Pharmacokinetics and Safety Data After Switching From Injectable CAB + RPV to Oral B/F/TAF

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Conclusions

- In virologically suppressed (VS) people with HIV (PWH) switching from cabotegravir (CAB) + rilpivirine (RPV) to bictegravir (BIC)/emtricitabine/tenofovir alafenamide (B/F/TAF), BIC trough and 2-hour post-dose plasma concentrations were generally within expected ranges in the presence of residual CAB and RPV
- Week 24 safety analysis showed that B/F/TAF was well tolerated, despite the overlapping exposures of the integrase strand transfer inhibitors CAB and BIC, with no study drug-related serious or severe treatment-emergent adverse events (TEAEs) and no study drug discontinuations due to TEAEs
- These data support switching from injectable CAB + RPV to oral B/F/TAF when needed or desired in VS PWH
- Further data on efficacy, safety, treatment satisfaction, and experiences from the EMPOWER study will be presented at IDWeek 2025 (Atlanta, GA, USA)

Plain Language Summary

- B/F/TAF is a daily pill for treating human immunodeficiency virus (HIV) that combines three medicines: bictegravir (B/BIC), emtricitabine (F), and tenofovir alafenamide (TAF)
- Another HIV treatment is cabotegravir (CAB) + rilpivirine (RPV), which is given as two injections once a month or once every 2 months
- The EMPOWER study looked at how well B/F/TAF works for people with HIV with low levels of the virus who used to take CAB + RPV every 2 months but could not carry on with these injections, or preferred to switch to a daily pill
- The study looked at whether CAB remaining in the blood after switching to B/F/TAF treatment would affect the levels of BIC or the safety of the treatment
- Levels of BIC in the blood over the 24 weeks after switching treatments were similar to those seen in other studies of B/F/TAF
- No one had drug-related serious or severe side effects within 24 weeks after switching treatments
- No one stopped taking B/F/TAF because of side effects 24 weeks after switching treatments
- This study shows that switching to B/F/TAF treatment was safe for people with HIV with low levels of the virus who were previously on CAB + RPV, with levels of BIC generally similar to those found in other studies of B/F/TAF

Introduction

- PWH on injectable CAB + RPV may discontinue injectable antiretroviral therapy for various reasons, including intolerance, adverse events, and personal preference[1,2]
- B/F/TAF is a guideline-recommended, once-daily oral treatment for HIV[3-5] that has shown high levels of efficacy and tolerability in clinical trials, including in VS individuals[6-10]
- Given the long half-lives of CAB and RPV,[11] switching to B/F/TAF involves overlapping exposures to the two integrase strand transfer inhibitors, CAB and BIC
- Since BIC, CAB, and RPV are not inhibitors or inducers of cytochrome P450 (CYP)3A and UDP glucuronosyltransferase (UGT)1A1, drug-drug interactions were not expected[12,13]; however, the overlap in CAB and BIC exposure has not been evaluated to date
- The Phase 4, prospective EMPOWER (**E**valuating **M**any **P**e**O**ple **W**ith HIV aft**ER** switching from CAB + RPV to B/F/TAF) study assessed the safety, pharmacokinetics, and efficacy of switching to B/F/TAF in VS PWH who were unable or unwilling to continue injectable CAB + RPV or expressed a preference to switch to oral therapy

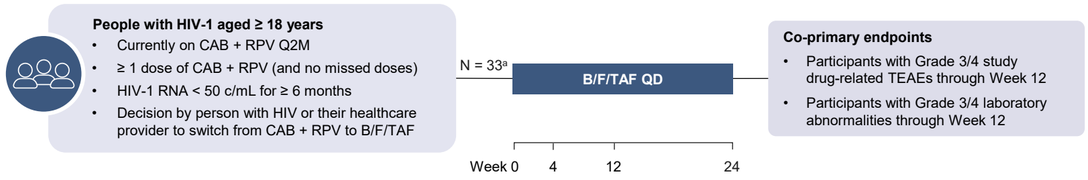
Objective

- To assess the plasma concentrations of BIC, CAB, and RPV, and safety of once-daily oral B/F/TAF, in VS PWH who switched from injectable CAB + RPV administered every 2 months (Q2M)

Methods

- EMPOWER (NCT06104306) was a Phase 4, single-group, open-label, prospective, multicenter study to evaluate the safety, pharmacokinetics, and efficacy of B/F/TAF in VS PWH who switched from CAB + RPV Q2M to daily B/F/TAF due to intolerance, adverse events, or personal preference

Study Design



[a]In total, 36 participants were screened, of whom 3 did not meet all eligibility criteria. Participants from France (n = 4) were not included in the pharmacokinetic analysis.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; CAB, cabotegravir; Q2M, every 2 months; QD, once daily; RPV, rilpivirine; TEAE, treatment-emergent adverse event.

