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Demonstration Project of Long-Acting Antiretroviral Therapy in a Diverse Population of People With HIV

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Abstract

Background: Intramuscular cabotegravir (CAB) and rilpivirine (RPV) is the only long-acting antiretroviral therapy (LA-ART) regimen approved for people with HIV (PWH). Long-acting ART holds promise for improving outcomes among populations with barriers to adherence but is only approved for PWH who have virologic suppression with use of oral ART before initiating injectables.

Objective: To examine LA-ART in a population of PWH that includes those with viremia.

Design: Observational cohort study.

Setting: Urban academic safety-net HIV clinic.

Patients: Publicly insured adults living with HIV with and without viral suppression, high rates of unstable housing, mental illness, and substance use.

Intervention: Demonstration project of long-acting injectable CAB–RPV.

Measurements: Descriptive statistics summarizing cohort outcomes to date, based on pharmacy team logs and electronic medical record data.

Results: Between June 2021 and November 2022, 133 PWH at the Ward 86 HIV Clinic were started on LA-ART, 76 of whom had virologic suppression while using oral ART and 57 of whom had viremia. The median age was 46 years (IQR, 25 to 68 years); 117 (88%) were cisgender men, 83 (62%) had non-White race, 56 (42%) were experiencing unstable housing or homelessness, and 45 (34%) had substance use. Among those with virologic suppression, 100% (95% CI, 94% to 100%) maintained suppression. Among PWH with viremia, at a median of 33 days, 54 of 57 had viral suppression, 1 showed the expected 2-$\log_{10}$ reduction in HIV RNA level, and 2 experienced early virologic failure. Overall, 97.5% (CI, 89.1% to 99.8%) were projected to achieve virologic suppression by a median of 33 weeks. The current virologic failure rate of 1.5% in the cohort is similar to that across registrational clinical trials at 48 weeks.

Limitation: Single-site study.

Conclusion: This project demonstrates the ability of LA-ART to achieve virologic suppression among PWH, including those with viremia and challenges to adherence. Further data on the ability of LA-ART to achieve viral suppression in people with barriers to adherence are needed.

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Although highly effective options for once-daily oral antiretroviral therapy (ART) to treat HIV are available, challenges with adherence to oral regimens persist. In a recent study using pharmacy records across the United States, more than 60% of people with HIV (PWH) had adherence rates below 90%, and more than 40% had adherence below 80% (1). In a retrospective cohort study across 31 countries from 2010 to 2019, only 79% of adults achieved virologic suppression 1 year after starting oral ART, with lower rates of suppression (65%) at 3 years (2). Adherence barriers span individual and structural factors, such as stigma, housing or food insecurity, insurance lapses or prohibitive copayments, mental illness, substance use, transportation issues, stockouts, or other competing priorities, all of which are likely to vary by country resources and patient population (3, 4). Long-acting injectable agents that are administered monthly or less frequently could circumvent some of these barriers.

Long-acting agents have been developed in other fields, such as for contraception (5), opioid use disorder, alcohol use disorder, and mental illness with psychosis (6), with the aim of increasing use in patients with challenges to taking daily pills. The field of long-acting ART (LA-ART) for HIV infection is relatively young. The U.S. Food and Drug Administration (FDA) approved a combination of 2 injectable antiretroviral medications—cabotegravir (CAB) and rilpivirine (RPV)—for administration every 4 weeks in both ART-naive and ART-experienced patients in January 2021, and a higher dose of each given every 8 weeks was approved in March 2022 (7). Several registrational trials (FLAIR [First Long-Acting

Injectable Regimen] [8], ATLAS [Antiretroviral Therapy as Long Acting Suppression] [9], and ATLAS 2-M [Antiretroviral Therapy as Long Acting Suppression every 2 Months] [10]) demonstrated noninferiority of long-acting CAB–RPV (LA CAB–RPV) in both treatment-naive and treatment-experienced patients. However, all 3 trials required an extended period of viral suppression during use of oral ART before the switch to long-acting injectables, and patients with any history of virologic failure were excluded. In an analysis of the registrational trials out to 48 weeks, the overall risk for virologic failure was low (1.3%) (11), and an updated analysis of the confirmed virologic failure rate at 152 weeks showed that the risk remained low (1.4%) (12). Factors that predicted failure included low RPV trough concentrations, HIV subtypes A1 and A6, body mass index (BMI) above 30 kg/m^2, and RPV-associated resistance mutations (11, 12).

