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Authors

Mehtani, Nicky J
Strough, Alix
Strieff, Sarah
et al.

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Authors: Nicky J. Mehtani MD MPH[1-3], Alix Strough RN[2], Sarah Strieff RN[2], Barry Zevin MD[2], Joanna Eveland MD[2], Elise D. Riley PhD MPH[3], Monica Gandhi MD MPH[3]

Affiliations:

[1] University of California, San Francisco; Department of Psychiatry & Behavioral Sciences

[2] San Francisco Department of Public Health, Whole Person Integrated Care

[3] University of California, San Francisco; Department of Medicine; Division of HIV, ID & Global Medicine

Corresponding Author:

Nicky J. Mehtani | nicky.mehtani@ucsf.edu

Ph: 916.708.7967 | Fax: 415.406.2860

Department of Psychiatry & Behavioral Sciences

University of California, San Francisco

675 Nelson Rising Lane

Sandler Neurosciences Bldg., Rm 510

San Francisco, CA 94143

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Running Head: Low-Barrier LA Antiretrovirals for PEH

Abstract

Background: Long-acting (LA) antiretrovirals may provide meaningful benefit to people who use drugs and people experiencing homelessness (PEH) who face disproportionate structural and psychosocial barriers in adhering to daily oral HIV antiretroviral therapy (ART) or pre-exposure prophylaxis (PrEP), but their use in these populations has not been studied.

Setting: The Maria X. Martinez Health Resource Center is a low-barrier (e.g., no appointment) community-based clinic serving San Francisco PEH.

Methods: A multidisciplinary care model with robust monitoring and outreach support was developed to provide LA-ART and LA-PrEP to eligible patients experiencing difficulties adhering to oral antiretrovirals. Feasibility was assessed by evaluating rates of HIV viremia and on-time injections among patients receiving LA antiretrovirals over the first 24 months of program implementation.

Results: Between November 2021 and November 2023, 33 patients initiated LA-ART or LA-PrEP (median age, 37 years; 27% transgender/non-binary; 73% non-White; 27% street homeless; 52% sheltered homeless; 30% with opioid use disorder; 82% with methamphetamine use disorder). Among 18 patients with HIV, 14 initiated LA-ART injections with detectable viremia (median CD4 count, 340 cells/mm^3; mean $\log_{10}$ viral load, 3.53; standard deviation [SD], 1.62), eight had never previously been virally suppressed, and all but one achieved or maintained virologic suppression (mean, 9.67 months; SD, 8.30). Among 15 LA-PrEP patients, all remained

HIV-negative (mean, 4.73 months; SD, 2.89). Of 224 injections administered total, 8% were delayed >7 days.

Discussion: The implementation of LA antiretrovirals is feasible in low-barrier, highly supportive clinical settings serving vulnerable PEH. Expansion of such programs will be critical to Ending the HIV Epidemic.

Key Words: Homelessness, people who use drugs, HIV, long acting antiretrovirals, cabotegravir, rilpivirine, lenacapavir, ART, PrEP

Background

People experiencing homelessness (PEH) face disproportionate structural and psychosocial barriers in adhering to daily oral HIV antiretroviral treatment (ART) and pre-exposure prophylaxis (PrEP) [1], compounding already sub-optimal rates of adherence found in the general population [2,3]. Burdens of food insecurity, substance use, mental illness, structural racism, incarceration, and lack of access to safe medication storage are exacerbated among PEH [1,4], ultimately resulting in decreased rates of HIV virologic suppression [1,4,5]. In San Francisco, only 27% of PEH and 64% of people who inject drugs (PWID) were virally suppressed in 2021 compared to 73% of housed people with HIV (PWH) [6]. Low rates of virologic suppression and PrEP uptake have, in turn, led to increased HIV transmission within these communities [7], such that 1 in 4 new HIV diagnoses in San Francisco occur in PEH or PWID [6]— an approximate doubling over the past decade. While extraordinary advancements in HIV pharmacotherapy over the past three decades have transformed HIV into a chronic, often asymptomatic, and preventable condition, this success has not been realized equally across populations. Adherence strategies specific to the needs of PEH may help narrow this gap [7].

