P088

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Outcomes After Switching From 144 Weeks of Blinded DTG/ABC/3TC or DTG+F/TAF to 96 Weeks of Open-label B/F/TAF

Chloe Orkin,[1] Andrea Antinori,[2] Jürgen Rockstroh,[3] Santiago Moreno Guillén,[4] Claudia Martorell,[5] Jean-Michel Molina,[6] Adriano Lazzarin,[7] Franco Maggiolo,[8] Yazdan Yazdanpanah,[9] Kristen Andreatta,[10] Hailin Huang,[10] Jason Hindman,[10] Hal Martin,[10] Jared Baeten,[10] Anton Pozniak[11]

[1]Queen Mary University of London, UK; [2]Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani, Roma, Italy; [3]Medizinische Klinik und Poliklinik I, Universitätsklinikum Bonn, Germany; [4]Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain; [5]Infectious Diseases and the Research Institute, Springfield, Massachusetts, US; [6]University of Paris, France; [7]IRCCS Ospedale San Raffaele, Milano, Italy; [8]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; [9]Hôpital Bichat-Claude Bernard, Paris; [10]Gilead Sciences, Inc., Foster City, California, US; [11]Chelsea and Westminster Hospital, London

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

Introduction

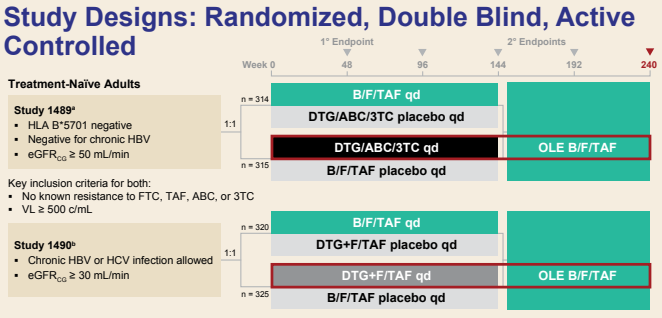
- HIV guidelines offer switch strategies for people with HIV-1 (PWH) who are virologically suppressed (eg, history consistent with no integrase [IN] strand transfer inhibitor [INSTI] resistance mutations), but long-term clinical follow-up after the regimen switch is often lacking
- Bictegravir/emtricitabine (FTC)/tenofovir alafenamide (B/F/TAF) is a guideline-recommended regimen for most PWH and is indicated for those with no antiretroviral treatment history or as a switch regimen in virologically suppressed PWH
- In addition, it is recommended for rapid initiation due to its high barrier to resistance, favorable drug-drug interaction profile, and once-daily dosing without food restrictions[1-9]

Objective

- To evaluate 96-week outcomes on open-label (OL) B/F/TAF that followed 144 weeks of blinded dolutegravir (DTG)–based treatment in two Phase 3 studies of PWH initiating treatment

Methods

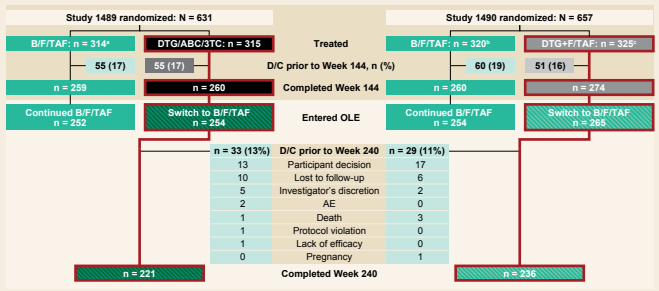
Study Designs: Randomized, Double Blind, Active Controlled



[a]GS-US-380-1489 (ClinicalTrials.gov NCT02607930); [b]GS-US-380-1490 (NCT02607956). 3TC = lamivudine; ABC = abacavir; $eGFR_{CG}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; OLE = OL extension; VL = viral load.

