Long-term Follow-up After a Switch to Bictegravir, Emtricitabine, and Tenofovir Alafenamide From Dolutegravir, Abacavir, and Lamivudine

Indira Brar,[1] Peter Ruane,[2] Douglas Ward,[3] Jean-Michel Molina,[4] Anthony Mills,[5] Mezgebe Berhe,[6] Cynthia Brinson,[7] Moti Ramgopal,[8] Paul Benson,[9] Keith Henry,[10] Hailin Huang,[11] Kristen Andreatta,[11] Hal Martin[11]

[1]Henry Ford Hospital, Detroit, MI; [2]Ruane Medical & Liver Health Institute, Los Angeles, CA; [3]Dupont Circle Physicians Group, Washington, DC; [4]Hôpital Saint-Louis, Paris, France; [5]Southern California Men's Medical Group, Los Angeles; [6]North Texas Infectious Diseases Consultants, Dallas, TX; [7]Central Texas Clinical Research, Austin, TX; [8]Midway Research Center, Fort Pierce, FL; [9]Be Well Medical Center, Berkeley, MI; [10]Hennepin Healthcare, Minneapolis, MN; [11]Gilead Sciences, Inc., Foster City, CA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
800-445-3235

Introduction

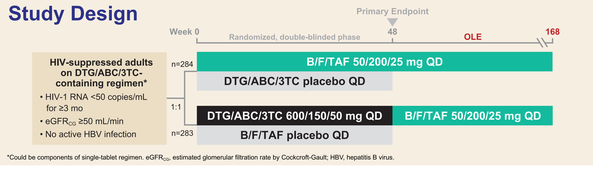
- Modern antiretrovirals provide high HIV suppression rates; safety and tolerability often drive regimen choice
- The single-tablet regimen bictegravir (BIC; B), emtricitabine (FTC; F), and tenofovir alafenamide (TAF; B/F/TAF) is a US DHHS, EACS, and IAS-USA guidelines-recommended regimen,[1-3] with demonstrated safety and efficacy, and a high barrier to resistance
- Previously reported primary results from the present Phase 3 study (GS-US-380-1844; NCT02603120) demonstrated that switching to B/F/TAF was noninferior to continuing dolutegravir (DTG), abacavir (ABC), and lamivudine (3TC) in virologically suppressed adults at Week 48[4]
  - Both treatments were well tolerated
  - No treatment-emergent viral resistance to B/F/TAF was observed

Objectives

- To assess efficacy and safety data through Week 168 for study GS-US-380-1844 participants who enrolled in the open-label extension (OLE)

Methods

Study Design

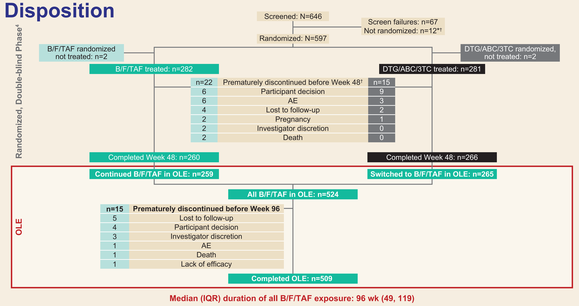


*Could be components of single-tablet regimen. $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; HBV, hepatitis B virus.

- Phase 3, randomized, double-blind, multicenter, active-controlled study
  - Australia, Europe, and North America
  - Primary endpoint: proportion with HIV-1 RNA ≥50 copies/mL at Week 48
- OLE objectives: to evaluate efficacy and safety after additional exposure to B/F/TAF
  - All B/F/TAF group included all participants with ≥1 dose of B/F/TAF; baseline for DTG/ABC/3TC to B/F/TAF group was measured from start of B/F/TAF in OLE

Results

Disposition



Median (IQR) duration of all B/F/TAF exposure: 96 wk (49, 119)

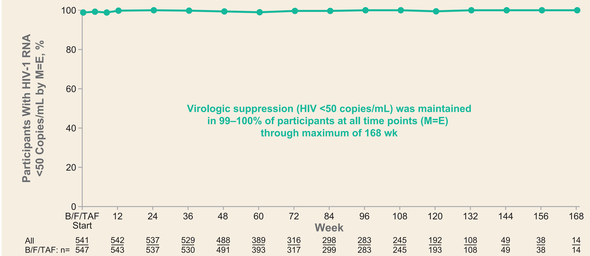
*12 participants met all eligibility criteria and were not randomized: withdrew consent (n=7), lost to follow-up (n=4), and outside of visit window (n=1); †Previously reported.[4] AE, adverse event; IQR, interquartile range.