In January 2021, intramuscular cabotegravir/rilpivirine (CAB/RPV) was introduced as the first publicly available long-acting (LA) regimen for HIV treatment after phase III clinical trials demonstrated it to be highly effective, tolerable, and non-inferior to oral ART among both ART-naïve and ART-experienced patients [8-10]. FDA approval of CAB/RPV was followed by approvals for intramuscular cabotegravir (CAB) for HIV PrEP in December 2021 [11-12] and subcutaneous lenacapavir (LEN) administered with an optimized background regimen for multi-

drug-resistant HIV in December 2022 [13]. CAB/RPV is currently FDA-approved only for patients with baseline HIV virologic suppression—reflecting the characteristics of participants in clinical trials upon which regulatory approval was based [8-10]. However, real-world demonstration projects at academic medical centers have suggested that CAB/RPV may provide robust virologic suppression even among patients with baseline HIV viremia who have experienced challenges adhering to oral ART [14-17], although data from compassionate use settings have been more mixed [18].

Such a "direct-to-inject" approach of providing LA antiretrovirals at 4- and 8-week intervals or even less frequently to patients with baseline viremia opens possibilities for innovative treatment methodologies that may mitigate structural barriers to medication adherence and provide strategic benefit to PEH and people who use drugs [7,14-16]. While recent qualitative studies demonstrate significant interest in the use of LA antiretrovirals among these populations, they also highlight logistical concerns, including needs for delivery within community-based settings and alternative care sites [19,20]. To date, no published studies have evaluated the feasibility of administering LA-ART or LA-PrEP in homeless health centers or community-based clinics designated to serve patients known to have a high burden of co-morbid substance use and mental illness. Here, we describe observational findings from an innovative, multidisciplinary program that has expanded LA antiretroviral access to PEH through a low-barrier municipal clinic.

Methods

Clinical Setting

Operating within the San Francisco Department of Public Health's Whole Person Integrated Care (WPIC) program, the Maria X. Martinez (MXM) Health Resource Center provides transitional primary care and urgent care to PEH in San Francisco, California. Due to inherent difficulties of appointment management in the context of homelessness, MXM utilizes an open-access clinic model, through which patients can access on-site medical and behavioral health care, labs, and other services on a drop-in basis 8 hours-per-day, 6 days-per-week at an accessible location near San Francisco's Tenderloin district, where a significant proportion of PEH in the city reside. During the 2021-22 fiscal year, MXM provided care to 6,965 PEH or unstably housed adults (68% cisgender men, 30% cisgender women, 2% transgender or non-binary, 30% Black, 17% Hispanic), the majority of whom receive government insurance (64% Medicaid, 13% MediCare, 7% county-specific programs) or are uninsured (13%). Medical services at MXM occur in collaboration with multidisciplinary street outreach teams and satellite clinical sites co-located at syringe access programs, homeless shelters, and other organizations frequented by PEH.

Description of the WPIC Long-Acting Antiretrovirals Program

Adapted from guidelines developed by the San Francisco General Hospital HIV clinic ("Ward 86") [14, 21], the LA-ART and LA-PrEP protocols implemented at WPIC are tailored to meet the needs of PEH and people who use drugs, the majority of whom do not have reliable access to cellphones or consistent locations of residence. In an effort to provide low-barrier access within MXM's existing open-access care model, eligibility criteria for initiating LA antiretrovirals are intentionally streamlined. Consistent with the CAB/RPV protocol developed at Ward 86 [21], MXM patients with HIV are not required to be virally suppressed prior to the initiation of injections, as this would preclude access to PEH who experience consistent barriers to oral ART

consumption. However, all patients must demonstrate (a) a willingness to receive injections and lab draws on schedule, (b) an understanding of the long-term risks associated with delayed injections, (c) familiarity with recommended contingencies if LA antiretrovirals are interrupted, (d) pre-existing care engagement through WPIC with ≥3 nursing or medical provider visits over the preceding 3 months, and (e) an intention to continue residing in San Francisco for ≥12 months.

