

ORIGINAL ARTICLE

Rapid start with bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) as initial treatment in people with human immunodeficiency virus-1 (HIV-1): A systematic literature review of clinical and patient-reported outcomes

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Abstract

Background: Treatment guidelines recommend rapid antiretroviral therapy (ART) initiation among eligible people with HIV to improve treatment outcomes and reduce HIV transmission. Bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF), an integrase strand transfer inhibitor-based single-tablet regimen, is recommended for rapid start in US and European guidelines. This systematic literature review synthesized evidence on the efficacy, safety and effect on patient-reported outcomes (PROs) of B/F/TAF rapid start among newly diagnosed people with HIV.

Methods: MEDLINE, Embase, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials databases were searched in January 2024, supplemented by searches of conference proceedings and clinical trial records. English-language interventional studies of B/F/TAF rapid start among ART-naïve people with HIV reporting efficacy, safety or PROs were eligible. Study quality was assessed using York Centre for Reviews and Dissemination or Risk Of Bias In Non-randomized Studies of Interventions checklists. Results were synthesized narratively.

Results: Across eight included studies, 745 people with HIV received B/F/TAF rapid start, 171 received rapid start comparators and 255 received non-rapid start comparators. At Weeks 24 and 48, 80%–94% and 74%–96% of people with HIV treated with B/F/TAF rapid start achieved viral load <50 copies/mL, respectively. Treatment discontinuation due to adverse events was 0%–3%, and grade 3/4 adverse events occurred in 0%–3% of people with HIV receiving B/F/TAF rapid start. Rapid start improved engagement in care over traditional non-rapid start approaches, and B/F/TAF rapid start reduced anxiety and improved quality of life

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among people with HIV. Limitations of the review included heterogeneous study definitions of “rapid start” and limited data availability.

Conclusions: B/F/TAF rapid start was efficacious, safe and associated with high engagement in care and improved PROs.

KEYWORDS

adherence, engagement in care, immediate start, quality of life, safety, viral suppression

INTRODUCTION

Human immunodeficiency virus (HIV) remains a significant global health challenge, affecting an estimated 39.9 million people in 2023, including 1.3 million new infections [1]. Antiretroviral therapy (ART) aims to suppress viral replication to induce and maintain an undetectable viral load, preserve and improve immune function and reduce the risk of HIV transmission [2].

Most HIV treatment guidelines recommend a ‘test and treat approach’, where ART is initiated as soon as possible, including same-day initiation or within 7 days after diagnosis [3–6]. Rapid ART improves health outcomes by improving viral suppression, decreasing transmission risk and enhancing patient linkage to and engagement in HIV care [7–10]. Rapid ART may also mitigate HIV-related stigma, which can negatively impact health outcomes by impeding HIV diagnosis, engagement in care, and treatment initiation and adherence [9, 11, 12]. Moreover, Undetectable = Untransmittable (‘U=U’) as a concept has empowered people with HIV who have an undetectable viral load to feel confident that they cannot transmit HIV to their sexual partners, resulting in reduced internalized stigma and anxiety [13].

The guidelines also recommend that initial ART regimens consist of an integrase strand transfer inhibitor (INSTI) and a nucleos(t)ide reverse transcriptase inhibitor (NRTI) backbone [3–6]. Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), a U.S Food and Drug Administration (FDA)-approved, INSTI-based single-tablet ART regimen, has demonstrated high rates of viral suppression, good safety and tolerability, and a high barrier to resistance in the treatment of HIV [14–17]. B/F/TAF is well suited to rapid start treatment because it can be initiated before receipt of lab results, is effective against hepatitis B virus, does not require HLA-B*5701 or pre-existing resistance mutation testing and is less likely to result in the development of drug resistance [18, 19]. Despite this, a comprehensive review of current literature on rapid start outcomes among people with HIV receiving B/F/TAF is lacking.

This systematic literature review (SLR) seeks to synthesize the evidence on the efficacy, safety and patient-

reported outcomes (PROs) of B/F/TAF rapid start among people with HIV-1 who are newly diagnosed.

METHODS

The SLR was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and a pre-specified protocol. MEDLINE, Embase, the Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Trials databases were searched in January 2024 using search terms for “HIV,” “B/F/TAF,” and relevant study designs (Tables S1–S3). Electronic database searches were supplemented with searches of relevant, available conference proceedings from the past 3 years (2021–2023), the World Health Organization international clinical trials registry platform and hand searches of bibliographies of relevant SLRs or meta-analyses identified in the electronic databases (Tables S4 and S5).

Interventional studies in people who were newly diagnosed with HIV, ART-naïve and initiating B/F/TAF rapid start were eligible for inclusion. Treatment was considered rapid start when initiated within 14 days of HIV diagnosis, or when defined as such by study authors. The latter criteria intentionally allowed ‘rapid start’ definitions beyond those used in major treatment guidelines to be included in the SLR to provide insight into real-world variability in rapid start ART within the context of controlled, interventional study designs. Eligible studies reported at least one relevant efficacy outcome (e.g., viral suppression, engagement in care), safety outcome (e.g., treatment discontinuation, adverse events [AE]) or PRO (e.g., treatment satisfaction, health-related quality of life [HRQoL]). Observational studies and publications not in English were excluded (full eligibility criteria reported in Table S6).

Identified records were reviewed in two stages. First, the titles and abstracts were reviewed against the SLR eligibility criteria. Second, the full texts of potentially relevant records were reviewed and those meeting the eligibility criteria were included. At each stage, records were reviewed by two independent reviewers who reached consensus on eligibility. Where necessary, a third reviewer was consulted.

Key study characteristics, participant characteristics and relevant study outcomes for all reported timepoints and subgroups were extracted into a pre-specified grid in Microsoft Excel by one reviewer. The accuracy and completeness of extracted data were verified by a second, independent reviewer. The quality of included randomized controlled trials (RCTs) was appraised using the University of York's Centre for Reviews and Dissemination checklist. Non-randomized interventional study (e.g., single-arm trial) quality was appraised using the Risk Of Bias In Non-randomized Studies of Interventions tool. Each study was appraised by one reviewer and verified by a second reviewer.

During manuscript development, the authors became aware that four of the six studies initially captured only as congress proceedings in the SLR were subsequently published as peer-reviewed manuscripts reporting additional relevant information such as expanded methodological details, additional timepoints and novel outcomes. To ensure that all available data from these studies were considered, these results have been incorporated into the manuscript.

Data were synthesized narratively. All studies reporting on a relevant outcome were grouped for synthesis. For efficacy and safety outcomes, only data reported at or beyond Week 24 of follow-up were synthesized, as earlier timepoints (e.g., Week 4 or Week 12) were considered unlikely to be clinically meaningful.

RESULTS

Included studies

A total of 690 records were identified from electronic databases, of which 8 were included in this SLR. A total of 3434 records were identified through supplementary searches, of which 17 were included. Ultimately, 25 publications reporting on 8 unique studies were included in the SLR (Figure S1). Six additional publications reporting on four of the studies initially included in the SLR only as congress proceedings were identified by the authors during manuscript development, and new relevant data were extracted.

