# Long-term Efficacy and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in ART-Naïve Adults

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## Introduction

- The single-tablet regimen bictegravir (BIC; B), emtricitabine (FTC; F), and tenofovir alafenamide (TAF; B/F/TAF) is an EACS, US Dept of Health & Human Services, and International Antiviral Society–USA guidelines-recommended regimen,[1–3] with demonstrated safety and efficacy, and a high barrier to resistance
- We report long-term (Week 144) results pooled from two Phase 3 studies of treatment-naïve adults living with HIV comparing randomized treatment with B/F/TAF to 1 of 2 recommended dolutegravir (DTG)–containing regimens: DTG/abacavir (ABC)/lamivudine (3TC) in Study 1489 and DTG + F/TAF in Study 1490

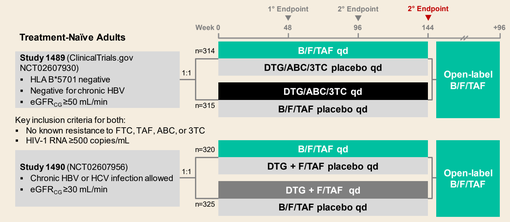
[1]**EACS European AIDS Clinical Society. Guidelines Version 9.1, October 2018. https://www.eacsociety.org/files/2018_guidelines-9.1-english.pdf; [2]Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.** Dep of Health and Human Services. https://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL003510.pdf; [3]Saag MS, et al. JAMA 2018;320:379-96.

## Objectives

- To evaluate the safety and efficacy of B/F/TAF and DTG-containing regimens in treatment-naïve adults living with HIV based on a pooled analysis from two phase 3 studies

## Methods

### Randomized, double-blind, active-controlled studies



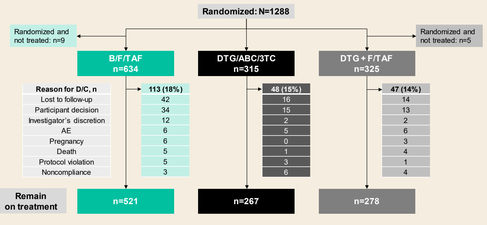

$eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen.

### Baseline Characteristics

| | Pooled | Study 1489 | | Study 1490 | |
|---|---|---|---|---|---|
| | B/F/TAF n=634 | B/F/TAF n=314 | DTG/ABC/3TC n=315 | B/F/TAF n=320 | DTG + F/TAF n=325 |
| Median age, y (range) | 32 (18–71) | 31 (18–71) | 32 (18–68) | 33 (18–71) | 34 (18–77) |
| Men, % | 89 | 91 | 90 | 88 | 89 |
| Race/ethnicity, % | | | | | |
| Black or African descent | 33 | 36 | 36 | 30 | 31 |
| Hispanic/Latino | 24 | 23 | 21 | 26 | 25 |
| Median HIV-1 RNA, log10 copies/mL (IQR) | 4.4 (4.0–4.9) | 4.4 (4.0–4.9) | 4.5 (4.0–4.9) | 4.4 (4.0–4.9) | 4.5 (4.0–4.8) |
| HIV-1 RNA >100,000 copies/mL, % | 19 | 17 | 16 | 21 | 17 |
| Median CD4 cell count, cells/µL (IQR) | 442 (293–590) | 443 (299–590) | 450 (324–608) | 440 (289–591) | 441 (297–597) |
| CD4 count <200 cells/µL, % | 13 | 11 | 10 | 14 | 10 |
| Asymptomatic HIV infection, % | 90 | 91 | 91 | 89 | 89 |
| Median eGFRCG, mL/min (IQR) | 122 (104–143) | 126 (108–146) | 123 (107–144) | 120 (101–142) | 121 (103–145) |

CD4, cluster of differentiation-4; IQR, interquartile range.

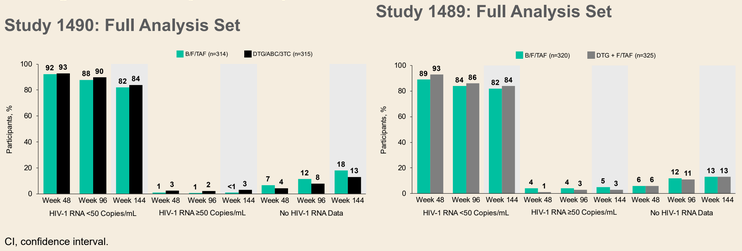
### Pooled Participant Disposition From Baseline to Week 144




AE, adverse event; D/C, discontinuation.