Several ongoing implementation studies of LA CAB–RPV in Europe and the United States show high rates of virologic suppression, but these studies started CAB–RPV only in patients with virologic suppression concomitant with the design of the clinical trials (13–15). Data on LA CAB–RPV in those with barriers to adherence that preclude successful oral therapy are limited. The pharmaceutical company's compassionate use program before drug approval showed that only 16 of 28 patients with viremia when starting LA CAB–RPV (57%) achieved virologic suppression (16). The U.S.-based OPERA (Observational Pharmacoepidemiology Research and Analysis) cohort reported results in October 2022 from 21 patients with viremia who were started on LA CAB–RPV, 19 (91%) of whom achieved suppression (17). To address the gap in the literature on the use of LA CAB–RPV in real-world populations, we launched a demonstration project of administration of LA-ART to patients with viral suppression who expressed a desire to switch or those with viremia who were experiencing challenges with adherence to daily oral ART. We reported on initial findings in August 2022 (18) and now present updated outcomes in our cohort, representing what is, to our knowledge, the largest demonstration project of the use of injectable ART in a population that includes patients initiating injections with unsuppressed viral loads.

Methods

The Ward 86 HIV Clinic, one of the oldest HIV clinics in the country, opened in January 1983 and now treats more than 2600 patients. Ward 86 is located within San Francisco General Hospital, the county hospital of the University of California, San Francisco (UCSF) tri-hospital system. The mission of San Francisco General Hospital is to care for low-income patients; 96% of the patients at Ward 86 are insured by Medicaid and Medicare, and 4% have municipal insurance or are uninsured. The Ward 86 patient population has high rates of unstable housing (approximately one third), major mental illness (38%), and self-reported substance use (mainly methamphetamines) (35%). The overall virologic suppression rate in the clinic is 87%, with patients with viremia usually reporting 1 or more barriers to adherence to daily oral ART, including housing or food insecurity, substance use, a focus on other subsistence needs, and stigma (19). Many of these patients are seen in a Ward 86 clinical program called POP-UP (Positive-health Onsite Program for Unstably-housed Populations), a low-barrier drop-in care model that serves PWH who experience

homelessness or unstable housing, do not have viral suppression, and have difficulty attending scheduled appointments (20).

When approval of LA-ART was anticipated in late 2020, we developed a program for the administration of LA-ART, which was subsequently named the SPLASH program (Special Program of Long-Acting Antiretrovirals to Stop HIV). The SPLASH team at Ward 86, which comprises clinic leadership, the pharmacy supervisor, a pharmacy technician, researchers, and leadership of the POP-UP clinical program, created a protocol for eligibility, referral, injection administration, follow-up, laboratory monitoring, and late injections (21). Program development drew on established implementation strategies to support provider referral, patient initiation and persistence, and ongoing monitoring and evaluation.

The inclusion criteria for participation in SPLASH were a desire to switch to LA CAB–RPV in patients with virologic suppression or demonstration of an inability to adhere to daily oral ART in patients with documented viremia, as well as a verbal expression of willingness to visit the clinic regularly for injections. Minor resistance mutations were initially allowed, but our original inclusion criteria (18) were subsequently tightened to exclude patients with even minor mutations in the reverse transcriptase (RT) gene that conferred RPV resistance or mutations in the integrase gene that conferred CAB resistance on historical viral genotypes obtained from the medical record. Patients were asked to voice commitment to visit the clinic every 4 weeks for injections and provide contact information at every visit for injection reminders, including contact information of friends or family members. If patients maintained or achieved virologic suppression for at least 3 months with LA CAB–RPV administered every 4 weeks, they could transition to dosing every 8 weeks at higher doses. Patients with chronic hepatitis B infection were maintained on oral hepatitis B treatment.

