First Demonstration Project of Long-Acting Injectable Antiretroviral Therapy for Persons With and Without Detectable HIV Viremia in an Urban HIV Clinic

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Running Head: LAI-ART in an Urban HIV Clinic

ABSTRACT

Background: Long-acting injectable antiretroviral therapy (LAI-ART) is approved for treatment-naïve or experienced people living with HIV (PLWH) based on trials that only included participants with viral suppression. We performed the first LAI-ART demonstration project to include PLWH unable to achieve or maintain viral suppression due to challenges adhering to oral ART.

Methods: Ward 86 is a large HIV clinic in San Francisco that serves publicly insured or underinsured patients. We started patients on LAI-ART via a structured process of provider referral, multidisciplinary review (MD, RN, pharmacist), and monitoring for on-time injections. Inclusion criteria were willingness to receive monthly injections and a reliable contact method. Descriptive statistics evaluated program outcomes.

Results: Between June 2021-April 2022, 51 patients initiated LAI-ART, with 39 receiving at least two follow-up injections by database closure (median age 46; 90% cisgender men, 61% non-White, 41% marginally housed, 54% currently using stimulants). Of 24 patients initiating injections with viral suppression (median CD4 706), 100% (95% CI 86-100%) maintained viral suppression. Of 15 patients initiating injections with detectable viremia (median CD4 99, mean log10 viral load 4.67 SD 1.16), 12 (80%; 95% CI 55-93%) achieved viral suppression and the other 3 had a 2-log viral load decline by a median of 22 days.

Conclusions: This small demonstration project of LAI-ART in a diverse group of patients with high levels of substance use and marginal housing demonstrated promising early treatment outcomes, including in those with detectable viremia due to adherence challenges. More data on LAI-ART in hard-to-reach populations are needed.

Keywords: HIV/AIDS, long-acting antiretroviral therapy, injectable cabotegravir and rilpivirine, viral suppression, engagement in care

Introduction

Treatment for HIV benefits people living with HIV (PLWH)[1-4] and eliminates onward transmission,[5] both crucial to the visionary goal of "Ending the HIV Epidemic (EHE)."[6] Despite advances in the tolerability and efficacy of oral antiretroviral therapy (ART),[7,8] the Centers for Disease Control and Prevention (CDC) estimates that only ~60% of those with diagnosed HIV achieve sustained viral suppression.[9] Disparities in viral suppression exist by lower income, younger age, Black race, Hispanic ethnicity, mental illness, and substance use.[10-12] Structural and societal drivers of these disparities include lack of access to care,[13] inability to meet subsistence needs,[14] homelessness and unstable housing,[15] HIV-related stigma,[16] language barriers,[17] medical mistrust,[18,19] and structural racism.[20]

In an HIV treatment landscape where the benefits of ART are experienced unevenly due to these challenges, an exciting recent development is the advent of long-acting antiretroviral therapy (LA-ART). Due to its extended dosing interval, long-acting ART (LA-ART) has the potential to mitigate many barriers to daily oral ART adherence, including pill fatigue, pills as a reminder of living with HIV, fear of inadvertent disclosure from possessing pills, not having a place to store pills safely, and inability to sustain a routine around daily pill-taking.[21,22] In January 2021, the Federal Drug Administration (FDA) approved a combination of two injectable antiretroviral medications, cabotegravir (CAB) and rilpivirine (RPV), given every four weeks, subsequently approving the option of an eight-week dosing interval in February 2022 and removing the requirement for an oral CAB/RPV lead-in in March 2022. Of note, since the clinical trials[23-25] forming the basis for regulatory approval enrolled only virally suppressed participants, the FDA has approved the medication only for those with viral suppression.

As the real-world rollout of long-acting injectable CAB/RPV (CAB/RPV-LA) begins, approaches that enable its use in PLWH with challenges adhering to oral ART are of paramount importance, given the potential for individual and public health benefit. While CAB/RPV-LA provides an additional treatment option for those stably suppressed on oral ART as studied in clinical trials, it also offers the opportunity to treat PLWH unable to take a daily oral regimen to achieve or maintain viral suppression. We describe a patient-centered CAB/RPV-LA care delivery program in an academic HIV clinic serving

urban PLWH with high levels of psychosocial and economic vulnerability and present early clinical outcome data of this demonstration project.

Study Setting and Population

Ward 86 is one of the oldest HIV clinics in the United States and the safety-net HIV clinic for the city and county of San Francisco. The clinic serves over 2,400 PLWH ≥18 years of age (85% cisgender men, 13% cisgender women, 2% transgender women and men, 21% Black, 27% Hispanic) who have government insurance (i.e., Medicaid, Medicare) or are covered through a municipal program for uninsured San Francisco residents. The clinic-wide viral suppression rate is ~84%[26] and prior analyses have shown that ~10% of patients have chronic viremia.[27] Patients without viral suppression at Ward 86 have high rates of stimulant use, mental illness, and marginal housing.[15,28,29] In 2019, the clinic developed a comprehensive multidisciplinary drop-in primary care model called POP-UP to better meet the needs of chronically virally non-suppressed patients with marginal housing who struggle to engage in traditional HIV care, which resulted in an increase in viral suppression from 0% to 55% for those enrolled.[30]

