Renal Outcomes in People With HIV-1 and Renal Impairment Treated With B/F/TAF in Randomized Trials

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Conclusions

- In a retrospective analysis of renal outcomes in PWH with mild to moderate renal impairment (eGFR$_{CG}$ 30–< 90 mL/min) at baseline, eGFR$_{CG}$ remained stable with up to 5 years of B/F/TAF treatment
- Only 1 (< 0.1%) participant with renal impairment discontinued B/F/TAF due to a renal TEAE (acute kidney injury unrelated to B/F/TAF)
- Overall, renal TEAEs were infrequent, occurring in < 3% (28/1069) of participants with renal impairment; there were no occurrences of proximal renal tubulopathy or Fanconi syndrome
  - The rate of renal TEAEs was similar to that with other antiretroviral regimens[1-9]
- Changes in eGFR$_{CG}$ and the occurrence of renal safety events were generally consistent between those with renal impairment at baseline versus those without renal impairment (eGFR$_{CG}$ ≥ 90 mL/min)

Plain Language Summary

- Many people living with the human immunodeficiency virus (HIV) have conditions that affect their kidneys
- This analysis combined information from nine different studies. It looked at whether the HIV treatment bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is safe for people with HIV and kidney disease
- This study looked at over 1000 people who had mildly to moderately reduced kidney function and were taking B/F/TAF. The researchers examined how kidney function changed over time while taking this medication
  - The study also looked to see if anyone developed a new kidney-related condition and if anyone had to stop taking B/F/TAF because of these conditions
- The results showed that kidney function remained the same and did not worsen with B/F/TAF use in people with HIV who have conditions affecting their kidneys
  - Kidney function after taking B/F/TAF was the same as in people with HIV taking B/T/TAF who did not have conditions affecting their kidneys
- Only one person stopped taking B/F/TAF because of a new condition affecting their kidneys; the doctors did not think this condition was caused by B/F/TAF
- Less than 3% of people in this study had a new condition related to their kidneys while taking B/F/TAF
- This suggests B/F/TAF could be a good option for people with HIV whose kidney function was mildly to moderately reduced

Introduction

- People with HIV (PWH) tend to experience more comorbidities with age than people without HIV[10]
- Chronic kidney disease (CKD) is a common comorbidity in PWH,[11] and its prevalence among PWH is likely to increase as the population gets older
- With the need for long-term antiretroviral therapy in PWH, it is critical to establish the renal safety of HIV treatments
- Tenofovir alafenamide–based regimens have a superior renal safety profile compared with tenofovir disoproxil fumarate–based regimens,[12,13] improving treatment options for PWH with mild to moderate renal impairment[14]

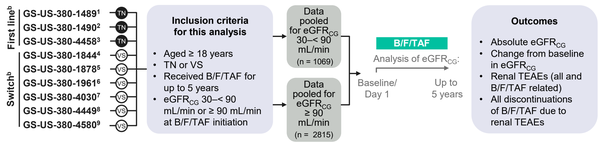
Objective

- To assess renal outcomes through 5 years in PWH with mild to moderate renal impairment receiving bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), using pooled data from nine studies

Methods

Study Design

B/F/TAF Phase 3/3b randomized trials[a]



[a]GS-US-380-4449 was not randomized (single-group study). [b]Includes participants randomized to comparator group during the randomized phase who switched to B/F/TAF in the extension phase. B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; TEAE, treatment-emergent adverse event; TN, treatment-naïve; VS, virologically suppressed.