After education at provider meetings and e-mail communications, clinic providers are asked to provide referrals for their patients to the program through the electronic medical record. The supervising pharmacist at Ward 86 reviews referrals and meets with patients for education and counseling. The SPLASH team meets every 2 weeks to review patients initiating LA CAB–RPV and to troubleshoot concerns. Injections are administered in the clinic with drop-in access and, on rare occasions, in the community using mobile outreach. Patients are counseled on the importance of on-time injections at each visit and reminded of upcoming visits via outreach calls.

As per the package insert for LA CAB–RPV and our protocol, patients who are more than 7 days late for LA-ART are asked to reinstitute daily oral therapy to cover the pharmacokinetic tail of LA-ART to avoid drug resistance and treatment failure. Our protocol called for administration of the induction dose of LA CAB–RPV (600 and 900 mg, respectively) if the injection was more than 2 weeks late, so we report on late injections as being 7 or more days and/or 14 or more days late. In patients starting LA-ART with unsuppressed viral loads, we measured HIV viral loads monthly until the viral load was less than 30 copies/mL (the lower limit of quantification for our laboratory’s assay), then every 3 months thereafter; a viral genotype was sent at the first maintenance injection for every patient who remained viremic. Of note, high BMI is associated with lower CAB

trough concentrations (12, 22), and using a longer needle to administer the LA CAB–RPV injections in patients with a BMI above 30 kg/m^2 helps the drug distribute to the intramuscular compartment, increasing CAB levels (23). Therefore, our protocol stipulated from its inception that a 2-inch needle be used to administer LA-ART in patients with high BMI. We have shared our SPLASH protocol with the public on the San Francisco Getting to Zero website and update the protocol as new data emerge or as we update evaluations of our program (21).

Statistical Analysis

For this analysis, we present data on the number of patients referred and their dispositions. We defined the analytic cohort as patients who had at least 1 injection by 4 November 2022 and thus were expected to have at least 2 follow-up injections by database closure on 9 January 2023. Descriptive statistics summarize patient characteristics, the median and range of the number of injections received, and viral suppression outcomes, stratified by viral load less than 30 copies/mL or at or above 30 copies/mL at LA-ART initiation. For patients initiating LA-ART with a viral load of 30 copies/mL or above, we present a Kaplan–Meier estimate of time to viral suppression, defined as viral load below 30 copies/mL. We calculated 95% CIs for proportions using the bias-ascertained Wilson method. On-time injections were defined as injections given 28 ± 7 days from the initial injection or, if the patient transitioned to dosing every 8 weeks, 56 ± 7 days between injections.

The UCSF Institutional Review Board approved data abstraction and analysis for this study.

Role of the Funding Source

The funders had no role in the design, conduct, or analysis of the study or the decision to submit the manuscript for publication.

Results

Between 8 June 2021 and 4 November 2022, 303 patients were referred for LA CAB–RPV, of whom 72 patients or their providers had decided against LA CAB–RPV, 51 patients were in the process of being evaluated by the pharmacy team at the time of database closure, 14 were ineligible because of resistance mutations, and 8 either transferred out or died before they could start injections, leaving 157 patients who had initiated LA CAB–RPV. The analytic cohort with virologic data by the time of database closure comprised 133 patients with a median age of 45 years (IQR, 38 to 54 years). Sixteen (12%) were cisgender or transgender women, 83 (62%) had non-White race or ethnicity, 56 (42%) were experiencing unstable housing or homelessness, 31 (23%) were enrolled in the POP-UP program, 45 (34%) endorsed stimulant use, and 16 (12%) were receiving other long-acting injections, such as anti-psychotics, naltrexone, or hormones (Table). During the observation period, 30 patients transitioned to CAB–RPV injections every 8 weeks, and 4 patients received ongoing injections in the community through collaborations with street medicine and home health. The median follow-up for the entire cohort was 33 weeks (range, 10 to 83 weeks).