## Results

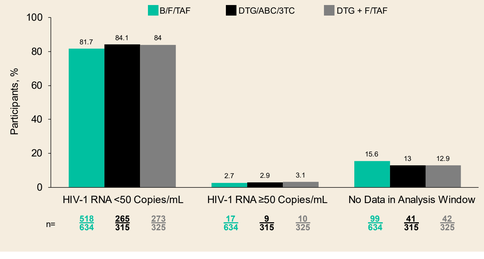
### Virologic Outcome by FDA Snapshot at Weeks 48, 96 and 144




CI, confidence interval.

- Difference in HIV-1 RNA <50 copies/mL by FDA Snapshot at Week 144: -2.6% (95% CI -8.5%, 3.4%)
- B/F/TAF was noninferior to DTG/ABC/3TC
- Difference in HIV-1 RNA <50 copies/mL by FDA Snapshot at Week 144: -1.9% (95% CI -7.8%, 3.9%)
- B/F/TAF was noninferior to DTG + F/TAF

### Pooled Virologic Outcomes by FDA Snapshot at Week 144




- Per-protocol analysis of HIV-1 RNA <50 copies/mL
  - Overall population: B/F/TAF 100% vs DTG/ABC/3TC 99% vs DTG + F/TAF 99%
  - HIV RNA >100,000 copies/mL at baseline: B/F/TAF 100% vs DTG/ABC/3TC 97% vs DTG + F/TAF 100%
  - CD4 <200 cells/µL at baseline: B/F/TAF 100% vs DTG/ABC/3TC 92% vs DTG + F/TAF 100%

## Results (Cont'd)

### Virologic Resistance Results at Week 144

| | Overall | | |
|---|---|---|---|
| Participants, n | B/F/TAF n=634 | DTG/ABC/3TC n=315 | DTG + F/TAF n=325 |
| Met criteria for resistance testing* | 8 | 6 | 7 |
| NRTI resistance detected | 0 | 0 | 0 |
| INSTI resistance detected | 0 | 0 | 0 |

*Performed for participants with confirmed HIV-1 RNA ≥50 copies/mL, with confirmation sample being ≥200 copies/mL or ≥200 copies/mL at last visit, and no resuppression of HIV-1 RNA to <50 copies/mL while on study drug. INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor.

- No treatment-emergent resistance to any components of the regimens was detected in any treatment group
- 1 participant with baseline DTG resistance (Q148H + G140S) was randomized to B/F/TAF, suppressed <50 copies/mL at Week 4, and remained suppressed at Week 144

### Adverse Events Through Week 144

| | Overall | | |
|---|---|---|---|
| All Grades ≥10% of Any Group, % | B/F/TAF n=634 | DTG/ABC/3TC n=31 | DTG + F/TAF n=325 |
| Diarrhea | 19 | 18 | 16 |
| Headache | 16 | 18 | 18 |
| Nasopharyngitis | 14 | 17 | 19 |
| Upper respiratory tract infection | 14 | 19 | 16 |
| Nausea* | 11 | 24 | 13 |
| Syphilis | 11 | 16 | 10 |
| Back pain | 10 | 12 | 12 |
| Fatigue | 10 | 12 | 11 |
| Insomnia | 9 | 11 | 7 |
| Oropharyngeal pain | 7 | 11 | 6 |

*p <0.001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test.

### Study Drug-Related Adverse Events Through Week 144

| | Overall | | |
|---|---|---|---|
| All Grades, % | B/F/TAF n=634 | DTG/ABC/3TC n=315 | DTG + F/TAF n=325 |
| Any drug-related AE* | 26 | 42 | 29 |
| AEs occurring in ≥5% of any group | | | |
| Nausea* | 4 | 18 | 5 |
| Headache | 5 | 5 | 3 |
| Diarrhea | 5 | 4 | 3 |

*p <0.0001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test

- B/F/TAF had lower rates of study drug-related AEs, nausea, and study drug-related nausea than DTG/ABC/3TC (p <0.001)

### Adverse Events Leading to Discontinuation Through Week 144

| Overall | | |
|---|---|---|
| B/F/TAF n=634 | DTG/ABC/3TC n=315 | DTG + F/TAF n=325 |
| n=6 (1%) | n=5 (2%) | n=6 (2%) |
| Cardiac arrest (Day 28) | Nausea and generalized rash (Day 4)* | Erythema and pruritus (Day 112) |
| Atypical chest pain (Day 31)* | Thrombocytopenia (Day 50)* | Depression (Day 420)* |
| Sleep disorder, dyspepsia, tension headache, depressed mood, and insomnia (Day 65)* | Steatorrhea (Day 134)* | Lipoatrophy (Day 464)* |
| Paranoia (Day 302) | Depression (Day 248)* | Depression (Day 532)* |
| Abdominal distension (Day 304)* | Renal failure (Day 621) | Supraventricular tachycardia (Day 597) |
| Depression (Day 337)* | | Large B-cell lymphoma (Day 1009) |
| 6 deaths reported:<br>• Cardiac arrest during septic shock (Day 28)<br>• Gastric adenocarcinoma (Day 376)<br>• Hypertensive heart disease & congestive heart failure (Day 412)<br>• Suicide (Day 656)<br>• Recreational drug overdose (Day 771)<br>• Sudden cardiac death (Day 1060) | 1 death reported:<br>• Recreational drug overdose (Day 812) | 4 deaths reported:<br>• Unknown cause (Day 174)<br>• Pulmonary embolism (Day 266)<br>• Lymphoma (Day 422)<br>• Unknown cause (Day 771) |