- Data from nine B/F/TAF Phase 3/3b trials were pooled:
  - Eight randomized studies: NCT02607930 (GS-US-380-1489),[1] NCT02607956 (GS-US-380-1490),[2] NCT03547908 (GS-US-380-4458),[3] NCT02603120 (GS-US-380-1844),[4] NCT02603107 (GS-US-380-1878),[5] NCT02652624 (GS-US-380-1961),[6] NCT03110380 (GS-US-380-4030),[7] NCT03631732 (GS-US-380-4580)[9]
  - One single-group study: NCT03405935 (GS-US-380-4449)[8]

Results

Baseline Demographics and Disease Characteristics by Baseline eGFR$_{CG}$

	30–< 90 mL/min (Renal Impairment)				≥ 90 mL/min (No Renal Impairment) n = 2815
	30–< 45 mL/min (Stage 3b eGFR$_{CG}$) n = 8	45–< 60 mL/min (Stage 3a eGFR$_{CG}$) n = 86	60–< 90 mL/min (Stage 2 eGFR$_{CG}$) n = 975	Overall n = 1069	
Age, years, median (Q1, Q3)	70 (61, 75)	62 (54, 67)	52 (43, 59)	53 (44, 60)	39 (31, 49)
Female sex at birth, n (%)	2 (25)	34 (40)	296 (30)	332 (31)	642 (23)
Race, n (%)					
White	5 (63)	45 (52)	492 (51)	542 (51)	1374 (49)
Black	2 (25)	33 (38)	321 (33)	356 (33)	998 (35)
Asian	0	5 (6)	110 (11)	115 (11)	240 (9)
Other[a]	1 (13)	3 (3)	52 (5)	56 (5)	203 (7)
Hispanic or Latine ethnicity, n (%)	1 (13)	12 (14)	148 (15)	161 (15)	529 (19)
eGFR$_{CG}$, mL/min, median (Q1, Q3)	40.8 (38.6, 42.5)	55.8 (51.0, 58.2)	78.6 (72.0, 84.8)	77.7 (69.6, 84.6)	116.8 (102.7, 136.8)
Treatment history, n (%)					
Treatment naïve	0	5 (6)	79 (8)	84 (8)	670 (24)
Virologically suppressed	8 (100)	81 (94)	896 (92)	985 (92)	2145 (76)

[a]Includes American Indian or Alaska Native; Native Hawaiian or Other Pacific Islander; other race; and participants with Not Permitted designation (when local regulators did not allow collection of race/ethnicity information). eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; Q, quartile.

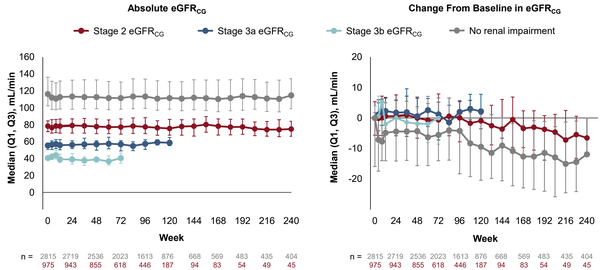
Baseline Characteristics

- Participants with more advanced CKD had a higher median age than those with less advanced CKD or no renal impairment

Treatment Duration With B/F/TAF

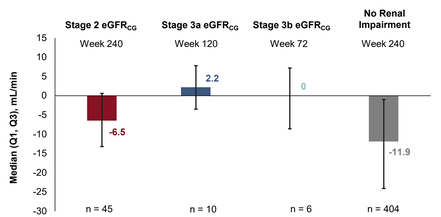
- Median (quartile [Q]1, Q3) duration of B/F/TAF treatment was 83.4 (52.4, 101.9) weeks for the overall study population with renal impairment (Stage 2-3b eGFR$_{CG}$) and 96.0 (64.1, 131.9) weeks for those without renal impairment
- By eGFR$_{CG}$ stage, median (Q1, Q3) [range] treatment duration was:
  - Stage 2 eGFR$_{CG}$: 84.3 (52.4, 103.4) [0.1-277.0] weeks
  - Stage 3a eGFR$_{CG}$: 72.5 (52.1, 96.0) [2.1-259.3] weeks
  - Stage 3b eGFR$_{CG}$: 95.4 (70.3, 101.8) [60.0-111.3] weeks

eGFR$_{CG}$ Change From Baseline Through 5 Years



Timepoints are shown for up to 5 years (240 weeks) or the last timepoint at which the number of participants with data was ≥ 5.
eGFR$_{CG}$: Stage 2, 60–< 90 mL/min; Stage 3a, 45–< 60 mL/min; Stage 3b, 30–< 45 mL/min; no renal impairment, ≥ 90 /mL/min.
eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; Q, quartile.

