Comparison of HIV-1 Intermittent Viremia for Two Drug (DTG+RPV) vs Three Drug Current Antiretroviral Therapy in the SWORD-1 and SWORD-2 Studies

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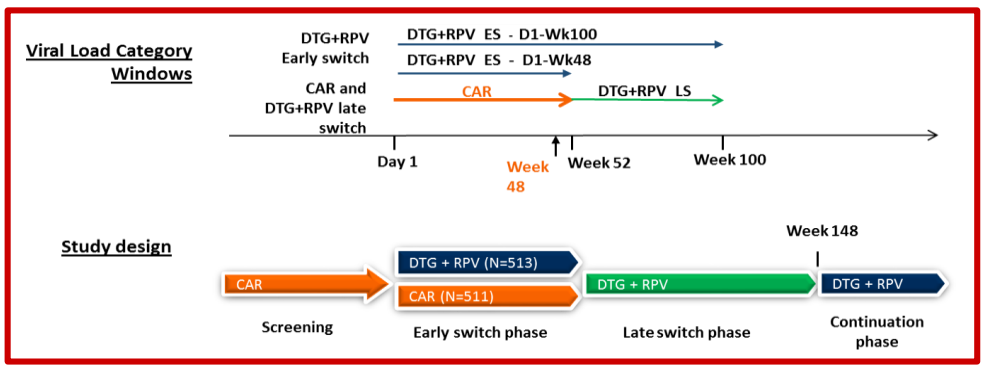
Introduction

- The overall goal of HIV therapy is to maintain lifelong virologic suppression over the entire course of a patient's treatment
- The clinical significance and management of subjects who have transient "blips" remains controversial; however, their appearance may lead to concerns about the durability of an ART regimen
- We assessed elevated viral loads over 2 years of therapy with the 2-drug regimen (2DR) of DTG+RPV vs remaining on 3-drug current antiretroviral regimen (CAR)

Methods

- SWORD-1 and SWORD-2 are identical open-label, multicentre, global, phase III, non-inferiority studies evaluating efficacy and safety of switching from CAR to DTG+RPV once daily in HIV-1-infected adults, with HIV-1 RNA <50 c/mL (viral load [VL] <50 c/mL) and no history of virologic failure
- Subjects either switched to DTG+RPV on Day 1 (Early Switch [ES] DTG+RPV arm) or remained on CAR (CAR arm) and switched to DTG+RPV at Week 52 (Late Switch [LS] DTG+RPV arm) if still on study and suppressed
- ES DTG+RPV D1–Week 100 represents subjects randomized to DTG+RPV at Day 1 with cumulative data from Day 1 through Week 100

Figure 1. Study Design



- US Food and Drug Administration Snapshot algorithm uses 50 c/mL as a cutoff for viral suppression
- We divided subjects within each of the following groups with ≥1 post-Baseline on-treatment VL ≥50 c/mL into 2 major categories:
  - (1) Subjects with ≥1 VL between 50 and 200 c/mL and no VL ≥200 c/mL
  - (2) Subjects with ≥1 VL ≥200 c/mL

Results

Table 1. Viral Load Categories and Subjects Observed per Category

Study regimen and time frames / VL categories	ES DTG+RPV D1–Wk48 N = 513	CAR D1–Wk48 N = 511	LS DTG+RPV Wk52–Wk100 N = 477	ES DTG+RPV D1–Wk100 N = 513
1. VL between 50 and 200 c/mL and no VL ≥200 c/mL				
1a. ≥1 VL ≥50 and <200 c/mL, and adjacent VL <50 c/mL (**"blip"**)	34 (6%)	28 (5%)	20 (4%)	48 (9%)
1b. ≥2 consecutive VL between 50 and 200 c/mL	1 (<1%)	1 (<1%)	3 (1%)	4 (1%)
2. VL ≥200 c/mL				
2a. 1 VL ≥200 c/mL and no 2 consecutive VL ≥50 c/mL	2 (<1%)	5 (1%)	5 (1%)	5 (1%)
2b. 2 consecutive VL ≥50 c/mL with ≥1 VL ≥200 c/mL	2 (<1%)	3 (1%)	4 (1%)	6 (1%)
Total (all categories)	39 (8%)	37 (7%)	32 (7%)	63 (12%)

- Through Week 100 across treatment groups, 10 subjects met CVW criteria[1]
  - 6 out of 10 CVW subjects had no intermittent blips; 3 had a single blip; and only 1 subject had 2 blips (Subject A in Table 2) before having a VL measurement meeting SVW criterion that was subsequently confirmed