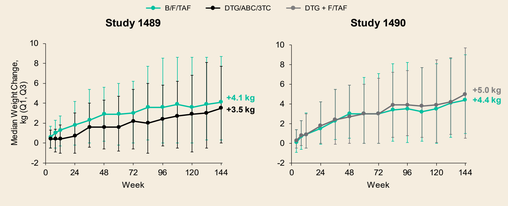
*p <0.0001: B/F/TAF vs DTG/ABC/3TC based on Fisher exact test.

### Laboratory Abnormalities Through Week 144

| | Overall | | |
|---|---|---|---|
| ≥5% of Any Overall Group, % | B/F/TAF n=634 | DTG/ABC/3TC n=315 | DTG + F/TAF n=325 |
| Any Grade 3 or 4 lab abnormality | 26 | 25 | 23 |
| Increased creatine kinase | 7 | 8 | 4 |
| Increased fasting LDL | 4 | 5 | 6 |

LDL, low-density lipoprotein.

### Weight Change Through Week 144




Q, quartile.

### Weight Changes at Week 144

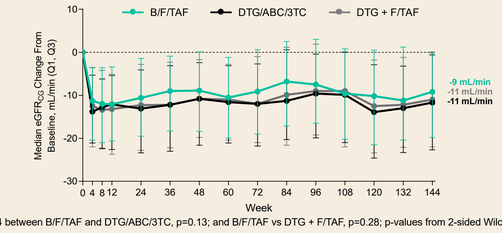
| | Study 1489 | | Study 1490 | |
|---|---|---|---|---|
| Week 144 | B/F/TAF n=314 | DTG/ABC/3TC n=315 | B/F/TAF n=320 | DTG + F/TAF n=325 |
| Participants, % | | | | |
| ≥5% weight gain | 52 | 48 | 53 | 55 |
| ≥10% weight gain | 29 | 25 | 30 | 32 |
| Weight loss or no change from baseline | 24 | 26 | 21 | 22 |
| Mean weight change from baseline, kg (SD) | 5.3 (9.2) | 4.3 (7.8) | 5.6 (8.3) | 5.7 (7.8) |

SD, standard deviation.

- An AE of weight increase was reported for B/F/TAF 3%, DTG/ABC/3TC 4%, and DTG + F/TAF 3%, and weight decrease for B/F/TAF 1%, DTG/ABC/3TC 1%, and DTG + F/TAF 3%

### Change From Baseline in eGFR Through Week 144

Overall

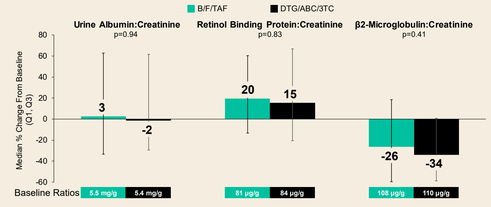



Differences at Week 144 between B/F/TAF and DTG/ABC/3TC, p=0.13; and B/F/TAF vs DTG + F/TAF, p=0.28; p-values from 2-sided Wilcoxon rank-sum test.

- Changes in eGFR were consistent with inhibition of tubular creatinine secretion via organic cation transporter-2 by DTG or BIC
- There were no D/Cs due to renal AEs in B/F/TAF or DTG + F/TAF group
- There was 1 D/C due to renal failure in DTG/ABC/3TC group not attributed to study drug

### % Change From Baseline in Quantitative Proteinuria at Week 144

Study 1489

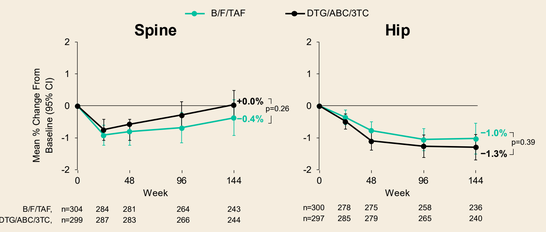



Difference in % change from baseline for each marker tested between treatment groups by Wilcoxon rank sum test; urine protein tests performed for Study 1489 only.