Results

Participant Disposition From Baseline to Week 240



[a]2 participants randomized and not treated; [b]7 randomized and not treated; [c]5 randomized and not treated. AE = adverse event; D/C = discontinuation.

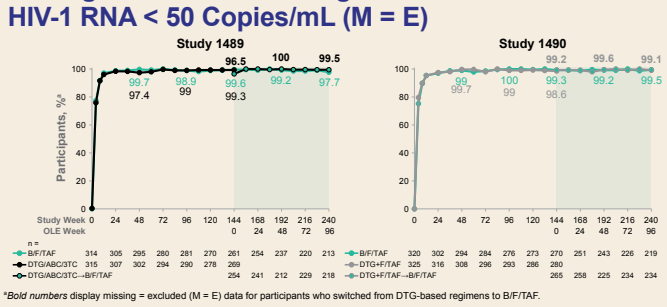
Characteristics at B/F/TAF Start[a]

	Study 1489 DTG/ABC/3TC→B/F/TAF n = 254	Study 1490 DTG+F/TAF→B/F/TAF n = 265
Median age, y (Q1, Q3)	36 (30, 45)	38 (30, 48)
Female sex at birth, n (%)	29 (11)	26 (10)
Race/ethnicity, n (%)		
Black or African descent	94 (37)	80 (30)
Hispanic/Latinx ethnicity	54 (21)	73 (28)
Median body weight, kg (Q1, Q3)	83.0 (72.6, 94.3)	81.7 (71.0, 96.0)
HIV-1 RNA 50 to < 200 copies/mL, n (%)	3 (1)	1 (< 1)
HIV-1 RNA ≥ 200 copies/mL, n (%)	6 (2)	1 (< 1)
Median CD4 count, cells/mm³ (Q1, Q3)	766 (599, 1023)	730 (550, 958)
Asymptomatic HIV infection, n (%)	229 (90)	234 (88)
Median $eGFR_{CG}$, mL/min (Q1, Q3)	116 (99, 138)	111 (95, 135)

[a]All participants completed 144 weeks on blinded DTG/ABC/3TC or DTG+F/TAF before entering OLE. CD4 = cluster of differentiation-4; Q = quartile.

- In participants who switched from DTG/ABC/3TC or DTG+F/TAF, median durations of exposure (Q1, Q3) to B/F/TAF were 96 weeks (95.7, 96.3) in Study 1489 and 96 weeks (95.9, 96.4) in Study 1490

Virologic Outcomes Through Week 240/OLE Week 96: HIV-1 RNA < 50 Copies/mL (M = E)



[a]Study week for participants initially randomized to B/F/TAF and OLE week for participants who switched from DTG-based regimens. M = F = missing = failure.

- Participants who switched from DTG-based regimens had similar rates of virologic suppression (M = F) to participants initially on B/F/TAF

Virologic Outcomes on B/F/TAF: HIV-1 RNA < 50 Copies/mL (M = F)

[a]Study week for participants initially randomized to B/F/TAF and OLE week for participants who switched from DTG-based regimens. M = F = missing = failure.

- Participants who switched from DTG-based regimens had similar rates of virologic suppression (M = F) to participants initially on B/F/TAF

Virologic Resistance During OLE: Weeks 144-240

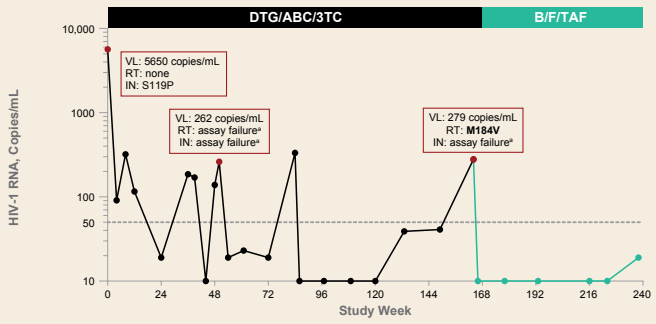
n	Study 1489 DTG/ABC/3TC→B/F/TAF n = 254	Study 1490 DTG+F/TAF→B/F/TAF n = 265
Met criteria for resistance testing[a]	3	1
NRTI resistance detected	0	0
INSTI resistance detected	0	0