Most included studies were interventional, single-arm studies of B/F/TAF rapid start (5/8 studies; Table 1). Three studies were comparative; one was a non-randomized study including a B/F/TAF non-rapid start comparator arm [20]. Two studies were RCTs: BIC Test&Treat (T&T) included a darunavir/cobicistat/F/TAF (D/C/F/TAF) rapid start comparator arm [21, 22], and Wang 2024 included a B/F/TAF non-rapid comparator arm, as well as efavirenz + lamivudine + tenofovir disoproxil fumarate (EFV + 3TC + TDF) rapid and non-rapid start arms [23, 24]. The non-rapid start arms were reported only in the extracted conference proceedings, while the published manuscript reported only the rapid start cohorts; the rapid

start cohorts in the manuscript were slightly larger than those reported in the conference proceedings due to a longer enrollment period [24].

Sample sizes ranged from 30 to 471 participants. Across all studies, 745 people with HIV received B/F/TAF rapid start, 171 received rapid start comparator regimens and 255 received non-rapid start comparator regimens. In 7/8 included studies, rapid start was defined as treatment initiation within 14 days of diagnosis [20, 21, 23, 25–28]; two of these studies assessed treatment initiation on the same day as the first appointment with a specialist [25, 27]. In the remaining study, a rapid start cut-off was not defined but occurred a median of 16 days after diagnosis for participants without lab results and a median of 28 days after diagnosis for participants with lab results (Table 1) [29]. Overall, median time from diagnosis to rapid start initiation ranged from 3 to 28 days.

All studies reported efficacy outcomes and seven studies reported safety outcomes at or beyond Week 24. Six studies reported PROs. The primary outcomes of most studies (5/8) assessed measures of virologic efficacy. The primary outcomes for three respective studies were engagement in HIV care [20], time to clinical or virologic failure [26], and the proportion of participants who were ineligible to receive other rapid ART regimens (Table 1) [28, 32].

Participant baseline characteristics

The mean or median age of enrolled participants ranged from 28 to 45 years (Table 2). In all studies, more than three-quarters of participants were male, with the Wang 2024 study only enrolling men who have sex with men [24]. Race and ethnicity were heterogeneous across the six reporting studies.

Mean or median baseline CD4 count ranged from 340 to 568 cells/mm³ in 7/8 reporting studies. Mean baseline viral load ranged from 4.7 to 5.6 log copies/mL and median baseline viral load ranged from 4.3 to 6.0 log copies/mL, with these values ≤ 4.8 log copies/mL in 5/7 reporting studies. In the Rainbow study, which only enrolled people with HIV who had a CD4 count < 200 cells/mm³ or who already experienced an acquired immunodeficiency syndrome (AIDS)-defining event, median baseline CD4 count was 90 cells/mm³ and median baseline viral load was 6.0 log copies/mL [26, 27].

Virologic efficacy

Viral suppression and virologic failure

Viral suppression was reported by all eight studies, virologic failure by six and resistance analyses by four. At

TABLE 1 Summary of characteristics of studies included in the SLR.

Study name	Study design ^a	Country	Treatment arms (<i>n</i> enrolled)	Rapid start definition	Primary outcome(s)
Benidir 2022 [20]	Single center non-RCT	United States	B/F/TAF rapid start (<i>n</i> = 65) B/F/TAF non-rapid start (<i>n</i> = 42)	≤7 days after diagnosis	Retention in HIV care at 1 year, defined as: 1. Keeping ≥3 visits within the first 12 months of care 2. Attending a clinic visit between months 9–12 of care 3. Experiencing no gaps in care >6 months
BIC-NOW [27, 30, 31]	Multicenter phase IV non-RCT	Spain	B/F/TAF rapid start (<i>n</i> = 208)	Same day as specialist appointment	HIV RNA in plasma at Week 24 and Week 48
BIC T&T [21, 22]	Multicenter phase III RCT	United Kingdom	B/F/TAF rapid start (<i>n</i> = 19) D/C/F/TAF rapid start (<i>n</i> = 17)	≤14 days after diagnosis without lab results	Virologic response at Week 12 (time-weighted average change from baseline to Week 12 in HIV RNA)
BIFAST [29]	Single center phase IV non-RCT	Spain	B/F/TAF rapid start (<i>n</i> = 59) ^b	Median 16 days (without lab results) or median 28 days (with lab results) after diagnosis	Time from the first determination of CD4 and HIV viral load to HIV viral load <50 copies/mL
FAST [25]	Multicenter phase IV non-RCT	France	B/F/TAF rapid start (<i>n</i> = 118)	Same day as specialist appointment without lab results	Virologic suppression at Month 6 (plasma HIV RNA <50 copies/mL per the Snapshot method)
Wang 2024 [23, 24]	Multicenter RCT	China	B/F/TAF rapid start (<i>n</i> = 132) (enrollment period: March 2021 to April 2022) EFV + 3TC + TDF rapid start (<i>n</i> = 126) (enrollment period: March 2021 to April 2022) B/F/TAF non-rapid start (<i>n</i> = 91) (enrollment period: March 2021 to April 2022) EFV + 3TC + TDF non-rapid start (<i>n</i> = 122) (enrollment period: March 2021 to April 2022) B/F/TAF rapid start	≤14 days after diagnosis	Virologic suppression at Week 48 (plasma HIV RNA <50 copies/mL per the FDA Snapshot method)

TABLE 1 (Continued)

Study name	Study design ^a	Country	Treatment arms (<i>n</i> enrolled)	Rapid start definition	Primary outcome(s)
Rainbow [26]	Single center phase IV non-RCT	Italy	<u>(<i>n</i> = 146) (enrollment period: March 2021 to July 2022)</u> <u>EFV ± 3TC ± TDF rapid start</u> <u>(<i>n</i> = 154) (enrollment period: March 2021 to July 2022)</u> B/F/TAF rapid start (<i>n</i> = 30)	≤7 days after diagnosis	Time to clinical or virologic failure, defined as: - Virologic reasons that include: - HIV RNA reduction <1 log₁₀ copies/mL by Week 12 - HIV RNA ≥200 copies/mL at or after Week 24 - HIV RNA ≥50 copies / mL at or after Week 48 - Viral rebound, defined as: - HIV RNA to >200 copies/mL after having achieved HIV RNA <50 copies/mL - Rebound of HIV RNA by >1 log₁₀ copies/mL from nadir value in patients whose viral load has never been <50 copies/mL - Clinical reasons that include: - Change of regimen before Week 48 because of toxicity, unmanageable drug–drug interactions or IRIS - Death due to any cause - Any new or recurrent AIDS defining event - Any new serious non-AIDS defining event
Test&Treat [28, 32]	Single center non-RCT	Spain	B/F/TAF rapid start (<i>n</i> = 100)	≤7 days of diagnosis without lab results	Proportion of patients non-eligible to receive other early ART regimens: - Presence of HLA-B* 5701 or lack of HLA test - Major genotypic resistance mutations - CD4 count <200 cells/mm³ - Viral load >100 000 copies/mL - Comorbidities such as osteopenia

(Continues)

TABLE 1 (Continued)

Study name	Study design ^a	Country	Treatment arms (<i>n</i> enrolled)	Rapid start definition	Primary outcome(s)
					6. Framingham risk score >10% at 10 years
					7. Kidney disease (eGFR <50 mL/min)
					8. Concomitant medication that can cause potential interactions with antiretrovirals
					9. HBV coinfection (HBsAg positivity) or lack of serology

Note: Underlined text indicates data that were retroactively extracted from the full-text of the peer-reviewed manuscript that was published after completion of the systematic literature review.