Providers and clinic staff receive in-service education on CAB/RPV, CAB, LEN, and internal referral processes through regular provider meetings and the distribution of detailed protocols. PWH interested in LA-ART are referred by their primary providers to a lead HIV physician, who screens electronic medical record data to identify potential medical contraindications, including presence of RPV- or CAB-associated resistance mutations on current or prior HIV RNA genotypes, co-medications known to affect CAB and/or RPV drug levels, or co-morbidities that raise concerns for immune reconstitution inflammatory syndrome. While RPV-associated resistance is generally considered a contraindication, exceptions for compassionate use are made on a case-by-case basis for immunosuppressed patients with single RPV-associated mutations demonstrating a prolonged inability to take oral ART. Following the availability of LEN in December 2022, these patients are also considered for the adjunctive use of LEN + CAB/RPV, and initiation of LEN + CAB is considered as a salvage regimen in settings in which a CAB/RPV patient develops RPV resistance with retained CAB susceptibility.

After screening, an in-person visit is conducted during which a provider evaluates the patient's interest in and understanding of expectations regarding LA-ART or LA-PrEP initiation, reviews

risks and contingencies associated with treatment interruptions, and documents contact information for multiple patient associates (i.e., friends, family, case managers, etc.), along with permission to contact them in the event of delayed injections (i.e., >1 day). During this visit, labs are drawn, LA medications are ordered for delivery to MXM from a partnering pharmacy, and the patient is asked to return within 7 days to receive their first loading dose injection. In baseline HIV viremic patients, an HIV RNA viral load and genotype are drawn monthly until viral suppression is reached, after which a viral load is drawn every 3 months (or more frequently in the event of delayed injections). PWH demonstrating sustained virologic suppression for ≥6 months on CAB/RPV dosed every 4 weeks may be considered for a switch to the FDA-approved 8-week dosing interval. For PrEP patients on CAB administered every 8 weeks, an HIV RNA viral load and HIV Ag/Ab are recommended with each injection.

Protocol features aiming to address the unique barriers faced by PEH include exclusive use of a direct-to-inject approach (i.e., without the requirement for an oral medication lead-in or baseline virologic suppression), facilitation of drop-in injection visits and on-site labs at MXM 6-days per week, and enhanced follow-up and tracking support provided by a multidisciplinary team. This team—which has included a physician lead (dedicating approximately 5-10% full-time equivalents [FTE]), a street-based outreach nurse (10-20% FTE), and, variably, one or two health workers and a clinic-based nurse (0-15% FTE each)—meets weekly to individualize care plans, review upcoming injection due dates, and coordinate the provision of reminders to patients and/or their community-based contacts over the preceding week. In the event of delayed injections, street-based outreach is mobilized and multiple modes of contact (i.e., phone, text, email, letter) are used to notify all relevant patient associates. If a CAB/RPV dose is delayed >9

days, an HIV RNA viral load and genotype are drawn at the time of the injection and, if delayed >14 days, re-induction with the loading dose (i.e., CAB 600mg/RPV 900mg) is conducted. For PrEP patients on CAB (600mg every 8 weeks), re-induction with two doses spaced 4 weeks apart is conducted if an injection is delayed >28 days. Due to limited personnel resources, LA-ART and LA-PrEP provision are prioritized among immunosuppressed PWH demonstrating difficulty adhering to oral ART, PrEP candidates with significant HIV risk factors, and/or those routinely frequenting MXM or WPIC satellite clinical sites. To improve access, reduce street-based outreach needs, and support adherence to recommended protocols, the provision of $10 gift cards to incentivize on-time injections and lab draws was initiated in May 2023.