[a]Resistance testing performed for participants with confirmed HIV-1 RNA ≥ 200 copies/mL or ≥ 200 copies/mL at last visit, with no resuppression of HIV-1 RNA to < 50 copies/mL while on study drug. NRTI = nucleoside reverse-transcriptase (RT) inhibitor.

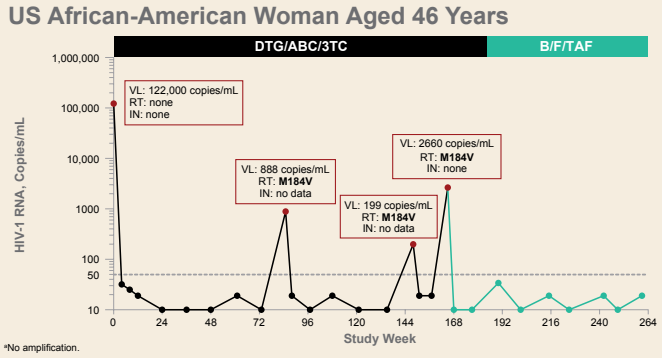
- No participant in the final resistance analysis population developed treatment-emergent resistance during long-term treatment with B/F/TAF
- Two participants on blinded DTG/ABC/3TC had HIV-1 RNA ≥ 200 copies/mL at time of switch, both of whom were later found to have M184V and resuppressed on OL B/F/TAF

Participants With Resistance

UK White Man Aged 24 Years



US African-American Woman Aged 46 Years



[a]No amplification.

Adverse Events During OLE: Weeks 144-240

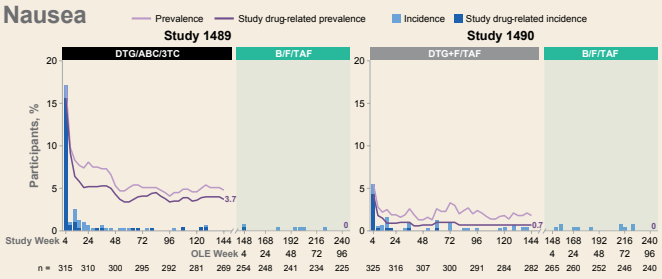
Participants, %	DTG/ABC/3TC→B/F/TAF n = 254	DTG+F/TAF→B/F/TAF n = 265
Any AE	84	81
Any grade study drug-related AE	5	3
All occurred in 1 participant unless otherwise specified	Diarrhea (n = 3), weight increased (n = 2), nausea, headache, abnormal dreams, vomiting, LDL increased, obesity, blood cholesterol increased, libido increased, myalgia, alopecia, pruritic rash	Headache, fatigue, flatulence, weight increased, weight decreased, back pain, diabetes mellitus, lethargy, migraine, oropharyngeal pain

LDL = low-density lipoprotein.

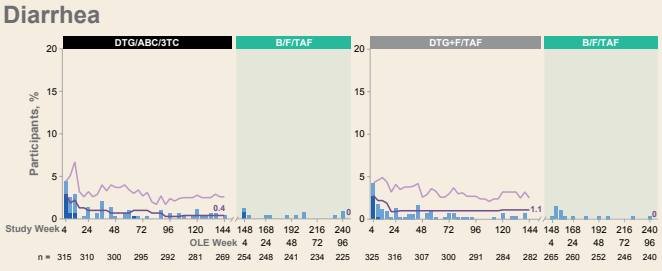
- A Grade 3 drug-related AE occurred in 1 participant (diabetes mellitus in a participant switching from DTG+F/TAF); no Grade 4 AEs were reported
- Nausea and diarrhea were the 2 most commonly reported AEs in the blinded phase of Studies 1489 and 1490[4]

Nausea and Diarrhea Incidence and Prevalence Through Week 240

Nausea



Diarrhea



Hashmarks indicate transition from randomized phase to OLE; prevalence reset at OLE start.

