Low Incidence of Treatment-Emergent Resistance to Bictegravir/ Emtricitabine/Tenofovir Alafenamide Under Real-World Adherence Conditions Among People With HIV in the United States, 2018-2024

TUPEB131

Sara N Levintow[1], Paul McDwyer[2], Ziwei Yin[2], Wenyi Wang[2], Michelle L D'Antoni[2], Travis Lim[2]

[1]IQVIA, Durham, NC, USA; [2]Gilead Sciences, Inc., Foster City, CA, USA

Conclusions

- Emergent resistance-associated mutations (RAMs) were rare among people receiving bictegravir/ emtricitabine/tenofovir alafenamide (B/F/TAF), supporting the high barrier to resistance in a real-world population
- To our knowledge, this is the largest assessment of the emergence of RAMs to date, enabled by real-world data, while previous studies have been trial- or cohort-based
- Although the incidence rates of emergent RAMs were higher among people with lower adherence, all rates remained low (<1 per 100 person-years [PY])
- Clinical impacts of emergent RAMs on B/F/TAF may vary:
  - M184V/I alone is most common; B/F/TAF may still be effective in achieving suppression consistent with prior reports[1]
  - INSTI + NRTI resistance is complex to manage and could increase risk of virologic failure
- Limitations include difficulty in knowing the appropriate denominator: only 8139 of 108,721 had baseline genotyping prior to B/F/TAF initiation, and reasons for resistance testing were unknown
  - 8139 in study may overrepresent people with history of virologic failure and overestimate rates
  - Only able to identify emergent RAMs for people with testing over follow-up
  - Findings may not generalize to all people using B/F/TAF

Plain Language Summary

- This study looked at HIV drug resistance, which happens when the virus changes in ways that make treatments less effective
- Drug-resistant virus can still multiply (replicate) even when people are taking HIV medication
- We found that resistance was rare in people taking a commonly prescribed HIV treatment
  - This treatment combines three medicines: bictegravir, emtricitabine, and tenofovir alafenamide
- Most people taking this treatment did not develop resistance
- People who developed resistance may have missed doses of their medication
- How resistance affects treatment depends on what kind of changes happen in the virus
  - In some cases, the treatment could still work well

Introduction

- Emergent RAMs have been rarely observed for integrase strand transfer inhibitor (INSTI)-based regimens with high barriers to resistance, such as B/F/TAF
- Prior studies in clinical trials and cohorts have used different denominators with varying lengths of follow-up for estimates of RAM emergence, making interpretation difficult
  - 0 of 1306 (0%) with emergent RAMs *(denominator: people randomized to B/F/TAF)* through weeks 48, 96, and/or 144 in a pooled analysis of Phase 3 studies in the USA[2]
  - 8 of 2797 (0.3%) with emergent RAMs *(denominator: people receiving B/F/TAF as first- or second-line therapy*) at any time over three years in an observational analysis of the French national database[3]
  - 6 of 3383 (0.2%) with emergent RAMs *(denominator: people receiving B/F/TAF as second or greater line of therapy)* at any time over three years in an observational analysis of the French national database[4]
- To confirm the high barrier to resistance to B/F/TAF in real-world settings, this study aimed to capture a larger population, incorporate adherence data, and account for varying follow-up with incidence rates

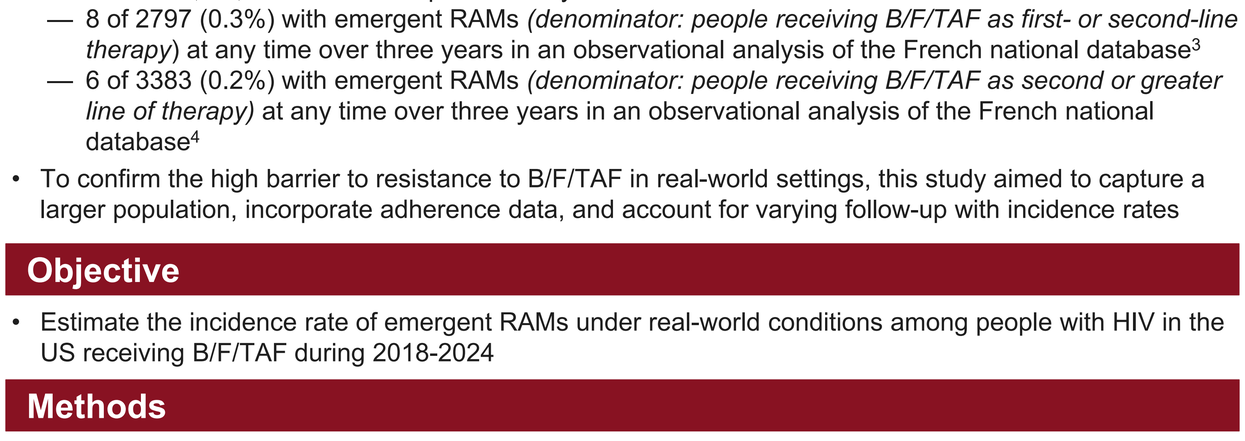
Objective

- Estimate the incidence rate of emergent RAMs under real-world conditions among people with HIV in the US receiving B/F/TAF during 2018-2024