In the cohort, 57 (43%) patients initiating LA-ART had viremia and 76 (57%) had virologic suppression with oral ART before starting use of injectables. Among the 76 patients who

started with virologic suppression, the median CD4 cell count was 0.615×10^9 cells/L and the median number of injections was 7.5 (IQR, 4 to 10; range, 1 to 17). In this group, 100% (95% CI, 94% to 100%) maintained viral suppression over the follow-up period. Five patients in this group chose to resume oral ART after use of injectable agents, citing injection site reactions, and 3 patients returned to oral ART after finding it logistically difficult to visit the clinic every 4 to 8 weeks.

Among 57 patients who were started on injectables with viremia, the median CD4 cell count was 0.215×10^9 cells/L, the mean $\log_{10}$ viral load was 4.21 (SD, 1.30), and the median number of injections was 7 (IQR, 5 to 11; range, 2 to 18). In this group, 54 of 57 achieved virologic suppression by a median of 33 days (IQR, 28 to 56 days). Two had documented virologic failure, both soon after initiation. Beyond the 2 cases of virologic failure, 1 additional patient developed viral rebound after initial suppression; the genotype failed to amplify, and he immediately achieved resuppression with oral ART (darunavir–cobicistat–tenofovir alafenamide–emtricitabine). This patient had a BMI of 32 kg/m^2 and inadvertently was not given his injection with the longer 2-inch needle, which may have contributed to low drug levels (11). A proviral HIV DNA test performed in this patient did not show development of any new mutations in the RT or integrase gene, but oral ART was continued. One patient (who started LA-ART with an HIV viral load of 66 764 copies/mL) needed 2 injections before the viral load was suppressed to less than 100 copies/mL, and the suppression outcome of less than 30 copies/mL was not achieved until after the fifth injection. Finally, a fifth patient in this group had an HIV viral load of 182 copies/mL by 5 injections, and we added lenacapavir to the LA CAB–RPV.

Of the 2 patients with early virologic failure in the viremic group, 1 patient had a decrease in viral load less than 2 $\log_{10}$ at the first maintenance injection (from 214 540 to 39 293 copies/mL). A nonnucleoside reverse transcriptase inhibitor (NNRTI) mutation (L100I) was present on genotypic testing at this time, and injections were discontinued. The patient had not chosen to initiate oral ART as of database closure, and additional genotypic testing showed a new Y181I mutation in the RT gene. Risk factors for failure were a V179V/I mutation in the RT gene at baseline and rifabutin use 2 weeks before initiation of LA CAB–RPV. The second patient with failure was also noted to have a decrease in viral load of less than 2 $\log_{10}$ at the first maintenance injection (from 137 134 to 4371 copies/mL) and, although the HIV viral load at the third injection was less than 30 copies/mL, genotypic testing was successful and showed an E138K mutation in the RT gene and an R263K mutation in the integrase gene. The baseline genotype resistance test had a minor integrase strand transferase inhibitor (INSTI) mutation (T97A). As of database closure, this patient was declining oral ART.

On-time injections occurred for 74% (CI, 66% to 81%) of the cohort. Thirty-four patients were late at least once, for a total of 52 episodes of lateness overall, 5 of which required reinitiation of the induction dose of injectable CAB–RPV (600 and 900 mg) because dosing was 14 or more days late. Six patients successfully used oral ART bridging when there was an anticipated inability to visit the clinic for injections.

The Figure shows the Kaplan–Meier plot of the viral load results for the 57 patients who started LA-ART with viremia. The Kaplan–Meier analysis estimated a probability of 97.5% (CI, 89.1% to 99.8%) of reaching virologic suppression by 33 weeks (range, 10 to 83 weeks).

