowledgments
Special thanks to the participating patients and investigators of the JUNGLE study centers: CIM/Muenster; GP Isarpraxis/Munich; ICH/Hamburg; IZ Steglitz/Berlin; Klinikum Osnabrueck/Osnabrueck; Klinikum Rechts der Isar/Munich; MEDCENTER/Weimar; MVZ Karlsplatz/Munich; Novopraxis/Berlin; Praxis City Ost/Berlin; Praxis Cordes/Berlin; Praxis Ebertplatz/Cologne; Praxis Heuchel/Chemnitz; Praxis Hohenstaufenring/Cologne; Praxis Kaiserdamm/Berlin; Praxis Knechten/Aachen; Praxis UBN/Berlin; Praxis Wuensche/Berlin; PRINZMED/Munich; UNI Essen/Essen; UNI Hamburg/Hamburg; UNI Tuebingen/Tuebingen; WIR/Bochum; ZIMI/Munich.
Support in medical writing was provided by MUC Research. The study is sponsored by ViiV Healthcare, Germany.

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