Baseline Characteristics*

		All B/F/TAF n=547
Age, y		47 (21–71)
Female at birth		58 (11)
Race/ethnicity	White	397 (73)
	Black or African descent	116 (21)
	Hispanic/Latino	96 (18)
CD4 cells/μL		709 (536, 905)
HIV disease status	Asymptomatic HIV	474 (87)
	Symptomatic HIV	18 (3)
	AIDS	55 (10)
$eGFR_{CG}$, mL/min		98 (83, 118)
Body mass index, kg/m²		26 (24, 29)
Hepatitis C coinfection (randomized phase: n=563)		1 (0.2)

*Data are n (%) or median (IQR), except age, which is median (range). CD4, cluster of differentiation-4.

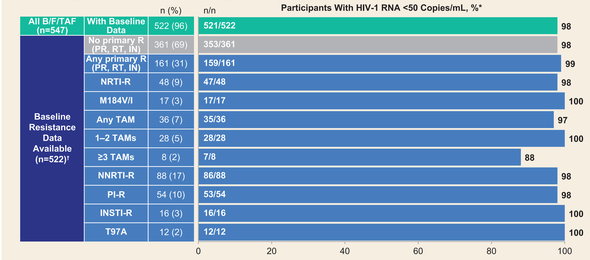
Virologic Outcomes (M=E)



M=E, missing = excluded.

- Median (IQR) baseline CD4 cell count: 709 (536, 905) cells/μL; changes from baseline: -17 (-120, 65) at Week 48 (n=476) and -9 (-100, 108) at Week 96 (n=279)
- No participant developed resistance to B/F/TAF

Virologic Outcomes by Archived Resistance



*1 participant with ≥3 thymidine analog mutation (TAMs; also counted in nucleoside reverse transcriptase [RT] inhibitor [NRTI]-resistance [R] and any TAM categories) had 56 copies/mL at last visit and resuppressed on commercial B/F/TAF; outcomes determined by last on-treatment observation carried forward analysis through end of study; †Derived from cumulative historical and/or proviral genotypes. IN, integrase; INSTI, IN strand transfer inhibitor; NNRTI, non-NRTI; PI, protease (PR) inhibitor.

- High efficacy was also achieved in participants with archived resistance

Overall Safety

n (%)	All B/F/TAF n=547
Any AE	446 (82)
Any Grade 3 or 4 AE	33 (6)
Any treatment-related AE*	39 (7)
Any serious AE	47 (9)
Any AE leading to discontinuation†	7 (1)
Death‡	3 (1)
Grade 3 or 4 laboratory abnormalities	96 (18)

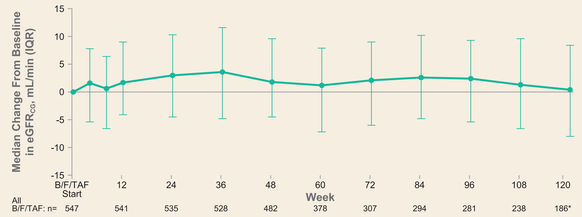
*Most treatment-related AEs were Grade 1; most common was headache (2%); †1 participant had AE leading to discontinuation in OLE (treatment-related headache); ‡Treatment-emergent deaths: 2 previously reported (Week 48) not considered related to treatment by investigator and 1 during OLE (hypertensive cardiovascular disease in White man aged 60 y with medical history of hypertension and hypercholesterolemia) not considered related to treatment.

Most Common AEs and Laboratory Abnormalities

n (%)	All B/F/TAF n=547
Most common AEs (>5% of participants)	
Upper respiratory tract infection	77 (14)
Nasopharyngitis	57 (10)
Diarrhea	53 (10)
Arthralgia	35 (6)
Back pain	31 (6)
Headache	31 (6)
Sinusitis	31 (6)
Bronchitis	29 (5)
Syphilis	28 (5)
Most common Grade 3 or 4 laboratory abnormalities (>2% of participants)	
Increased LDL	23 (4)
Increased creatine kinase	17 (3)
Hyperglycemia	13 (2)
Increased amylase	12 (2)
Increased ALT	11 (2)
Glycosuria	11 (2)

ALT, alanine aminotransferase; LDL, low-density lipoprotein.

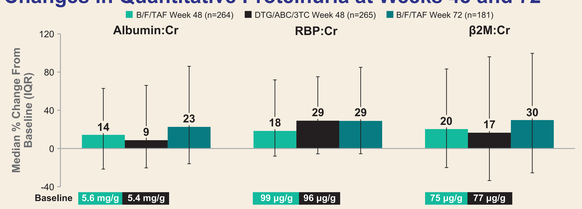
Change From Baseline in $eGFR_{CG}$



*Low participant numbers out to Week 168 (n=12); median change at Week 168: -1.2 mL/min.

- No discontinuations due to renal-related AEs and no cases of renal proximal tubulopathy

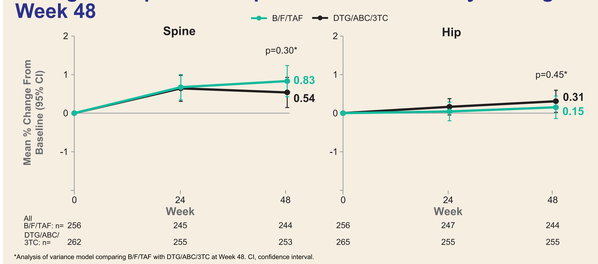
Changes in Quantitative Proteinuria at Weeks 48 and 72



β2M, β2-microglobulin; Cr, creatinine; RBP, retinol-binding protein.