Methods

- **Data source:** Medical and pharmacy claims and laboratory records from HealthVerity™ Marketplace, representing people in the US insured under commercial, Medicare, or Medicaid plans
- **Inclusion criteria:** Aged ≥18 years, diagnosed with HIV-1, treatment-naïve or experienced, initiated B/F/TAF in 2018-2024, and documented genotypic resistance testing prior to initiation or within 90 days
- **Follow-up period:** From B/F/TAF initiation (index) until the earliest of the RAM outcome or censoring (regimen switch, insurance disenrollment, end of study)
- **Adherence assessment:** Percentage of days covered (PDC) by prescription fills for 90-day periods following regimen initiation
- **Resistance assessment:** Extracted genotyping results from laboratory records and applied interpretation system from Stanford HIV drug resistance database (HIVdb) to identify RAMs conferring any level of resistance (high, intermediate, low, potential-low)[5]

Study Schematic



Outcome Assessment

RAMs were defined as follows:

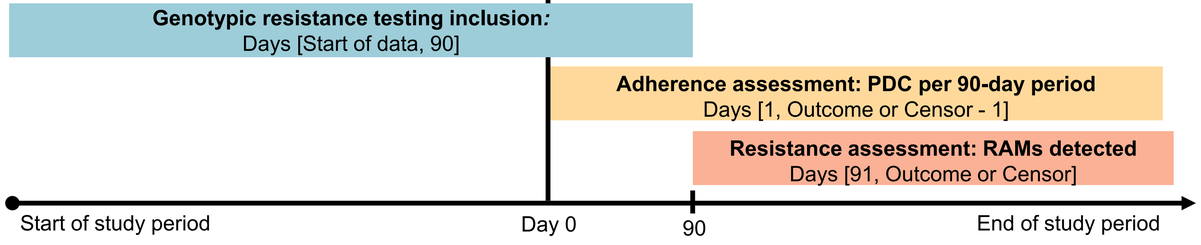
- **Specific to regimen:** RAM was associated with resistance to one or more regimen components
- **Newly detected:** RAM was first documented after 90 days of follow-up on regimen
- **Linked to adherence:** PDC was assessed for the 90 days prior to RAM detection
- **Linked to viremia:** Genotypic test performed was for plasma RNA (not proviral DNA) or there was a viral load measure ≥200 copies/ml within 90 days of RAM detection
- **Verified using positive control:** RAMs were confirmed to be higher for people on regimens containing elvitegravir or raltegravir (first-generation INSTIs) vs. bictegravir, cabotegravir, or dolutegravir

Emergent RAMs met all the above criteria, plus the following:

- **Confirmed absence in baseline genotype:** Genotyping results were available pre-index or within the first 90 days, and RAM was not detected

Statistical Analysis

- **Person-time:** The person-time denominator accumulated in 90-day periods over follow-up, stratified by PDC 0-65%, 65-85%, and 85-100%, reflecting thresholds associated with virologic response[1,6,7]
- **Incidence:** Rates (95% CIs) were estimated with Poisson regression, corresponding to people with RAM outcomes per 100 person-years (PY), overall and by PDC in the past 90 days



Results

Study Population

N = 883,916 People diagnosed with HIV-1 in the database

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N = 188,910 Initiated B/F/TAF (index) during February 2018-November 2024 study period

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N = 109,932 Enrolled in insurance ≥180 days pre- to ≥90 days post-index

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N = 108,721 Aged ≥18 years, no HIV-2 diagnoses during baseline period

↓

N = 8139 Documented resistance testing pre-index or ≤90 days post-index

Of 108,721 people on B/F/TAF, 8139 had baseline genotypes and were the focus of analysis

Characteristics of the Study Population, Overall on B/F/TAF and for the Subset With Baseline Genotypes

	Overall Population n = 108,721	Subset With Baseline Genotypes n = 8139
Treatment naïve, n (%)	56,631 (52%)	4776 (59%)
Age, years, median (interquartile range)	45 (33-55)	40 (31-52)
Sex, n (%)		
Male	80,960 (74%)	6022 (74%)
Female	27,761 (26%)	2117 (26%)
US region, n (%)		
South	35,842 (33%)	3308 (41%)
Northeast	21,143 (19%)	1685 (21%)
West	19,999 (18%)	1137 (14%)
Midwest	14,176 (13%)	694 (9%)
Multiple	3098 (3%)	294 (3%)
Missing	14,463 (13%)	1021 (13%)
Insurance type, n (%)		
Commercial	39,108 (36%)	2532 (31%)
Medicaid	40,395 (37%)	3459 (42%)
Medicare	5318 (5%)	272 (3%)
Multiple	10,160 (9%)	822 (10%)
Missing	13,740 (13%)	1054 (13%)
Year of initiation, n (%)		
2018-2019	36,349 (33%)	1486 (18%)
2020	16,574 (15%)	1131 (14%)
2021	14,120 (13%)	1029 (13%)
2022	16,157 (15%)	1172 (14%)
2023	13,916 (13%)	1728 (21%)
2024	11,605 (11%)	1593 (20%)

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide.

