Cabotegravir + Rilpivirine Long-Acting Outcomes by Sex at Birth, Age, Body Mass Index, Race, and Ethnicity: A Subgroup Analysis of the Phase 3b SOLAR Study

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Key Takeaways

- **We present outcomes within key subgroups (sex at birth, age, body mass index [BMI], race, and ethnicity) who received cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 2 months (Q2M) in the Phase 3b SOLAR study.**
- **Switching to CAB + RPV LA Q2M from bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) was efficacious for the maintenance of virologic suppression in people living with HIV-1 (PLWH) across all subgroups evaluated.**
- **CAB + RPV LA Q2M was well tolerated and provided psychosocial benefits, including alleviation from the fear of inadvertent disclosure and anxiety surrounding adherence related to daily oral therapy.**
- **Treatment satisfaction improved from baseline across subgroups in participants who switched to CAB + RPV LA vs. continuing BIC/FTC/TAF, with 87–95% of participants in the LA arm preferring CAB + RPV LA vs. BIC/FTC/TAF.**

Introduction

- CAB + RPV LA administered Q2M is the first and only complete LA regimen recommended for virologically suppressed PLWH.[1–3]
- The less frequent dosing offered by CAB + RPV LA may help address some concerns associated with daily oral therapy, including fear of disclosure, stigma, anxiety around medication adherence, and the daily reminder of HIV status.[4]
- The Phase 3b SOLAR study (NCT04542070) demonstrated noninferior efficacy of switching to CAB + RPV LA Q2M vs. continuing daily oral BIC/FTC/TAF at Month 12, with 90% of switch participants preferring LA therapy.[5]
- Here, we present outcomes within key subgroups (sex at birth, age, BMI, race, and ethnicity) who received CAB + RPV LA.

Methods

- SOLAR is an open-label switch study that enrolled virologically suppressed PLWH to either switch to CAB + RPV LA dosed Q2M or continue daily oral BIC/FTC/TAF.
- The primary analysis was based on the modified intention-to-treat exposed (mITT-E) population.*
- In this *post hoc* analysis, data from participants receiving CAB + RPV LA were stratified by sex at birth (male and female), age (<35, 35–<50, and ≥50 years), BMI (<30 and ≥30 kg/m^2), race (White, Black, Asian, and Other races), and ethnicity (Hispanic or Latinx and not Hispanic or Latinx) and are summarized descriptively.
- Treatment satisfaction was assessed using the HIV Treatment Satisfaction Questionnaire status version (HIVTSQs).
- Psychosocial outcomes were measured using a three-item questionnaire.

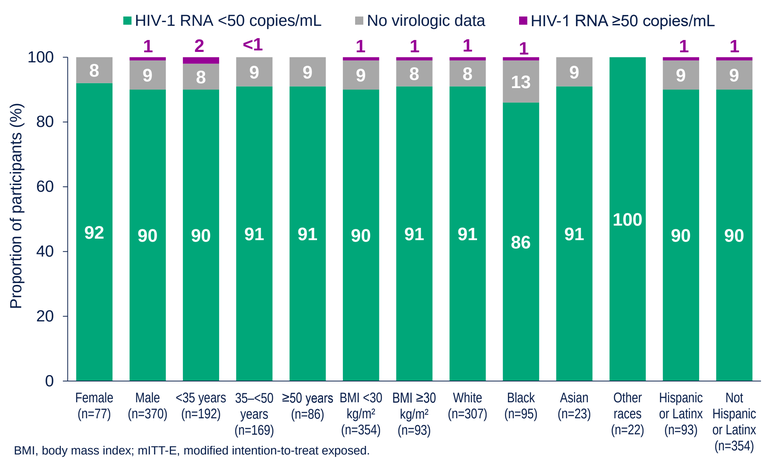
Endpoints Assessed at Month 11/12:†

- Proportion of participants with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL (FDA Snapshot algorithm).
- Incidence of confirmed virologic failure (CVF; two consecutive HIV-1 RNA ≥200 copies/mL).
- Change from baseline in CD4$^+$ cell counts.
- Safety and tolerability.
- Treatment preference and treatment satisfaction (HIVTSQs).
- Psychosocial outcomes (three single-item questions exploring how often: an individual feared disclosure of their HIV status; an individual had anxiety relating to adherence requirements; taking HIV medication was an uncomfortable daily reminder of their HIV status).