Data Collection & Analysis

Data for patients receiving LA antiretrovirals were extracted from the medical record and an internal tracking log developed by WPIC's multidisciplinary LA antiretrovirals team. This log includes patients' contact information, co-morbidities, injection dates, and, when applicable, HIV RNA viral load, genotype, and CD4 cell count measurements from the time of LA antiretroviral initiation to the present. Descriptive statistics were used to characterize patients who received LA antiretrovirals over the program's initial 24 months, between November 10, 2021-November 9, 2023. This included the median and range numbers of total injections administered and proportions administered late, stratified by LA-ART and LA-PrEP status. Late injections were defined as those administered >37 days following the last injection for PWH on 4-week CAB/RPV dosing and >65 days following the last injection for PWH on 8-week CAB/RPV dosing and PrEP patients on 8-week CAB maintenance dosing. Virologic suppression after initiation of injections was defined as an HIV RNA viral load <30 copies/mL on the

measurement most proximal to database closure. The University of California-San Francisco provided Institutional Review Board exemption to publish findings from this quality improvement project.

Results

Between November 2021-November 2023, 33 patients initiated LA antiretrovirals through WPIC, including 18 PWH who started CAB/RPV (four of whom also received LEN) and 15 PrEP candidates who initiated CAB (Table 1). The median age was 37 years (interquartile range, 31-44), and the cohort included nine (27%) transgender or non-binary persons, six (18%) cisgender women, and 24 (73%) patients of non-White race/ethnicity. At the time of LA initiation, 27 (82%) patients did not have reliable access to a cellphone, nine (27%) were street homeless, 17 (52%) were staying at homeless shelters or other non-permanent residences, and the remaining seven (21%) had been housed within the preceding 6 months. Co-morbid psychiatric diagnoses included opioid use disorder (n=10; 30%), methamphetamine use disorder (n=27; 82%), depression or post-traumatic stress disorder (n=21; 64%), schizophrenia or schizoaffective disorder (n=6; 18%), and bipolar disorder (n=6; 18%). Twelve patients received other long-acting injectable medications (antipsychotics, n=6; estrogen, n=8; testosterone, n=1).

Among the 18 PWH initiated on LA-ART, 14 were viremic at baseline, including eight who had never previously been virally suppressed in the outpatient setting and four with known baseline RPV resistance mutations. Two patients were initiated on CAB/RPV in collaboration with the San Francisco General Hospital HIV Clinic (“Ward 86”) and have earlier data captured in

previously published demonstration projects [14,15]. After a mean of 9.67 months since initiating LA-ART (SD: 8.30; range: 1-24 months), 17 out of 18 (94%) patients achieved or maintained virologic suppression (Figure 1), three of whom transitioned to the 8-week CAB/RPV dosing interval. Among the 172 total doses of CAB/RPV administered over the 24 months, 159 (93%) were administered on-time, with one patient late for four injections, three patients late for two injections, and three patients late for one injection each (Table 2). Six episodes of lateness required re-induction with the loading dose (CAB 600mg/RPV 900mg). One patient was routinely administered injections at a syringe access program, three received injections at their housing units or shelters, and two received one-time administrations while in custody at a local jail. The remaining 136 (79%) LA-ART injections were administered at MXM.

Of the four PWH with baseline RPV resistance, two initiated CAB/RPV alone (one with a V179D and the other with a V108I) and two received CAB/RPV + LEN (one with a V179D and the other with a remote history of Y181C + K101E discovered two months following CAB/RPV initiation, when the patient had already virally suppressed). After delayed receipt of CAB/RPV injections in the context of increased substance use and mental health challenges, both patients initiated on CAB/RPV alone acquired further resistance mutations—one to only RPV and the other to both CAB and RPV—ultimately requiring LA-ART discontinuation within six months of initiation (Table 2, Patients E and G). However, both also experienced substantial improvements in symptoms and CD4 counts following LA-ART initiation (from 18 to 343 cells/mm^3 and 189 to 322 cells/mm^3, respectively), had never previously been virally suppressed as outpatients, and remained unable to adhere to oral ART following CAB/RPV discontinuation. Given continued CAB sensitivity on subsequent HIV RNA genotypes, after 6 months off

CAB/RPV, the first patient was re-inducted onto CAB + LEN, with which his viral load re-suppressed.

