Switch to Bictegravir/F/TAF From DTG and ABC/3TC

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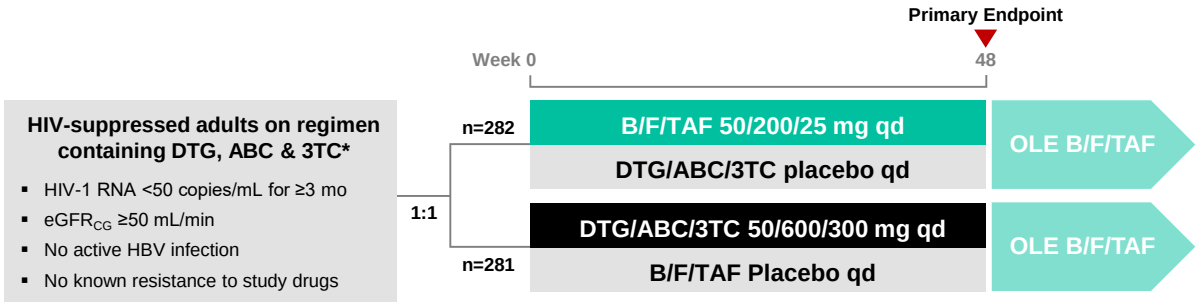
Introduction

- Bictegravir (BIC, B) is a novel, unboosted, potent INSTI with a high in vitro barrier to resistance and low potential for drug-drug interactions[1,2]
  - Co-formulated with emtricitabine and tenofovir alafenamide as a single-tablet regimen (B/F/TAF)
  - Dosed once-daily with or without food
- In three large phase 3 trials, B/F/TAF was noninferior to:
  - dolutegravir (DTG)-containing regimens in treatment naive patients[3,4]
  - boosted ATV or DRV-containing regimens in virologically suppressed patients[5]
  - No treatment emergent viral resistance to B/F/TAF was identified through Week 48
- We assessed the efficacy and safety of switching from DTG/Abacavir/3TC (DTG/ABC/3TC) to B/F/TAF

1. Gallant JE, et al. J Acquir Immune Defic Syndr 2017;75:61-6; 2. Tsiang M, et al. Antimicrob Agents Chemother 2016.60:7086-97; 3. Gallant J, et al Lancet 2017; 4. Sax PE, et al. Lancet 2017. 5. Daar, ID Week 2017, Abstract 67504.

Study 380-1844: Design



- Phase 3, randomized, double-blind, multicenter, active-controlled study (NCT02603120): North America, Europe, Australia
- Primary endpoint: proportion with HIV-1 RNA ≥50 copies/mL at Week 48
  - Noninferiority margin of 4% based on FDA snapshot algorithm

*Could be components of single-tablet regimen. OLE, open label extension.

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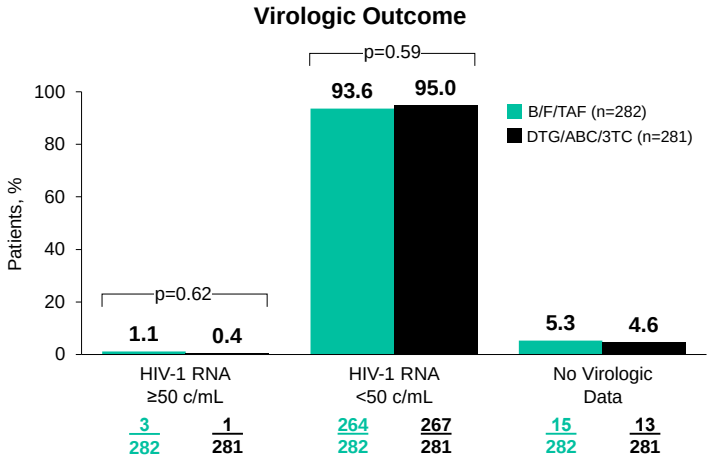
Baseline Characteristics