*After consultation with a blinded external expert, 11 participants were excluded from the intention-to-treat exposed (ITT-E) population (n=681) due to critical findings related to significant and persistent non-compliance to protocol entry criteria at one study site.
†Participants receiving CAB + RPV LA starting with injections (without an oral lead-in) were assessed at Month 11, whereas participants receiving CAB + RPV LA with an oral-lead in were assessed at Month 12. Month 11/12 is referred to as Month 12 throughout.

Results

Figure 1. Month 12 Snapshot Efficacy Across Subgroups (mITT-E Population)



BMI, body mass index; mITT-E, modified intention-to-treat exposed.

- Rates of virologic suppression (HIV-1 RNA <50 copies/mL) with CAB + RPV LA ranged 86–100% across subgroups, and rates of non-response (HIV-1 RNA ≥50 copies/mL) ranged 0–2% (**Figure 1**).
- Mean changes from baseline in CD4$^+$ cell counts were similar between subgroups (range, 26–69 cells/mm^3).
- Overall, 2/447 (<1%) participants had CVF; both were male (sex at birth), <35 years of age, White (not Hispanic or Latinx), and had a BMI <30 kg/m^2. The participants had no baseline RPV resistance-associated mutations and had HIV-1 subtypes AE and B.
  - Additionally, a third participant from the site that was excluded from the main analysis met the CVF criterion in the ITT-E population. This participant was male (sex at birth), 35–<50 years of age, White (not Hispanic or Latinx), BMI ≥30 kg/m^2, and had HIV-1 subtype C* with failed resistance assay analysis at baseline.

*Participant had HIV-1 subtype C at Month 3. Baseline analysis failed.

Table 1. Safety Summary Through Month 12 Excluding Injection Site Reactions (ISRs) Across Sex at Birth, Age, and BMI Subgroups

	Sex at birth		Age (years)			BMI (kg/m^2)	
ITT-E population Parameter, n (%)	**Female (n=79)**	**Male (n=375)**	**<35 (n=192)**	**35–<50 (n=173)**	**≥50 (n=89)**	**<30 (n=357)**	**≥30 (n=97)**
Any AE	60 (76)	289 (77)	143 (74)	141 (82)	65 (73)	272 (76)	77 (79)
Drug-related	19 (24)	71 (19)	37 (19)	37 (21)	16 (18)	74 (21)	16 (16)
Any Grade ≥3 AE	6 (8)	36 (10)	10 (5)	19 (11)	13 (15)	28 (8)	14 (14)
Drug-related	1 (1)	6 (2)	0	3 (2)	4 (4)	5 (1)	2 (2)
Leading to withdrawal	2 (3)	13 (3)	4 (2)	7 (4)	4 (4)	10 (3)	5 (5)
Drug-related	1 (1)	8 (2)	2 (1)	4 (2)	3 (3)	7 (2)	2 (2)
Any serious AE	3 (4)	17 (5)	6 (3)	7 (4)	7 (8)	12 (3)	8 (8)
Drug-related	0	3 (<1)	0	1 (<1)	2 (2)	2 (<1)	1 (1)

AE, adverse event; BMI, body mass index; ITT-E, intention-to-treat exposed.

