CLINICAL OUTCOMES DURING CUSTOMIZE: A HYBRID III IMPLEMENTATION-EFFECTIVENESS STUDY FOCUSED ON IMPLEMENTATION OF CABOTEGRAVIR PLUS RILPIVIRINE (CAB + RPV) LA IN US HEALTHCARE SETTINGS

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Introduction

- Cabotegravir (CAB) and rilpivirine (RPV) is the first complete long-acting (LA) injectable regimen recommended by treatment guidelines for the maintenance of virologic suppression in people living with HIV-1[1-3]
- Limited data exist evaluating the feasibility, acceptability, and resource requirements of implementing this novel healthcare provider–administered therapy and subsequent clinical outcomes in US healthcare settings
- This analysis reports key efficacy, safety, and adherence outcomes after 12 months of CAB + RPV LA implementation in CUSTOMIZE

Methods

- CUSTOMIZE is a phase IIIb, single-arm, hybrid III implementation-effectiveness study at 8 US clinical sites that enrolled virologically suppressed participants with HIV-1 infection
  - Clinics were located in Sacramento, CA; Kansas City, MO; Dallas, TX; Detroit, MI; Atlanta, GA; Jackson, MS; Jacksonville, FL; and Miami, FL
- Key secondary endpoints evaluated efficacy and safety measures of once-monthly CAB + RPV LA, adherence to injection dosing schedule, and length of clinic visit
  - Plasma HIV-1 RNA and adverse event (AE) assessments occurred at Months 1, 2, 4, 6, 8, 10, and 12
  - Injection site reactions (ISRs) were documented at each monthly visit
  - Total time spent in clinic from arrival to departure was recorded at Months 1, 5, and 11
- CAB + RPV therapy began with a 1-month oral lead-in of CAB 30 mg + RPV 25 mg to assess individual tolerability before transitioning to monthly CAB 400 mg + RPV 600 mg LA intramuscular injections
  - Injections were scheduled with a −7-day dosing window around the target injection visit date at Months 2 and 3 (second and third injections) and a ±7-day dosing window starting at Month 4 (fourth injection)

Results

- Of 115 participants enrolled, 109 (95%) received ≥1 CAB + RPV LA injection, and 102 (89%) completed through Month 12
  - 6 participants withdrew before receiving a CAB + RPV LA injection because of protocol deviation (n=3), AE (n=1), physician decision (n=1), or withdrawn consent (n=1)
- 86% of participants were men, 57% were White, 37% were Black or African American, and median (range) body mass index was 27 (17-55) kg/m^2 (Table 1)

Table 1. Baseline Demographics

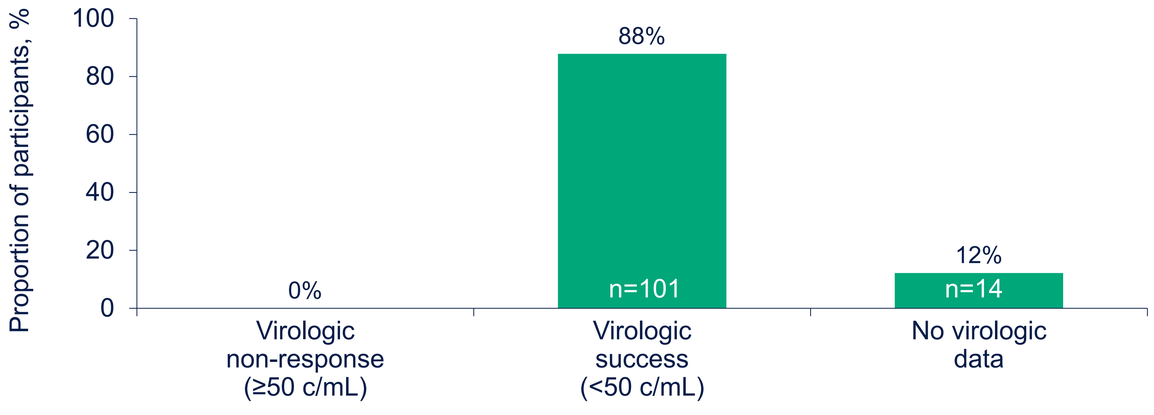
Parameter	CAB + RPV LA Q1M (N=115)
Age, mean (range), y	39 (20-65)
≥50, n (%)	27 (23)
Male, n (%)	99 (86)
Race and ethnicity, n (%)	
White	66 (57)
Black or African American	42 (37)
Hispanic or Latino	30 (26)
Body mass index, median (range), kg/m^2	27 (17-55)

Q1M, every 1 month.