- There were no cases of proximal renal tubulopathy reported in any group

### % Change in Spine and Hip BMD Through Week 144

Study 1489

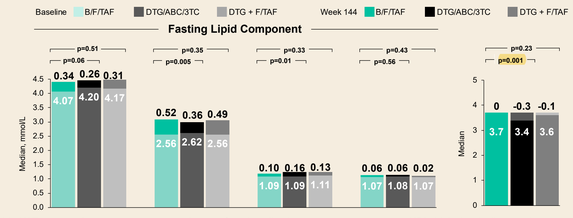



Comparison of B/F/TAF vs DTG/ABC/3TC at Week 144 by analysis of variance model; bone mineral density (BMD) measured by dual-energy x-ray absorptiometry in Study 1489 only.

- Changes in BMD from baseline were similar between groups

### Change From Baseline in Fasting Lipids at Week 144

Overall




p-values from 2-sided Wilcoxon rank-sum test to compare changes from baseline between treatment groups. HDL, high-density lipoprotein.

- Fasting lipids increased in all groups after treatment initiation
- Differences between groups in changes from baseline in fasting lipids were not clinically relevant
- Similar percentages of participants in each group received lipid-modifying agents at study entry (B/F/TAF 5.0%, DTG/ABC/3TC 2.2%, and DTG + F/TAF 5.5%) and initiated treatment during the study (B/F/TAF 4.7%, DTG/ABC/3TC 5.1%, and DTG + F/TAF 4.9%)

## Conclusions

- At Week 144, B/F/TAF remained noninferior to either DTG-based triple therapy regimen in treatment-naïve participants with high rates of virologic suppression in all treatment arms
- There was no treatment-emergent resistance to any of these triple-therapy treatment regimens
- B/F/TAF was associated with fewer treatment-related AEs than DTG/ABC/3TC (p <0.001)
  - Nausea and treatment-related nausea were less common with B/F/TAF vs DTG/ABC/3TC (p <0.001)
- Changes from baseline in BMD and renal markers for B/F/TAF were similar to DTG/ABC/3TC
  - There were no cases of proximal renal tubulopathy in any treatment arm
  - No participant discontinued B/F/TAF due to renal or bone-related AEs
- There were no clinically relevant differences between arms in median changes from baseline in fasting lipids and no differences in proportions initiating lipid-lowering medications
- This 3-year long-term follow-up demonstrates treatment with B/F/TAF was effective, and may offer better safety and tolerability over other guideline-recommended regimens

## References & Acknowledgments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**Study 1489:** Albrecht H, Angel J, Antinori A, Arribas Lopez JR, Asmuth DM, Baumgarten A, Bennani Y, Benson P, Berhe M, Bordon J, Brar I, Brinson C, Brunetta J, Charest L, Cindrich R, Clarke A, Clotet B, Cook P, Cotte L, Coulston DR, Crofoot GE, Cruickshank FA, Cunningham D, Daar E, DeJesus E, De Wet JJ, Dietz C, Edelstein H, Estrada Perez V, Fichtenbaum C, Flamm J, Gallant J, Gathe JC, Girard P-M, Grossberg R, Gupta S, Hagins D, Hardy W, Hare CB, Henn S, Henry WK, Hileman C, Hite A, Hsiao CB, Jain M, Johnson M, Kasper K, Kinder CA, Klein D, Koenig E, Lazzarin A, LeBlanc R, LeBouche B, Lucasti C, Maggiolo F, Mallolas Masferrer J, Mayer C, McDonald C, McGowan JP, Meybeck A, Mills A, Miralles Alvarez C, Molina J-M, Moreno Guillen S, Mounzer K, Newman C, Orkin C, Osiyemi O, Palmieri PJ, Para M, Parks DA, Parsons C, Petroll A, Pierone G, Podzamczer D, Polk C, Portilla Sogorb J, Post F, Pozniak A, Prelutsky DJ, Pugliese P, Rachlis A, Ramgopal MN, Rashbaum BS, Richmond GJ, Roman A, Roberts A, Rockstroh J, Ross JD, Ruane PJ, Rubio Garcia R, Saag M,Santana-Bagur JL, Santiago Colon L, Schrader S, Scribner A, Shalit P, Shamblaw DJ, Shon A, Sims J, Slim J, Stellbrink H-J, Stephan C, Tebas P, Thompson MA, Towner WJ, Ustianowski A, Van Dam C, Vanderkerckhove L, Vandercam B, Vanig T, Voskuhl G, Wade BH, Walker D, Waters L, Wilkin A, Wohl DA, Wohlfeiler M, Workowski K, Wurapa A, Yazdanpanah Y, Young B, Zurawski C;

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## Disclosures

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