Table 2. Safety Summary Through Month 12 Excluding ISRs Across Race and Ethnicity Subgroups

	Race				Ethnicity	
ITT-E population Parameter, n (%)	**White (n=313)**	**Black (n=96)**	**Asian (n=23)**	**Other races (n=22)**	**Hispanic or Latinx (n=95)**	**Not Hispanic or Latinx (n=359)**
Any AE	239 (76)	72 (75)	19 (83)	19 (86)	68 (72)	281 (78)
Drug-related	58 (19)	23 (24)	6 (26)	3 (14)	13 (14)	77 (21)
Any Grade ≥3 AE	25 (8)	14 (15)	3 (13)	0	3 (3)	39 (11)
Drug-related	5 (2)	2 (2)	0	0	0	7 (2)
Leading to withdrawal	9 (3)	5 (5)	1 (4)	0	2 (2)	13 (4)
Drug-related	7 (2)	2 (2)	0	0	2 (2)	7 (2)
Any serious AE	15 (5)	4 (4)	1 (4)	0	3 (3)	17 (5)
Drug-related	3 (<1)	0	0	0	0	3 (<1)

AE, adverse event; ISR, injection site reaction; ITT-E, intention-to-treat exposed.

- The incidence of AEs, including drug-related AEs, was generally similar across subgroups (**Tables 1** and **2**).
- Overall, the most commonly reported drug-related AEs were pyrexia (3%), headache (2%), fatigue (2%), and diarrhea (2%).
- No deaths occurred due to AEs in any subgroup.

Table 3. ISR Summary (Event-Level) Across Sex at Birth, Age, and BMI Subgroups

	Sex at birth		Age (years)			BMI (kg/m^2)	
Participants with injections Parameter	**Female (n=77)**	**Male (n=368)**	**<35 (n=188)**	**35–<50 (n=170)**	**≥50 (n=87)**	**<30 (n=349)**	**≥30 (n=96)**
Number of injections, n	1051	4901	2529	2283	1140	4678	1274
ISR events, n*	405	1510	749	803	363	1530	385
Pain, n (% of injections)	218 (21)	1176 (24)	546 (22)	606 (27)	242 (21)	1157 (25)	237 (19)
Nodule, n (% of injections)	30 (3)	54 (1)	44 (2)	28 (1)	12 (1)	45 (<1)	39 (3)
Grade 3, n (% of ISR events)†	7 (2)	22 (1)	9 (1)	18 (2)	2 (<1)	28 (2)	1 (<1)
Median duration (IQR), days	4 (2–8)	3 (2–5)	3 (2–6)	3 (2–5)	3 (2–4)	3 (2–5)	4 (3–7)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)‡	5 (6)	6 (2)	4 (2)	6 (4)	1 (1)	9 (3)	2 (2)

*A single injection could result in more than one ISR. †There were no Grade 4 or Grade 5 ISRs. ‡Includes participants who discontinued due to ISR AEs, and an additional participant who withdrew from the study citing injection intolerability. This also includes one participant who was excluded from the primary analysis (mITT-E) population.
AE, adverse event; BMI, body mass index; IQR, interquartile range; ISR, injection site reaction; ITT-E, intention-to-treat exposed; mITT-E, modified intention-to-treat exposed.

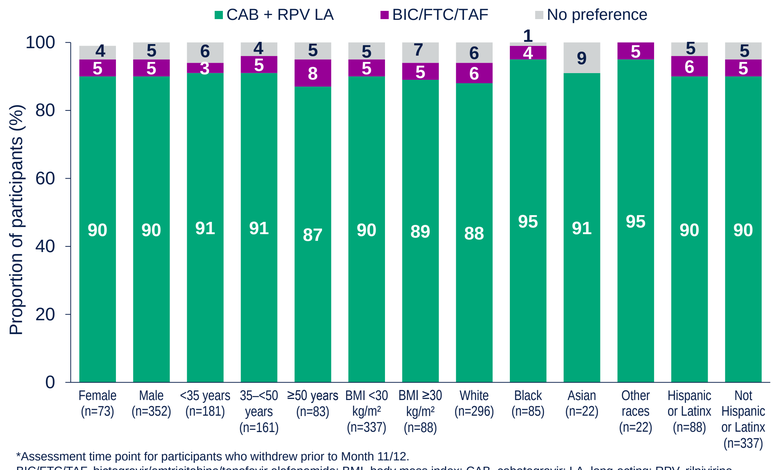
Table 4. ISR Summary (Event-Level) Across Race and Ethnicity Subgroups