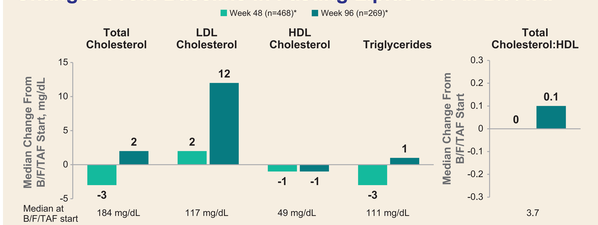
- No differences between B/F/TAF and DTG/ABC/3TC in quantitative measures of proteinuria or biomarkers of renal tubular dysfunction
- Week 48 previously presented; additional data at Week 72 were assessed for B/F/TAF participants not yet unblinded, but on study

Changes in Spine and Hip Bone Mineral Density Through Week 48



*Analysis of variance model comparing B/F/TAF with DTG/ABC/3TC at Week 48. CI, confidence interval.

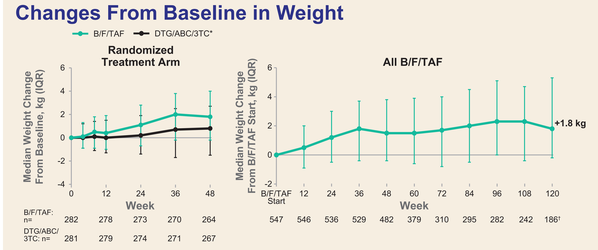
Changes From Baseline in Fasting Lipids for All B/F/TAF



*Weeks after switch to B/F/TAF. HDL, high-density lipoprotein.

- Fasting lipids were generally stable, with slight increases in LDL
- 17 participants (3%) initiated lipid-modifying agents during the study

Changes From Baseline in Weight



*Shown for reference; †Low participant numbers out to Week 168 (n=12); median change at Week 168: +2.1 kg.

- Weight increased, with median changes from baseline ranging from +0.5 to +2.3 kg

Conclusions

- In the long-term OLE of this Phase 3 study, people living with HIV who switched to B/F/TAF from DTG/ABC/3TC demonstrated:
  - Continued high rates of virologic suppression, with no emergent resistance
  - High efficacy in participants with archived resistance
  - Safety and tolerability of B/F/TAF through 168 wk
    - Changes from baseline in body weight in the all B/F/TAF group were consistent with the Week-48 data
    - No discontinuations due to renal-related AEs and no cases of renal proximal tubulopathy

References: 1. Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV; 7/10/19; **2.** EACS Guidelines Version 10.1 October 2020; **3.** Saag MS, et al. JAMA 2018;320:379-96; **4.** Molina JM, et al. Lancet HIV 2018;5:e357-65. **Acknowledgments:** We extend our thanks to the participants, their families, and all participating study investigators and staff: **Australia:** D Baker, M Bloch, D Smith; **Belgium:** L Vandekerckhove; **Canada:** L Charest, J de Wet, K Kasper, RP LeBlanc, B LeBouche; **France:** J-M Molina, G Pialoux, P Pugliese, F Raffi; **Germany:** K Arasteh, A Baumgarten, M Bickel, J Bogner, S Esser, H Jäger, J Rockstroh, H-S Stellbrink; **Italy:** A Antinori; **Spain:** A Antela, B Clotet Sala, M Gutierrez, LF Lopez-Cortes, MJ Pérez, D Podzamczer, A Rivero Roman; **UK:** AE Clark, MA Johnson, J Ross, G Schembri, AP Ustianowski; **USA:** H Albrecht, J Bartczak, P Benson, D Berger, M Berhe, I Brar, C Brinson, JH Burack, BP Cook, D Coulston, C Cretcios, GE Crofoot Jr, FA Cruickshank, E DeJesus, C Dietz, MP Dube, H Edelstein, C Fichtenbaum, J Flamm, JE Gallard, JC Gathe Jr, R Grossberg, DP Hagins, WK Henry, RK Hsu, M Johnson, CA Kinder, D Klein, A LaMarca, K Lichtenstein, N Lin, CT Martorelli, A Mills, JO Morales Ramirez, K Mounzer, CL Newman, G Oguchi, O Osiyemi, C Parsons, P Peyrani, G Pierone Jr, DJ Prelutsky, M Ramgopal, B Rashbaum, GJ Richmond, PJ Ruane, L Santiago, AJ Scarsella, SR Schrader, A Scribner, P Shalit, C Shikuma, ASO Shon, J Slim, J Stephens, WJ Towner, TJ Vanig, BH Wade, MB Wohlfeiler, AK Wurapa. BG Yangco. This study was funded by Gilead Sciences, Inc.