PE2/68

Outcomes 48 Weeks After Switching From DTG/ABC/3TC or DTG + F/TAF to B/F/TAF

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Introduction

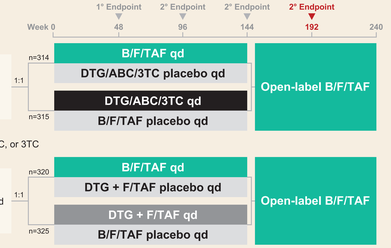
- Bictegravir (B; BIC)/emtricitabine (F; FTC)/tenofovir alafenamide (TAF; B/F/TAF) is a guidelines-recommended, single-tablet regimen for people with HIV-1 (PWH)[1-3]
- B/F/TAF has a high barrier to resistance, favorable drug-drug interaction profile, and ability to be given once daily without food restrictions
- Safety and efficacy through Week 144 have been demonstrated in two Phase 3 studies (GS-US-380-1489 [ClinicalTrials.gov NCT02607930] and GS-US-380-1490 [NCT02607956]) of B/F/TAF compared with 3-drug dolutegravir (DTG)–containing regimens in treatment-naïve adults[4-8]
  - All participants were offered enrollment in an open-label extension (OLE) after completing 144 wk of the randomized portions of the studies

Objective

- To evaluate 48-wk outcomes on B/F/TAF in an OLE that followed 144 wk of blinded DTG-based treatment in two Phase 3 studies of treatment-naïve PWH

Methods

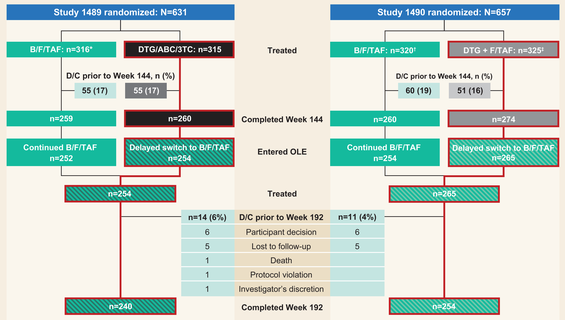
Study Designs: Randomized, Double Blind, Active Controlled



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.

Results

Participant Disposition From Baseline to Week 192



*2 participants randomized and not treated; †7 randomized and not treated; ‡5 randomized and not treated. D/C, discontinuation.

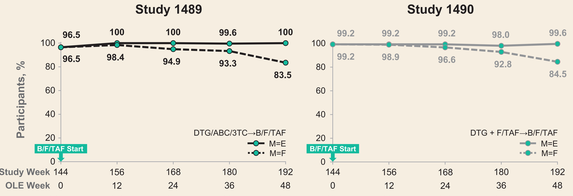
Characteristics at B/F/TAF Start*

	Study 1489 DTG/ABC/3TC→B/F/TAF n=254	Study 1490 DTG + F/TAF→B/F/TAF n=265
Median age, y (range)	36 (22–71)	38 (21–80)
Female 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 (IQR)	83 (73, 94)	82 (71, 96)
HIV-1 RNA ≥50 copies/mL, n (%)	9 (4)	2 (1)
Median CD4 cells/μL (IQR)	766 (599, 1023)	730 (550, 958)
Asymptomatic HIV infection, n (%)	229 (90)	234 (88)
Median $eGFR_{CG}$, mL/min (IQR)	116 (99, 138)	111 (95, 135)

*All participants completed 144 wk on blinded DTG/ABC/3TC or DTG + F/TAF before entering OLE. CD4, cluster of differentiation-4; IQR, interquartile range.

Virologic Outcomes: Weeks 144–192

HIV-1 RNA <50 Copies/mL



*Participants with nonmissing HIV-1 RNA at each visit. M=E, missing=excluded; M=F, missing=failure.