Discussion

We report on a demonstration project of LA-ART in a publicly insured population of PWH with high rates of substance use and unstable housing, including those with viremia. The main finding showed that LA-ART maintained virologic suppression in those who were receiving suppressive oral ART before switching, and nearly all patients who did not have virologic suppression and were not using oral ART before LA-ART initiation achieved suppression. The overall confirmed virologic failure rate in this cohort of patients receiving LA-ART was 1.5% at a median of 33 weeks, which is similar to the virologic failure rate (1.3%) seen across the registrational clinical trials at 48 weeks (11). The 2 instances of failure despite on-time injections in our cohort occurred soon after LA-ART initiation, which was similar to the majority of failures in the registrational trials (68% occurred before 24 weeks) (8–12). For 19% of patients with viremia, the virologic suppression seen with LA-ART was the first time these patients had ever achieved suppression, which shows the power of LA-ART to circumvent typical barriers to adherence and help advance the goals of the Ending the HIV Epidemic initiative (24, 25).

Approximately three quarters of injections were on time, and despite late injections, retention in the injection program was high. These early adopters may have been highly motivated to persist with injections, but we hypothesize that strong relationships with clinic providers and staff supported retention. Indeed, a robust commitment to the program on the part of Ward 86 staff helped underpin its success.

This project is one of the only ones that deliberately used LA-ART in a real-world population with a high prevalence of adherence challenges and viremia. Although LA-ART for patients with viremia is not recommended in current treatment guidelines because of a lack of randomized controlled trial data, accumulating data from observational cohorts on the success of this regimen in persons who cannot take oral ART may eventually lead to a change in the recommendations. The fact that our confirmed virologic failure rate to date is analogous to that of the pooled analysis in the clinical trials of LA CAB–RPV to date is heartening. Moreover, the 2 failures occurred soon after initiation and were likely due to the presence of minor mutations in NNRTIs or INSTIs, so we hope that sustainability of virologic suppression in other cohort members will be maintained. Of note, the 2 patients who had virologic failure had no other options for treatment, as they both were simply unable to adhere to oral ART and have not started oral ART since the virologic failure. In addition, both patients experienced viral load reductions that would not have occurred with oral ART. We have since strengthened our protocol to ensure that any patient with even minor resistance mutations is excluded.

A recent model showed that the overall virologic suppression rate in patients who have barriers to adherence is approximately 22% (26). Long-acting ART therefore offers a novel

and promising therapeutic approach that can benefit patients who struggle with adherence. For instance, injections can help to mitigate privacy concerns by reducing the risk for unintended HIV disclosure and the stigma associated with consuming oral ART regimens in group settings, such as shelters. Long-acting anti-psychotics were being administered in 8% of the patients in this cohort, which highlights the possibility of treating mental illness and HIV simultaneously. Long-acting treatments for opioid or alcohol use disorder could also be simultaneously administered in patients with concomitant substance use. Stigma also plays a significant part in adherence difficulties in low- and middle-income countries, suggesting a role for LA-ART worldwide. When weighing benefits and risks of LA CAB–RPV in populations who struggle with adherence to oral ART, the alternative outcome is not perfect adherence to oral ART but rather ongoing viremia and progression of HIV disease, which recalibrates the tipping point for use.

Whether LA-ART will change population health outcomes depends on the willingness of health care systems to use these medications to improve virologic suppression rates in populations with barriers to oral ART adherence. The “inverse care law” shows that the populations that could most benefit from an intervention are the least likely to receive it (27). Although the World Health Organization has not yet endorsed LA CAB–RPV for low- and middle-income countries, we hope that data from demonstration projects such as ours can help bolster a more expansive approach worldwide. Lenacapavir, which has recently been approved by the FDA for use in multidrug-resistant HIV, could play an additional role, especially in patients with NNRTI resistance. Although LA-ART holds considerable potential to be a game-changer for HIV treatment in patients experiencing barriers to oral ART adherence, additional data from demonstration projects will be needed to confirm sustainable benefits over time.

