Comparison of Viral Replication Below 50 c/mL for Two-Drug (DTG + RPV) Versus Three-Drug Current Antiretroviral Regimen (CAR) Therapy in the SWORD-1 and SWORD-2 Studies

P311

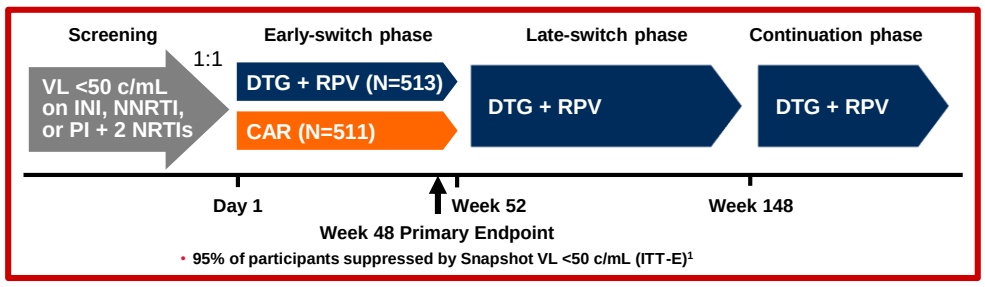
Mark Underwood,[1] Kostas Angelis,[2] Ruolan Wang,[1] Brian Wynne,[1] Veerle Van Eygen,[3] Libby Blair,[1] Lesley Kahl,[2] Tia Vincent,[4] Justin Koteff,[1] Michael Aboud[4]

[1]ViiV Healthcare, Research Triangle Park, NC, USA; [2]GlaxoSmithKline, Stockley Park, UK; [3]Janssen Pharmaceutica NV, Beerse, Belgium; [4]ViiV Healthcare, Brentford, UK

Introduction

- SWORD-1 and SWORD-2 are identical, open-label, multicentre, global, phase III, non-inferiority studies[1] evaluating efficacy and safety of switching from current antiretroviral regimen (CAR) to dolutegravir (DTG) + rilpivirine (RPV) once daily in HIV-1–infected adults, with HIV-1 RNA <50 c/mL (viral load [VL] <50 c/mL) for at least 6 months and no history of virologic failure.
- FDA Snapshot algorithm uses 50 c/mL as cutoff. The clinical significance and subject management implications of low-level quantitative and qualitative VL data remain controversial.

Figure 1. Study Design



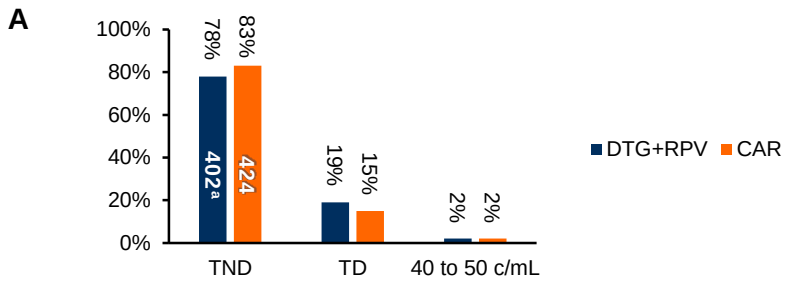
- 1024 participants were randomized and exposed across both studies.
- At Week 48, 95% of participants in each arm had Snapshot VL <50 c/mL[1] in the intention-to-treat–exposed (ITT-E) population.
- The Abbott RealTime HIV-1 assay measures quantitative HIV-1 RNA VL from 40 c/mL to 10,000,000 c/mL and generates qualitative target detected (TD) or target not detected (TND) results for VL <40 c/mL.
- We assessed the number of participants having 40 c/mL ≤ VL <50 c/mL, or TD or TND for those with VL <40 c/mL, over 48 weeks for the DTG + RPV two-drug regimen versus CAR (PI-, NNRTI-, or INSTI-based three-drug CAR).

Methods

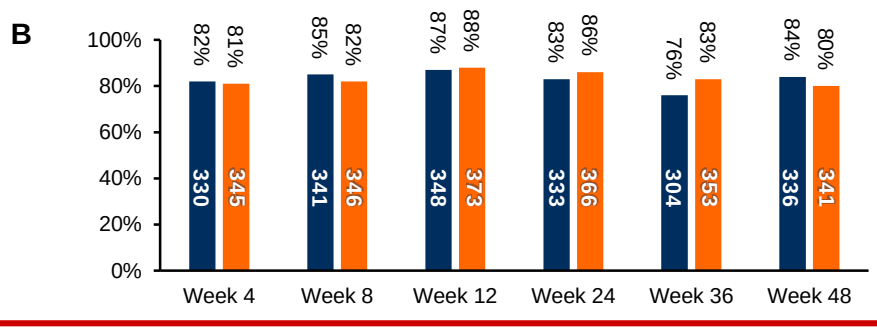
- We explored shifts from Baseline (Day 1), cumulative, and per visit classification of participants into >50 c/mL, 40 c/mL ≤ VL <50 c/mL, or TD/TND when <40 c/mL, across arms throughout 48 weeks.
- See footnotes in Figure 2A, Table 1, and Table 2 for analysis details.

