Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Adults Aged ≥ 65 Years: Week 72 Results from a Phase 3b, Open-Label Trial (GS-US-380-4449)

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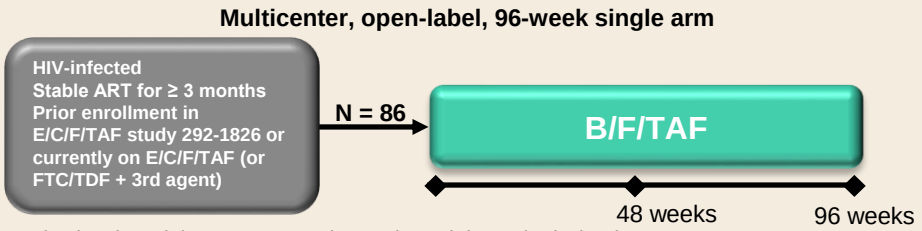
Poster P038

Background

- Almost 50% of people living with HIV (PLWH) are > 50 years old, collecting and evaluating data on long term safety in older patients is important.
- PLWH are at increased risk of co-morbidities and polypharmacy, so ensuring the safety and tolerability of ART in this population is critical.
- B/F/TAF is a small single-tablet regimen with few drug-drug interactions and a high barrier to resistance.
- Declines in bone mineral density and renal function occur due to aging.
- Tenofovir alafenamide (TAF) is a prodrug of tenofovir associated with 90% lower tenofovir plasma levels than tenofovir disoproxil fumarate (TDF), resulting in less renal and bone toxicity.

Methods

Figure 1: Study Design



Study sites in Belgium, France, Italy, Spain and the United Kingdom

Primary endpoints:
- HIV RNA < 50 copies/mL at Week 24 by FDA Snapshot algorithm

Secondary endpoints:
- HIV-1 RNA <50 copies/mL at Weeks 48, 72 and 96
- Safety and tolerability of B/F/TAF through 96 weeks

Key Inclusion Criteria

- Age ≥ 65 years at screening
- Currently receiving an antiretroviral regimen of E/C/F/TAF single tablet regimen (or FTC/TDF + 3rd agent if current or past participant in GS-US-292-1826) for ≥ 3 months*
- Documented plasma HIV-1 RNA < 50 copies/mL on current regimen for the last 2 visits preceding the Screening Visit
  - Transient detectable viremia or "blips" (HIV-1 RNA ≥ 50 and < 400 copies/mL) were acceptable
- Estimated GFR ≥ 30 mL/min (Cockcroft-Gault formula)

Study GS-US-292-1826 was an international open label, randomized 48 week study of the efficacy and safety of switching from a TDF-based regimen to E/C/F/TAF in 167 participants 60 years and older

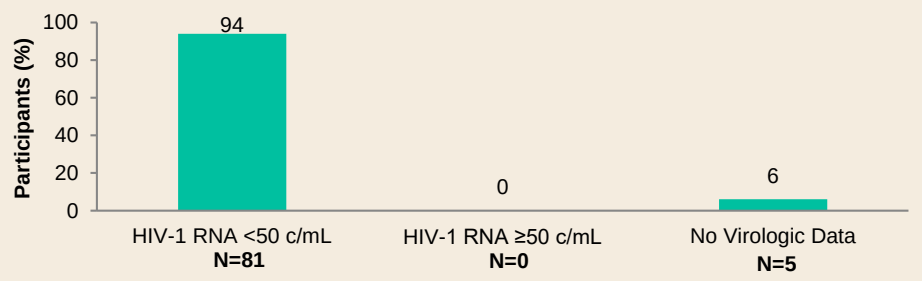
Results

Table 1: Baseline Demographics and Disease Characteristics

	B/F/TAF N=86
Median age, years (range)	69 (65-80)
Female, % (n)	13% (11)
Race, %, (n)*	
White	99% (82)
Black	1% (1)
Ethnicity, Hispanic/Latinx	14% (12)
Median weight (kg) (range)	78 (49-110)
Median estimated GFR_{CG}, mL/min (range)	76 (40-130)
Mode of Infection	
MSM (n)	46.5% (40)
Heterosexual (n)	46.5% (40)
HIV RNA < 50 copies/mL at baseline	98% (84)
Median CD4 count, cells/mm^3 (range)	676 (132-1385)
Baseline Regimen (n)	
EVG/COBI/FTC/TAF	92% (79)
RPV/FTC/TDF	5% (4)
EFV/FTC/TDF	1% (1)
EVG/COBI/FTC/TDF	1% (1)
NVP+FTC/TDF	1% (1)
Chronic Non-ARV Medications at Baseline, median (IQR)	3.0 (2, 5)
Baseline Chronic Medications by organ-system class	
Cardiovascular system	64% (55)
Gastrointestinal tract	63% (54)
Nervous system	44% (38)
Blood and blood forming organs	27% (23)
Musculoskeletal system	23% (20)
Genitourinary system and sex hormones	21% (18)

* 3 participants did not disclose race.

Figure 2: Virologic Outcomes at Week 72 (Snapshot Analysis)



- No participant had a HIV viral load ≥ 50 c/mL
- Median change in CD4 count was 53 cells/mm^3 (IQR: -49, 120) at W72

Results, cont'd.