Abbreviations: AIDS, acquired immunodeficiency syndrome; ART, antiretroviral therapy; B/F/TAF: bictegravir, emtricitabine, tenofovir alafenamide; D/C/F/TAF: darunavir, cobicistat, emtricitabine, and tenofovir alafenamide; EFV + 3TC + TDF, efavirenz + lamivudine + tenofovir disoproxil fumarate; eGFR, estimated glomerular filtration rate; FDA, United States Food and Drug Administration; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; IRIS, immune reconstitution inflammatory syndrome; RCT, randomized controlled trial; RNA, ribonucleic acid; SLR, systematic literature review.

^aAll included studies were open label studies.

^bBIFAST has been reported here as a single arm study, despite its description in-text as a multi-arm study, as it reports a single treatment arm analyzed in two cohorts treated as subgroups. No second intervention or comparator was assessed in this study.

Week 24, $\geq 80\%$ of intention-to-treat (ITT) or modified ITT (mITT) population participants treated with B/F/TAF rapid start achieved viral suppression, defined as viral load <50 copies/mL (Table 3) [22, 23, 25–27, 29, 32]. In Wang 2024, at Week 24, significantly more participants receiving B/F/TAF rapid start achieved viral suppression compared with EFV + 3TC + TDF rapid start participants (94% vs. 75%, $p < 0.001$) [23]. In subgroup analyses, $\geq 60\%$ of participants with baseline viral load $\geq 100\,000$ copies/mL achieved viral load <50 copies/mL at Week 24: 78% (7/9 participants) in BIFAST [29] and 70% (35/50 participants) in FAST [25]. Among participants in FAST with baseline viral load >500 000 copies/mL, 62% (13/21) achieved viral suppression [25].

Virologic failure at Week 24 was <10% in two reporting studies (Table 3) [25, 29]. The publication on FAST noted that failure did not appear due to treatment non-adherence based on assessment of plasma B/F/TAF concentrations and no emergent resistance mutations were identified; all 11 participants who failed had median baseline viral loads between 247 713 and 10 000 000 copies/mL [25].

At Week 48, 74%–96% of participants treated with B/F/TAF rapid start achieved viral load <50 copies/mL (Table 3) [22, 24–27, 32]. The proportion of participants experiencing virologic failure ranged from 0% to 13%, although definitions of virologic failure varied. No resistance mutations to B/F/TAF were identified in a total of 15 participants experiencing confirmed virologic failure [25, 27] or viral blips [26].

Benidir 2022 only reported viral suppression by study visit. At visit 4 (median 192.0 and 243.5 days after treatment initiation for B/F/TAF rapid and non-rapid start, respectively), viral suppression favored the rapid start arm, although the difference was not statistically significant (Table 3) [20]. Quantitative viral load findings are presented in Table S7 and time to viral suppression findings are presented in Table S8.

CD4 count and CD4/CD8 ratio

Changes in CD4 count or CD4/CD8 ratios were reported in five studies, four of which were single-arm B/F/TAF rapid start studies. Mean baseline CD4 count was 394 cells/ μ L in BIC-NOW, which increased by +313 cells/ μ L at Week 48, while mean baseline CD4 count was 365 cells/ μ L in T&T, which increased by +206 cells/ μ L at Week 48. Median baseline CD4 count was 369 cells/ μ L in FAST, which increased by +230 cells/ μ L at Week 48. In all three studies, 1.6–1.8-fold increases were seen in CD4/CD8 ratios from baseline to Week 48 (Table S9) [24, 25, 27, 32]. Wang 2024, the only RCT that reported both CD4 count and CD4/CD8

TABLE 2 Baseline characteristics of people with HIV enrolled in studies included in the SLR.

Study	Treatment arm (sample size)	Age, mean (SD) or median (Q1, Q3)	Male, n (%)	Race/ethnicity, n (%)	CD4 count, mean (SD) or median (Q1, Q3), cells/mm ³	Viral load, mean (SD) or median (Q1, Q3), log copies/mL
Benidir 2022 [20]	B/F/TAF rapid start (n = 65)	28 (24, 36)	56 (86)	White: 28 (44)	351 (183, 514)	4.7 (4.2, 5.4)
				Black: 24 (38)		
	B/F/TAF non-rapid start (n = 42)	35 (28, 48)	33 (79)	Other: 12 (19)	476 (336, 716)	4.7 (4.0, 5.6)
				Hispanic: 11 (18) ^a		
				White: 27 (64)		
				Black: 13 (31)		
	B/F/TAF rapid start (n = 208)	36 (11)	182 (88)	Other: 2 (5)	394 (252)	5.6 (6.2)
				Hispanic: 2 (5) ^a		
BIC T&T [21, 22]	B/F/TAF rapid start (n = 19)	34 (13.7)	19 (100)	NR	452 (254)	4.86 (0.71)
				White: 11 (58)		
	D/C/F/TAF rapid start (n = 17)	37 (9.4)	15 (88)	Hispanic: 2 (11)	568 (246)	4.71 (1.03)
				Black: 2 (11)		
				Asian: 3 (16)		
				Other: 1 (5)		
				White: 8 (47)		
				Hispanic: 2 (12)		
BIFAST [29]	B/F/TAF rapid start without lab data (n = 20)	32 (26, 39)	19 (95)	Black: 4 (24)	454 (286, 725)	NR
				Asian: 1 (6)		
	B/F/TAF rapid start with lab data (n = 39)	35 (30, 42)	38 (97)	Other: 2 (12)	404 (238, 668)	NR
				European: 14 (70)		
FAST [25]	B/F/TAF rapid start (n = 112)	36 (28, 47)	98 (88)	Latin American: 6 (30)	369 (240, 570)	4.8 (4.4, 5.5)
				European: 22 (56)		
Wang 2024 [23, 24] ^b	B/F/TAF rapid start (n = 132) (enrollment period: March 2021 to April 2022)	29 (25, 38)	132 (100)	Latin American: 17 (44)	342 (241, 450)	4.3 (3.8, 5.0)
				Asian: 110 (83)		
	EFV + 3TC + TDF rapid start (n = 126) (enrollment period: March 2021 to April 2022)	29 (25, 35)	126 (100)	Asian: 109 (87)	342 (243, 449)	4.4 (4.0, 4.8)

(Continues)

TABLE 2 (Continued)