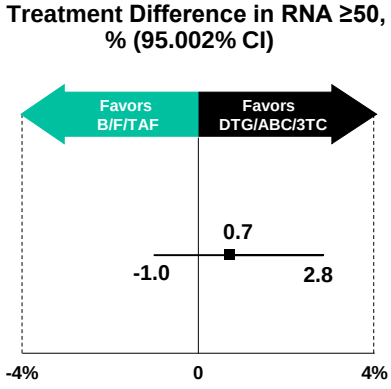
Study 380-1844

	B/F/TAF n=282	DTG/ABC/3TC n=281
Median age, years (range)	47 (21-71)	45 (20-70)
Male, %	88	90
Race, %		
White	73	73
Black or African descent	21	22
Hispanic/Latino Ethnicity, %	16	19
Median CD4 cell count, cells/μL (IQR)	732 (554,936)	661 (478,874)
Median $eGFR_{CG}$, mL/min (IQR)	101(84,119)	101(85,122)

Virologic Outcome at Week 48

Study 380-1844





- Switching to B/F/TAF was noninferior to remaining on DTG/ABC/3TC

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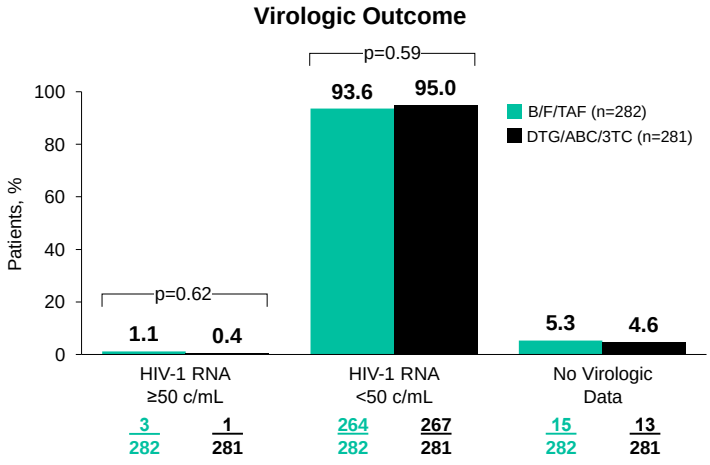
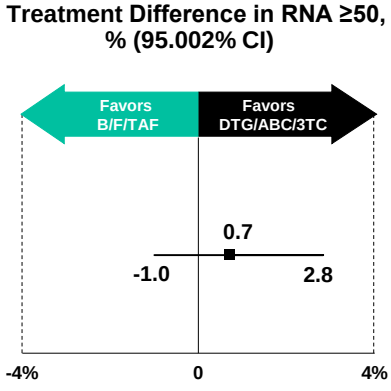
Virologic Outcome at Week 48

Study 380-1844





- Switching to B/F/TAF was noninferior to remaining on DTG/ABC/3TC
- No participant developed treatment-emergent resistance

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Adverse Events Leading to Study Drug Discontinuation

Study 380-1844

Patients, n (%)	B/F/TAF n=282	DTG/ABC/3TC n=281
Overall	**6 (2)**	**2 (1)**
Headache	2	1
Vomiting	1	0
Cerebrovascular accident	1	0
Abnormal dreams	1	0
Suicidal ideation*	1	0
Pruritis	0	1

*Not considered related to study treatment by investigator.

- 2 deaths occurred in the B/F/TAF arm, unrelated to study medication:
  - Male, 71 years old: sudden death, atherosclerotic CVD on autopsy
  - Female, 46 years old: alcohol and opioid toxicity

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Most Common Adverse Events Through Week 48

Study 380-1844

Patients, n (%)	B/F/TAF n=282	DTG/ABC/3TC n=281
Any AE (all grades)	**225 (79.8)**	**225 (80.1)**
AEs occurring in ≥5% of patients		
Upper respiratory tract infection	29 (10)	27 (10)
Nasopharyngitis	20 (7)	22 (8)
Headache	19 (7)	21 (7)
Diarrhea	24 (9)	14 (5)
Arthralgia	19 (7)	10 (4)
Insomnia	8 (3)	14 (5)

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Study Drug-Related AEs Through Week 48

Study 380-1844

All Grades	B/F/TAF n=282	DTG/ABC/3TC n=281	p-Value
Any study drug-related AE, n (%)	**23 (8)**	**44 (16)**	**0.01**
Study drug-related AE in ≥1%, n (%)			
Headache	7 (3)	8 (3)	
Abnormal dreams	1 (<1)	5 (2)	
Flatulence	0	5 (2)	
Nausea	0	5 (2)	
Diarrhea	2 (<1)	4 (1)	
Fatigue	1 (<1)	3 (1)	
Insomnia	0	3 (1)	

p-value from Fisher exact test

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Laboratory Abnormalities Through Week 48