Median Change From Baseline in eGFR$_{CG}$



Timepoints are shown for up to 5 years (240 weeks) or the last timepoint at which the number of participants with data was ≥ 5.
eGFR$_{CG}$: Stage 2, 60–< 90 mL/min; Stage 3a, 45–< 60 mL/min; Stage 3b, 30–< 45 mL/min; no renal impairment, ≥ 90 /mL/min.
eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; Q, quartile.

Change From Baseline in eGFR

- eGFR remained stable in all groups, with a small reduction in eGFR$_{CG}$ among participants with Stage 2 eGFR$_{CG}$ (median [Q1, Q3] change: -6.5 [-13.2, 0.6] mL/min at Week 240) and participants without renal impairment (median [Q1, Q3] change: -11.9 [-24.1, -1.0] mL/min at Week 240)

Renal TEAEs

	eGFR$_{CG}$ 30–< 90 mL/min (Renal Impairment) n = 1069	eGFR$_{CG}$ ≥ 90 mL/min (No Renal Impairment) n = 2815
Any renal TEAE, n (%)	28 (2.6)	71 (2.5)
Acute kidney injury	10 (0.9)	14 (0.5)
Creatinine renal clearance decreased	6 (0.6)	5 (0.2)
Proteinuria	5 (0.5)	39 (1.4)
Blood creatinine increased	4 (0.4)	8 (0.3)
Renal impairment	4 (0.4)	0
Renal failure	2 (0.2)	4 (0.1)
Glomerular filtration rate decreased	1 (< 0.1)	0
Protein urine present	0	4 (0.1)
Albuminuria	0	2 (< 0.1)
Blood creatinine abnormal	0	1 (< 0.1)
Blood urea increased	0	1 (< 0.1)
Urine output decreased	0	1 (< 0.1)

eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; TEAE, treatment-emergent adverse event.

Renal TEAEs in Participants Receiving B/F/TAF

- Overall, 28 (2.6%) participants with renal impairment reported renal treatment-emergent adverse events (TEAEs); 7 (0.7%) were related to B/F/TAF
- Renal TEAEs occurred in 71 (2.5%) of participants without renal impairment, with 22 (0.8%) related to B/F/TAF
- The most common renal TEAEs were acute kidney injury (n = 10, 0.9%) in participants with renal impairment and proteinuria (n = 39, 1.4%) in participants without renal impairment
  - There were no cases of proximal renal tubulopathy or Fanconi syndrome

Discontinuation of B/F/TAF Due to Renal TEAEs

	eGFR$_{CG}$ 30–< 90 mL/min (Renal Impairment) n = 1069	eGFR$_{CG}$ ≥ 90 mL/min (No Renal Impairment) n = 2815
Renal TEAE leading to B/F/TAF discontinuation, n (%)	1 (< 0.1)	0
Acute kidney injury	1 (< 0.1)	0

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; TEAE, treatment-emergent adverse event.

- **Only 1 (< 0.1%) participant discontinued B/F/TAF after 3 months due to a moderate renal TEAE of acute kidney injury, judged by investigator to be unrelated to B/F/TAF**
  - The participant was a 68-year-old male with Stage 2 eGFR$_{CG}$ and HIV-1 RNA < 50 copies/mL at baseline. They were receiving therapy for ongoing hyperlipidemia and hypertension at baseline, as well as an anticancer treatment with known association with kidney complications prior to discontinuation

Limitations

- Cystatin C–based eGFR was not evaluated, as in all trials included in the study, eGFR was calculated using the Cockcroft-Gault equation

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