Restarting Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) After Virologic Rebound: A Pooled Analysis of Studies in People With HIV-1

Poster eP.A.086

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Key Findings

- The majority of participants who experienced virologic rebound after virologic control achieved viral resuppression with B/F/TAF within 30 days
- No treatment-emergent resistance was observed in participants with persistent viremia, supporting the high barrier to resistance of B/F/TAF

Conclusion

- This study indicates that continuation of B/F/TAF treatment is effective in achieving HIV-1 resuppression following virologic rebound

Introduction

- Management of HIV-1 virologic rebound in the absence of treatment resistance includes reinitiating ARV therapy to regain virologic suppression[1,2]
- Most ARV agents are studied for their ability to suppress HIV-1 as first-line therapy, or in people who already have virologic suppression and are switching treatment regimens
- B/F/TAF is a recommended treatment for HIV-1[1–3]; however, data on the efficacy of B/F/TAF in people with HIV-1 with viremia who are treatment experienced are limited

Objective

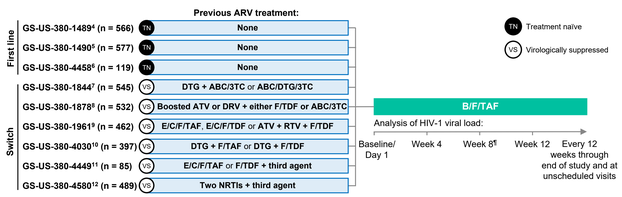
- To examine outcomes following virologic rebound in people with HIV-1 receiving B/F/TAF

Methods

Study Design

- We performed a pooled analysis of nine Phase 3, randomized, multicenter studies:

- Adults (≥ 18 years of age)*
- No documented or suspected resistance to FTC or TFV†
- $eGFR_{CG}$ ≥ 30 mL/min or ≥ 50 mL/min, depending on study‡
- HIV-1 RNA < 50 c/mL for ≥ 3 months prior to screening§ (switch studies)
- Receiving a stable ARV regimen for ≥ 3 months prior to screening§ (switch studies)



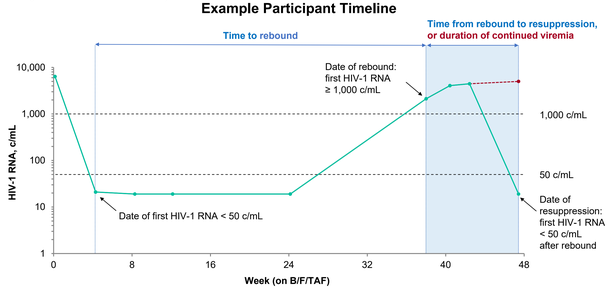
n values show the number of participants with ≥ 1 postbaseline HIV-1 RNA measurement on B/F/TAF during each study. *People with both HIV-1 and HBV for Study 4458; women for Study 1961; age ≥ 65 years for Study 4449; identifying as Black, African American or mixed race, including Black, for Study 4580; †Except NRTI resistance was permitted in Study 4030; FTC resistance was permitted in Study 4580; and resistance to the following drugs was not permitted in certain studies: INSTIs (Studies 4030 and 4580), DTG (Study 1844), EVG (Study 1961) and BIC (Study 4449); ‡≥ 30 mL/min for Studies 1490, 4030 and 4449; ≥ 50 mL/min for Studies 1489, 4458, 1844, 1878, 1961 and 4580; §≥ 6 months for Studies 1878, 4030 (if there was documented or suspected NRTI resistance prior to screening) and 4580; ¶Studies 4449 and 4580 did not include a scheduled Week 8 visit.

Endpoints on B/F/TAF Treatment

- **Virologic rebound events:** One or more viral load (VL) of ≥ 1,000 c/mL after virologic suppression (< 50 c/mL), indicative of suboptimal adherence
  - Categorized as subsequent virologic suppression, continued viremia or not evaluable (virologic rebound at last assessment)
- **Time to rebound:** Time between date of first HIV-1 RNA < 50 c/mL and date of rebound
- **Time from rebound to resuppression:** Time between date of rebound and date of first HIV-1 RNA < 50 c/mL after rebound
- **Duration of continued viremia:** Time from first HIV-1 RNA ≥ 1,000 c/mL in rebound to last HIV-1 RNA measurement for a continued viremia event
- **Cumulative study drug adherence** over the duration of the study, calculated for participants who returned ≥ 1 pill bottle and had calculable drug adherence
  - Categorized as < 85% versus ≥ 85% adherence*
- **Virologic resistance testing**, performed after a confirmed VL of ≥ 200 c/mL or unconfirmed ≥ 200 c/mL at key study endpoint or last study visit

