P006

B/F/TAF vs DTG/ABC/3TC or DTG + F/TAF in Treatment-Naïve Adults With High Baseline Viral Load or Low Baseline CD4 Count in 2 Phase 3 Randomised, Controlled Clinical Trials: Week 96 Results

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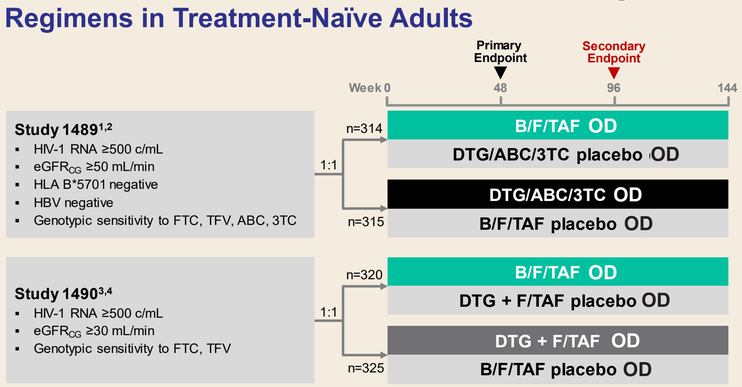
Introduction

- Early initiation of HIV therapy is recommended worldwide and is associated with improvements in morbidity and mortality as well as better immunologic recovery and lower chance of virologic failure with drug resistance[1-9]
  - However, many patients still present late in the course of disease with high HIV-1 viral load and low CD4 counts[10,11]
- Coformulated bictegravir/emtricitabine (FTC)/tenofovir (TFV) alafenamide (B/F/TAF, Biktarvy®, Gilead) was non-inferior to dolutegravir (DTG)-based regimens in 2 recent studies in treatment-naïve people living with HIV through the Week 48 primary endpoint,[12,13] as well as at the secondary Week 96 endpoint (Studies 1489 and 1490)[14,15]
  - No participant failed with virologic resistance
  - No differences were noted between arms in treatment response in participants with baseline HIV-1 viral load >100,000 copies/mL or with CD4 count <200 cells/μL

Methods

Study Design
Studies 1489 & 1490: B/F/TAF vs DTG-containing Regimens in Treatment-Naïve Adults



ABC, abacavir; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft Gault; FTC, emtricitabine; HBV, hepatitis B virus; HLA, human leukocyte antigen; TFV, tenofovir; 3TC, lamivudine.

- HIV-1 infected, treatment-naïve adults in Australia, Europe, Latin America, and North America were randomised in 2 double-blind, multi-centre, active-controlled non-inferiority trials
- Randomisation for each study was stratified by the following:
  - HIV-1 viral load (≤100,000, >100,000–≤400,000, or >400,000) copies/mL at screening
  - CD4+ cell count (<50, 50–199, or ≥200 cells/μL) at screening
  - Region (US vs non-US) at randomisation
- These studies were conducted in accordance with the Declaration of Helsinki and were approved by central or site-specific review boards or ethics committees
- All participants gave written informed consent
- **Full Analysis Set (FAS):**
  - Includes all participants randomised into the study who received ≥1 dose of study medication
- **Pre-Specified Per-Protocol Analysis Set**
  - Includes all participants who had on-treatment HIV-1 RNA in the Week 96 window or who discontinued due to lack of efficacy
  - Excludes participants from the FAS who violated entry criteria due to genotype or prohibited medication, or adherence to study medication <2.5th percentile
- Primary endpoint for each study: proportion of participants with plasma HIV-1 viral load <50 copies/mL at Week 48 by snapshot algorithm
- Secondary endpoint for each study: proportion of participants with plasma HIV-1 viral load <50 copies/mL at Week 96 by snapshot algorithm
- A prespecified analysis pooled all data from the individual studies through Week 96
- In this pooled analysis, participants were grouped into 3 treatment groups:
  - B/F/TAF: all participants randomised to B/F/TAF in Studies 1489 or 1490
  - DTG/ABC/3TC: all participants randomised to DTG/ABC/3TC in Study 1489
  - DTG + F/TAF: all participants randomised to DTG + F/TAF in Study 1490