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References

1. McComsey GA, Lingohr-Smith M, Rogers R, et al. Real-world adherence to antiretroviral therapy among HIV-1 patients across the United States. Adv Ther. 2021;38:4961–4974. doi:10.1007/s12325-021-01883-8 [PubMed: 34390465]
2. Han WM, Law MG, Egger M, et al. ; IeDEA collaboration. Global estimates of viral suppression in children and adolescents and adults on antiretroviral therapy adjusted for missing viral load measurements: a multiregional, retrospective cohort study in 31 countries. Lancet HIV. 2021;8:e766–e775. doi:10.1016/S2352-3018(21)00265-4 [PubMed: 34856180]
3. Pugh LE, Roberts JS, Viswasam N, et al. Systematic review of interventions aimed at improving HIV adherence to care in low- and middle-income countries in sub-Saharan Africa. J Infect Public Health. 2022;15:1053–1060. doi:10.1016/j.jiph.2022.08.012 [PubMed: 36063721]
4. Locher C, Messerli M, Gaab J, et al. Long-term effects of psychological interventions to improve adherence to antiretroviral treatment in HIV-infected persons: a systematic review and meta-analysis. AIDS Patient Care STDS. 2019;33:131–144. doi:10.1089/apc.2018.0164 [PubMed: 30844307]

5. Teal S, Edelman A. Contraception selection, effectiveness, and adverse effects: a review. JAMA. 2021;326:2507–2518. doi:10.1001/jama.2021.21392 [PubMed: 34962522]
6. Taub S, Krivoy A, Whiskey E, et al. New approaches to antipsychotic medication adherence - safety, tolerability and acceptability. Expert Opin Drug Saf. 2022;21:517–524. doi:10.1080/14740338.2021.1983540 [PubMed: 34541978]
7. U.S. Food and Drug Administration. FDA Approves Cabenuva and Vocabria for the Treatment of HIV-1 Infection. 27 January 2021. Accessed at www.fda.gov/drugs/human-immunodeficiency-virus-hiv/fda-approves-cabenuva-and-vocabria-treatment-hiv-1-infection on 29 December 2022.
8. Orkin C, Bernal Morell E, Tan DHS, et al. Initiation of long-acting cabotegravir plus rilpivirine as direct-to-injection or with an oral lead-in in adults with HIV-1 infection: week 124 results of the open-label phase 3 FLAIR study. Lancet HIV. 2021;8:e668–e678. doi:10.1016/S2352-3018(21)00184-3 [PubMed: 34656207]
9. Swindells S, Lutz T, Van Zyl L, et al. Week 96 extension results of a phase 3 study evaluating long-acting cabotegravir with rilpivirine for HIV-1 treatment. AIDS. 2022;36:185–194. doi:10.1097/QAD.0000000000003025 [PubMed: 34261093]
10. Jaeger H, Overton ET, Richmond G, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 96-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. Lancet HIV. 2021;8:e679–e689. doi:10.1016/S2352-3018(21)00185-5 [PubMed: 34648734]
11. Cutrell AG, Schapiro JM, Perno CF, et al. Exploring predictors of HIV-1 virologic failure to long-acting cabotegravir and rilpivirine: a multivariable analysis. AIDS. 2021;35:1333–1342. doi:10.1097/QAD.0000000000002883 [PubMed: 33730748]
12. Orkin C, Schapiro JM, Perno CF, et al. Expanded multivariable models to assist patient selection for long-acting cabotegravir + rilpivirine treatment: clinical utility of a combination of patient, drug concentration, and viral factors associated with virologic failure over 152 weeks. HIV Glasgow 2022, Glasgow, United Kingdom, 23–26 October 2022. Presentation no. 044.
13. Collins LF, Corbin-Johnson D, Asrat M, et al. Early experience implementing long-acting injectable cabotegravir/rilpivirine for human immunodeficiency virus-1 treatment at a Ryan White-funded clinic in the US South. Open Forum Infect Dis. 2022;9:ofac455. doi:10.1093/ofid/ofac455 [PubMed: 36147599]
14. De Wit S, Rami A, Bonnet F, et al. CARISEL: a hybrid III implementation effectiveness study of implementation of cabotegravir plus rilpivirine long acting (CAB + RPV LA) in EU health care settings. Key clinical and implementation outcomes by implementation arm. Open Forum Infect Dis. 2022;9(Suppl 2). doi:10.1093/ofid/ofac492.107
15. Borch J, Scherzer J, Jonsson-Oldenbüttel C, et al. 6-month outcomes of every 2 months long-acting cabotegravir and rilpivirine in a real-world setting - effectiveness, adherence to injections, and patient-reported outcomes of people living with HIV in the German CARLOS cohort. HIV Glasgow 2022, Glasgow, United Kingdom, 23–26 October 2022. Presentation no. O43.
16. D'Amico R, Cenoz Gomis S, Moodley R, et al. Compassionate use of long-acting cabotegravir plus rilpivirine for people living with HIV-1 in need of parenteral antiretroviral therapy. HIV Med. 2023;24:202–211. doi:10.1111/hiv.13370 [PubMed: 35945163]
17. Sension MG, Hsu RK, Fusco JS, et al. Real-world use of long-act ing cabotegravir + rilpivirine in the US: effectiveness in the first year. Open Forum Infect Dis. 2022;9(Suppl 2). doi:10.1093/ofid/ofac492.105
18. Christopoulos KA, Grochowski J, Mayorga-Munoz F, et al. First demonstration project of long-acting injectable antiretroviral therapy for persons with and without detectable human immunodeficiency virus (HIV) viremia in an urban HIV clinic. Clin Infect Dis. 2023;76:e645–e651. doi:10.1093/cid/ciac631 [PubMed: 35913500]
19. Christopoulos KA, Hartogensis W, Glidden DV, et al. The Lorenz curve: a novel method for understanding viral load distribution at the population level. AIDS. 2017;31:309–310. doi:10.1097/QAD.0000000000001336 [PubMed: 27831945]
20. Hickey MD, Imbert E, Appa A, et al. HIV treatment outcomes in POP-UP: drop-in HIV primary care model for people experiencing homelessness. J Infect Dis. 2022;226:S353–S362. doi:10.1093/infdis/jiac267 [PubMed: 35759251]