Study	Treatment arm (sample size)	Age, mean (SD) or median (Q1, Q3)	Male, n (%)	Race/ethnicity, n (%)	CD4 count, mean (SD) or median (Q1, Q3), cells/mm ³	Viral load, mean (SD) or median (Q1, Q3), log copies/mL
Rainbow [26]	EFV + 3TC + TDF non- rapid start (n = 122) (enrollment period: March 2021 to April 2022)	35 (28, 44)	122 (100)	Asian: 113 (93)	350 (208, 460)	4.3 (3.6, 4.7)
	B/F/TAF rapid start (n = 146) (enrollment period: March 2021 to July 2022)	31 (27, 40)	146 (100)	Han: 133 (91.1)	340 (242, 446)	4.4 (3.8, 5.0)
	EFV ± 3TC ± TDF rapid start (n = 154) (enrollment period: March 2021 to July 2022)	32 (27, 38)	154 (100)	Han: 142 (95.3)	334 (242, 449)	4.5 (4.0, 4.9)
Test&Treat [28, 32]	B/F/TAF rapid start (n = 30)	45 (38, 58)	25 (83)	White: 27 (90) Hispanic: 2 (7) Asian: 1 (3)	90 (39, 147)	6.0 (5.4, 6.4)
	B/F/TAF rapid start (n = 100)	32 (27, 38)	79 (79)	Latin American: 64 (64) European: 34 (34) Asian: 1 (1) African: 1 (1)	365 (213)	4.7 (4.2, 5.2)

Note: Underlined text indicates data that were retroactively extracted from the full-text of the peer-reviewed manuscript that was published after completion of the systematic literature review. Italicized values were calculated based on data reported by the publications.

Abbreviations: B/F/TAF: bictegravir, tenofovir alafenamide; D/C/F/TAF: darunavir, cobicistat, emtricitabine, and tenofovir alafenamide; EFV + 3TC + TDF, efavirenz + lamivudine + tenofovir disoproxil fumarate; NR, not reported; Q1, first quartile; Q3, third quartile; SD, standard deviation; SLR, systematic literature review.

^aHispanic was reported separately from racial categories; participants may be included in both a racial category and the Hispanic category.

^bNo baseline characteristics were reported for the B/F/TAF non-rapid start arm.

TABLE 3 Summary of viral suppression and virologic failure findings.

Study name	Timepoint	Treatment arm	Outcome definition	n/N (%)	p value
Viral suppression					
BIFAST [29]	Week 24 ^a	B/F/TAF rapid start (ITT)	Viral load <50 copies/mL	50/59 (84.4)	NR
Wang 2024 [23, 24] ^b	Week 24	B/F/TAF rapid start (enrollment period: March 2021 to April 2022)	Viral load <50 copies/mL (FDA Snapshot method)	101/108 (93.5)	NR
		EFV + 3TC + TDF rapid start (enrollment period: March 2021 to April 2022)		68/91 (74.7)	<0.001 vs. B/F/TAF rapid start
		EFV + 3TC + TDF non-rapid start (enrollment period: March 2021 to April 2022)		67/88 (76.1)	0.16 vs. EFV + 3TC + TDF rapid start
	Week 48 ^a	B/F/TAF rapid start (ITT) (enrollment period: March 2021 to July 2022)	Viral load <50 copies/mL (FDA Snapshot method)	140 (95.9)	NR
		EFV + 3TC + TDF rapid start (ITT) (enrollment period: March 2021 to July 2022)		118 (79.2)	NR
		B/F/TAF rapid start (mITT)			NR
BIC-NOW [27, 30, 31]	Week 24	B/F/TAF rapid start (ITT)	Viral load <50 copies/mL	142/160 (88.8)	NR
	Week 48 ^a	B/F/TAF rapid start (ITT)		175/208 (84.1)	NR
		B/F/TAF rapid start (mITT)		NR/NR (96.8)	NR
Rainbow [26]	Week 24	B/F/TAF rapid start	Viral load <50 copies/mL	24/30 (80.0)	<0.001 vs. baseline
	Week 48	B/F/TAF rapid start		27/30 (90.0)	<0.001 vs. baseline
FAST [25]	Week 24 ^a	B/F/TAF rapid start (ITT)	Viral load <50 copies/mL (FDA Snapshot method)	90/112 (80.4)	NR
	Week 48 ^a	B/F/TAF rapid start (ITT)		95/112 (84.8)	NR
BIC T&T [21, 22]	Week 24	B/F/TAF rapid start	Viral load <50 copies/mL	16/19 (84.2)	NR
	Week 48	D/C/F/TAF rapid start		12/17 (70.6)	NR
		B/F/TAF rapid start		14/19 (74)	NR
		D/C/F/TAF rapid start		11/17 (65)	NR
Test&Treat [28, 32]	Week 24	B/F/TAF rapid start (ITT with observed data)	Viral load <50 copies/mL	83/92 (90)	<0.001 vs. baseline
		B/F/TAF rapid start (ITT)	Viral load <50 copies/mL (FDA Snapshot analysis)	82/100 (82)	NR

(Continues)

TABLE 3 (Continued)

Study name	Timepoint	Treatment arm	Outcome definition	n/N (%)	p value
Benidir 2022 [20]	Week 48	B/F/TAF rapid start (ITT with observed data)	Viral load <50 copies/mL	80/87 (92)	<0.001 vs. baseline
		B/F/TAF rapid start (ITT)	Viral load <50 copies/mL (FDA snapshot analysis)	78/100 (78)	NR
	Visit 3 (median 118.0 days)	B/F/TAF rapid start	Undetectable viral load	19/25 (76.0)	≥0.05
	Visit 3 (median 238.5 days)	B/F/TAF non-rapid start		12/16 (75.0)	
	Visit 4 (median 192.0 days)	B/F/TAF rapid start		9/9 (100.0)	≥0.05
Virologic failure	Visit 4 (median 243.5 days)	B/F/TAF non-rapid start		3/4 (75.0)	
	Visit 5 (median days NR)	B/F/TAF rapid start		3/3 (100.0)	≥0.05
	Visit 5 (median days NR)	B/F/TAF non-rapid start		1/1 (100.0)	
BIFAST [29]	Week 24	B/F/TAF rapid start (ITT)	Viral load >50 copies/mL	4/59 (6.8)	NR
	Week 24	B/F/TAF rapid start (ITT)	Two consecutive plasma viral load measurements ≥50 copies/mL as of Week 24	11/112 (9.8)	NR
	Week 48	B/F/TAF rapid start (ITT)		14/112 (12.5)	NR
BIC-NOW [27, 30, 31]	Week 48	B/F/TAF rapid start (PP)	Two consecutive HIV viral load measurements >50 copies/mL following previous undetectability under B/F/TAF treatment	3/178 (1.7)	NR
	Week 48	B/F/TAF rapid start	Clinical or unconfirmed virologic failure (viral blips that did not meet the definition of protocol-defined virologic failure ^c)	3/30 (10.0)	NR
Test&Treat [28, 32]	Week 24	B/F/TAF rapid start (ITT)	Protocol-defined virologic failure ^c	0/30 (0)	NR
	Week 48	B/F/TAF rapid start (ITT)	Viral load ≥50 copies/mL	11/100 (11)	NR
				8/100 (8)	NR

TABLE 3 (Continued)

Study name	Timepoint	Treatment arm	Outcome definition	n/N (%)	p value
Wang 2024 [23, 24]	Week 48	B/F/TAF rapid start (ITT) (enrollment period: March 2021 to July 2022) EFV + 3TC + TDF rapid start (ITT) (enrollment period: March 2021 to July 2022)	Viral load >200 copies/mL after at least 24 weeks of ART	0 (0) 1 (0.7)	NR NR

Note: Underlined text indicates data that were retroactively extracted from the full-text, peer-reviewed manuscript that was published after completion of the systematic literature review. Italicized values were calculated based on data reported by the publications.

