P001

A Phase 3, Randomised, Controlled Clinical Trial of Bictegravir in a Fixed-Dose Combination, B/F/TAF, vs DTG/ABC/3TC in Treatment-Naïve Adults at Week 96

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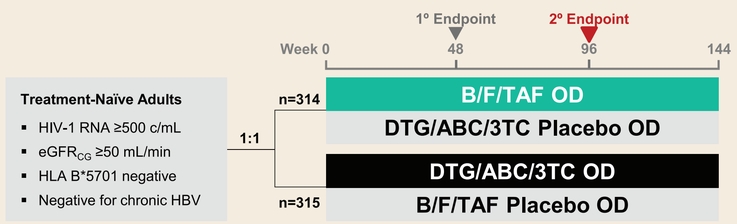
Introduction

- Bictegravir, a novel, potent INSTI with a high barrier to resistance, was coformulated with emtricitabine and tenofovir alafenamide into a single-tablet regimen (B/F/TAF) and is approved in the US, Europe, Australia, and Canada as Biktarvy®
  - Unboosted, once daily dosing without regard to food
- B/F/TAF was non-inferior at Week 48 to standard-of-care comparators, with no treatment-emergent resistance, and was well tolerated in five randomised phase 3 studies in adults, including a study of 470 women[1-5]
- The current trial compares B/F/TAF to coformulated dolutegravir, abacavir, and lamivudine (DTG/ABC/3TC) in treatment-naïve adults and is ongoing in a double blind fashion to W144
  - B/F/TAF is associated with significantly fewer "bothersome" symptoms, primarily GI and neuropsychiatric, than DTG/ABC/3TC by patient reported outcomes (PRO)[6]
  - Similar bone and renal profiles were observed at Week 48[1]
- We now report cumulative efficacy and safety results through Week 96

Methods

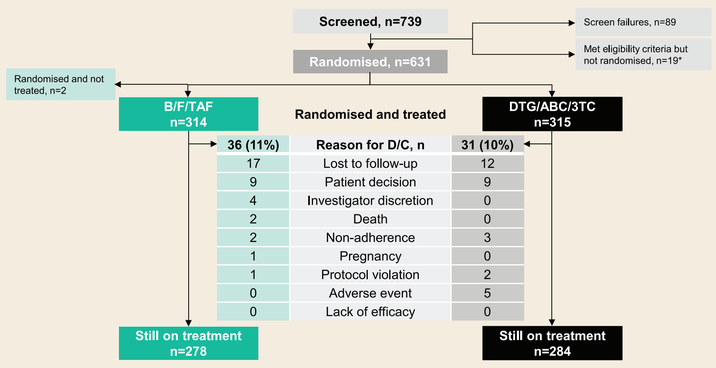
GS-US-380-1489 Study Design



ClinicalTrials.gov NCT02607930; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation.

- Phase 3, randomised, double-blind, active-controlled study
  - Stratified by HIV-1 RNA, CD4 cell count, geographic region (North America, Europe)
- Primary endpoint: proportion with HIV-1 RNA <50 copies/mL at Week 48
  - B/F/TAF 92.4% vs DTG/ABC/3TC 93.0% with HIV-1 RNA <50 c/mL (p=0.78)
- Secondary endpoint: proportion with HIV-1 RNA <50 copies/mL at Week 96
  - Non-inferiority margin of 12% based on FDA Snapshot algorithm

Participant Disposition From Baseline to W96



* Lost to follow-up (n=8), withdrew consent (n=6), investigator's discretion (n=2), adverse event (n=1), outside of visit window (n=1), other (n=1).

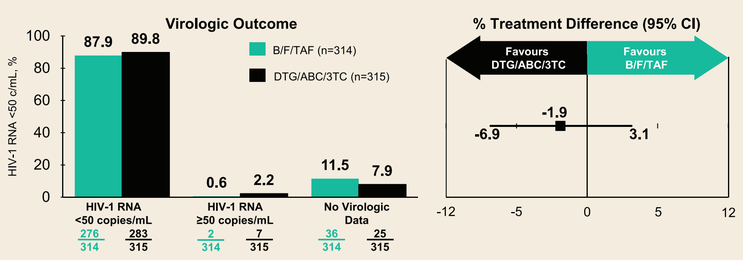
Results

Baseline Characteristics

	B/F/TAF n=314	DTG/ABC/3TC n=315
Age, median years (range)	31 (18-71)	32 (18-68)
Male, %	91	90
Race/ethnicity, %		
Black or African descent	36	36
White	58	57
Hispanic/Latino ethnicity	23	21
HIV-1 RNA, median log_{10} c/mL (IQR)	4.42 (4.03, 4.87)	4.51 (4.04, 4.87)
HIV-1 RNA >100,000 c/mL, %	17	16
CD4 cell count, median cells/µL (IQR)	443 (299, 590)	450 (324, 608)
CD4 count <200 cells/µL, %	11	10
Asymptomatic HIV infection, %	91	91
$eGFR_{CG}$, median mL/min (IQR)	126 (108, 146)	123 (107, 144)

c, copies; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; IQR, interquartile range.