Results

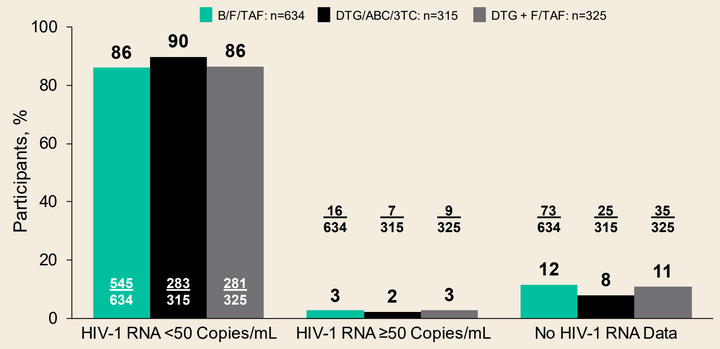
Pooled Baseline Characteristics

	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + FTC/TAF n=325
Median age, y (range)	32 (18–71)	32 (18–68)	34 (18–77)
Male, %	89	90	89
Race/ethnicity, %			
Black or African descent	33	36	31
Hispanic/Latino	25	21	25
Median HIV-1 RNA, log_{10} copies/mL (Q1, Q3)	4.42 (4.00, 4.88)	4.51 (4.04, 4.87)	4.45 (4.03, 4.84)
HIV-1 RNA >100,000 copies/mL, %	19	16	17
Median CD4 cell count, cells/μL (Q1, Q3)	442 (293, 590)	450 (324, 608)	441 (297, 597)
CD4 count <200 cells/μL, %	13	10	10
HBV coinfection, %*	1	Excluded	2
HCV coinfection, %†	1	1	2
Median $eGFR_{CG}$, mL/min (Q1, Q3)	122 (104, 143)	123 (107, 144)	121 (103, 145)

*Positive HBV surface antigen and/or isolated positive HBV core antigen with HBV DNA ≥20 IU/mL; †Positive hepatitis C virus (HCV) antibody and HCV RNA ≥15 IU/mL. Q, quartile.

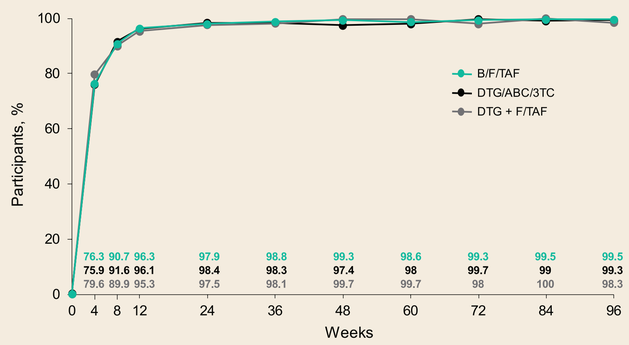
Results (cont'd)

Virologic Outcome at Week 96
FDA Snapshot Analysis FAS[12-15]



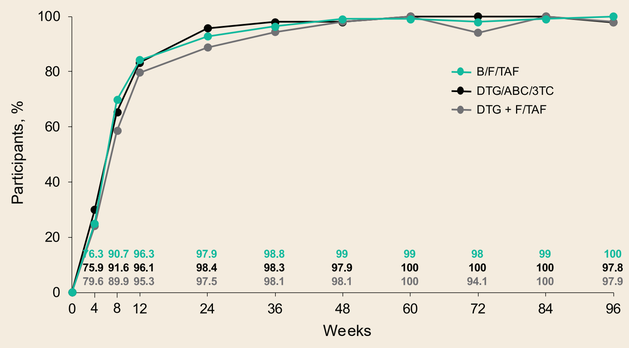
- HIV-1 RNA was <50 copies/mL for 86% of participants on B/F/TAF, 90% on DTG/ABC/3TC, and 86% on DTG + F/TAF; these differences were not statistically different between arms and the secondary endpoint of noninferiority at Week 96 was met
- There was no emergent resistance to B/F/TAF and DTG-containing regimens in treatment-naïve participants
- There were no treatment differences in the pooled analysis based on age, sex, race, baseline HIV-1 viral load, baseline CD4 count or region at Week 96

Virologic Response by Visit (FAS):
HIV-1 RNA <50 copies/mL, Missing=Excluded Analysis



