GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Comparison With CAB + RPV IM Q2M

This document is in response to your request for information regarding the efficacy and safety of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) compared with cabotegravir and rilpivirine intramuscular injections once every 2 months (CAB + RPV IM Q2M) in people with HIV-1 (PWH).

This document summarizes information from a study that was not sponsored by Gilead Sciences, Inc. For additional information regarding this study, please refer to its sponsor.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.

Summary

Clinical Data on BIC/FTC/TAF vs CAB + RPV IM Q2M

The SOLAR study was a phase 3b, randomized, open-label study that compared the efficacy and safety of CAB + RPV IM Q2M with BIC/FTC/TAF in virologically suppressed PWH.[1]

- At Month 12, CAB + RPV IM Q2M showed noninferior efficacy compared with BIC/FTC/TAF, with <1% of participants (1/223) receiving BIC/FTC/TAF and 1% of participants (5/447) receiving CAB + RPV IM Q2M demonstrating HIV-1 RNA ≥50 c/mL in the mITT-E population.
- No participants receiving BIC/FTC/TAF had CVF or treatment-emergent resistance. Three participants receiving CAB + RPV IM Q2M had CVF, 2 of whom had both INSTI and RPV (NNRTI) treatment-emergent resistance.
- Through Months 11 to 12, 1% of participants (2/227) receiving BIC/FTC/TAF and 72% of participants (327/454) receiving CAB + RPV IM Q2M experienced any drug-related AE.

Clinical Data on BIC/FTC/TAF vs CAB + RPV IM Q2M

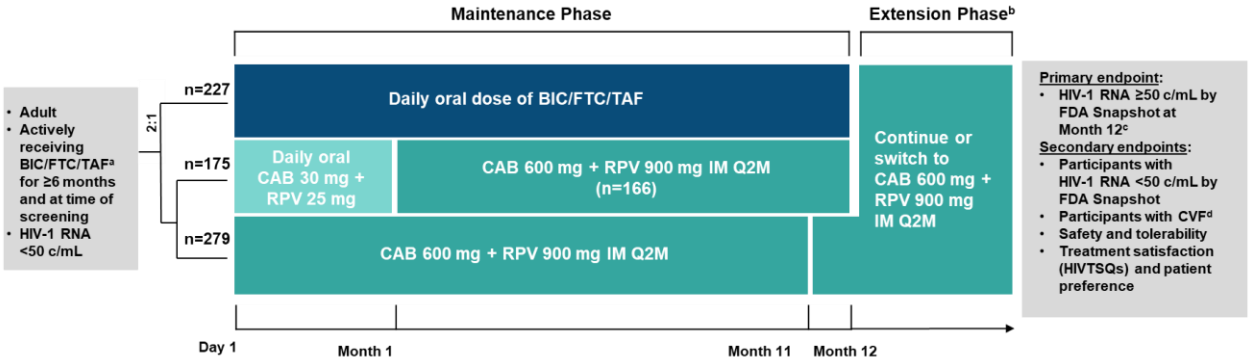
Switch Onto Long-Acting Regimen (SOLAR) Study

Study design and demographics[1]

A ViiV-sponsored, phase 3b, randomized, open-label, multicenter, active-control, non-inferiority study evaluated the safety and efficacy of CAB + RPV compared with BIC/FTC/TAF in virologically suppressed PWH. Participants with an undetectable HIV-1 RNA (<50 c/mL) who had been on BIC/FTC/TAF as a first or second regimen for ≥6 months

were randomly assigned in a 2:1 ratio to continue daily oral BIC/FTC/TAF or switch to CAB + RPV for 12 months. Participants who were assigned to receive CAB + RPV were able to choose to either start with a 1-month OLI or with SWI. Key exclusion criteria included any history of non-INSTI regimen and known or suspected presence of RAMs to any component BIC/FTC/TAF or CAB + RPV.