*Categorization based on a prior study.[13]

Example Participant Timeline



Results

Baseline Demographics and Clinical Characteristics

Characteristic	Participants with any virologic rebound n = 96	Participants without any virologic rebound n = 3,672	*P*-value* (with vs. without virologic rebound)
Treatment naïve, n (%)†	53 (55.2)	689 (18.8)	< 0.0001‡
Virologically suppressed, n (%)†	43 (44.8)	2983 (81.2)	
Age, years, median (IQR)§	36 (26–46)	44 (33–53)	0.0029
Sex at birth, n (%) Male / Female	78 (81.3) / 18 (18.8)	2,724 (74.2) / 948 (25.8)	0.9915
Race, n (%)¶ American Indian, Alaska Native, Native Hawaiian or Pacific Islander	2 (2.0)	23 (0.6)	< 0.0001‖
Asian	5 (5.2)	263 (7.2)	
Black	51 (53.1)	1,287 (35.1)	
White	34 (35.4)	1,870 (51.1)	
Other or not permitted	4 (4.2)	229 (6.2)	
Hispanic or Latinx, n (%)¶	21 (21.9)	660 (18.0)	0.5881
HIV-1 RNA < 50 c/mL, n (%)§	40 (41.7)	2,937 (80.0)	0.0051
CD4 count, cells/µL, median (IQR)§	487 (324–738)	645 (463–855)	0.1095
CD4 count < 200 cells/µL, n (%)§	17 (17.7)	145 (3.9)	0.0040

Total N = 3,772; however, four participants from first-line studies (1489, 1490, 4458) who never achieved HIV-1 RNA < 50 c/mL on B/F/TAF were excluded. **P*-value was from the CMH test (categorical data) or the two-sided van Elteren test (continuous data), stratified by participant population type (treatment naïve vs. virologically suppressed); †Studies 1489, 1490 and 4458 randomized B/F/TAF groups. For Studies 1489 and 1490, participants in ABC/DTG/3TC group (n = 252) and participants in DTG + F/TAF group (n = 264) switching to B/F/TAF in open-label extension phase were included in virologically suppressed group; ‡For rebound status by participant population type, *P*-value was from Fisher exact test; §Defined at the first dose date of B/F/TAF; ¶Participants who reported "not permitted" were excluded from percentage and *P*-value calculations; ‖*P*-value is from the CMH test for comparing percentage of Black race between groups.

- Compared with participants without virologic rebound, those with rebound were more likely to be treatment naïve, younger, Black, have baseline VL ≥ 50 c/mL or baseline CD4 cell count < 200 cells/µL

Virologic Rebound Events

- In total, 110 virologic rebound events were identified in 96 (2.5%) of the 3,772 participants

Baseline Genotype Resistance Data for Participants With Virologic Rebound

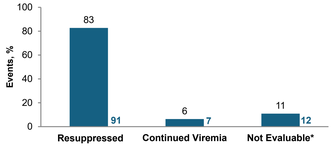
	INSTI-R n = 89	NRTI-R n = 95	PI-R n = 95	NNRTI-R n = 95
Participants with pre-existing primary resistance, % (n)	1 (1)	6 (6)	2 (2)	20 (19)
List of primary resistance substitutions, (n)	E92G (1)	M41L (2) D67N (1) L74V (1) K219N/Q (2) K70R (2) M184V (2)	M46I (1) I84V (1) T74P (1)	K103N/S (12) E138A/G/K (5) G190A/Q (2) L100I (1) Y181C (1) M230I (1)

Outcomes Following Virologic Rebound

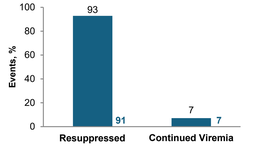
Virologic Rebound Events

- In total, 83% (91/110) of virologic rebound events were followed by subsequent resuppression
- Excluding nonevaluable virologic rebound events (virologic rebound at last assessment), resuppression was noted in 93% (91/98) of virologic rebound events

Total Rebound Events (Events = 110)



Not Evaluable* = Excluded (Events = 98)

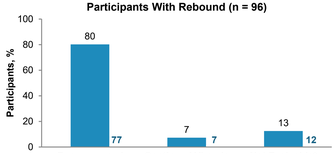


Values in blue denote number of events. *Virologic rebound at last assessment.