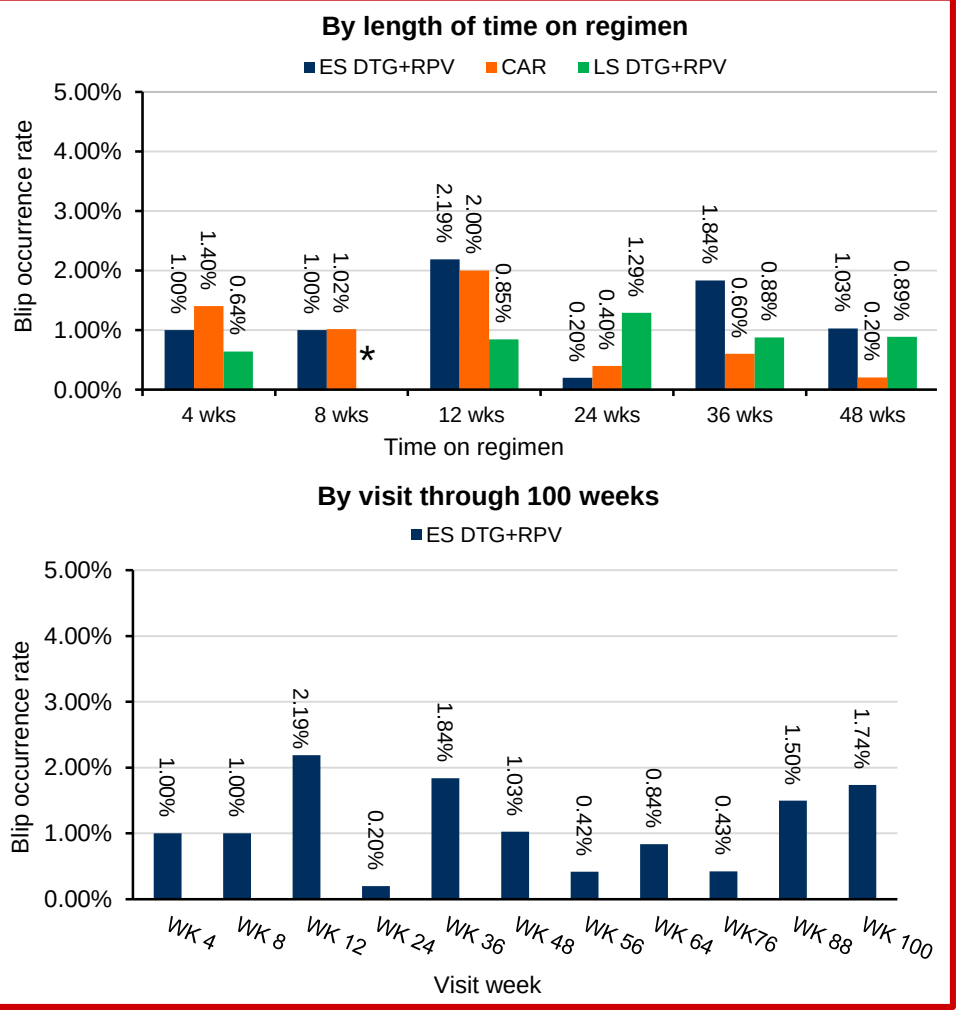
Table 2. Occurrence of Blips Prior to Participants Meeting CVW

Subject ID	A	B	C	D	E
Treatment arm	CAR	CAR	ES DTG+RPV	ES DTG+RPV	LS DTG+RPV
# of Blips	2	1	0	0	0
Subject ID	**F**	**G[a]**	**H[a]**	**I[a]**	**J[a]**
Treatment arm	LS DTG+RPV	ES DTG+RPV	ES DTG+RPV	ES DTG+RPV	ES DTG+RPV
# of Blips	0	1	0	1	0

[a]Subjects in DTG+RPV arm that met CVW in year two.

CVW – Confirmed virologic withdrawal: HIV-1 RNA ≥200 c/mL following prior VL ≥50 c/mL.

Figure 2. Rates of Blips Through Week 100



*There was no Week 8 visit for the late switch subjects.

- Blip occurrences by treatment arm over time demonstrate overall diverse numbers as expected for virologic blips caused by stochastic non-adherence, intercurrent illness,[2] or immunizations[3]

Conclusions

- The incidence of blips was low, fluctuated, and occurred at a similar rate among subjects receiving DTG+RPV 2-drug regimen and subjects receiving 3-drug (CAR) regimen
- All other categories of VL >50 c/mL occurred infrequently in all groups
- Viral blips were not associated with CVW
- DTG+RPV 2DR is as effective at preventing intermittent low-level viremia as 3-drug ART

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References: 1. Aboud et al. AIDS 2018; Amsterdam, the Netherlands. **2.** Donovan et al. *J Infect Dis*. 1996;174:401-403. **3.** Günthard et al. *J Infect Dis*. 2000;181:522-531.