Study 380-1844

Grade 3 or 4 Lab Abnormalities, n (%)	B/F/TAF n=282	DTG/ABC/3TC n=281
Any	**47 (17)**	**32 (11)**
in ≥ 2% of patients		
LDL elevation	14 (5)	13 (5)
Increased amylase	7 (2)	0
ALT elevation	6 (2)	0
CK elevation	6 (2)	6 (2)
Fasting hyperglycemia	6 (2)	2 (<1)

- No cases of rhabdomyolysis
- All amylase elevations were transient and not associated with pancreatitis; 4/7 cases had normal lipase
- Grade 3 and 4 ALT abnormalities were not study treatment related, did not result in study drug interruption, and were associated with other AEs: acute HCV infection (n=3), acute HAV infection (n=1), alcohol abuse (n=1), and NASH (n=1)

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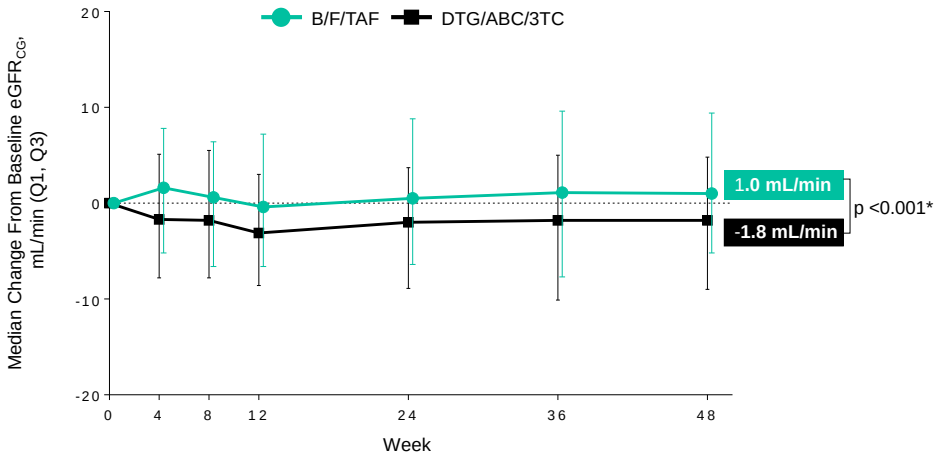
Change in $eGFR_{CG}$ Over Time

Study 380-1844



- No discontinuations due to renal AEs and no cases of renal tubulopathy in either arm

*From 2-sided Wilcoxon rank-sum test.

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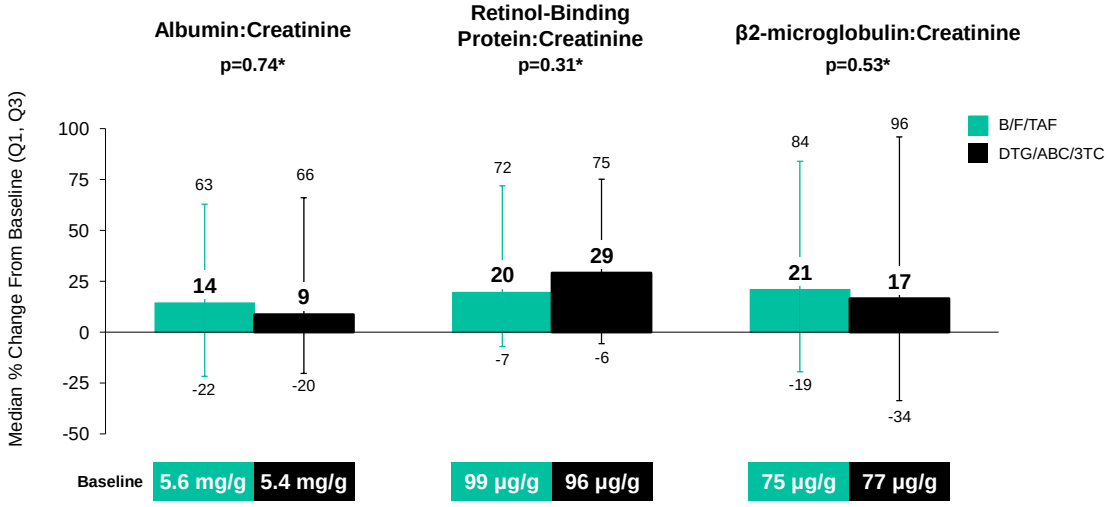
Changes in Quantitative Proteinuria at Week 48

Study 380-1844



*From 2-sided Wilcoxon rank-sum test for % change from baseline at Week 48 for each marker for treatment comparison.

