Dolutegravir (DTG) Plus Lamivudine (3TC) Versus DTG Plus Tenofovir/Emtricitabine (TDF/FTC) Fixed-Dose Combination in the GEMINI Studies - Viral Load Rebound Including 'Blips' Through 48 Weeks

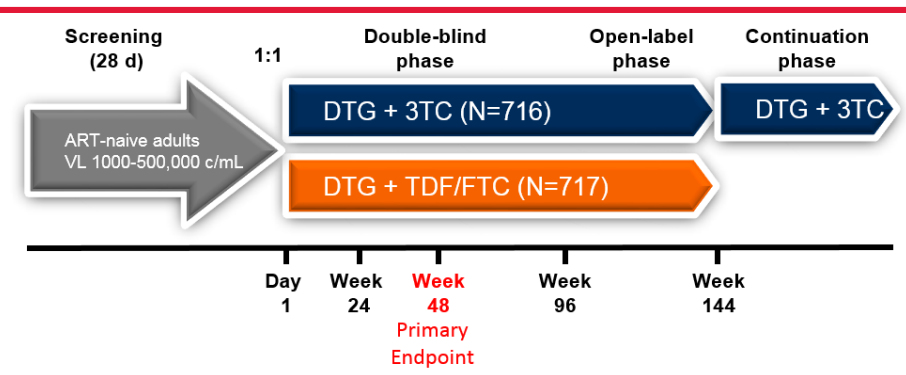
MOPEB231

Mark Underwood,[1] Ruolan Wang,[1] Joseph Horton,[2] Choy Man,[1] Jörg Sievers,[3] Rimgaile Urbaityte,[4] Brian Wynne,[1] Allan Tenorio,[1] Keith Pappa,[1] Justin Koteff,[1] Martin Gartland,[1] Michael Aboud[3]

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

Background

- GEMINI-1 and GEMINI-2 are identical double-blind, multicentre, randomized, phase III, non-inferiority studies comparing dolutegravir + lamivudine (DTG + 3TC) two-drug regimen (2DR) with DTG + tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) three-drug regimen (3DR) once daily in HIV-1-infected ART-naive adults, with screening HIV-1 RNA viral load (VL) <500,000 c/mL.
- DTG + 3TC was non-inferior to DTG + TDF/FTC through 48 weeks, with 91% (655/716) versus 93% (669/717), respectively, achieving VL <50 c/mL using FDA snapshot algorithm, pooled analysis.[1]
- We assessed VL rebound through 48 weeks of therapy.



Methods

- VL rebound after suppression to <50 c/mL was assessed in two major participant categories (see Table 1): (1) with only VL ≥50 and <200 c/mL, or (2) at least one VL ≥200 c/mL.
  - Each of these major categories was further divided into a single non-consecutive occurrence or ≥ two consecutive occurrence sub-categories.
  - A '**blip**' is defined here as VL of 50-<200 c/mL with adjacent values <50 c/mL.
  - A third Table 1 category included those that never suppressed to <50 c/mL.
- Confirmed virologic withdrawal (CVW) criteria for resistance testing were: VL decrease <1 $\log_{10}$ c/mL by Week 12, with subsequent confirmation, unless VL <200 c/mL; or confirmed VL ≥200 c/mL on or after Week 24; or confirmed VL ≥200 c/mL after prior confirmed VL <200 c/mL.
- VL rebound and CVW categories were assessed by Baseline (BL) VL.

