HIV-1 REPLICATION AT <50 C/ML TO 148 WEEKS FOR SWORD-1/SWORD-2 STUDIES WITH DTG + RPV

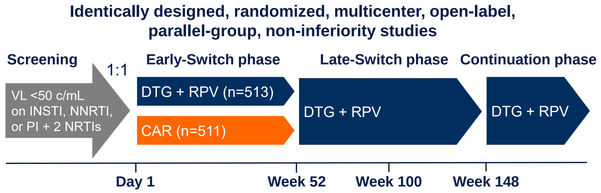
M Underwood,[1] K Angelis,[2] R Wang,[1] J Horton,[3] V Van Eygen,[4] J Matthews,[1] L Kahl,[5] J van Wyk,[5] B Wynne[1]

[1]ViiV Healthcare, Research Triangle Park, NC, USA; [2]GlaxoSmithKline, Stockley Park, UK; [3]Parexel International, Durham, NC, USA; [4]Janssen Pharmaceutica, Beerse, Belgium; [5]ViiV Healthcare, Brentford, UK

Introduction

- The SWORD studies demonstrated non-inferiority of switch to dolutegravir (DTG) + rilpivirine (RPV) vs continuing a 3- or 4-drug current antiretroviral regimen (CAR) for 48 weeks and also demonstrated durable suppression to HIV-1 RNA <50 c/mL over 3 years
- The clinical significance of low-level viral load (VL) <50 c/mL remains unclear
- Previous assessment of low-level qualitative HIV-1 RNA using undetectable (Target Not Detected; TND) and detectable (Target Detected; TD) measures showed similar levels of TND for participants receiving DTG + RPV 2-drug regimen (2DR) compared with those who continued their CAR through Week 48[1]
- We present here longer-term HIV-1 RNA data, focusing on low-level qualitative VL data, and including quantitative VL ≥40 c/mL, from the phase III SWORD HIV-1 studies up to Week 148

Figure 1. Study Design



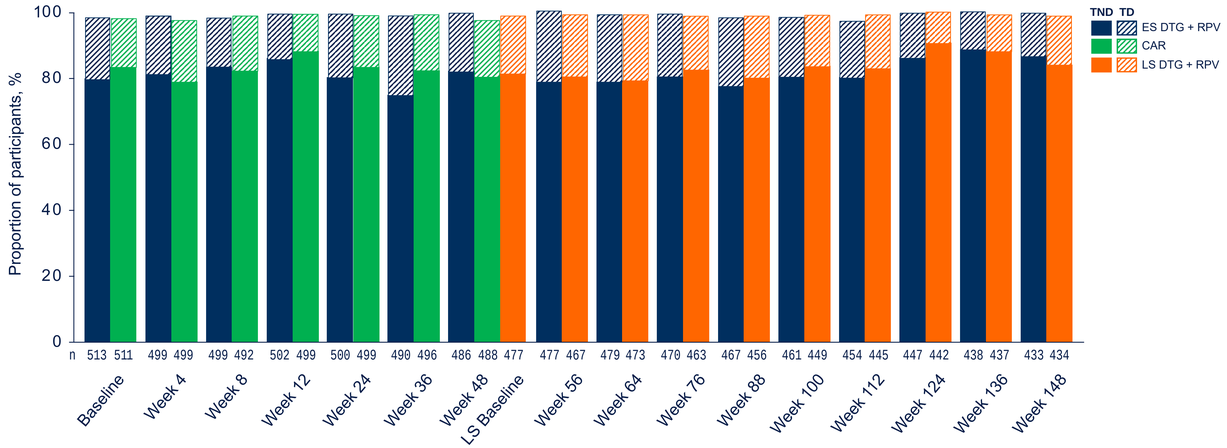
Methods

- Adults with VL <50 c/mL for ≥6 months were randomized to switch to DTG + RPV (Early-Switch [ES] DTG + RPV group) for 148 weeks or continue CAR. CAR participants with VL <50 c/mL at Week 48 switched at Week 52 (Late-Switch [LS] DTG + RPV group) to receive DTG + RPV for 96 weeks
- The Abbott RealTime assay measures VL quantitatively from 40 c/mL to 10,000,000 c/mL; when VL <40 c/mL it reports qualitative Target Detected (TD) or Target Not Detected (TND) results
- We assessed participants' TND and TD status for those with VL <40 c/mL over time, overall and by Baseline TD or TND status. We also assessed quantitative VLs ≥40 to <50 c/mL, ≥50 to <200 c/mL, and ≥200 c/mL for participants overall
- In "by visit" analyses, the latest VL within each visit is considered. Participants who discontinued from study before reaching a specific timepoint (ie, Week 100, Week 148) are not included in the summaries of the respective timepoint
- Baseline for the LS group is defined as the last VL assessment (usually from the Week 48 visit) before switch to DTG + RPV at Week 52. Per study switch criteria, no participants had VL ≥50 c/mL at LS Baseline