Abbreviations: ART: antiretroviral therapy; B/F/TAF: bictegravir, emtricitabine, tenofovir alafenamide; EFV + 3TC + TDF, efavirenz + lamivudine + tenofovir disoproxil fumarate; FDA, United States Food and Drug Administration; HIV, human immunodeficiency virus; (m) ITT, (modified) intention-to-treat; NR, not reported; PP, per protocol.

^aPP analyses also reported.

^bViral suppression was not reported for the B/F/TAF non-rapid start arm.

^cProtocol-defined virologic failure was defined as the failure to achieve a virologic response and/or the presence of viral rebound. Virologic response was defined as either a reduction HIV RNA >1 log₁₀ copies/mL by Week 12, HIV RNA ≤200 copies/mL at or after Week 24, and HIV RNA ≤50 copies/mL at Week 48. Viral rebound was characterized as HIV-1 RNA >200 copies/mL following the attainment of HIV-1 RNA <50 copies/mL or with an increase of more than 1 log₁₀ copies/mL from the lowest value, confirmed after a 2-week period.

ratio outcomes, reported that the B/F/TAF rapid start arm (*n* = 146) had higher increases in CD4 count (223 vs. 181 cells/μL) and CD4/CD8 ratio (0.36 vs. 0.29) than the EFV + 3TC + TDF rapid start arm (*n* = 149) (Table S9) [24]. The fifth study, Rainbow, included participants who presented with advanced disease. At Week 48, mean CD4 count increased from 133 cells/μL to 309 cells/μL, and mean CD4/CD8 ratio increased from 0.18 to 0.44 (Table S9) [26].

Safety

Study discontinuations

Study discontinuations were reported by seven studies (Table 4). For participants treated with B/F/TAF rapid start, loss to follow-up was 0%–14% among 674 participants across seven studies [21, 23, 25–27, 29, 32], and treatment discontinuation due to AEs was 0%–3% among 482 participants across four studies [23, 25, 26, 30, 31]. At Week 24, fewer participants discontinued B/F/TAF rapid start due to AEs (0%) compared with EFV + 3TC + TDF rapid start (5%) in Wang 2024 (Table 4) [23].

Adverse events

B/F/TAF rapid start was well tolerated in the six studies reporting AEs (Table 4). AEs were reported either as the number of participants who experienced any event, or as the number of events that occurred across all participants. Wang 2024 reported that treatment-related AEs (TRAEs) occurred in fewer participants receiving B/F/TAF rapid start (21/146) compared with EFV + 3TC + TDF rapid start (39/149) [24]. In four studies, 0%–3% of B/F/TAF rapid start participants experienced Grade 3/4 AEs; whether these events were treatment-related was not reported [22, 24, 30–32]. In T&T, Grade 3 AEs were detected in three participants, and there were five serious AEs (SAEs), including two Grade 4 AEs, creatinine kinase increase and autolytic attempt [32].

Two additional studies reported the number of Grade 3/4 AE or SAE events, but not the number of participants who experienced any Grade 3/4 AE or SAE (Table 4). In FAST, 11 Grade 3/4 AEs or SAEs occurred following B/F/TAF rapid start treatment, including one death due to suicide, none of which were deemed treatment-related [25]. In Rainbow, 209 AEs occurred in 30 participants receiving B/F/TAF rapid start, of which 16 were Grade 3/4 AEs and 6 were SAEs. Of these, 2 SAEs were considered treatment-

TABLE 4 Study discontinuations and AEs at the latest available timepoint.

Study name	Timepoint	Treatment arm	Study discontinuations		Adverse events	
			Outcome definition	n/N (%)	Grade 3/4 AEs, n/N (%)	TRAEs, n/N (%)
BIC T&T [21, 22]	Week 48	B/F/TAF rapid start	Loss to follow-up	2/19 (10.5)	0/19 (0)	NR
		D/C/F/TAF rapid start		4/17 (23.5)	0/17 (0)	NR
		B/F/TAF or D/C/F/TAF rapid start	Study withdrawal	1/36 (2.8)	NR	NR
BIC-NOW [27, 30, 31]	Week 48	B/F/TAF rapid start	Study discontinuations due to AEs	0/208 (0)	0/208 (0)	NR
			Loss to follow-up	20/208 (9.6)	0/178 (0)	NR
BIFAST [29]	Week 24	B/F/TAF rapid start	Loss to follow-up	4/59 (6.8)	NR	NR
			Study discontinuations	1/59 (1.7)	NR	NR
FAST [25]	Week 48	B/F/TAF rapid start (ITT)	Study discontinuations	14/112 (12.5)	Grade 3/4 AEs or SAEs: 11 events/NR (NR)	Grade 3/4 AEs or SAEs: 0/112 (0)
			Due to treatment failure ^a	1/112 (0.9)		
			Due to AEs	3/112 (2.7)		
			Due to study withdrawal	4/112 (3.6)		
			Due to loss to follow-up	3/112 (2.7)		
			Due to baseline resistance ^b	3/112 (2.7)		
Wang 2024 [23, 24]	Week 24	B/F/TAF rapid start (enrollment period: March 2021 to April 2022)	All-cause mortality	1/112 (0.9)	NR	NR
			Study discontinuations	1/132 (0.8)	2/108 (1.9)	15/108 (13.9)
			Due to AEs	0/132 (0)		
		EFV + 3TC + TDF rapid start (mITT) ^c (enrollment period: March 2021 to April 2022)	Due to loss to follow-up	1/132 (0.8)		
			Study discontinuations	13/121 (10.7)	1/91 (1.1)	29/91 (31.9)
			Due to treatment failure	1/121 (0.8)		
			Due to AEs	6/121 (5.0)		
			Due to loss to follow-up	4/121 (3.3)		NR
			Due to death	1/121 (0.8)		
			Due to baseline resistance	1/121 (0.8)		
		B/F/TAF non-rapid start (enrollment period: March 2021 to April 2022)	Study discontinuations	9/91 (9.9)	NR	NR
			Due to study withdrawal	1/91 (1.1)		
			Due to loss to follow-up	8/91 (8.8)		
		EFV + 3TC + TDF non-rapid start (enrollment period: March 2021 to April 2022)	Study discontinuations	18/122 (14.8)	NR	NR
			Due to AEs	5/122 (4.1)		
			Due to study withdrawal	5/122 (4.1)		
			Due to loss to follow-up	4/122 (3.3)		
			Due to baseline resistance	2/122 (1.6)		
			Due to non-compliance	2/122 (1.6)		

TABLE 4 (Continued)