Figure 1. SOLAR: Study Design[1]



[a]One prior INSTI-containing regimen was allowed if BIC/FTC/TAF was a second-line regimen >6 months prior to screening. Change in regimen must have been for safety/tolerability or reasons unrelated to treatment failure.
[b]Extension phase continued until CAB + RPV IM Q2M were either commercially available or locally approved, the participant no longer showed clinical benefit, or for other protocol-defined reasons.
[c]Based on the mITT-E population, which excluded 11 participants due to study site non-compliance with protocol entry criteria.
[d]Defined as two consecutive assays of HIV-1 RNA ≥200 c/mL.

Table 1. SOLAR: Baseline Demographics and Disease Characteristics (mITT-E Population)[1]

Key Demographics and Characteristics		BIC/FTC/TAF (n=223)	CAB + RPV IM Q2M (n=447)
Age, median (range), years		37 (18–66)	37 (18–74)
≥50 years, n (%)		42 (19)	86 (19)
Female sex at birth,[a] n (%)		41 (18)	77 (17)
Race, n (%)	White	156 (70)	307 (69)
	Black	49 (22)	95 (21)
	Asian	11 (5)	23 (5)
	Other	7 (3)	22 (5)
BMI, median (IQR), kg/m^2		25.4 (23.4–29.6)	26 (23.3–29.4)
Duration on previous ART, median, years		2.47	2.58
CD4 count, median (IQR), cells/mcL		640 (459–846)	649 (477–850)
CD4 count category, n (%)	<350 cells/mcL	28 (13)	54 (12)
	350 to <500 cells/mcL	35 (16)	74 (17)
	≥500 cells/mcL	159 (71)	319 (71)

Abbreviation: ART=antiretroviral treatment.
[a]Twelve transgender female participants, 1 transgender male participant, and 1 gender non-conforming participant were included.

Efficacy results

A total of 681 participants underwent randomization, and 670 participants were included in the mITT-E analyses. At Months 11 to 12, rates of virological suppression demonstrated noninferior efficacy of CAB + RPV IM Q2M compared with BIC/FTC/TAF. From baseline to

Months 11 to 12, the median change in CD4 count was +20 and +39 cells/mcL in the BIC/FTC/TAF and CAB + RPV IM Q2M groups, respectively.[1]

Table 2. SOLAR: Efficacy Outcomes at Months 11 to 12 (mITT-E Population)[1]

Efficacy Outcome, n (%)	BIC/FTC/TAF (n=223)	CAB + RPV IM Q2M (n=447)
HIV-1 RNA <50 c/mL	207 (93)	403 (90)
HIV-1 RNA ≥50 c/mL	1 (<1)	5 (1)
No data on virologic status	15 (7)	39 (9)

From baseline through Month 12, viral blips were reported in 4% of participants in both the BIC/FTC/TAF group (n/N=9/223) and the CAB + RPV IM Q2M group (n/N=19/447); of the participants with viral blips, 11% (1/9) and 5% (1/19), respectively, had HIV-1 RNA ≥50 c/mL at Month 12. Neither of the 2 participants in the mITT-E population who received CAB + RPV IM Q2M and developed CVF had viral blips through Month 12.[2]

Resistance analysis through 12 months[1,3]

No participant who received BIC/FTC/TAF met the CVF criterion for resistance analysis. Two participants who received CAB + RPV IM Q2M in the mITT-E population had on-treatment RAMs. One participant who developed on-treatment RPV (NNRTI) and INSTI RAMs at CVF later resuppressed during long-term follow-up on DRV/c, FTC, and TAF (Participant 1, Table 3). The second participant who developed RPV and INSTI RAMs at CVF also achieved viral resuppression on BIC/FTC/TAF followed by DRV/c, FTC, and TAF (Participant 2, Table 3).

A third participant from the ITT-E population who received CAB + RPV IM Q2M also met the CVF criterion and had RPV RAMs in the genotype at failure (Participant 3, Table 3), but it is unknown if these were present at baseline since the retrospective assessment of peripheral blood mononuclear cells was not successful. This participant later achieved viral resuppression on BIC/FTC/TAF.