21. Getting to Zero SF. Ward 86 shares updated clinical considerations and recommendations for starting patients on CAB/RPV LA therapy. Accessed at https://gettingtozerosf.org/ward-86-shares-clinic-hiv-long-acting-injectable-antiretroviral-protocol on 8 May 2023.

22. Elliot E, Polli JW, Patel P, et al. Combined analysis of ATLAS, FLAIR, ATLAS-2M: efficacy and safety of switch to LA CAB + RPV by BMI class. 18th European AIDS Conference, London, United Kingdom, 27–30 October 2021. Abstract no. BPD1/8.

23. Jucker BM, Fuchs EJ, Lee S, et al. Multiparametric magnetic resonance imaging to characterize cabotegravir long-acting formulation depot kinetics in healthy adult volunteers. Br J Clin Pharmacol. 2022;88:1655–1666. doi:10.1111/bcp.14977 [PubMed: 34240449]

24. Pyra M, Motley D, Bouris A. Moving toward equity: fostering transdisciplinary research between the social and behavioral sciences and implementation science to end the HIV epidemic. Curr Opin HIV AIDS. 2022;17:89–99. doi:10.1097/COH.0000000000000726 [PubMed: 35225249]

25. Hojilla JC, Gandhi M, Satre DD, et al. Equity in access to long-acting injectables in the USA. Lancet HIV. 2022;9:e145–e147. doi:10.1016/S2352-3018(22)00031-5 [PubMed: 35131041]

26. Chen W, Gandhi M, Sax P, et al. Projected benefits of long-acting ART (LA-ART) in PWH viremic not taking oral therapy. Conference on Retroviruses and Opportunistic Infections, Seattle, Washington, 19–22 February 2023. Abstract no. 519.