Among the 15 patients initiated on LA-PrEP, after a mean of 4.73 months (SD: 2.89; range: 0-11 months), none acquired HIV, 12 remained on CAB, and three discontinued injections. Reasons for discontinuing LA-PrEP included pain from injection site reactions, resolution of risk factors, housing transitions, and/or changes in mental health status. Among the 52 doses of CAB administered in total, 47 (90%) were administered on-time, with one patient late for two injections, three late for one injection each, and one episode of lateness requiring re-induction with two doses of CAB 600mg dosed one month apart (Table 3). Six patients experienced delays >7 days between their initial lab draw and first injection, requiring labs to be re-drawn on the day of treatment initiation, and CAB was prescribed to five additional patients who expressed interest in LA-PrEP yet did not return to initiate injections for ≥3 months. Seven LA-PrEP patients were routinely administered injections by a street outreach or shelter health nurse at their respective residences, including two in tents, three at a homeless shelter, and two within housing units, and one patient received a single injection while in jail custody. The remaining 27 (52%) LA-PrEP injections were administered on-site at MXM.

Conclusion

The implementation of LA antiretrovirals for the treatment and prevention of HIV was feasible in the context of a low-barrier, municipal public health clinic designated to serve homeless and unstably housed patients with a high burden of co-morbid substance use and severe mental

illness. While this pilot program represents a small cohort over only a 24-month period, the rate of sustained virologic suppression observed among PWH initiated on LA-ART was high (94%), despite the majority having baseline viremia, and all LA-PrEP patients remained HIV free over the study period. Moreover, the substantial representation of populations underserved in traditional primary care settings—including dual-diagnosed, transgender, Black, and Hispanic patients, in addition to eight PWH who had never previously been virally suppressed as outpatients—supports findings from qualitative studies suggesting the unique potential of LA antiretrovirals in addressing barriers to HIV- and PrEP-related care [19,20].

The program described here operated with limited direct personnel support—between 0-20% FTE from a lead physician, outreach nurse, and, variably, a clinic-based nurse and one or two health workers. However, implementation of LA antiretrovirals was also supported through endorsement by MXM's full medical and nursing provider teams to learn and execute protocols. In addition, this program necessarily involved the expansion of injection delivery into community-based settings—including a local jail, tent encampments, homeless shelters, housing units, and syringe access programs—for 14 (42%) patients. As a result, the support of providers from these sites and the availability of a street-based outreach nurse skilled in locating patients, administering injections, and obtaining labs in the field was critical. While this level of staffing was sufficient for maintaining oversight over a relatively small cohort of patients, the program's sustainability and opportunities for expansion would be enhanced by increased availability of dedicated personnel, back-up support in the event of provider absences, and, ideally, full-time patient navigators to support complex patients with the initiation and continuation of LA-ART or LA-PrEP. Clinics serving PEH should thus consider instituting capacity limits on the total

number of patients initiated on LA antiretrovirals dependent on the availability of personnel to support mobile outreach. The development of robust partnerships with case management programs may also mitigate the need for intensive outreach by clinical personnel. While providing mobile phones to patients to support outreach could also be considered, text-messaging interventions have failed to demonstrate efficacy in improving visit adherence or rates of HIV viral suppression in prior studies, in part due to high cellphone turnover among PEH [22]. Future implementation studies investigating patient-centered approaches to support communication with PEH may improve care retention in this population.