The 3 participants who received CAB + RPV IM Q2M with CVF did not have late injections outside of the dosing window (+7 days). The participants' plasma drug concentrations were above the respective paIC$_{90}$ (CAB, 0.166 mcg/mL; RPV, 12 ng/mL) and phase 3 benchmarks (CAB, 0.65 mcg/mL; RPV, 17.3 ng/mL) at SVF timepoints.

Table 3. SOLAR: Participants With CVF Who Received CAB + RPV IM Q2M[1,3]

Participant (Population)	SVF Timepoint, Months	HIV-1 RNA at SVF/CVF, c/mL	RAMs at Baseline	RAMs at CVF	Phenotypic Sensitivity to RPV/CAB at SVF, FC
1 (mITT-E)	6	1327/ 1409	None	RPV: M230L INSTI: Q148R	3.2/3.1
2 (mITT-E)	11	6348/ 419	INSTI: G140G/R	RPV: K101E INSTI: G118R	1.9/8.4
3 (ITT-E)	3	3797/ 928	Assay failed	RPV: E138E/K + Y181Y/C	4.2/analysis failed

Abbreviation: FC=fold change.

Safety results[1,3]

Through Month 12, 1% of participants (2/227) who received BIC/FTC/TAF experienced any drug-related AE, compared with 72% (327/454) in the CAB + RPV IM Q2M group. AEs,

excluding ISRs, are summarized in Table 4. A summary of ISRs reported by participants who received CAB + RPV IM (SWI and OLI groups) is shown in Table 5.

Table 4. SOLAR: AEs, Excluding ISRs, Through Month 12 (ITT Population)[1,3]

AEs, n (%)		BIC/FTC/TAF (n=227)	CAB + RPV IM Q2M (n=454)
Any AE		172 (76)	349 (77)
Drug-related AEs		2 (<1)	90 (20)
AEs that led to withdrawal		2 (<1)	15 (3)
Drug-related AEs that led to withdrawal		0	9 (2)[a]
Any Grade ≥3 AEs		26 (11)	42 (9)
Drug-related Grade ≥3 AEs		0	7 (2)
Any serious AEs		15 (7)	21 (5)
Drug-related serious AEs		0	3 (<1)[b]
Common AEs (≥10%)	COVID-19 infection	39 (17)	74 (16)
	Headache	12 (5)	49 (11)

[a]During the OLI period (each, n=1): limb discomfort/paresthesia/dysesthesia, dizziness, fatigue, deafness/ear congestion/fatigue, participant-reported blood pressure fluctuation, and diarrhea/joint stiffness; during the IM injection period (each, n=1): myocardial infarction, increase in ALT, and fatigue/pyrexia.
[b]Increase in ALT (n=2) and acute myocardial infarction (n=1).

Table 5. SOLAR: ISRs in CAB + RPV IM Q2M Groups (ITT-E Population)[3a]

Event		SWI CAB + RPV IM Q2M (n=279)	OLI CAB + RPV IM Q2M (n=175)
Injections, n		3742	2228
ISR events,[a] n		1181	734
ISR symptom	Pain, n (% of injections)	887 (24)	507 (23)
	Discomfort, n (% of injections)	65 (2)	56 (3)
	Nodule, n (% of injections)	56 (2)	28 (1)
	Grade 3,[b] n (% of ISR events)	10 (<1)	19 (3)
Duration of ISR, median (IQR), days		3 (2–5)	3 (2–5)
Participants who withdrew secondary to injection-related reasons,[c] n (% of participants with injections)		8 (3)	3 (2)

[a]One injection could be associated with multiple ISRs. Data on grading was missing for 1 ISR in the SWI group.
[b]No Grade 4 or 5 ISRs were reported.
[c]Included 1 participant who discontinued due to ISR AEs, 1 participant who withdrew from the study secondary to injection intolerability, and 1 participant who was excluded from the primary analysis of the mITT-E population for unknown reasons.