Results

Table 1. Cumulative Elevated Viral Load Frequencies by Category

Categories	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
1. Participants with VLs between 50-<200 c/mL and no VL ≥200 c/mL after suppression to <50 c/mL	**98 (14%)**	**101 (14%)**
1a. VLs between 50-<200 c/mL with adjacent values <50 c/mL ('**blips**')	83 (12%)	93 (13%)
1b. ≥ Two consecutive VLs between 50-<200 c/mL	15 (2%)	8 (1%)
2. Participants with at least one VL ≥200 c/mL after suppression to <50 c/mL	**19 (3%)**	**22 (3%)**
2a. A single VL ≥200 c/mL with adjacent VLs <200 c/mL	14 (2%)	19 (3%)
2b. ≥ Two consecutive VLs ≥200 c/mL (CVW)	5* (<1%)	3** (<1%)
3. Participant VL never suppressed to <50 c/mL most had only Day 1 (Baseline) visits	**8 (1%)**	**7 (1%)**
Total (all categories)	**125**	**130**

NOTE: *One CVW in DTG + 3TC arm never achieved <50 c/mL, thus is counted in category 3. **One CVW in DTG + TDF/FTC arm was confirmed after Wk 48 at Wk 60, thus is counted in category 2a in this analysis.

- The proportion of participants with elevated VLs (Table 1) was comparable across arms; most participant VL rebounds that occurred were 'blips' between 50 and 200 c/mL.
- By Week 48, six participants in the DTG + 3TC group (0.8%) and four in the DTG + TDF/FTC group (0.6%) met CVW criteria.
  - Most CVWs are in category 2b (Table 1 and footnote).

Table 2. CVW Occurrences by BL VL

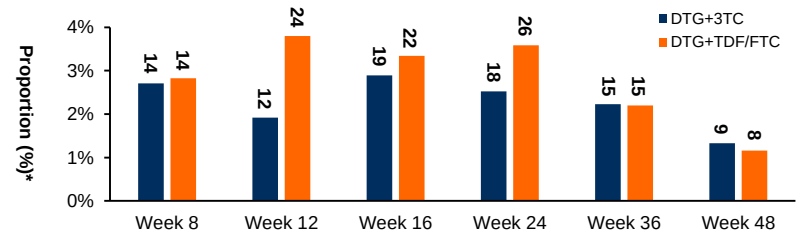
	All participants		≤100,000 c/mL		>100,000 c/mL	
	DTG + 3TC	DTG + TDF/FTC	DTG + 3TC	DTG + TDF/FTC	DTG + 3TC	DTG + TDF/FTC
n	716	717	576	564	140	153
CVW	6	4	4	3	2	1

- The number of CVWs was low with similar occurrence across arms regardless of BL VL (Table 2).

CVW Participants - Key Results

- No CVW participants in either arm had blips prior to CVW.
- No CVW participants had treatment-emergent resistance.

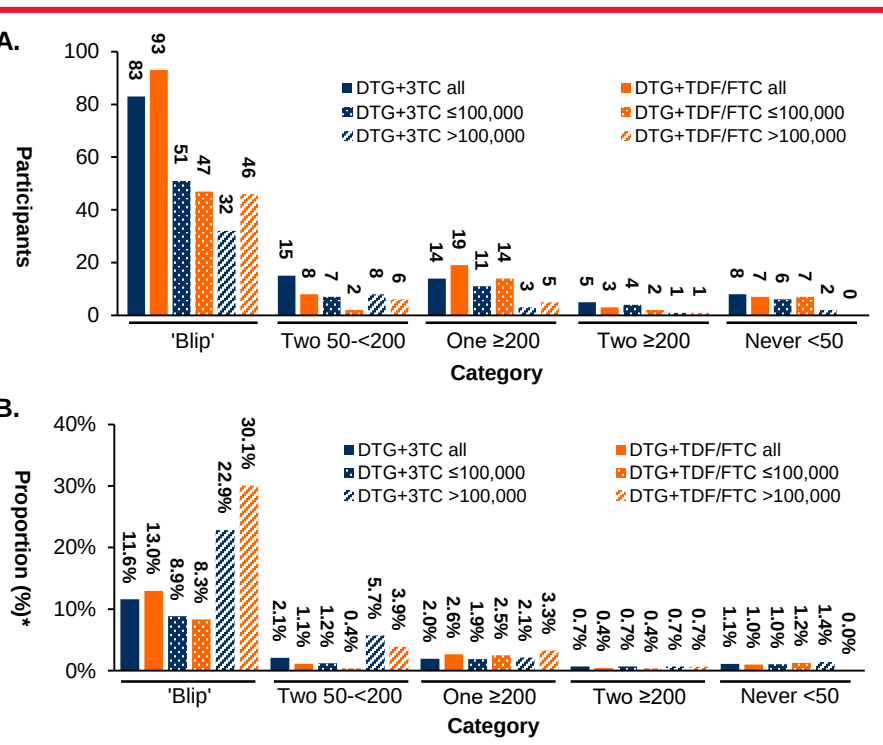
Figure 1. Blip Frequencies and Number by Visit Week