Programs may also consider the initial roll out of LA-PrEP prior to LA-ART medications, as the relative risks associated with interrupted or delayed LA-PrEP injections are lower. Unlike CAB/RPV, CAB as LA-PrEP can also more flexibly be administered in mobile treatment settings due to a lack of refrigeration requirement. Of note, in the current analysis, 25 (48%) LA-PrEP vs. 36 (21%) LA-ART injections were administered at locations outside of clinic. However, seronegative PEH interested in and able to initiate LA-PrEP may represent a more psychosocially stable patient population than homeless PWH interested in LA-ART. Such a discrepancy in degrees of vulnerability was likely reflected in the current cohort given that only one LA-PrEP vs. six LA-ART injections were delayed by >14 days (Tables 2 & 3).

The experiences of two patients who acquired extensive resistance to RPV and/or CAB due to treatment interruptions demonstrate the inherent risks involved in providing LA-ART to PEH who face significant psychosocial distress, underscoring the limitations of CAB/RPV as well as needs for improved structural supports and mental health treatments for this population. These

incidents have resulted in tightening of the clinic's protocols, including requirements for increased clinical engagement prior to LA-ART initiation, considerations for adjunctive LEN + CAB/RPV, and further limitations to permissible baseline resistance mutations in contexts of compassionate use. Nonetheless, the substantial improvements in immunosuppression and persistent difficulties in oral ART adherence experienced by both patients, even with intensive case management support, raises ethical questions with respect to limiting the use of LA-ART among highly vulnerable populations. For one of these patients, we suspect that resolution of severe AIDS symptoms following CAB/RPV initiation promoted increased subsequent interest in clinical engagement, ultimately allowing for re-induction onto CAB + LEN, with which his HIV viral load re-suppressed. However, this combination of antiretrovirals notably requires further study.

The high frequency of lab monitoring required for patients on CAB/RPV and CAB was also a challenge for many patients, several of whom have difficulties with blood draws due to histories of injection drug use. On some occasions, if a patient found the protocolized frequency of blood draws untenable, on-time administration of LA antiretrovirals was prioritized without labs if HIV RNA viral loads were obtained at a minimum of 6-month intervals. Our experience suggests that LA-PrEP uptake could be improved by reducing the recommended frequency of lab draws to every other injection (i.e., every 4 months). In addition, six out of 15 LA-PrEP patients experienced a >7-day lag between their initial lab draw and first dose, and another five patients never returned to initiate injections, suggesting that facilitation of same-day LA-PrEP starts through the use of point-of-care fingerstick HIV testing and an on-site stock supply of CAB could reduce unprotected periods. The use of small monetary incentives for on-time injections

and lab draws may also mitigate these challenges. Early data following implementation of incentives at MXM in May 2023 indicate a pre-post reduction in delayed injections (11% vs. 6%). However, these differences should be interpreted with caution, as data are based on small numbers and several temporal factors may contribute.

Importantly, most patients were insured through a Medicaid program that fully covers the costs of CAB/RPV, CAB, and LEN, which may not be true in other geographic locations. This pilot initiative was also supported through partnership with a local pharmacy that supplied all LA antiretrovirals, allowing for streamlined communication regarding medication orders, deliveries, and clinic inventory. However, a clinic-based pharmacy technician to oversee medication procurement would be invaluable in facilitating program expansion.

In summary, the implementation of LA antiretrovirals was successful in addressing barriers to oral ART and PrEP use among particularly vulnerable PEH and unstably housed patients. While significant personnel resources and multidisciplinary support are crucial to the operation of this program and longer-term studies are necessary, findings from this pilot evaluation are promising. If effective scale-up is possible, HIV disparities may be markedly reduced, which will be critical in progressing toward national goals to End the HIV Epidemic.