- Additional pharmacokinetic (PK) and safety endpoints presented in this analysis included:
  - Plasma concentrations of BIC, CAB, and RPV measured using sparse PK sampling (Day 1, Week 4, Week 12, and Week 24, as appropriate)
  - TEAEs, study drug-related TEAEs, treatment-emergent Grade 3 or 4 laboratory abnormalities, and study drug discontinuations due to TEAEs through Week 24
- A single plasma PK sample was collected on Day 1 prior to dose
- A single trough plasma PK sample was collected ~23-24 hours after the previous B/F/TAF dose and prior to B/F/TAF dosing at Weeks 4, 12, and 24
- A single plasma PK sample was collected ~2 hours after B/F/TAF dose at Weeks 4, 12, and 24
- Plasma concentrations of BIC, CAB, and RPV are presented using descriptive statistics for the PK Analysis Set, which included all enrolled participants who received ≥ 1 dose of study drug and had ≥ 1 plasma PK measurement
  - Participants from France were not included in the PK analysis
- Safety outcomes were assessed in the Safety Analysis Set, which included all enrolled participants who received ≥ 1 dose of study drug
- Further analyses will be presented at IDWeek 2025 (Atlanta, GA, USA):
  - Efficacy (participants with HIV-1 RNA < 50 c/mL at Week 12 and Week 24)
  - B/F/TAF discontinuation through Week 12 and Week 24
  - Treatment satisfaction

Results

Baseline Demographic and Clinical Characteristics

	Participants Switching to B/F/TAF N = 33
Age, years, median (Q1, Q3)	48 (36, 59)
Sex assigned at birth, n (%)	
Male	24 (73)
Female	9 (27)
Race, n (%)	
White	18 (55)
Black	6 (18)
Other	5 (15)
Not permitted	4 (12)
Ethnicity, n (%)	
Not Hispanic or Latine	20 (61)
Hispanic or Latine	11 (33)
Not permitted	2 (6)
BMI, kg/m², median (Q1, Q3)	28.3 (23.7, 32.6)
$CrCl_{CG}$, mL/min, median (Q1, Q3)	109.0 (91.8, 138.6)
HIV-1 RNA, n (%)	
< 50 c/mL	31 (94)
≥ 50 c/mL	2[a] (6)
CD4 count, cells/µL, mean (SD)	689 (241)
Previously switched from B/F/TAF to CAB + RPV,[b] n (%)	11 (33)
Time on CAB + RPV, years, median (Q1, Q3)	1.4 (0.5, 2.1)
Time between last CAB + RPV dose and B/F/TAF initiation, days, median (Q1, Q3)	54 (49, 57)

- 29 participants were from North America and were included in the PK analysis
  - Participants from France (n = 4) were not included in the PK analysis
- 29 participants completed study and study drug treatment through Week 24
- Four participants prematurely discontinued the study drug
  - Two participants discontinued due to their own decision, one of whom switched to clinician-prescribed B/F/TAF
  - One participant died[c]
  - One participant was lost to follow-up after Week 12

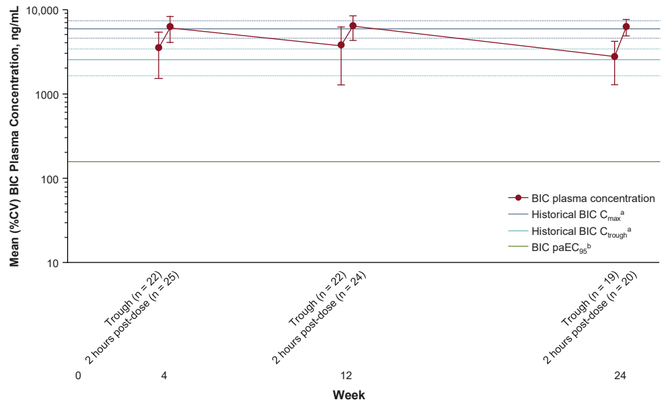
Data are shown for the Safety Analysis Set.
[a]Viral load values at baseline: 61 c/mL and 51 c/mL. [b]Prior antiretroviral therapy is based on available data. [c]Cause of death was a bicycle accident (reported term).
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; c, copies; CAB, cabotegravir; CD4, cluster of differentiation 4; $CrCl_{CG}$, estimated creatinine clearance by Cockcroft-Gault equation; Q, quartile; RPV, rilpivirine.