Study name	Timepoint	Treatment arm	Study discontinuations		Adverse events	
			Outcome definition	n/N (%)	Grade 3/4 AEs, n/N (%)	TRAEs, n/N (%)
Rainbow [26]	Week 48	B/F/TAF rapid start (ITT) (enrollment period: March 2021 to July 2022)	Study discontinuations	1/146 (0.7)	Grade 3: 0/146 (0)	21/146 (14.4)
			Due to loss to follow-up	1/146 (0.7)	Grade 4: 0/146 (0)	
			Study discontinuations	24/149 (16.1)	Grade 3: 1/149 (0.7)	39/149 (26.2)
			Due to suicide	1/149 (0.7)	Grade 4: 1/149 (0.7)	
			Due to AEs	11/149 (7.4)		
		EFV ± 3TC ± TDF rapid start (ITT) (enrollment period: March 2021 to July 2022)	Due to adverse effect	11/149 (7.4)		
			Due to loss to follow-up	5/149 (3.4)		
			Due to virological failure	1/149 (0.7)		
			Due to EFV primary resistance	6/149 (4)		
			Loss to follow-up	0/30 (0)	16/209 events (7.7)	15/209 events (7.2)
Test&Treat [28, 32]	Week 48	B/F/TAF rapid start	Study discontinuations	1/30 (3.3)		
			Regimen switch due to TB diagnosis	1/30 (3.3)		
			Due to AEs	0/30 (0)		
			Study discontinuations	16/100 (16)	Grade 3: 3/100 (3)	3/100 (3%)
			Physicians' decision	1/100 (1)	Grade 4: 2/100 (2)	
		B/F/TAF rapid start	Moved away	1/100 (1)		
			Premature discontinuation of study treatment ^d	3/100 (3)		
			Loss to follow-up	11/100 (11)		

Note: Underlined text indicates data that were retroactively extracted from the full-text of the peer-reviewed manuscript that was published after completion of the systematic literature review. Italicized values were calculated based on data reported by the publications. Loss to follow-up presented in alignment with study reporting, either considered as a study discontinuation or separate.

Abbreviations: AE, adverse event; B/F/TAF, bictegravir, emtricitabine, tenofovir alafenamide; D/C/F/TAF, darunavir, cobicistat, emtricitabine, and tenofovir alafenamide; DOR, doravirine; EFV + 3TC + TDF, efavirenz + lamivudine + tenofovir disoproxil fumarate; (m)ITT, (modified) intention-to-treat; NR, not reported; SAE, serious adverse event; TB, tuberculosis; TRAE, treatment-related adverse event.

^aVirologic failure (patients with two consecutive plasma viral load measurements ≥ 50 copies/mL as of Week 24).

^bThe authors noted that 1 participant had baseline lamivudine/emtricitabine resistance and 2 had possible baseline bictegravir resistance (E157Q); however, updated local guidance no longer advises that people with the E157Q mutation switch regimens.

^cmITT analysis set excludes 5 participants who withdrew consent and were never treated.

^dThree prematurely discontinued (at weeks 12, 23, 24) the study treatment but remained on follow-up one participant reported difficulties attending appointments but maintained B/F/TAF off-study, and two reported tolerability problems, with one switching to DOR plus F/TDF and the other to darunavir/cobicistat D/C/F/TAF.

related, both immune reconstitution inflammatory syndrome (IRIS) [26]. No other studies reported on IRIS.

Engagement in care

Engagement in HIV care was reported by four studies. Engagement in care at Year 1 was the primary outcome of the US single-center study Benidir 2022, defined as meeting the following criteria: (1) attending ≥ 3 visits within the first 12 months of care, (2) attending ≥ 1 visit between Months 9 and 12, and (3) experiencing no gaps in care > 6 months. Of the patients enrolled long enough to participate in Visit 2, a total of 50/55 B/F/TAF rapid start participants (91%) and 31/41 non-rapid start participants (76%) were engaged (median follow up: 6 weeks and 9 weeks, respectively). Of the remaining patients enrolled at Visit 4, 9/16 rapid start (56%; median follow up: 27 weeks) and 2/22 non-rapid start participants (9%; median follow up: 35 weeks) met these criteria [20].

The single-arm trials Rainbow ($N = 30$) and T&T ($N = 100$) both reported that all participants receiving B/F/TAF rapid start attended the latest reported follow-up visit (Week 48 and Week 4, respectively) [26, 28]. Engagement in care was similarly high across B/F/TAF rapid and non-rapid start arms in Wang 2024, with 93% of rapid start participants (239/258) and 87% of non-rapid start participants (185/213) continuing treatment at Week 24 ($p = 0.053$) [23].

Patient-reported outcomes

Six studies reported PROs (Table 5) [24–27, 29, 32].

Adherence

Three studies collected participant-reported treatment adherence to B/F/TAF rapid start; no adherence data were reported for comparator arms. Adherence was overall high and stable, with most participants self-reporting $\geq 90\%$ adherence through Week 48. Adherence in BIC-NOW ($N = 208$) was 90%–100% at Week 48 as assessed by the Simplified Medication Adherence Questionnaire [27, 30, 31]. In FAST ($N = 112$), 84%–85% of participants reported $> 95\%$ adherence in the preceding 4 weeks at Weeks 24 and 48 [25]. In Rainbow ($N = 30$), an average of 55% of participants reported $\geq 95\%$ adherence and 10% reported $< 85\%$ adherence; however, data were missing for 32% of participants and objective adherence data were not reported [26]. Wang 2024 evaluated adherence by pill count but did not report adherence for the B/F/TAF rapid start and EFV

+ 3TC + TDF rapid start arms; however, it was reported that all participants who remained on treatment had good adherence (≥ 95) [24].

Treatment satisfaction

Treatment satisfaction with B/F/TAF rapid start was high among four reporting studies [25, 27, 29, 32]. Two studies reported improvements in satisfaction with B/F/TAF rapid start treatment over time; however, quantitative data were not clearly reported for all timepoints [25, 29]. Additionally, FAST reported favorable opinions of the effectiveness of same-day initiation and continuation of B/F/TAF treatment despite moderate stress levels [25]. In T&T, 81% of participants reported they were very satisfied with B/F/TAF [32].

Mood and health-related quality of life

Two studies reported improvements in anxiety from baseline to Week 48 with B/F/TAF rapid start treatment [25, 26]. The improvement was statistically significant in FAST as measured by the State-Trait Anxiety Inventory [25]. BIFAST similarly reported improved self-perception from baseline to Week 24, which was defined as decreases in anxiety and depression scores with associated increases in happiness and optimism. However, the PRO assessment methods in this study were unclear [29]. Rainbow and BIC-NOW reported a statistically significant improvement in health-related quality of life scores, measured by EQ-5D, from baseline to Week 48 with B/F/TAF rapid start. Small increases in mean SF-12 scores, another measure of HRQoL, and Beck Depression Inventory II scores were also reported, but these differences were not significant [26].

In Wang 2024, a lower proportion of patients with B/F/TAF rapid start treatment reported grade 3/4 insomnia (as assessed by the Pittsburgh Sleep Quality Index) than patients with EFV + 3TC + TDF rapid start (61.7% vs. 70.1%) at Week 48. The patients with B/F/TAF rapid start also reported lower rates of anxiety (10.5% vs. 18.0%) and depression (6.8% vs. 11.2%) (as measured by the Hospital Anxiety and Depression Scale) than the EFV + 3TC + TDF arm. PROs significantly improved from baseline to Week 48 for the patients with B/F/TAF rapid start treatment, but not for patients with EFV + 3TC + TDF rapid start [24].