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Figure 1. HIV-1 RNA viral load measurements of patients initiated on Long-Acting (LA) Cabotegravir/Rilpivirine (CAB/RPV), San Francisco Department of Public Health Whole Person Integrated Care, n = 18 (November 2021-November 2023)

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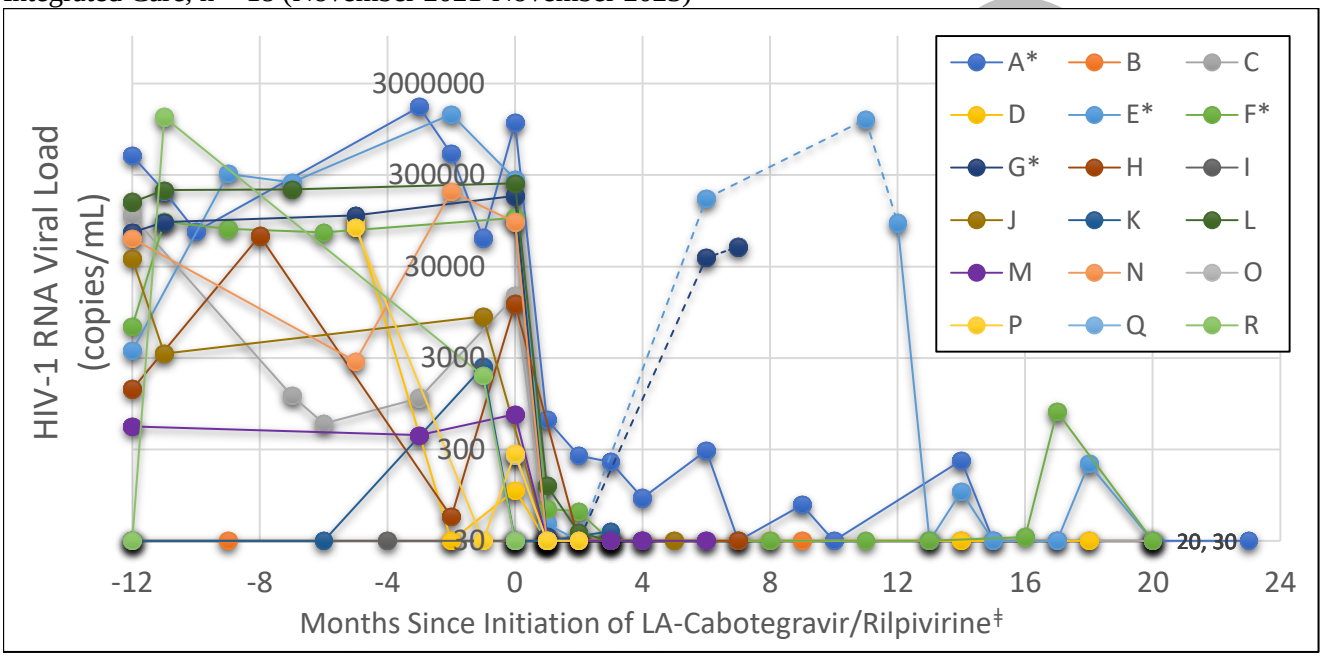

* *Patients A, E, F, and G experienced viremia following CAB/RPV initiation, which was related to delayed receipt of injections and/or treatment interruptions (Table 2).*

‡ *For each patient, HIV-1 RNA viral load values depicted at 12 months prior to CAB/RPV initiation represent those available most proximally from the electronic medical record within 12-24 months prior to CAB/RPV initiation.*

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Table 1. Characteristics of patients initiated on Long-Acting (LA) Antiretrovirals (ARVs), San Francisco Department of Public Health Whole Person Integrated Care, N = 33 (November 2021-November 2023)

Patient Characteristics	n	[%]
LA ARV(s) Received		
Intramuscular cabotegravir/rilpivirine (ART)	18	[55%]
Subcutaneous lenacapavir (ART)*	4	[12%]
Intramuscular cabotegravir (PrEP)	15	[45%]
Age (years)		
≤ 24	2	[6%]
25-34	12	[36%]
35-49	16	[48%]
≥ 50	3	[9%]
Gender		
Cisgender man	18	[55%]
Cisgender woman	6	[18%]
Non-binary	1	[3%]
Transgender woman	8	[24%]
Race/Ethnicity		
Black	15	[45%]
Hispanic	7	[21%]
White (non-Hispanic)	9	[27%]
Multiracial/other	10	[30%]