	Race				Ethnicity	
Participants with injections Parameter	**White (n=307)**	**Black (n=94)**	**Asian (n=22)**	**Other races (n=22)**	**Hispanic or Latinx (n=94)**	**Not Hispanic or Latinx (n=351)**
Number of injections, n	4098	1246	300	308	1260	4692
ISR events, n*	1414	324	97	80	338	1577
Pain, n (% of injections)	1043 (25)	209 (17)	87 (29)	55 (18)	289 (23)	1105 (24)
Nodule, n (% of injections)	45 (1)	36 (3)	1 (<1)	2 (<1)	6 (<1)	78 (2)
Grade 3, n (% of ISR events)†	20 (1)	6 (2)	0	3 (4)	3 (<1)	26 (2)
Median duration (IQR), days	3 (2–5)	3 (3–7)	4 (3–5)	3 (2–3)	3 (2–4)	3 (2–5)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)‡	8 (3)	3 (3)	0	0	2 (2)	9 (3)

*A single injection could result in more than one ISR. †There were no Grade 4 or Grade 5 ISRs. ‡Includes participants who discontinued due to ISR AEs, and an additional participant who withdrew from the study citing injection intolerability. This also includes one participant who was excluded from the primary analysis (mITT-E) population.
AE, adverse event; IQR, interquartile range; ISR, injection site reaction; ITT-E, intention-to-treat exposed; mITT-E, modified intention-to-treat exposed.

- ISR profiles were generally comparable across subgroups (**Tables 3** and **4**).
- Most ISRs were Grade 1 or 2 (96–100%), short-lived (median, 3–4 days), with few participants discontinuing due to injection-related reasons.

Figure 2. Treatment Preference at Month 12 (or Withdrawal*) Across Subgroups



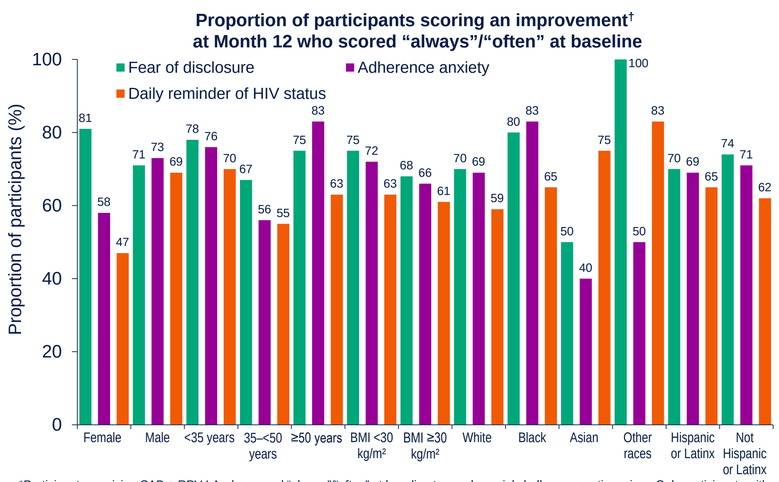
*Assessment time point for participants who withdrew prior to Month 11/12.
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.

- Across all subgroups, most participants preferred CAB + RPV LA vs. BIC/FTC/TAF, with preference ranging from 87% in the ≥50 years subgroup to 95% in the Black and Other races subgroups (**Figure 2**).

- Treatment satisfaction was high at baseline across subgroups, with HIVTSQs* total mean scores ranging from 54.5/66.0 to 59.5/66.0.
  - Female, 58.0; Male, 57.9; <35 years, 56.7; 35–<50 years, 58.6; ≥50 years, 59.1; BMI <30 kg/m^2, 57.4; BMI ≥30 kg/m^2, 59.5; White, 58.5; Black, 56.7; Asian, 54.5; Other races, 58.1; Hispanic or Latinx, 58.3; Not Hispanic or Latinx, 57.8.
- Improvements in HIVTSQs* total mean scores from baseline to Month 12 were observed across subgroups, ranging from +3.0 to +5.9.
  - Month 12: Female, +3.9; Male, +4.3; <35 years, +5.8; 35–<50 years, +3.0; ≥50 years, +3.0; BMI <30 kg/m^2, +4.6; BMI ≥30 kg/m^2, +3.0; White, +3.6; Black, +5.9; Asian, +4.0; Other races, +5.5; Hispanic or Latinx, +4.7; Not Hispanic or Latinx, +4.1.