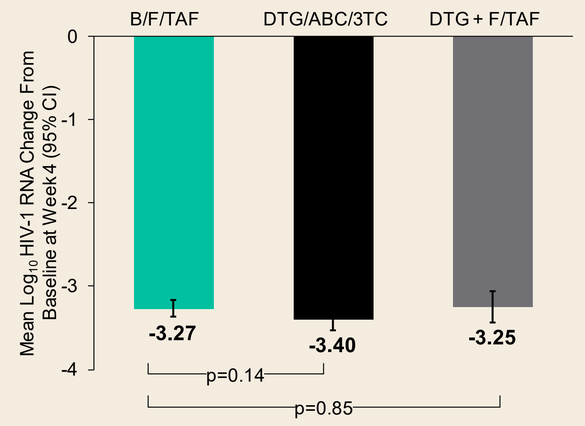
- All arms showed rapid suppression of viraemia, with the majority of participants <50 copies/mL by Week 4[12-15]

Virologic Response by Visit (FAS):
HIV-1 RNA <50 copies/mL, Missing=Excluded Analysis
Baseline HIV-1 RNA >100,000 copies/mL



- Virologic response rates by visit were also rapid and similar between treatment arms in participants with high baseline VL

Mean Change From Baseline in HIV-1 RNA at Week 4
Baseline HIV-1 RNA >100,000 Copies/mL



p-values were calculated using analysis of variance model adjusted by region stratum.

- For participants with baseline HIV-1 RNA >100,000 copies/mL, mean changes from baseline of HIV-1 RNA at Week 4 were similar between those taking B/F/TAF, DTG/ABC/3TC, and DTG + F/TAF

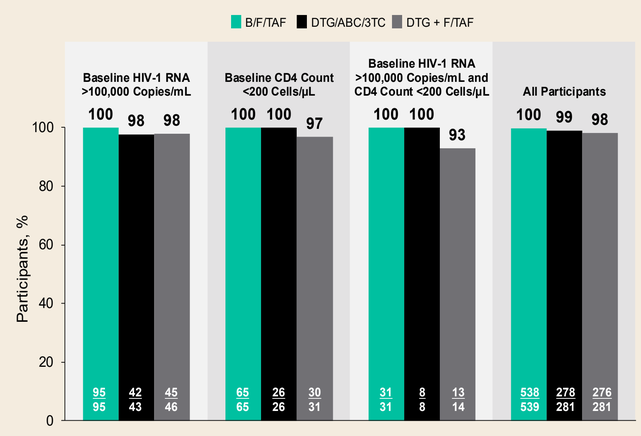
Participant Disposition: Per-Protocol Analysis Set

	B/F/TAF	DTG/ABC/3TC	DTG + F/TAF
FAS, n	634	315	325
AE leading to D/C, n (%)	6 (<1)	5 (2)	5 (2)
D/C due to lack of efficacy, n	0	0	0
Per-protocol analysis set, n (%)	539 (85)	281 (89)	281 (86)
Total participants excluded, n (%)	95 (15)	34 (11)	44 (14)
Reasons for exclusion, n (%)*			
No data in window	88 (14)	29 (9)	39 (12)
Excluded genotype	0	0	0
Prohibited medication	0	1 (<1)	0
Adherence <2.5th percentile	14 (2)	9 (3)	7 (2)

*Participant may fit >1 exclusion criterion from per-protocol analysis set. AE, adverse event; D/C, discontinuation.

- AEs leading to study drug D/C were low in all treatment groups
- The leading cause for exclusion from the per-protocol analysis set was no data in study window due to loss to follow-up or missed study visit

HIV-1 RNA <50 Copies/mL at Week 96
Pooled Per-Protocol Analysis Set



Conclusions

- At Week 96 in each study:
  - Treatment responses were similar among participants treated with B/F/TAF and DTG comparators regardless of HIV-1 RNA or CD4 count at baseline
  - No participant failed with treatment-emergent resistance
- Pooled analyses at Week 96 in the FAS showed:
  - Rapid rates of virologic decline in B/F/TAF-treated participants, with similar findings in DTG-based comparator arms
  - Mean changes from baseline in HIV-1 RNA at Week 4 were similar between the B/F/TAF and DTG-based comparator arms in participants with high baseline HIV-1 viral load
- In the pooled per-protocol analysis at Week 96:
  - 100% of participants treated with B/F/TAF had HIV-1 RNA <50 copies/mL regardless of high viral load, low CD4 count, or having both high viral load and low CD4 count at baseline
- These data support the use of B/F/TAF in patients presenting with high viral load and low CD4 counts

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