Housing Status (at time of LA ARV initiation)		
Street homeless	9	[27%]
Sheltered homeless	17	[52%]
Unstably housed (i.e., housed < 6 months)	7	[21%]
Access to Cellular Phone		
None	19	[58%]
Sometimes or intermittently	8	[24%]
Always or usually	6	[18%]
HIV Transmission Risk Factor(s)		
MSM or transgender/nonbinary	22	[67%]
Injection drug use history	20	[61%]
Sex work or partner known to have HIV	12	[36%]
Substance Use or Mental Health Condition(s)		
Methamphetamine use disorder	27	[82%]
Opioid use disorder	10	[30%]
Depression or post-traumatic stress disorder	21	[64%]
Schizophrenia or schizoaffective disorder	6	[18%]
Bipolar disorder	6	[18%]
Baseline HIV Labs (LA-ART patients, n = 18)		
CD4 count < 200 cells/mm^3	6	[33%]
HIV viral load > 30 copies/mL	14	[78%]

** Two patients initiated lenacapavir (LEN) + cabotegravir/rilpivirine (CAB/RPV) due to baseline RPV resistance; a third initiated LEN + CAB after developing confirmed virologic*

failure to RPV on CAB/RPV; and a fourth initiated LEN adjunctively after developing low-level viremia on CAB/RPV.

Table 2. Clinical outcomes following delayed receipt of Long-Acting Cabotegravir/Rilpivirine (CAB/RPV) injections for HIV treatment, San Francisco Department of Public Health Whole Person Integrated Care (November 2021-November 2023)

Patient ID	Injection Number	Days Delayed ǂ	Developed HIV-1 RNA Viremia? ¥	Clinical Outcome(s)
A	7th 10th 11th 15th	18* 14 15* 10	No Low-level No Low-level	• No genotypic evidence of RPV or CAB resistance • CAB/RPV continued
B	10th	14	No	• CAB/RPV continued
C	8th	17*	No	• CAB/RPV continued
E	5th 13th	83* 14	Yes Low-level	• Resistance to RPV (V179D, M230, Y181C) • CAB/RPV discontinued after 5th injection • Started on CAB + lenacapavir (LEN) at 12 months
F	14th 18th	13 14	No Low-level	• No genotypic evidence of RPV or CAB resistance • CAB/RPV continued with LEN added adjunctively
G	3rd 5th	10 19*	No Yes	• Resistance to RPV and CAB (V108I, K101K, K103R, E138K, Y181C, E138K,

				G140S, Q148R) • CAB/RPV discontinued
I	2nd	15*	No	• CAB/RPV continued

ǂ *Number of days delayed are based on a 28-day injection cycle for CAB/RPV maintenance dosing.*

¥ *"Yes" to HIV-1 RNA viremia indicates a viral load ≥1000 copies at the time of the delayed injection, while "Low-level viremia" indicates a viral load between 30-1000 copies and "No" indicates a viral load that is undetectable or <30 copies.*

* *Delay required re-induction with the loading dose (CAB 600mg/RPV 900mg).*

Table 3. Clinical outcomes following delayed receipt of Long-Acting Cabotegravir (CAB) injections for HIV pre-exposure prophylaxis, San Francisco Department of Public Health Whole Person Integrated Care (November 2021-November 2023)

Patient ID	Injection Number	Days Delayed ǂ	Developed HIV-1 RNA Viremia?	Clinical Outcome(s)
U	5th	52*	No	• CAB continued
V	2nd	11	No	• CAB continued
	4th	12	No	
W	4th	13	No	• CAB continued
AB	3rd	13	No	• CAB continued

ǂ *Number of days delayed are based on a 56-day injection cycle for CAB maintenance dosing.*

23. * *Delay required re-induction with the loading dose (two doses of CAB 600mg one month apart).*