Weight change[4]

At Month 12, the median (IQR) weight change was +0.05 (-2.3 to +1.95) kg in the BIC/FTC/TAF group and -0.4 (-2.95 to +2.1) kg in the CAB + RPV IM Q2M group. By Month 12, a total of 4% of participants (9/213) in the BIC/FTC/TAF group and 3% of participants (11/408) in the CAB + RPV IM Q2M group experienced a weight increase of ≥10%. Changes in BMI remained numerically similar overall, and there were no clinically relevant changes in the proportion of participants with metabolic syndrome or insulin resistance from baseline through Month 12.

Treatment satisfaction[5]

The mean adjusted baseline HIVTSQs score was 58.38 for the BIC/FTC/TAF group and 57.88 for the CAB + RPV IM Q2M group. From baseline to Month 6, there was

a -0.4 (95% CI: -1.41 to +0.61) change in score for the BIC/FTC/TAF group and a +3.86 (95% CI: 3.14–4.57) change in score for the CAB + RPV IM Q2M group, with an adjusted difference of 4.26 (95% CI: 3.02–5.49; *P*<0.001). From Month 6 to Month 12, there was a -1.59 (95% CI: -2.71 to -0.47) change in score for the BIC/FTC/TAF group and a +3.36 (95% CI: 2.59–4.13) change in score for the CAB + RPV IM Q2M group, with an adjusted difference of 4.95 (95% CI: 3.59–6.31; *P*<0.001). Changes from baseline to Month 12 in HIVTSQs scores reflected greater patient satisfaction in the CAB + RPV IM Q2M group than in the BIC/FTC/TAF group.

References

1. Ramgopal MN, Castagna A, Cazanave C, et al. Efficacy, safety, and tolerability of switching to long-acting cabotegravir plus rilpivirine versus continuing fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV, 12-month results (SOLAR): a randomised, open-label, phase 3b, non-inferiority trial. *The lancet. HIV.* 2023;10(9):e566-e577.
2. Latham C, Urbaityte R, Sutton K, Sutherland-Phillips D, Spreen W, D'Amico R. HIV-1 RNA Blips and Low-Level Viral Replication: SOLAR (CAB + RPV LA vs. BIC/FTC/TAF) [Poster 627]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 03-06, 2024; Denver, CO.
3. Ramgopal MN, Castagna A, Cazanave C, et al. Efficacy, safety, and tolerability of switching to long-acting cabotegravir plus rilpivirine versus continuing fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV, 12-month results (SOLAR): a randomised, open-label, phase 3b, non-inferiority trial. [Supplementary Appendix]. *The lancet. HIV.* 2023;10(9):e566-e577.
4. Tan DHS, Antinori A, Eu B, et al. Weight and Metabolic Changes With Long-Acting Cabotegravir and Rilpivirine or Bictegravir/Emtricitabine/Tenofovir Alafenamide. *J Acquir Immune Defic Syndr.* 2025;98(4):401-409.
5. Ramgopal M, Castagna A, Cazaneve C. Solar 12-Month Results: Randomized Switch Trial of CAB+RPV LA vs Oral B/FTC/TAF. [Poster]. Paper presented at: Conferences on Retroviruses and Opportunistic Infections (CROI). 19-22 February 2023, 2023; Seattle, Washington.

Abbreviations

AE=adverse event
BIC=bictegravir
c/mL=copies/mL
CAB=cabotegravir
CD4=cluster of differentiation 4
CVF=confirmed virologic failure
DRV/c=darunavir/cobicistat
FTC=emtricitabine
HIVTSQs=HIV Treatment Satisfaction Questionnaire status version
IM=intramuscular
INSTI=integrase strand transfer inhibitors
ISR=injection site reaction
ITT-E=intent-to-treat exposed
mITT-E=modified intent-to-treat exposed
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
OLI=oral lead-in
paIC$_{90}$=protein-adjusted 90% inhibitory concentration
PWH=people with HIV
Q2M=once every 2 months
RAM=resistance associated mutation
RPV=rilpivirine
SOLAR=Switch Onto Long-Acting Regimen
SVF=suspected virologic failure
SWI=start with injections
TAF=tenofovir alafenamide

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Biktarvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.