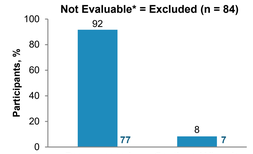
Outcomes in Participants With Virologic Rebound

- In total, 80% (77/96) of participants who had ≥ 1 virologic rebound event achieved resuppression after last rebound
- When nonevaluable events (virologic rebound at last assessment) were excluded, resuppression was achieved in 92% (77/84) of participants with virologic rebound after last rebound

Participants With Rebound (n = 96)



Not Evaluable* = Excluded (n = 84)



Values in blue denote number of participants. *Virologic rebound at last assessment.

Characteristics of Virologic Rebound Events

	Days, median (IQR)	Number of events
Time to virologic rebound	273 (148–503)	110
Time from rebound to resuppression	23 (19–38)	91
Duration of continued viremia before discontinuation of B/F/TAF	30 (14–87)	7*

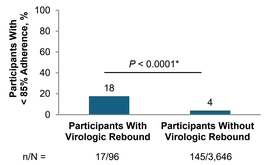
*Of seven participants with continuing viremia, one switched to DRV + RTV + F/TDF and one switched to DRV/COBI + RPV; both subsequently resuppressed. Follow-up data were not available for the remaining five participants.

- The median (IQR) HIV-1 VL at rebound was 6,840 (2,120–22,200) c/mL
- No treatment-emergent resistance was observed in participants with continued viremia

For characteristics of participants with continued viremia, please scan the QR code

Study Drug Adherence

- A significantly greater proportion of participants with virologic rebound versus without virologic rebound had < 85% adherence to study drugs



Participants who returned ≥ 1 pill bottle and had calculable drug adherence were included. **P*-value from CMH test stratified by participant population type (treatment naïve vs. virologically suppressed).

References: **1.** European AIDS Clinical Society. https://www.eacsociety.org/media/guidelines-11.1_final_09-10.pdf (accessed Aug. 9, 2023). **2.** DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed Aug. 3, 2023). **3.** Gandhi RT, et al. JAMA 2023;329:63-84. **4.** Gallant J, et al. Lancet 2017;390:2063-2072. **5.** Sax PE, et al. Lancet 2017;390:2073-2082. **6.** Avihingsanon A, et al. Lancet HIV Jul. 2023 [ePub]. doi: 10.1016/S2352-3018(23)00151-0. **7.** Molina JM, et al. Lancet HIV 2018;5:e357-e365. **8.** Daar ES, et al. Lancet HIV 2018;5:e347-e356. **9.** Kityo C, et al. J Acquir Immune Defic Syndr 2019;82:321-328. **10.** Sax PE, et al. Clin Infect Dis 2021;73:e485-e493. **11.** Maggiolo F, et al. Infect Dis Ther 2021;10:775-788. **12.** Hagins D, et al. J Acquir Immune Defic Syndr 2021;88:86-95. **13.** Sax P, et al. CROI 2020, Poster 495.

Acknowledgments: These studies were sponsored by Gilead Sciences. We thank all study participants and all participating study investigators and staff. Medical writing support was provided by Anne Errichelli, DPhil (Aspire Scientific Ltd, U.K.), and was funded by Gilead.

Disclosures: **AP:** grants or contracts from Gilead and ViiV Healthcare (paid to institution). **CO:** grants or contracts from AstraZeneca, Gilead, Janssen, MSD and ViiV Healthcare (paid to institution); payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Gilead, Janssen, MSD and ViiV Healthcare; President of the Medical Women's Federation (unpaid); governing council member of the International AIDS Society (unpaid). **AB:** speakers' bureaus for AbbVie, BMS, Gilead and Janssen; advisory boards for AbbVie, BMS, Gilead and MSD. **KM:** research grants and honoraria for speakers' bureaus and advisory boards from Gilead, GSK/ViiV Healthcare, Janssen and Merck; honorarium for advisory board participation with Epividian. **JRA:** personal fees for speaking and participation in advisory boards from Alexa, Gilead, Janssen, Merck and ViiV. **MLD**, **HH**, **HL**, **KA**, **LV**, **CC**, **JTH** and **HM:** employees of Gilead and own stocks/shares in Gilead. **FM** and **YY:** nothing to disclose.

Abbreviations: 3TC, lamivudine; ABC, abacavir; ARV, antiretroviral; ATV, atazanavir; B/BIC, bictegravir; c, copies; C/COBI, cobicistat; CD, cluster of differentiation; CMH, Cochran–Mantel–Haenszel; DRV, darunavir; DTG, dolutegravir; E/EVG, elvitegravir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft–Gault equation; F/FTC, emtricitabine; HBV, hepatitis B virus; INSTI, integrase strand-transfer inhibitor; IQR, interquartile range; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; R, resistance; RPV, rilpivirine; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir; TN, treatment naïve; VL, viral load; VS, virologically suppressed.