- Among participants randomized to DTG/ABC/3TC (Study 1489) or DTG+F/TAF (Study 1490), the incidence and prevalence of nausea and diarrhea declined numerically after switching to B/F/TAF in the OLE

Adverse Events Leading to Discontinuation During OLE: Weeks 144-240

Participants, n	DTG/ABC/3TC→B/F/TAF n = 254	DTG+F/TAF→B/F/TAF n = 265
AE leading to premature D/C	Seizure unrelated to study drug on OLE Day 335/Study Week 192	
	Weight increase attributed to study drug during blinded phase Day 29, D/C on OLE Day 506/Study Week 228	
Death	Seizure unrelated to study drug on OLE Day 335/Study Week 192	Malignant neoplasm of urinary bladder unrelated to study drug on OLE Day 659/Study Week 240
	Unknown cause on OLE Day 677/Study Week 270	Unknown cause on Study Week 60
		Unknown cause on OLE Day 320/Study Week 207

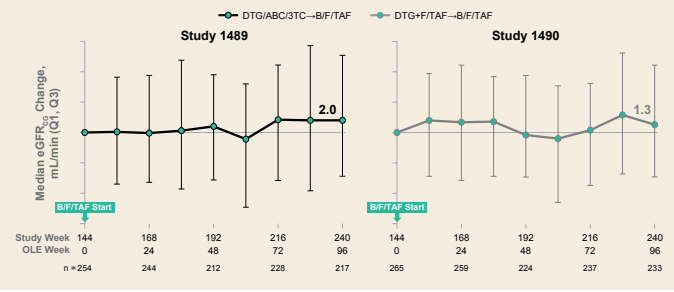
- Across both studies, 2/519 participants (0.4%) experienced an AE that led to drug D/C after switching

Laboratory Abnormalities During OLE: Weeks 144-240

Participants, %	DTG/ABC/3TC→B/F/TAF n = 254	DTG+F/TAF→B/F/TAF n = 265
Any Grade 3 or 4 laboratory abnormality	13	16
≥ 2% in either group		
Increased amylase	2[a]	2[a]
Increased AST	2	1
Increased creatine kinase	4	3
Fasting hyperglycemia	1	2
Nonfasting hyperglycemia	1	3
Increased fasting LDL	1	3
Glycosuria	1[b]	3[b]

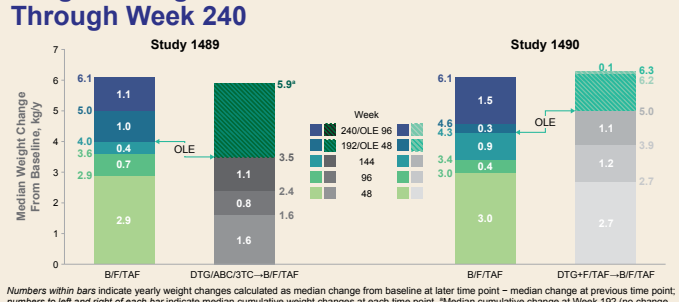
[a]No clinical symptoms of pancreatitis; [b]No cases of glycosuria occurred in participants without diabetes or concomitant hyperglycemia. AST = aspartate aminotransferase.

eGFR Changes During OLE: Weeks 144-240



- There were no reported cases of proximal renal tubulopathy and no D/Cs due to renal AEs for participants receiving B/F/TAF