Virologic Outcomes

- At Month 12, 88% (101/115) of participants maintained virologic suppression (HIV-1 RNA <50 c/mL), and no participants had HIV-1 RNA ≥50 c/mL (Figure 1)
  - 1 participant with missing data in the Month 12 window, due to COVID-19, maintained HIV-1 RNA <50 c/mL at all visits through Month 10 and remained undetectable at an unscheduled visit at Month 13
- No confirmed virologic failures (2 consecutive HIV-1 RNA measurements ≥200 c/mL) occurred through Month 12

Figure 1. Virologic Outcomes at Month 12 (FDA Snapshot Algorithm)



Outcome, n (%)	CAB + RPV LA Q1M (N=115)
HIV-1 RNA <50 c/mL	101 (88)
HIV-1 RNA ≥50 c/mL	0
No virologic data	14 (12)
Discontinued due to AE or death	5 (4)[a]
Discontinued for other reasons	8 (7)[b]
On study but missing data in window	1 (1)[c]

Q1M, every 1 month. [a]One death was reported due to diabetic ketoacidosis and drug abuse (both unrelated to study treatment). [b]Reasons include withdrawn consent (n=4), protocol deviation (n=3), and physician decision (n=1). [c]Due to COVID-19.

Safety

- ISRs were the most common overall AE, reported in 72% (78/109) of participants who received ≥1 injection through Month 12; no grade 4 or 5 ISRs were reported (Table 2)
- Excluding ISRs, arthralgia (14%), diarrhea (14%), fatigue (12%), and headache (11%) were the most common AEs
- Drug-related AEs were reported in 59% (n=68) of participants, with the most common non-ISR drug-related AEs being fatigue (5%) and headache (5%)

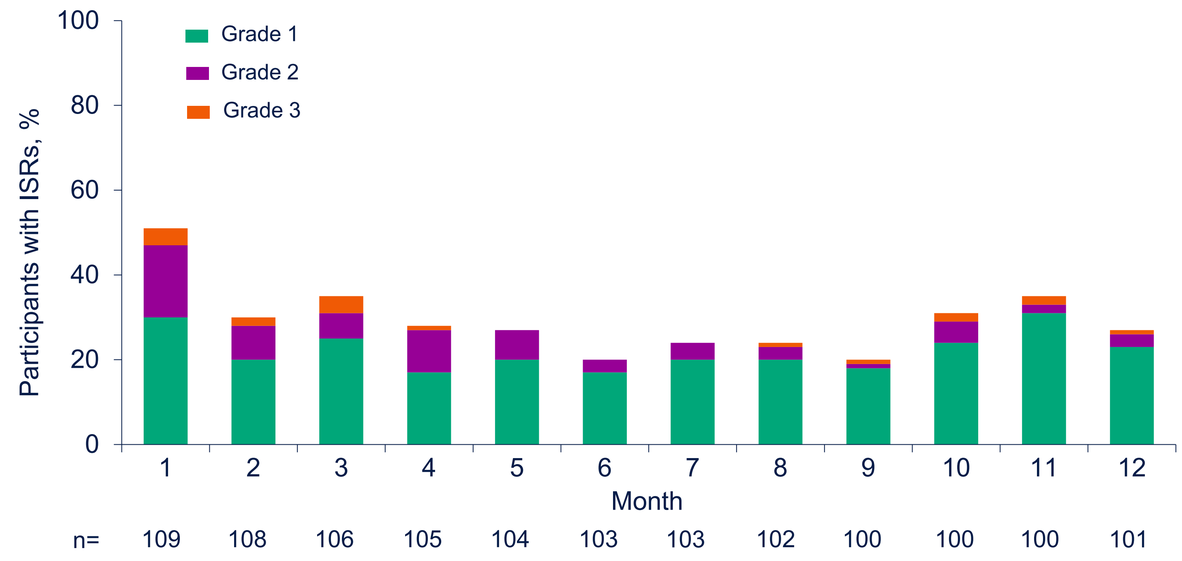
Table 2. Summary of AEs, Including ISRs

Event, n (%)	CAB + RPV LA Q1M (N=115)
Any AE	104 (90)
ISR events	78/109 (72)[a]
Grade ≥3 AEs	17 (15)
Drug-related AEs	68 (59)
Grade ≥3 drug-related AEs[b]	3 (3)[c]
Serious AEs	5 (4)[d]
AEs leading to withdrawal	6 (5)[e]

Q1M, every 1 month. [a]109 participants received ≥1 injection. [b]No grade 4 or 5 drug-related AEs were reported. [c]Injection site pain (n=2) and mental status changes (n=1). [d]5 participants reported 11 non-ISR serious AEs. [e]6 participants reported 14 events: injection site pain (n=2); arthralgia, back pain, diabetic ketoacidosis, diarrhea, drug abuse, insomnia, lipodystrophy, mental disorder, myalgia, nausea, psoriasis, and tendon pain (n=1 each).