Results

Figure 2. (A) Proportions by VL Category <50 c/mL at Baseline and (B) Proportions of TND by Week for Participants With Baseline TND



[a]The number of participants per category. Of four participants in the DTG + RPV arm with no Post-Baseline data, three had TND and one had TD at Baseline. Two with Baseline TND in CAR had no Post-Baseline VL, and are included here and per Snapshot algorithm in Table 2 (N=402 and N=424), but not in Table 1 analyses (TND DTG + RPV, N=399 and CAR, N=422).



- At Baseline, slight numerical differences were observed within the VL categories <50 c/mL between the DTG + RPV and CAR arms (Figure 2A)
- Similar proportions of participants with TND were observed at each visit in the DTG + RPV and CAR arms through Week 48 among participants with TND at Baseline (Figure 2B).

Table 1. Changes in Quantifiable and Non-Quantifiable VL Levels by Baseline VL Category Through Week 48

		DTG + RPV (N=513)			CAR (N=511)		
	Baseline	TND	TD	40-50 c/mL	TND	TD	40-50 c/mL
		399 (78%)	98 (19%)	12 (2%)	422 (83%)	76 (15%)	11 (2%)
Post-Baseline	≥50 c/mL[a]	21 (5%)	14 (14%)	4 (33%)	22 (5%)	13 (17%)	2 (18%)
	≥40-<50 c/mL[a]	12 (3%)	4 (4%)	2 (17%)	5 (1%)	6 (8%)	1 (9%)
	VL <40 & TD[a]	177 (44%)	61 (62%)	4 (33%)	172 (41%)	43 (57%)	7 (64%)
	VL <40 & TND[b]	189 (47%)	19 (19%)	2 (17%)	223 (53%)	14 (18%)	1 (9 %)

Post-Baseline categories are mutually exclusive; inclusion of participants into a category is based on highest VL observed (ie, from top to bottom rows). The percentages for Post-Baseline below solid line are calculated from the percentages at Baseline for categories above solid line. Four participants with TND and one with TD in the DTG + RPV arm and two with TND in the CAR arm at Baseline had no Post-Baseline on-treatment VL data and thus are not included here in Baseline totals. [a]In at least one time point after Baseline through Week 48. [b]In all time points Post-Baseline.

- By Baseline VL category, there were similar proportions of Post-Baseline categories between the DTG + RPV and CAR arms.
  - The proportions with TND at Baseline were 78% for DTG + RPV vs 83% for CAR (Figure 2A).
- Post-Baseline TD was more common with Baseline TD versus Baseline TND

Table 2. Snapshot Analysis for Participants With TND at Baseline Using <50 c/mL or TND as Endpoint at Week 48

Outcome	DTG + RPV (N=402)[a]	CAR (N=424)[a]	Crude diff. Prop. (95% CI)[b]	Adjust. diff. Prop. (95% CI)[c]
Virologic Success				
VL <50 c/mL[d]	383 (95%)	405 (96%)	—	—
VL <40 c/mL & TND	336 (84%)	341 (80%)	3.2% (-2.1%, 8.4%)	3.1% (-2.2%, 8.3%)
Virologic Failure[e]	47 (12%)	66 (16%)		
VL <40 & TD at Week 48 visit	45 (11%)	59 (14%)		
40 ≤ VL <50 at Week 48 visit	2 (<1%)	5 (1%)		
VL ≥50 at Week 48 visit	0	2 (<1%)		
No Virologic Data	19 (5%)	17 (4%)		
Disc. study due to AE or death	15 (4%)	3 (1%)		
Disc. study for other reasons while VL below 50 c/mL	4 (1%)	13 (3%)		
Missing data during window but on study	0	1 (<1%)		

Note: [a]Participants having TND at Baseline. [b]Difference: Proportion on DTG + RPV − Proportion on CAR. [c]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for stratifications factors: Baseline age (< or ≥50 years) and Baseline third agent (PI, NNRTI, INI). VL = viral load. [d]Endpoint VL <50 c/mL in participants with Baseline TND; details on virologic failures and no virologic data for this endpoint are not provided. [e]There were no virologic failures due to disc. for lack of efficacy, disc. for other reasons while VL not below 50 c/mL, or change in ART.

- Week 48 Snapshot success by VL measurement <50 c/mL was similar for participants with TND at baseline between the DTG + RPV and CAR arms.
- Week 48 Snapshot success by TND was similar across the DTG + RPV and CAR arms.

Conclusions

- Similar proportions of participants with TND were observed at each visit through Week 48 for the DTG + RPV and CAR arms.
- There were similar proportions of participants in the DTG + RPV and CAR arms with Post-Baseline TD and TND categories by Baseline category.
- Qualitative viremia by the TD measure was more common with Baseline TD than with Baseline TND.
- Using the more stringent TND data, there was no difference by Snapshot for the DTG + RPV two-drug regimen versus the CAR three-drug regimen at Week 48.

Acknowledgments: This study was funded by ViiV Healthcare. We thank everyone who has contributed to the success of these studies, including all study participants and their families; the SWORD-1 and SWORD-2 clinical investigators and their staff; and the ViiV Healthcare, GSK, and Janssen study teams. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by MedThink SciCom and funded by ViiV Healthcare.

Reference: 1. Llibre et al. *Lancet.* 2018;391:839-849.