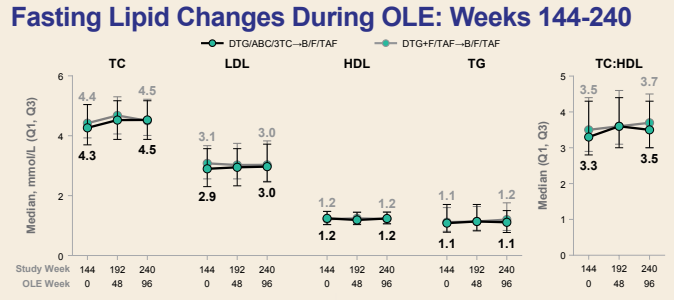
Weight Changes From Randomized Phase Baseline Through Week 240



Numbers within bars indicate yearly weight changes calculated as median change from baseline at later time point − median change at previous time point; *numbers to left and right of each bar* indicate median cumulative weight changes at each time point. [a]Median cumulative change at Week 192 (no change from Week 192 to 240).

- Significantly lower weight changes were observed at Week 144 for participants treated with DTG/ABC/3TC vs DTG+F/TAF: 3.5 vs 5.0 kg ($P = 0.02$)
- Between Weeks 144 and 240 of the OLE, greater weight changes were observed in participants who switched from DTG/ABC/3TC to B/F/TAF vs those who switched from DTG+F/TAF to B/F/TAF: 2.4 vs 1.3 kg ($P = 0.01$)
- Cumulative median weight changes at Week 240 were numerically similar for all treatment groups
- Switch from ABC to TAF has been associated with statistically significant weight gain, consistent with the loss of a weight suppressive effect of ABC noted in the first year[10,11]

Fasting Lipid Changes During OLE: Weeks 144-240



Participants, %	DTG/ABC/3TC→B/F/TAF n = 254	DTG+F/TAF→B/F/TAF n = 265
Taking lipid-lowering agents at B/F/TAF start	7	10
Initiated lipid-lowering agents while on B/F/TAF	2	5

HDL = high-density lipoprotein; TC = total cholesterol; TG = triglycerides.

- Small changes in lipids were observed among participants who switched to B/F/TAF for 48 weeks and few participants initiated lipid-lowering agents

Conclusions

- Over 5 years of follow-up in adults initially taking DTG/ABC/3TC or DTG+F/TAF who then switched to B/F/TAF and were followed for 96 weeks, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance to B/F/TAF
  - Two participants had HIV-1 RNA ≥ 200 copies/mL with M184V at the time of switching from DTG/ABC/3TC and both subsequently had sustained resuppression on B/F/TAF
  - Few AEs leading to D/C and no renal related D/Cs
  - Declines in incidence and prevalence of nausea and diarrhea after switching to B/F/TAF
  - Small median lipid changes and minimal impact on TC:HDL ratio
  - Similar cumulative weight changes at Year 5 for all groups, with greater weight changes in those who switched from DTG/ABC/3TC vs DTG+F/TAF, consistent with the loss of the weight-suppressive effect of ABC noted in Year 1
- These results provide additional long-term evidence of the safety and efficacy of B/F/TAF in PWH who switch from a DTG-containing regimen

References: **1.** DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV; 18 Dec 2019; **2.** EACS Guidelines Version 10.0 November 2019; **3.** Gallant J, et al. *Lancet*. 2017;390:2063-72; **4.** Orkin C, et al. *Lancet HIV*. 2020;7:e389-400; **5.** Pozniak A, et al. EACS 2021, poster PE2/68; **6.** Saag MS, et al. *JAMA*. 2018;320:379-96; **7.** Sax PE, et al. *Lancet*. 2017;390:2073-82; **8.** Stellbrink H-J, et al. *Lancet HIV*. 2019;6:e364-72; **9.** Wohl DA, et al. *Lancet HIV*. 2019;6:e355-63; **10.** Lakey W, et al. *AIDS Res Hum Retroviruses*. 2013;29:435-40; **11.** Sax PE, et al. *Clin Infect Dis*. 2020;71:1379-89.

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