- ISRs were reported in 718 of 2804 total injections and decreased in incidence after the first injection (Figure 2)
- Most ISRs were grade 1 (78%) or 2 (18%), with injection site pain being the most common (69%)
- Median duration of ISRs was 2 days, with 85% of ISRs resolving in <8 days
- 2 (2%) participants withdrew from the study because of injection site pain and injection intolerability after the first injection (n=1) or injection site pain after the sixth injection (n=1)

Figure 2. ISRs Through Month 12



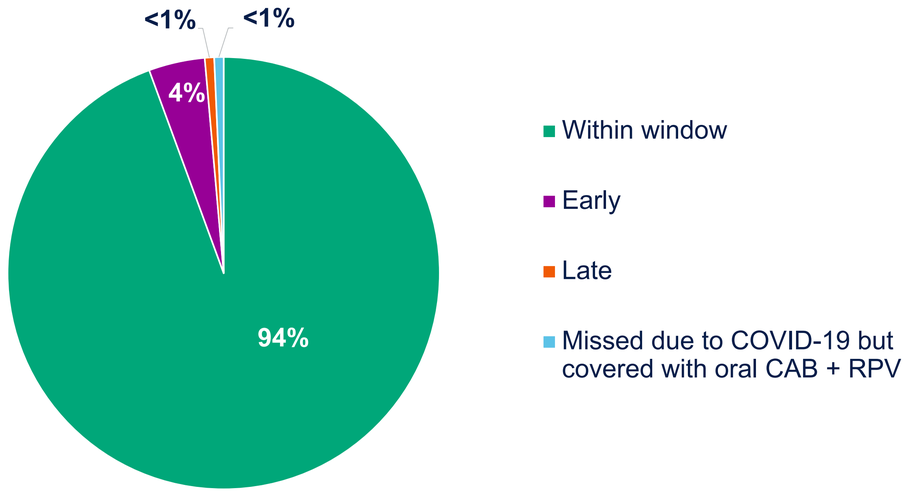
Event-level summary	CAB + RPV LA Q1M (N=109)[a]
Injections, n	2804
ISR event, n[b]	718
Pain, n (% of total injections)	494 (18)
Discomfort, n (% of total injections)	144 (5)
Grade 3 ISR, n (% of total injections)[c]	28 (1)
Median ISR duration, d	2
Participants withdrawing for injection-related reasons, n (%)	2 (2)

Q1M, every 1 month. [a]Participants receiving ≥1 injection. [b]Common ISRs reported in >1% of total injections. [c]No grade 4 or 5 ISRs were reported.

Adherence to Treatment Window

- Through Month 12, 94% (1076/1140) of expected injection visits occurred within the ±7-day dosing window, and <1% (8/1140) of injection visits took place >7 days late (range, 8-11 days; Figure 3)
- 4% (48/1140) of injection visits occurred >7 days early, most (40/48) of which took place 8 to 14 days early relative to the target treatment date
- 8 (<1%) injection visits were missed because of COVID-19, all of which were covered with oral CAB + RPV and had no disruption to continuous ART

Figure 3. Adherence to Treatment Window Through Month 12



Total Time Spent in Clinic

- Median (IQR) total time spent in clinic (wait time plus exam room time) for the first injection visit at Month 1 was 57 (47-70) minutes
- Subsequent injection-only visits were shorter, with median (IQR) total time spent in clinic of 35 (25-49) minutes at Month 5 and 34 (27-44) minutes at Month 11
- Median (IQR) exam room time decreased from 51 (42-65) minutes at Month 1 to 32 (26-41) minutes at Month 11

Conclusions

- Monthly CAB + RPV LA was highly effective in a diverse US population, with no confirmed virologic failures occurring after 12 months of treatment
- Although ISRs were frequent, most (96%) were mild or moderate in severity, decreased after the first injection, and few participants (2%) withdrew for injection-related reasons
- Most injection visits (94%) occurred within the ±7-day dosing window through 12 months of treatment, with <1% of injection visits impacted by COVID-19
- Time spent in clinic for injection visits decreased after the first injection visit
- Clinical outcomes through 12 months in the CUSTOMIZE implementation-effectiveness study provide support for monthly CAB + RPV LA as an effective and well-tolerated treatment option that is preferred by people living with HIV-1[4]

Acknowledgments

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