Quality assessment of included studies

Risk of bias of included studies was overall low to moderate. The two RCTs, Wang 2024 and BIC T&T,

TABLE 5 Summary of key PROs for people with HIV treated with B/F/TAF rapid start, including findings on treatment satisfaction, anxiety, depression, and overall HRQoL.

Study name	Assessment name and description	Timepoint	Reported outcome	N	p value
BIC-NOW [27, 30, 31]	EQ-5D, general satisfaction	Week 4	Median: 90 (IQR: 80–99)	NR	NR
		Week 48	Median: 90 (IQR: 80–95)	NR	NR
	EQ-5D, questionnaire score	Baseline	Mean: 0.940 (SD: 0.117)	208	NR
		Week 48	Mean: 0.959 (SD: 0.083)	208	0.012 vs. baseline
	EQ-5D-VAS (maximum score 100)	Baseline	VAS ≥90: 53.43%	208	NR
			VAS 80–89: 24.51%	208	NR
			VAS < 80: 22.06%	208	NR
		Week 24	VAS ≥90: 57.53%	208	0.759 vs. baseline
			VAS 80–89: 28.49%	208	0.226 vs. baseline
			VAS < 80: 13.98%	208	0.019 vs. baseline
		Week 48	VAS ≥90: 60.45%	208	0.367 vs. Week 24
			VAS 80–89: 22.60%	208	0.146 vs. Week 24
			VAS < 80: 16.95%	208	0.022 vs. Week 24
BIFAST [29]	Self-perception, ^a satisfaction with ART, and comfort with ART	Week 24	Improvement from Week 4	NR	NR
FAST [25]	STAI-Y, anxiety scale (scored 20–80)	Baseline	Mean: 52	NR	NR
		Week 48	Mean: 37	NR	<0.001 vs. baseline
	Stress around same-day ART initiation (maximum score 10)	NR	Mean: 6.3	NR	NR
	HIVTSQc, general/clinical and lifestyle/comfort satisfaction (5 items each scored 0–6, maximum score 30)	NR	Mean: 25.9–26.8	NR	<0.05 (timeframe of improvement NR)
	Satisfaction with same-day ART initiation and continuing B/F/TAF (maximum score 10)	NR	Mean: approximately 8–9; participants reported favorable opinions and felt that same-day ART initiation was better and more effective	NR	NR
Rainbow [26]	EQ-5D, general HRQoL (maximum score 100)	Baseline	Mean: 57	NR	0.001
		Week 48	Mean: 75	NR	
	SF-12, general HRQoL (maximum score 100)	Baseline	Mean 48	NR	NR
		Week 48	Mean: 51	NR	
	Beck Depression Inventory II (maximum score 63, score <20 indicates minimal to mild depression)	Baseline	Minimal-mild: 93% (25/27)	27	1.000
		Week 48	Minimal-mild: 95% (21/22)	22	
	Beck Anxiety Inventory (scored out of 63, score	Baseline	Minimal-mild: 85% (23/27)	27	0.678

(Continues)

TABLE 5 (Continued)

Study name	Assessment name and description	Timepoint	Reported outcome	N	p value
Test&Treat [28, 32]	<16 indicates minimal to mild anxiety)	Week 48	Minimal-mild: 91% (20/22)	22	0.706
	Pittsburgh Sleep Quality Index (scored out of 21, score ≤5 indicates good sleep quality)	Baseline	Good sleep quality: 80% (20/25)	25	
		Week 48	Good sleep quality: 86% (19/22)	22	
	<u>CESTA survey (five level scale)</u>	<u>Week 48</u>	<u>Very high satisfaction with global health status and disease control: 78%</u>	<u>83</u>	<u>NR</u>
			<u>Very satisfied with study treatment: 81%</u>	<u>83</u>	<u>NR</u>
			<u>High satisfaction with AEs: 70%</u>	<u>83</u>	<u>NR</u>
			<u>High satisfaction with number of pills: 82%</u>	<u>83</u>	<u>NR</u>
			<u>High satisfaction with daily doses: 81%</u>	<u>83</u>	<u>NR</u>
	<u>Wang 2024 [23, 24] (enrollment period: March 2021 to April 2022)</u>	<u>PROs (unspecified)</u>	<u>Median: 9.0 (IQR: 3.0, 19.5)</u>	<u>145</u>	<u>NR</u>
		<u>Week 48</u>	<u>Median: 5.0 (1.0, 13.0)</u>	<u>145</u>	<u>0.002 vs. baseline</u>
		<u>Pittsburgh Sleep Quality Index</u>	<u>Insomnia: 61.7% (82/132)</u>	<u>132</u>	<u>0.035 vs. EFV ± 3TC ± TDF rapid start arm</u>
		<u>Hospital Anxiety and Depression Scale</u>	<u>Anxiety: 10.5% (14/132)</u>	<u>132</u>	<u>0.65 vs. EFV ± 3TC ± TDF rapid start arm</u>
			<u>Depression: 6.8% (9/132)</u>	<u>132</u>	<u>1.0 vs. vs. EFV ± 3TC ± TDF rapid start arm</u>

Note: Underlined text indicates data that were retroactively extracted from the full-text of the peer-reviewed manuscript that was published after completion of the systematic literature review.

Abbreviations: AE, adverse event; ART, antiretroviral therapy; B/F/TAF, bictegravir, emtricitabine, tenofovir alafenamide; CESTA, Spanish Questionnaire of Satisfaction with Antiretroviral Treatment; EQ-5D, EuroQol five dimensions; HIVSTQc, Human Immunodeficiency Virus Treatment Satisfaction Questionnaire; HRQoL, health-related quality of life; NR, not reported; PRO, patient-reported outcome; SF-12, 12-Item Short Form Survey; STAI-Y, State-Trait Anxiety Inventory-Form Y; VAS, visual analogue scale.

^aImprovement in subjects' self-perception was defined as decrease of anxiety/depression symptoms and increase in happiness and optimistic perception about the future from baseline to Week 24.

had a moderate risk of bias due to their open-label designs and, in BIC T&T, more dropouts in the comparator arm than the B/F/TAF arm (Table S10) [22, 24]. Risk of bias was low in four of the six non-RCTs [25, 26, 29, 30]; however, Benidir 2022 had a serious risk of bias due to missing data, confounding and deviations from the intended intervention, and BIC-NOW had a moderate risk of bias due to missing data and potential selection of reported results (Table S11) [20, 30].

DISCUSSION

The findings of this systematic literature review support B/F/TAF's position as an optimal guideline-recommended rapid start regimen in treatment guidelines from high-income settings. B/F/TAF rapid start was highly efficacious, with viral suppression rates of 74%–96% by Week 48. In a comparative study, B/F/TAF rapid start demonstrated statistically significant superior efficacy versus EFV + 3TC + TDF rapid start [24]. B/F/TAF viral suppression rates were

comparable to real-world and clinical trial findings of B/F/TAF non-rapid start in people with HIV who are newly diagnosed [14, 15, 33]. Time to viral suppression with B/F/TAF rapid start was sparsely reported and data were not robust enough to draw conclusions.