Virologic Outcome at W96



c, copies; CI, confidence interval.

- At Week 96, non-inferiority confirmed by pre-specified analyses for HIV-1 RNA <50 c/mL:
  - Per-protocol: B/F/TAF 99.6% vs DTG/ABC/3TC 98.9%
  - Missing=Failure: B/F/TAF 87.9% vs DTG/ABC/3TC 90.8%
  - Missing=Excluded: B/F/TAF 98.9% vs DTG/ABC/3TC 99.3%
- Mean CD4 increase from baseline at Week 96:
  - B/F/TAF +287 cells/µL vs DTG/ABC/3TC +288 cells/µL (p=0.94)
- No participant developed treatment-emergent resistance through Week 96

Results (cont'd)

Resistance Analysis Population

	B/F/TAF n=314	DTG/ABC/3TC n=315
Resistance analysis population	0	5
Emergent resistance	0	0

- Virologic Rebound at or after Week 8
  - Confirmed virologic failure without resuppression
    - Two consecutive HIV-1 RNA tests ≥ 50 c/mL after achieving < 50 c/ml and HIV-1 RNA ≥ 200 c/mL at the confirmation test

      or
    - ≥1 log_{10} copies/mL increase in HIV-1 RNA from nadir
  - HIV-1 RNA ≥ 200 c/mL at Week 96 or last visit on study drug (did not require confirmation)
- The second, confirmatory sample was sent for resistance analysis, unless there was no follow-up sample

AEs Leading to Study Drug Discontinuation Through W96

B/F/TAF n=314	DTG/ABC/3TC n=315
0	5 (1.6%)
	Nausea,* rash* [Day 4]
	Thrombocytopenia* [Day 50]
	Chronic pancreatitis/steatorrhea* [Day 134]
	Depression* [Day 248]
	Renal failure [Day 621]

* Reported as Treatment-Related.

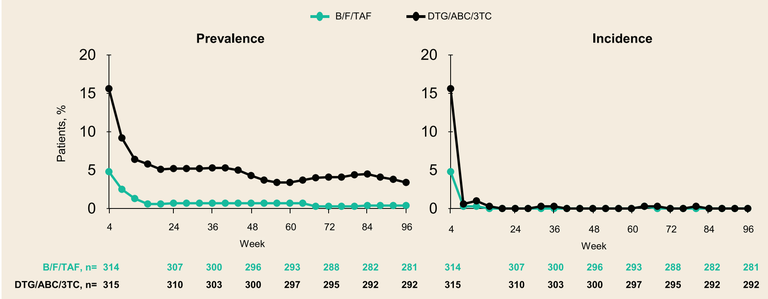
- 2 deaths were reported in the B/F/TAF arm:
  - Recreational drug overdose [Day 771]
  - Suicide [Day 656]

All Grade Adverse Events (≥10%) Through Week 96

All Grade, %	B/F/TAF n=314	DTG/ABC/3TC n=315	
Diarrhoea	15	16	
Headache	13	16	
Nausea	11	24	p <0.001*
Nasopharyngitis	11	12	
Upper respiratory tract infection	11	16	
Fatigue	9	11	
Syphilis	9	12	
Back pain	8	10	
Insomnia	7	10	

* Difference in nausea between treatment groups, Fisher exact test

Prevalence and Incidence of Nausea



Any Drug-related Adverse Events (≥3%) Through Week 96

All Grade, %	B/F/TAF n=314	DTG/ABC/3TC n=315	
Any drug-related AE	**28**	**40**	p=0.002*
Nausea	6	17	p <0.001†
Diarrhoea	6	4	
Headache	5	5	
Fatigue	3	3	