Table 2: Virologic Outcomes at Week 72 by FDA Snapshot

	B/F/TAF N=86
HIV-1 RNA < 50 c/mL	**81 (94%)**
HIV-1 RNA ≥ 50 c/mL	**0**
HIV-1 RNA ≥ 50 c/mL in W72 Window	0
DC Study Drug Due to Lack of Efficacy	0
DC Study Drug Due to AE and Last Available HIV-1 RNA ≥ 50 c/mL	0
DC Study Drug Due to Other Reasons and Last Available HIV-1 RNA ≥ 50 c/mL	0
No Virologic Data in W72 Window	**5 (5.8%)**
DC Study Drug Due to AE/Death and Last Available HIV-1 RNA < 50 c/mL	4 (4.7%)*
DC Study Drug Due to Other Reasons and Last Available HIV-1 RNA < 50 c/mL	0
Missing Data During Window but on Study Drug	1†

*1) abdominal discomfort (grade 2, drug-related), 2) alcohol withdrawal, 3) benzodiazepine withdrawal, 4) depressive disorder
† At W84, the participant had an HIV-1 RNA < 50 c/mL
c/mL, copies/mL; DC, discontinued

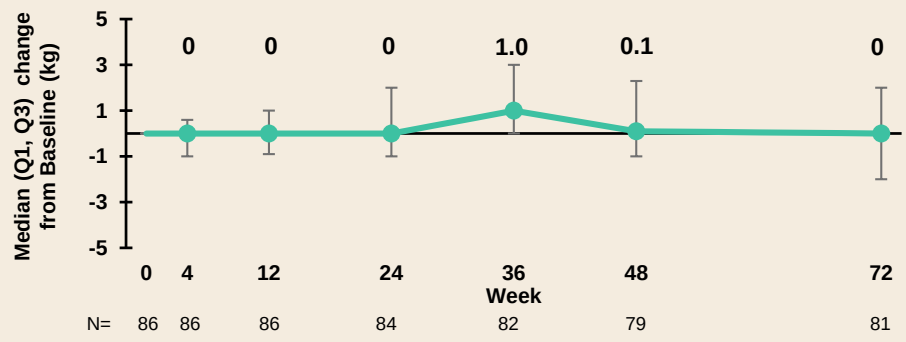
Table 3: Treatment-Emergent Adverse Events through Week 72

	B/F/TAF N=86; % (n)
Any Grades 2-4 Study Drug-Related AE	4.7% (4)
Any Grades 3-4 Study Drug-Related AEs	2.3% (2)
Grades 3 or 4 Laboratory Abnormalities	9% (8)
Any Study Drug-Related Serious AE	0
AEs Leading to Study Drug Discontinuation	4.7% (4)*
AEs Leading to Study Drug Discontinuation (drug-related)	2.3% (2)
Death	2†

*1) abdominal discomfort (grade 2, drug-related), 2) alcohol withdrawal, 3) benzodiazepine withdrawal, 4) irritability and sleep disorder (grade 4, drug-related)
† 1) 77 yo male with pre-existing depressive disorder led to suicide via a benzodiazepine overdose (study day 427), 2) 72 yo male developed and succumbed to pneumonia secondary to COVID-19 infection (study day 672); Neither death study drug-related

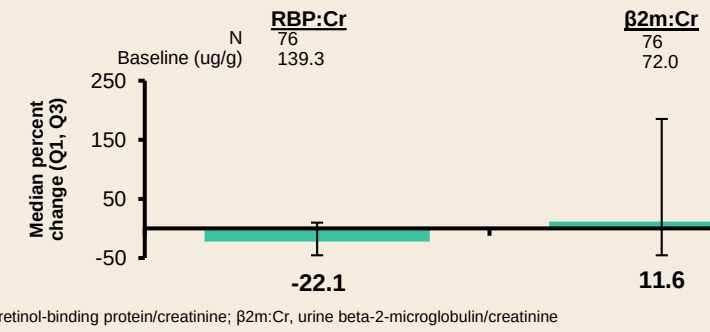
- There were no renal, bone or hepatic discontinuations

Figure 3: Weight: Median Change from Baseline through Week 72



- Median change in weight at Week 72 was 0.0 kg (IQR -2.0, 2.0)

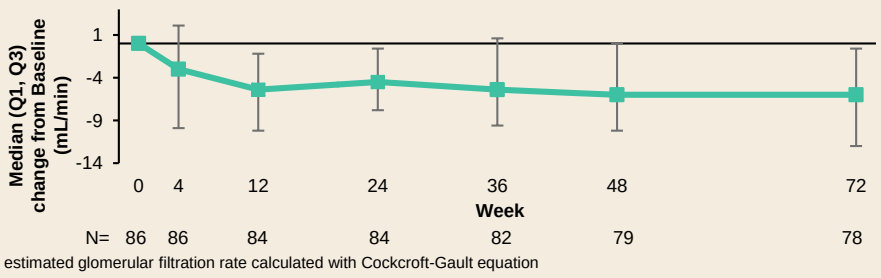
Figure 4: Renal Biomarker Changes (%) at Week 72



RBP:Cr, retinol-binding protein/creatinine; β2m:Cr, urine beta-2-microglobulin/creatinine

- 8% of participants switched from a TDF-based regimen to B/F/TAF

Figure 5: Estimated Glomerular Filtration Rate: Median Changes from Baseline through Week 72



$eGFR_{CG}$, estimated glomerular filtration rate calculated with Cockcroft-Gault equation

- $eGFR_{CG}$ decline is consistent with known inhibition of OCT2 creatinine transporter

Conclusion

- Switching to B/F/TAF is safe, effective and well tolerated in virologically suppressed adults ≥ 65 years through 72 weeks
  - High virologic suppression at 94% with no virologic failures and no treatment-emergent resistance
  - No renal, bone, or hepatic AEs resulting in discontinuation
  - Few drug-related AEs leading to discontinuation (2/86)
  - There were no serious drug-related AEs
  - eGFR decline is consistent with known inhibition of OCT2 creatinine transporter
  - Median weight was stable

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