Results

- 1024 participants were randomized and exposed (ES DTG + RPV, n=513; CAR, n=511) across both studies; 477 CAR participants switched to DTG + RPV at Week 52

Figure 2. Proportion of Participants With TND and TD by Visit Through Week 148 Presented by Arm and Treatment Group



- The proportions of participants with TND were similar through Week 148 across the ES DTG + RPV, CAR, and LS DTG + RPV groups
- Proportions with TND ranged from 75% to 88% for ES DTG + RPV, 79% to 88% for CAR, and 79% to 90% for LS DTG + RPV

Table 1. Proportions of Participants Who Maintained TND at Every Visit by Baseline Category

A. During 48 Weeks of Treatment

Comparator group[a]	Baseline[b] category		
	Overall	TND	TD
ES DTG + RPV	41% (198/486)	47% (180/383)	19% (18/94)
LS DTG + RPV	48% (215/449)	52% (189/367)	33% (25/76)
CAR	47% (229/488)	53% (215/408)	19% (13/70)

[a]For ES DTG + RPV and CAR, data are through Week 48, and for LS DTG + RPV, data are from Week 52 to Week 100. [b]Baseline is Day 1 for ES DTG + RPV and CAR, and LS Baseline (see Methods) for LS DTG + RPV.

- Similar proportions of participants had TND at all visits through 48 weeks receiving DTG + RPV (in the ES and LS groups) or receiving CAR treatment
- More participants in TND at Baseline category had TND at all visits compared with participants in TD at Baseline category

B. During 96 to 100, or 148 Weeks of Treatment

Comparator group[a]	Baseline[b] category		
	Overall	TND	TD
LS DTG + RPV at Week 148	36% (158/434)	40% (142/352)	20% (15/76)
ES DTG + RPV at Week 100	25% (113/461)	28% (102/362)	12% (11/90)
ES DTG + RPV at Week 148	20% (87/433)	23% (79/341)	10% (8/84)

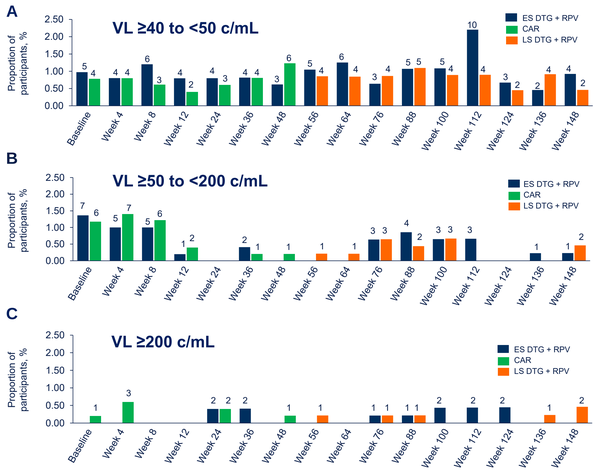
[a]LS DTG + RPV at Week 148 and ES DTG + RPV at Week 100 received, respectively, 96 or 100 weeks of DTG + RPV, ES DTG + RPV at Week 148 received 148 weeks of DTG + RPV. [b]Baseline is Day 1 for ES DTG + RPV, and LS Baseline (see Methods) for LS DTG + RPV.

- Respectively, about 1 in 10 participants with BL TD versus 1 in 5 participants with BL TND maintained TND at all visits during ~3 years of exposure to DTG + RPV

Discussion

- Qualitative measures of HIV-1 RNA replication have been noted to correlate with single-copy assay (SCA),[2] and can provide an estimate of viral replication that informs on comparative potency in clinical studies
- The clinical significance and patient management implications of low-level VL measurements have been assessed previously using qualitative data,[3,4] and additional data are needed to inform on this topic

Figure 3. Proportion of Participants With Viral Loads ≥40 c/mL Through Week 148



NOTE: The number of participants in the different categories is shown above the vertical bars at visit weeks. No number indicates there were no occurrences at those visits.

- Numbers and proportions of quantitative VLs ≥40 to <50 c/mL, ≥50 to <200 c/mL, and ≥200 c/mL were low and similar across groups through 148 weeks

Conclusions

- The proportions of participants with TND by visit under DTG + RPV remained high across all visits, with no decline observed through 148 weeks
- The proportions of participants with TND maintained for all visits were similar across DTG + RPV and CAR groups over 48 weeks of treatment
- The proportions of participants with VL ≥40 c/mL were low and comparable among treatment groups
- This is supportive evidence that long-term treatment with DTG + RPV is efficacious in virologic suppression to <50 c/mL

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References: 1. Underwood et al. HIV Glasgow 2018; Glasgow, UK. Poster P311. **2.** Tosiano et al. CROI 2019; Seattle, WA. Poster 0557. **3.** Doyle at al. *Clin Infect Dis.* 2012;54:724-732. **4.** Henrich et al. *PLoS One.* 2012;7:e50065.