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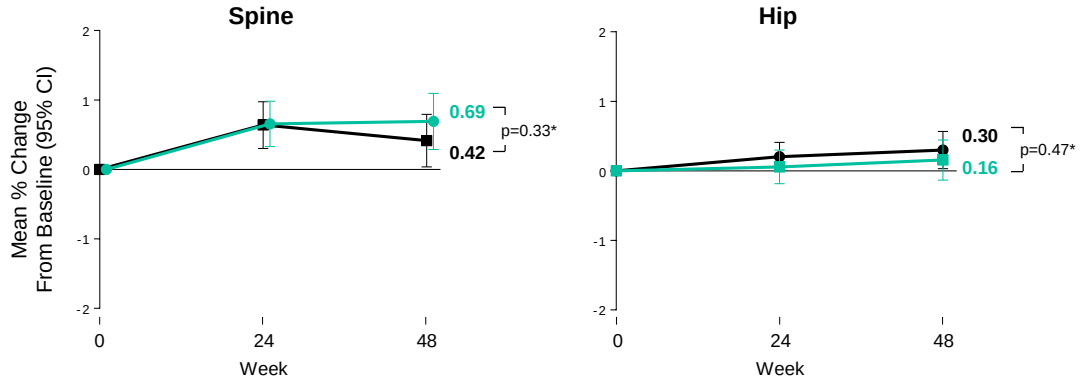
Changes in Spine and Hip BMD Through Week 48

Study 380-1844



B/F/TAF	n=256	244	233	256	246	229
DTG/ABC/3TC	n=262	253	244	265	253	242

*From ANOVA model for comparison of B/F/TAF vs DTG/ABC/3TC at Week 48.

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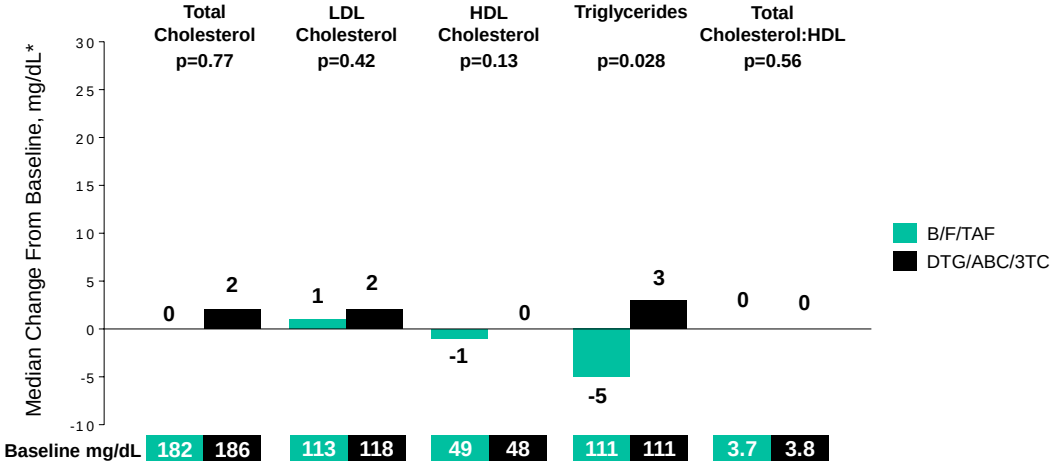
Fasting Lipid Changes at Week 48

Study 380-1844



*p-values from 2-sided Wilcoxon rank-sum test.

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Study 380-1844 Conclusions

- **Switching to B/F/TAF was non-inferior to remaining on DTG/ABC/3TC**
- **No treatment emergent resistance was observed in either arm**
- **B/F/TAF was well tolerated**
  - Adverse events were comparable between arms at Week 48
- **The lipid, bone and renal safety profiles of switching to B/F/TAF were comparable to remaining on DTG/ABC/3TC through 48 weeks of treatment**
- **B/F/TAF offers an effective and safe alternative to DTG/ABC/3TC**

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