Rates of AEs or study discontinuations due to AEs were low among people with HIV receiving B/F/TAF rapid start. B/F/TAF showed superior safety compared with EFV 400 mg + 3TC 300 mg + TDF 300 mg rapid start [24]. Similarly, in a real-world study by Lee et al. in which 88% of participants initiated ART within 14 days of HIV diagnosis, significantly fewer people with HIV receiving B/F/TAF discontinued treatment compared with those receiving dolutegravir/abacavir/3TC ($p = 0.017$), and fewer discontinuations were due to AEs ($p = 0.058$) [34]. This SLR identified limited data on IRIS, an excessive inflammatory response to opportunistic infections that can occur during initial ART treatment in people with HIV with a baseline CD4 count <200 cells/ μ L. Rainbow, which enrolled people who were newly diagnosed and presented with advanced disease, observed IRIS in 2/30 participants [26]. Some evidence shows that incidence of IRIS is generally comparable between INSTI-based regimens and other antiretroviral classes [35], and is not expected to be common for people initiating treatment during acute HIV infection, who often do not have advanced HIV disease. However, further research is needed to assess rapid start among those with advanced HIV disease.

Rapid ART, as part of the “test and treat” approach in HIV care, may enhance treatment adherence and long-term engagement in care [36, 37], which are vital to reducing viral replication, preventing resistance mutation development, improving health outcomes and reducing HIV transmission. Approximately 43% of HIV transmissions occur among people with HIV who are aware of their HIV status but not engaged in regular care [38]. In this SLR, treatment adherence by self-report and engagement in care up to 48 weeks were overall high for people with HIV receiving B/F/TAF rapid start, including among those presenting with advanced HIV [26]. Late HIV diagnosis increases risk of morbidity and mortality, which may be mitigated by rapid ART. In addition, two studies demonstrated higher engagement in care for rapid start regimens compared with non-rapid start regimens [20, 23]. By facilitating increased engagement in care and treatment adherence among people with HIV, B/F/TAF rapid start represents a potentially important aspect of future U=U initiatives through the reduction of HIV transmission and alleviation of internalized HIV stigma.

PRO data identified by this SLR may support the potential benefit of rapid ART on indicators of HIV-related stigma among people with HIV. Although none of the included studies utilized validated HIV-stigma

measuring tools, several demonstrated high treatment satisfaction, decreased anxiety and improved HRQoL with B/F/TAF rapid start. Rapid ART may help newly diagnosed people with HIV cope with their diagnoses, as demonstrated in a qualitative study [39]. Data suggest that people with HIV experience HIV-related stigma regardless of treatment timing, but those who initiated ART earlier did so partly to mitigate anticipated and internalized stigma, whereas those who initiated ART later expressed more anxiety around external or enacted stigma. Additionally, people who started ART later (non-rapid start) had the lowest care visit adherence, although the difference was not statistically significant [9]. In this SLR, improved engagement in care was observed with rapid ART compared with non-rapid ART, and PROs improved with B/F/TAF rapid start.

The review identified several limitations in the evidence. First, 6/8 included studies were initially available only as conference abstracts; however, following completion of the SLR, we identified that 4/6 were subsequently published as peer-reviewed manuscripts [22, 24, 30, 32]. To mitigate this limitation, the authors incorporated newly available data from these publications into the analysis, meaning only 2/8 studies are presented using only conference proceedings [20, 29]. As these two studies have not undergone peer review, their findings and risk of bias assessment should be interpreted with caution. Comparative analysis was also limited by the small number of unique interventional studies evaluating B/F/TAF rapid start, the predominance of single-arm designs, and heterogeneous outcome “rapid start” definitions. Notably, BIFAST included people with HIV initiating B/F/TAF rapid start after baseline lab results, leading to a longer median time to treatment initiation than other studies (28 days) [29]. Still, treatment initiation after lab results is not excluded by HIV treatment guideline definitions of “rapid start” and the study reflects real-world variability in rapid treatment timing [3]. Lastly, given more than three-quarters of the participants were male, the female sex was largely underrepresented.

Additionally, only English-language publications were included, which may have resulted in the exclusion of some studies. Conference searches encompassed only the past 3 years, so relevant records prior to these date limits will have been missed. However, this practice assumes that robust results presented earlier would have since been published in peer-reviewed journals.

This review itself had many strengths, including the use of a prespecified protocol and a comprehensive search strategy of multiple databases and grey literature sources. Furthermore, a robust, two-stage, dual-reviewer approach ensured accuracy in the inclusion

and exclusion of records. Accuracy was further promoted during data extractions, which were performed by one reviewer and verified by a second independent reviewer.

This review highlights the benefits of B/F/TAF rapid start, which is the only INSTI-based single-tablet regimen recommended for rapid start by most HIV treatment guidelines. High rates of viral suppression, low rates of AEs and study discontinuations, and favorable clinical engagement and PROs support B/F/TAF rapid start as an effective treatment option for people with HIV who are newly diagnosed. Rapid, effective and durable virologic suppression also offers benefits in the context of the current U=U strategy and may reduce internalized HIV-related stigma among people with HIV by mitigating anxiety around their own health and concern of HIV transmission to sexual partners. Future research should focus on further assessing the benefits of rapid start on PROs and stigma-related outcomes, as well as treatment adherence and engagement in care over longer follow-up durations to understand the impact of treatment on sustained engagement in healthcare. Future efforts should also study rapid start ART in treatment-naïve people with advanced HIV. While the recently completed LAPTOP study found that individuals with treatment-naïve advanced HIV treated with B/F/TAF had a better virologic response at Week 48 and a lower incidence rate of overall adverse events than those treated with D/C/F/TAF, it did not evaluate rapid initiation, highlighting the gap in available data on rapid start ART in this population [40]. Rapid ART initiation approaches with B/F/TAF offer promising clinical and quality of life benefits for people with HIV who are newly diagnosed and just starting therapy.

AUTHOR CONTRIBUTIONS

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: JG, JC, MoG, MiG, AA, HT, ML, EFK, DM, FAB, BGP, LD; drafting of the publication, or revising it critically for important intellectual content: JG, JC, MoG, MiG, AA, HT, ML, EFK, DM, FAB, BGP, LD; final approval of the publication: JG, JC, MoG, MiG, AA, HT, ML, EFK, DM, FAB, BGP, LD. All authors agree to be accountable for all aspects of the work. All authors agreed for the final version of the manuscript to be published.

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CONFLICT OF INTEREST STATEMENT

JG: Honoraria from Gilead Sciences, Inc. and ViiV Healthcare. JC: Received grants from Gilead Sciences, Inc. MoG: Nothing to disclose. MiG: Advisory honoraria from Gilead Sciences, Inc., Johnson & Johnson, and ViiV Healthcare. AAH: Received grants and personal fees from ViiV Healthcare; received personal fees from Gilead Sciences, Inc., Janssen, and Merck. HT: Received grants from Gilead Sciences, Inc. and ViiV Healthcare. ML, EFK: Employees of Costello Medical, which received funding from Gilead Sciences, Inc. for conducting this work. DM, FAB, BGP: Employees and shareholders of Gilead Sciences, Inc. LD: Nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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