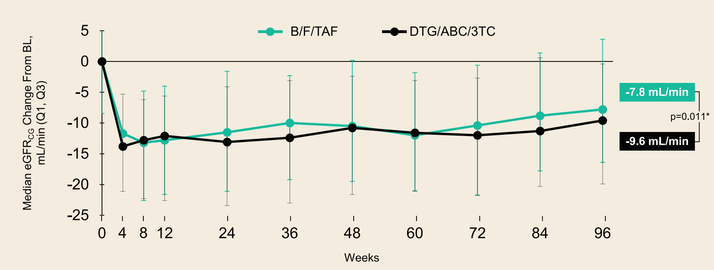
* Difference in overall treatment-related AEs between treatment groups, Fisher exact test.
† Difference in treatment-related nausea between treatment groups, Fisher exact test

Laboratory Abnormalities (≥2%) Through Week 96

Grade 3 or 4, %	B/F/TAF n=314	DTG/ABC/3TC n=315
CK	6	5
AST	4	3
LDL cholesterol	3	4
Neutropenia	3	4
Amylase	3	3

AST, aspartate aminotransferase; CK, creatine kinase; LDL, low-density lipoprotein

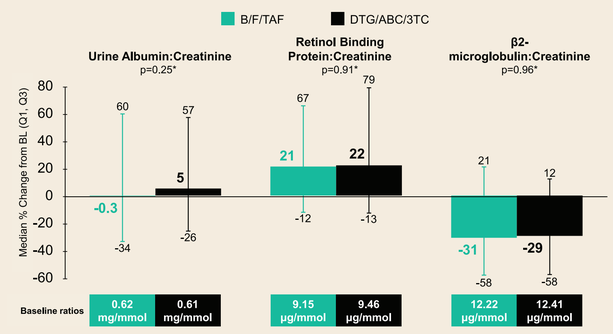
Change from Baseline in $eGFR_{CG}$ Through Week 96



BL, baseline; Q, quartile.
* 2-sided Wilcoxon rank sum test

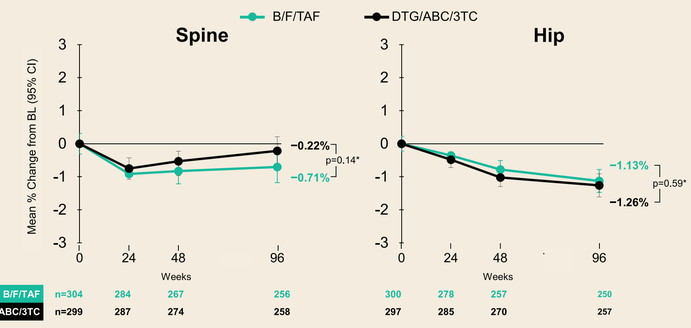
- No discontinuations due to renal adverse events and no proximal tubulopathy in the B/F/TAF arm

% Change from Baseline in Quantitative Proteinuria at W96



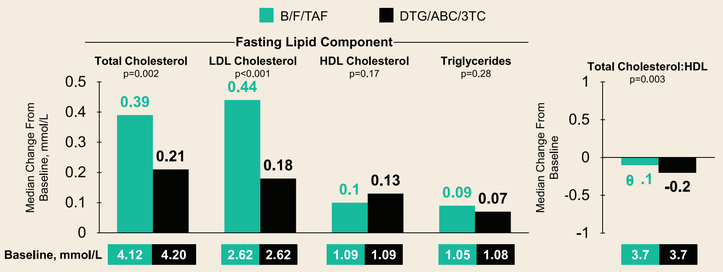
* Difference in percentage change from BL for each marker tested between treatment groups by Wilcoxon rank sum test

Mean % Changes in Spine and Hip BMD Through W96



CI, confidence interval.
* Comparison of B/F/TAF vs DTG/ABC/3TC at Week 96 by ANOVA model.

Fasting Lipid Changes at W96



P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

Conclusions

- Initial HIV-1 therapy with B/F/TAF was non-inferior to DTG/ABC/3TC at Week 96 by Snapshot algorithm with high rates of virologic suppression (HIV-1 RNA <50 copies/mL)
  - 87.9% B/F/TAF vs 89.8% DTG/ABC/3TC
- No treatment-emergent resistance
- B/F/TAF was well tolerated, with no AEs leading to discontinuation (vs 5 in the DTG/ABC/3TC arm)
  - Nausea was reported more frequently in the DTG/ABC/3TC arm (p<0.001)
  - More treatment-related AEs were reported in the DTG/ABC/3TC arm (p=0.002)
- Changes from baseline in bone mineral density and renal markers were comparable between treatment arms, with no cases of renal tubulopathy
- There were small differences in the change in median TC, LDL, and TC:HDL ratio, however, there was no difference in the proportion of participants initiating lipid-lowering agents between the two arms
- These results provide further evidence of longer-term safety, efficacy, and high barrier to resistance of B/F/TAF in people living with HIV-1

References

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