Plasma Concentrations of CAB and RPV Following Switch From CAB + RPV to B/F/TAF

	n	Mean (%CV) Concentration, ng/mL	
		CAB	RPV
Day 1: Pre-first B/F/TAF dose[a]	29	1650 (61.3)	68.3 (38.2)
Week 4: BIC trough timing[b]	22	929 (79.6)	57.8 (36.0)
Week 4: 2 hours post-B/F/TAF dose[b]	25	975 (78.1)	55.7 (37.9)
Week 12: BIC trough timing[b]	22	667 (147.0)	47.2 (47.4)
Week 12: 2 hours post-B/F/TAF dose[b]	24	647 (135.0)	45.4 (49.4)
Week 24: BIC trough timing[b,c]	19		37.1 (60.2)
Week 24: 2 hours post-B/F/TAF dose[b,c]	20		33.1 (52.5)

n = number of participants in the CAB/RPV PK Analysis Set with non-missing data, with measurements within the trough PK sampling window (20-28 hours inclusive after previous B/F/TAF dose and prior to next B/F/TAF dose) or post-dose PK sampling window (1.5-2.5 hours inclusive after B/F/TAF dose). Values below the limit of quantitation (25 ng/mL for CAB, 1 ng/mL for RPV) were treated as 0.
[a]For CAB + RPV administered as an injection every 2 months, geometric mean (5th, 95th percentile) CAB C_{trough}: 1600 (800, 3000) ng/mL, RPV C_{trough}: 68.9 (38.0, 119) ng/mL.[11]
[b]The residual CAB and RPV concentrations were measured at the corresponding BIC C_{trough} and post-B/F/TAF dose timepoints and do not represent C_{trough} or post-dose values for CAB or RPV since CAB and RPV were not administered during the study.
[c]Not calculated for CAB as more than a third of the values were below the limit of quantitation.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; CAB, cabotegravir; C_{trough}, concentration at the end of the dosing interval; CV, coefficient of variation; RPV, rilpivirine.

Plasma Concentration of BIC Following Switch From CAB + RPV to B/F/TAF



n = number of participants in the BIC PK Analysis Set with non-missing data, with measurements within the trough PK sampling window (20-28 hours inclusive after previous B/F/TAF dose and prior to next B/F/TAF dose) or post-dose PK sampling window (1.5-2.5 hours inclusive after B/F/TAF dose). Values below the limit of quantitation (20 ng/mL) were treated as 0. 2-hour post-dose concentrations were assessed 1.5-2.5 hours after B/F/TAF dose and do not necessarily represent the C_{max} values.
[a]Dashed lines indicate the range of %CV. Historical data in PWH on B/F/TAF from population PK analysis in Studies 1489, 1490, 1844, and 1878 (N = 1193): mean (%CV) BIC C_{max}: 6150 (22.9) ng/mL, mean (%CV) BIC C_{trough}: 2610 (35.2) ng/mL.[14] BIC T_{max}: 2-4 hours.[14]
[b]BIC $paEC_{95}$: 162 ng/mL.[14]
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; C_{max}, maximum concentration; C_{trough}, concentration at the end of the dosing interval; CV, coefficient of variation; $paEC_{95}$, protein-adjusted 95% effective concentration; PK, pharmacokinetic; PWH, people with HIV; T_{max}, time to maximum concentration.

Safety

- No participants experienced study drug-related Grade 3/4 TEAEs through Week 12 (co-primary endpoint) and Week 24
- Through Week 12, one (3%) participant experienced Grade 3 treatment-emergent laboratory abnormalities (reduced neutrophil and total white blood cell counts),[a] which were deemed unrelated to study drug
  - There was one additional Grade 3 treatment-emergent laboratory abnormality through Week 24 (increased low-density lipoprotein cholesterol level)
  - A total of 2 (6%) participants experienced Grade 3/4 treatment-emergent laboratory abnormalities through Week 24
- Through Week 24, 21 (64%) participants experienced TEAEs, of whom 7 (21%) experienced study drug-related TEAEs and 3 (9%) experienced Grade 3/4 TEAEs, which were deemed unrelated to study drug
- In total, 2 (6%) participants experienced serious TEAEs through Week 24; these were deemed unrelated to study drug
  - The serious TEAEs were upper abdominal pain, intestinal diverticulum, and gastrointestinal hemorrhage in one participant, and bicycle accident (leading to death)
- There were no study drug discontinuations due to TEAEs through Week 24

[a]Co-primary endpoint: Grade 3/4 treatment-emergent laboratory abnormalities through Week 12.

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