*Percentages were calculated from number of blips (Table 1, category 1a) using previously suppressed (<50 c/mL) participant Ns, respectively, for DTG + 3TC and DTG + TDF/FTC at Wk 8 (N=517) and (N=496); Wk 12 (N=625) and (N=632); Wk 16 (N=657) and (N=659); Wk 24 (N=714) and (N=726); Wk 36 (N=674) and (N=683); and Wk 48 (N=678) and (N=691). Bold numbers on chart are # of blips at given week visits. Individual participants can have had more than one blip.

- Similar 'blip' frequencies were seen across arms by visit week.
- Cumulative occurrences: DTG + 3TC (N=87); DTG + TDF/FTC (N=109).

Figure 2. Cumulative Participants With Elevated VLs by BL VL



*Percentages calculated with respective total Ns for DTG + 3TC and DTG + TDF/FTC of All (N=716) and (N=717); VL ≤100K (N=576) and (N=564); and VL >100K (N=140) and (N=153).

- Overall, similar occurrences and percentages of participants with 'blips' were seen across arms regardless of BL VL.
- Most VL elevations occurred in 'blip' category 1a, regardless of BL VLs (Figure 2A).
- The most frequent occurrences by percentage were in 'blip' category (Figure 2B).
  - The DTG + TDF/FTC arm when BL VL was >100,000 c/mL had the greatest proportion of 'blips' (Figure 2B). Since the number of participants in this subgroup is small, this result needs to be interpreted with caution.

Discussion

- Previous work for JULUCA (DTG + RPV) in the suppressed switch SWORD studies showed similar 'blip' frequencies between the DTG + RPV 2DR and the comparator 3DR arm.[2]
- Previously reported assessments of very-low-level viremia with qualitative HIV-1 RNA <40 c/mL for GEMINI studies at Week 48[3] showed similar frequency of patients across arms with undetectable VL, although the median time to undetectable VL was numerically shorter for DTG + 3TC patients versus DTG + TDF/FTC with BL VLs >100,000 c/mL.

Conclusions

- The occurrences of blips by visit were similar across arms.
- The incidence of participants with blips through 48 weeks was overall similar between the DTG + 3TC and DTG + TDF/FTC arms.
  - A higher percentage of blips occurred in participants receiving DTG + TDF/FTC than DTG + 3TC if BL VL was >100,000 c/mL, though participant number was low and caution in interpretation is warranted.
- Other assessed categories for VL ≥50 c/mL occurred infrequently in all groups, and the occurrences were similar.
- CVWs were not associated with prior VL blips.
- These data further reinforce the efficacy and potency of DTG + 3TC for the treatment of HIV.

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 GEMINI-1 and GEMINI-2 clinical investigators and their staff; and the ViiV Healthcare, PPD, and GSK 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.

References: 1. Cahn P, Sierra Madero JS, Arribas JR, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. *Lancet*. 2019;393(10167):143-155. **2.** Wang R, Underwood M, Koteff J, et al. 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. Presented at: HIV Glasgow; October 28-31, 2018; Glasgow, UK. Poster P313. **3.** Underwood M, Urbaityte R, Sievers J, et al. HIV replication at <40 c/mL for DTG + 3TC vs DTG + TDF/FTC in the GEMINI-1 & -2 studies. Presented at: Conference on Retroviruses and Opportunistic Infections; March 4-7, 2019; Seattle, WA. Poster 490.