*HIVTSQs total mean scores range from 0 (minimum, very dissatisfied) to 66 (maximum, very satisfied).

Figure 3. Psychosocial Outcomes Across Subgroups for Participants Who Reported Challenges* at Baseline



*Participants receiving CAB + RPV LA who scored "always"/"often" at baseline to psychosocial challenge questionnaires. Only participants with non-missing values at baseline and Month 12 were included.
Fear of disclosure: Female (n=27), Male (n=75); <35 years (n=46), 35–<50 years (n=36), ≥50 years (n=20); BMI <30 kg/m^2 (n=77), BMI ≥30 kg/m^2 (n=25); White (n=63), Black (n=30), Asian (n=4), Other races (n=5); Hispanic or Latinx (n=20), Not Hispanic or Latinx (n=82).
Adherence anxiety: Female (n=19), Male (n=93); <35 years (n=55), 35–<50 years (n=39), ≥50 years (n=18); BMI <30 kg/m^2 (n=83), BMI ≥30 kg/m^2 (n=29); White (n=74), Black (n=29), Asian (n=5), Other races (n=4); Hispanic or Latinx (n=26), Not Hispanic or Latinx (n=86).
Daily reminder of HIV status: Female (n=32), Male (n=75); <35 years (n=44), 35–<50 years (n=44), ≥50 years (n=19); BMI <30 kg/m^2 (n=84), BMI ≥30 kg/m^2 (n=23); White (n=66), Black (n=31), Asian (n=4), Other races (n=6); Hispanic or Latinx (n=23), Not Hispanic or Latinx (n=84).
†Moving from "always" at baseline to "sometimes"/"rarely"/"never"/"often" or "often" at baseline to "sometimes"/"rarely"/"never" after 12 months of therapy.
BMI, body mass index; CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.

- At baseline (prior to switching to CAB + RPV LA), 36% of participants in the Other races subgroup and 65% of participants in the Female subgroup reported "always"/"often" to at least one of the psychosocial challenge questions.
  - Female, 65%; Male, 45%; <35 years, 50%; 35–<50 years, 49%; ≥50 years, 47%; BMI <30 kg/m^2, 48%; BMI ≥30 kg/m^2, 52%; White, 47%; Black, 59%; Asian, 43%; Other races, 36%; Hispanic or Latinx, 48%; Not Hispanic or Latinx, 49%.
- For participants who reported challenges at baseline*, improvements† in psychosocial outcomes were observed across all subgroups at Month 12 (**Figure 3**).

*Participants receiving CAB + RPV LA who scored "always"/"often" at baseline to psychosocial challenge questionnaires.
†Moving from "always" at baseline to "sometimes"/"rarely"/"never"/"often" or "often" at baseline to "sometimes"/"rarely"/"never" after 12 months of therapy.

Conclusions

- Switching to CAB + RPV LA Q2M from BIC/FTC/TAF was efficacious for the maintenance of virologic suppression in PLWH, irrespective of sex at birth, age, BMI, race, or ethnicity.
- CVF was infrequent, with <1% of participants in the CAB + RPV LA Q2M arm reporting CVF through Month 12.
- CAB + RPV LA Q2M was well tolerated across subgroups, with most (96–100%) ISRs being mild to moderate in severity, short in duration (median, 3–4 days), and infrequently leading to withdrawal.
- Across subgroups, CAB + RPV LA Q2M also provided emotional well-being benefits, including alleviation from the fear of disclosure and anxiety surrounding adherence.
- Treatment satisfaction improved from baseline across all subgroups in participants who switched from BIC/FTC/TAF to CAB + RPV LA, with 87–95% preferring the LA therapy over daily oral treatment.

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