27. Tudor Hart J Commentary: three decades of the inverse care law. BMJ. 2000;320:18–19. [PubMed: 10671038]

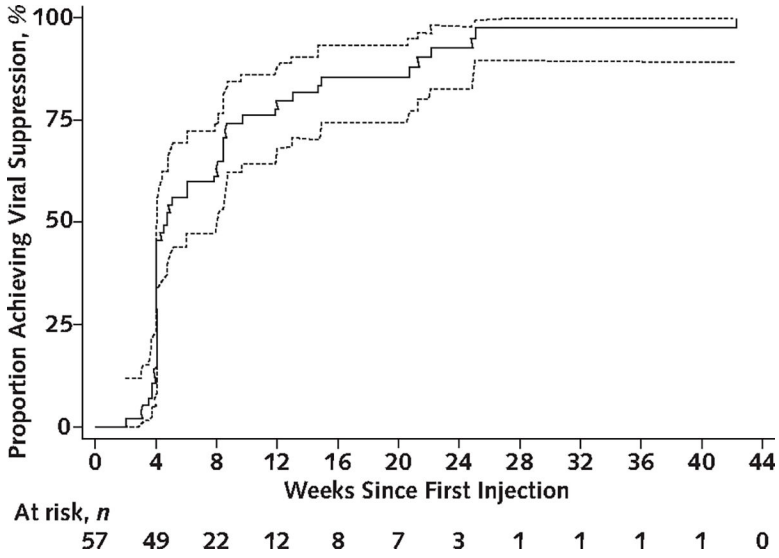

Figure.

Kaplan–Meier curve of probability of achieving virologic suppression (viral load <30 copies/mL) with long-acting antiretroviral therapy ($n = 57$).

The dashed lines indicate the 95% CI.

Table.

Patient Characteristics, by Virologic Suppression Status at Initiation of LA CAB-RPV [*]

Characteristic	Patients With Viremia (*n* = 57)	Patients With Virologic Suppression (*n* = 76)	Overall Sample (*n* = 133)
Median age(range),*y*	48.0 (25.0–68.0)	44.5 (29.0–68.0)	46.0 (25.0–68.0)
Gender, n (%)			
Cisgender man	51 (89.5)	66 (86.8)	117 (88.0)
Cisgender woman	5 (8.8)	6 (7.9)	11 (8.3)
Transgender woman	1 (1.8)	4 (5.3)	5 (3.8)
Race/ethnicity, *n* (%)			
Black	13 (22.8)	8 (10.5)	21 (15.8)
Latino/Latina	18 (31.6)	25 (32.9)	43 (32.3)
White	23 (40.4)	27 (35.5)	50 (37.6)
Multiracial/other	3 (5.3)	16 (21.1)	19(14.3)
Housing status, *n* (%) [†]			
Experiencing homelessness	6 (10.5)	3 (4.0)	9 (6.8)
Unstable	24 (42.1)	23 (30.3)	47 (35.3)
Stable	27 (47.4)	50 (65.8)	77 (57.9)
Insurance, *n* (%)			
Medicare, Medicaid, or both	55 (96.5)	73 (96.1)	128 (96.2)
ADAP	2 (3.5)	3 (4.0)	5 (3.9)
Current stimulant use, *n* (%) [†]	28 (49.1)	17 (22.4)	45 (33.8)
Mean $\log_{10}$ viral load (SD)	4.21 (1.30)	NA	NA
Median CD4 cell count(IQR), × 10^9*cells/L* [‡]	0.215 (0.075–0.402)	0.615 (0.395–0.818)	0.422 (0.219–0.749)

ADAP = AIDS Drug Assistance Program; LA CAB-RPV = long-acting cabotegravir-rilpivirine; NA = not applicable.

[*] Virologic suppression was defined as viral load <30 copies/mL.

[†] Housing status and stimulant use were reported by providers at the time of referral. Stable housing was defined as renting or owning. Unstable housing was defined as staying in a hotel or single room occupancy or with friends. Homelessness was defined as staying on the street or in a shelter.

[‡] Baseline CD4 cell count (n = 131) was defined as the measurement closest to and including the date of the first injection. The median time from CD4 cell measurement to the date of the first injection was 57 days (range, 0 to 882 days).