RAM Incidence Over Follow-Up

Rate of emergent RAMs was 0.47 per 100 PY in the subset with baseline genotypes, in which resistance testing was performed prior to or within 90 days of B/F/TAF initiation

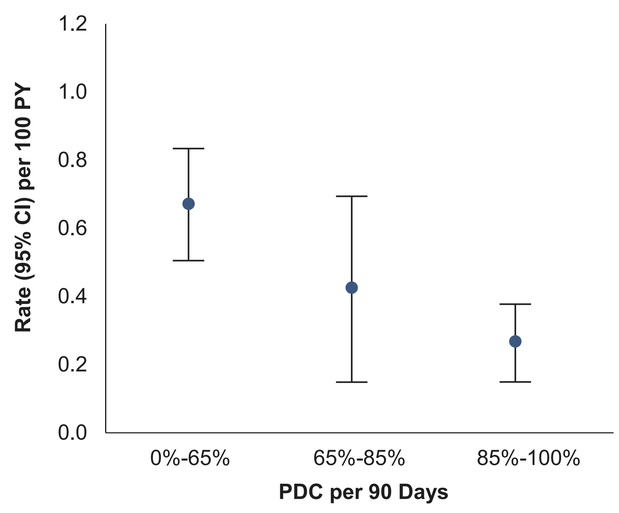
Rate of RAMs was 0.09 per 100 PY in the full population, most without baseline genotypes

Emergent RAM Incidence in B/F/TAF Subset With Baseline Genotypes

	N With Emergent RAMs	PY	Rate per 100 PY (95% CI)
Overall	89	18,921	0.47 (0.37-0.57)
PDC in past 90 days			
85%-100%	20	7748	0.26 (0.14-0.37)
65%-85%	9	2164	0.42 (0.14-0.69)
0%-65%	60	9009	0.67 (0.50-0.83)

B/F/TAF, bictegravir/ emtricitabine/tenofovir alafenamide; PDC, percentage of days covered; PY, person-years; RAM, resistance-associated mutation.

Emergent RAM Incidence by Adherence Level in B/F/TAF Subset with Baseline Genotypes



B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; PDC, percentage of days covered; PY, person-years; RAM, resistance-associated mutation.

Resistance Characterization

72 of 89 had emergent RAMs to one drug class, with INSTI mutations only or NRTI mutations only

Few INSTI RAMs conferred high resistance to bictegravir

Drug Class Resistance for 89 People With Emergent RAMs to B/F/TAF at First Detection of the Outcome Over Follow-Up

Drug Class Resistance	Number of People (%)
INSTI and NRTI mutations	17 (19%)
INSTI mutations only	12 (13%)
NRTI mutations only	
M184V/I only	41 (46%)
Other NRTI mutations	19 (21%)

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; RAM, resistance-associated mutation.

For additional details on the emergent RAMs, please scan the QR code

Resistance Classification From HIVdb Genotypic Susceptibility Score

BIC, bictegravir; FTC, emtricitabine; HIVdb, Stanford HIV drug resistance database; TAF, tenofovir alafenamide; RAM, resistance-associated mutation.

References: 1. Rolle CP, et al. *AIDS Res Ther*. 2025;22:126. **2.** Andreatta K, et al. *J Antimicrob Chemother*. 2025;80:281-91. **3.** Marcelin AG, et al. *J Antimicrob Chemother*. 2025;80:95-101. **4.** Marcelin AG, et al. AIDS. 2026;40:803-10. **5.** Stanford HIV Drug Resistance Database. https://hivdb.stanford.edu. **6.** Maggiolo F, et al. *J Int Assoc Provid AIDS Care*. 2022;21: 23259582221140208. **7.** Maggiolo F, et al. *Sex Transm Infect*. 2024;100:418-22.

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Disclosures: **SNL** is an employee of IQVIA and works exclusively on Gilead studies. **PM, WW, MLD'A,** and **TL** are employees of, and hold stock in, Gilead Sciences, Inc. **ZY** is an employee of The Lotus Group (Pine Brook, NJ, USA) and works exclusively on Gilead studies.

Correspondence: Travis Lim, Travis.Lim1@gilead.com.