- Participants who switched from DTG/ABC/3TC or DTG + F/TAF to B/F/TAF in the OLE maintained high levels of virologic suppression through Week 192/OLE Week 48 (M=E)
- Median CD4 changes from B/F/TAF start to Week 192/OLE Week 48, cells/μL (IQR): DTG/ABC/3TC→B/F/TAF, -6 (-113, 104); DTG + F/TAF→B/F/TAF, 14 (-83, 117)

Virologic Resistance Through Week 192

Participants, n	Baseline–Week 144 DTG/ABC/3TC n=315	Baseline–Week 144 DTG + F/TAF n=325	Week 144–Unblinding DTG/ABC/3TC n=269	Week 144–Unblinding DTG + F/TAF n=281	OLE B/F/TAF DTG/ABC/3TC→B/F/TAF n=254	OLE B/F/TAF DTG + F/TAF→B/F/TAF n=265
Met criteria for resistance testing*	6	7	4	1	1	1
NRTI resistance detected	0	0	2 (M184V)†	0	0	0
INSTI resistance detected	0	0	0	0	0	0

*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; †1 DTG/ABC/3TC participant developed M184V and had no resistance to integrase (IN); adherence by pill count was 93%; ‡ DTG/ABC/3TC participant developed M184V and had assay failure for IN; adherence by pill count was 86%. INSTI, IN strand transfer inhibitor; NRTI, nucleoside reverse-transcriptase (RT) inhibitor.

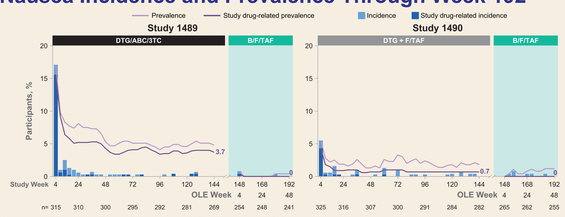
- No resistance to any components of B/F/TAF occurred in any group
- Post-Week 144 but prior to switch, 2 participants on blinded study drug of DTG/ABC/3TC developed M184V, switched to B/F/TAF, and achieved HIV-1 RNA <50 copies/mL at their next visit

Adverse Events: Weeks 144–192

Participants, %	DTG/ABC/3TC→B/F/TAF: n=254	DTG + F/TAF→B/F/TAF: n=265
Any AE	73	71
Any study drug-related AE	3	2
All occurred in 1 participant unless otherwise specified	Diarrhea (n=2), headache, abnormal dreams, alopecia, libido decreased, nausea, obesity, rash pruritic, and vomiting	Diabetes mellitus, fatigue, flatulence, headache, lethargy, migraine, and weight decreased

AE, adverse event.

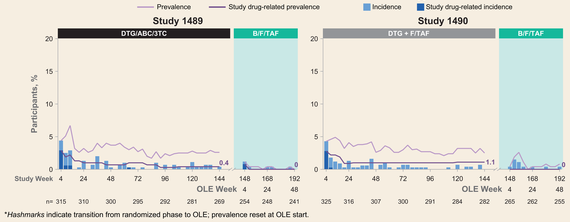
Nausea Incidence and Prevalence Through Week 192*



*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 declined numerically after switching to B/F/TAF in the OLE

Diarrhea Incidence and Prevalence Through Week 192*



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

- Among participants treated with DTG/ABC/3TC or DTG + F/TAF, the incidence and prevalence of diarrhea declined numerically after switching to B/F/TAF in the OLE

Adverse Events Leading to Discontinuation: Weeks 144–192

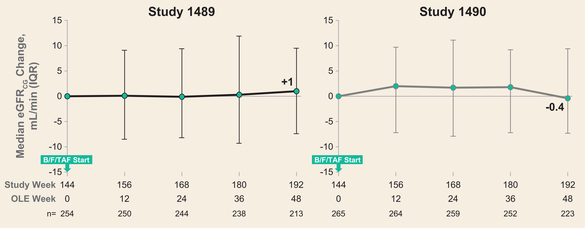
- 1 participant who switched from DTG/ABC/3TC to B/F/TAF (Study 1489) died due to seizure unrelated to study drug on OLE Day 335/Study Week 192

Laboratory Abnormalities: Weeks 144–192

Participants, %	DTG/ABC/3TC→B/F/TAF n=254	DTG+F/TAF→B/F/TAF n=265
Any Grade 3 or 4 laboratory abnormality	8	14
≥2% in either group		
Nonfasting hyperglycemia	1	3
Increased fasting LDL	1	3
Glycosuria	1	2

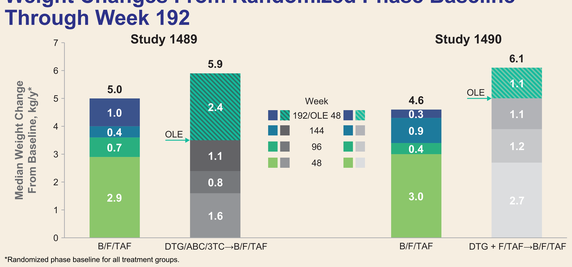
LDL, low-density lipoprotein.

eGFR Changes: Weeks 144–192



- No reported cases of proximal renal tubulopathy or D/C due to renal AEs were observed on B/F/TAF

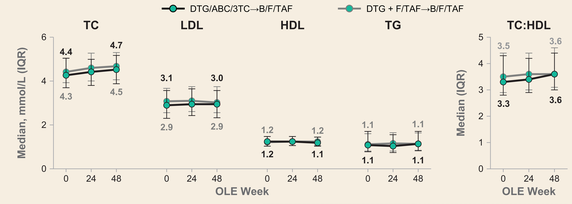
Weight Changes From Randomized Phase Baseline Through Week 192



*Randomized phase baseline for all treatment groups.

- Numerically greater weight changes were observed in those who switched from DTG/ABC/3TC (Study 1489) at OLE Week 48 postswitch than in those who switched from DTG + F/TAF (Study 1490): 2.4 vs 1.1 kg
- Switch from ABC to TAF has been associated with statistically significant weight gain, with one potential explanation being worse gastrointestinal tolerability with ABC vs TAF[9,10]
- The difference in weight gain in Study 1489 at Week 48 (1.3 kg less with DTG/ABC/3TC) was similar to the difference in additional weight gain at OLE Week 48 (+1.4 kg when switching from DTG/ABC/3TC to B/F/TAF)

Fasting Lipid Changes: Weeks 144–192



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	4

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 wk and small numbers of participants initiated lipid-lowering agents

Conclusions

- Over 4 y of follow-up of treatment-naïve PWH who were initially randomized to DTG/ABC/3TC or DTG + F/TAF for 144 wk and then switched to 48 wk of OL B/F/TAF, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance to B/F/TAF
  - Few AEs leading to D/C and no renal related D/Cs
  - Declines in nausea and diarrhea incidence and prevalence after switching from DTG/ABC/3TC or DTG + F/TAF to B/F/TAF
  - Small median lipid changes and minimal impact on TC:HDL ratio
  - Numerically greater weight changes in those who switched from DTG/ABC/3TC than from DTG + F/TAF
- These results confirm the safety and efficacy of B/F/TAF among people who switch from DTG/ABC/3TC or DTG + F/TAF

References: 1. DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV; 12/18/19; **2.** EACS Guidelines Version 10.0 November 2019; **3.** Saag MS, et al. JAMA 2018;320:379-96; **4.** Gallant J, et al. Lancet 2017;390:2063-72; **5.** Orkin C, et al. Lancet HIV 2020;7:e389-400; **6.** Sax PE, et al. Lancet 2017;390:2073-82; **7.** Stellbrink H-J, et al. Lancet HIV 2019;6:e364-72; **8.** Wohl DA, et al. Lancet HIV 2019;6:e355-63; **9.** Lakey W, et al. AIDS Res Hum Retroviruses 2013;29:435-40; **10.** Sax PE, et al. Clin Infect Dis 2020;71:1379-89.

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