Description of the Ward 86 Long-Acting Injectable ART Program

We developed a program to support patients and providers to initiate CAB/RPV-LA and to promote patient adherence to injections. Patients with or without viral suppression are allowed to enter the program. Key considerations for CAB/RPV-LA are willingness to receive two gluteal injections at each visit, attend regularly scheduled injection appointments, and resume oral ART if CAB/RPV-LA is interrupted, as well as providing a reliable form of communication (e.g. phone, text, MyChart) and an additional method of contact (e.g. friend, family member, case manager). Patients with any history of rilpivirine-associated resistance mutations are not considered for CAB/RPV-LA,[31] however, the program allows ≤1 integrase strand transfer inhibitor (INSTI) mutation.[23-25,32] The program also allows patients with hepatitis B infection if they are willing to continue or initiate hepatitis B directed treatment. Patients on medications known to decrease drug levels of CAB/RPV-LA[33] are not placed on injections.

Providers at Ward 86 received education on CAB/RPV-LA, the process of referral, and feedback on outcomes of CAB/RPV-LA in the clinic at regular provider meetings. A detailed clinic protocol provides additional guidance on referral considerations. Providers refer patients to the pharmacy team for consideration of CAB/RPV-LA via a structured electronic medical record (EMR) template. The clinic pharmacist reviews referrals for resistance mutations to INSTIs and non-nucleoside reverse transcriptase inhibitors (NNRTIs), drug-drug interactions, and hepatitis B status (to ensure maintenance/initiation of treatment for chronic hepatitis B). Patients recommended for CAB/RPV-LA are then scheduled for a pharmacist visit that includes education and counseling on the efficacy of therapy, potential side effects, including local injection site reactions, and the risks of interrupting regular injections. Patients are asked to agree to take fully active oral ART in case of interruption until injections can be resumed. A pharmacy technician oversees the process of insurance authorization and procurement of medications.

Our protocol favors a direct-to-inject (no oral lead-in) approach as approved by the FDA,[34] regardless of viral suppression status. The direct-to-inject (DTI) option removes the barrier of needing to adhere to oral ART for an additional month for those with adherence challenges as well as any obstacles related to taking oral rilpivirine with food or without gastric acid-reducing medications. Patients without viral suppression have individualized plans for injection adherence, including identification of community-based supports, e.g. case managers, home and street-based nursing services, community-based injection sites (including harm reduction sites), and receipt of small financial incentives (drawn from Ryan White or city-provided funds for adherence support) for visits or blood draws. All referred and active patients are reviewed in a biweekly multidisciplinary (i.e., physician, nursing, pharmacy) case conference, with additional discussion of POP-UP patients in a weekly POP-UP case conference.

After the first injection visit, the pharmacy team conducts a follow-up telephone visit within seven days to ensure tolerability. Injection appointment reminders and missed appointment follow-up calls/texts are performed by the pharmacy technician, who is bilingual in English and Spanish. For patients who start without viral suppression, an HIV viral load is repeated every 4 weeks until it is below the lower limit of detection for our laboratory's assay (<30 copies/mL), with resistance testing performed

at the second injection visit if the viral load remains detectable. Consideration of the FDA-approved 8-week dosing interval requires demonstration of sustained viral suppression for six months with every 4-week dosing based on data from the ATLAS 2-M study,[35,36] which found that confirmed virologic failure (CVF) occurred most commonly early in the 8-week arm (7/8 participants with CVF failed in the first 24 weeks).

If a patient plans to miss a scheduled injection by more than 7 days, patients are counseled to restart oral ART until injections are resumed; they are advised to keep one month of their prior oral ART regimen on hand for this purpose. In the event of an unplanned missed injection, the pharmacy technician immediately attempts to contact the patient (and if not reachable, their listed contacts). If repeated attempts using different modes of contact, i.e., phone, text, or letter, are unsuccessful, clinic staff pursue in-person outreach. If an injection is delayed by ten days or more, bloodwork for resistance testing is obtained in addition to viral load testing. Although modeling of CAB/RPV-LA pharmacokinetics suggests that an interval of 60 days is sufficient to continue the maintenance dose (CAB 400mg/RPV 600mg) after a missed visit,[37,38] we favor a more conservative approach and allow a shorter interval of 42 days (28 days plus up to 14 days late), after which time the initiation dose (CAB 600mg/RPV 900mg) is given.

Data Collection and Analysis

Data were extracted from pharmacy team logs and the medical record. Providers reported housing status and stimulant use (methamphetamines, cocaine) at the time of referral. Descriptive statistics were used to characterize patients who had initiated CAB/RPV-LA by February 10, 2022, and thus were expected to have at least two scheduled follow-up injections by the time of database closure (April 15, 2022). We present the median and range number of injections received by these patients and viral suppression outcomes, stratified by viral suppression status at the time of CAB/RPV-LA initiation. We calculated 95% confidence intervals (CI) for proportions using the modified Wilson method.[39] For patients initiating CAB/RPV-LA without viral suppression, we display viral load measurements over time. All patients described in this analytic sample were on q4 week dosing and had at least one viral load

measurement after initiating CAB/RPV-LA. On-time injections were defined as injections given 28 days +/- 7 days from the initial injection. Viral suppression after initiating injections was defined as viral load <30 copies/mL on the measurement most proximal to database closure. This study was approved by the University of California San Francisco Institutional Review Board under protocol number 20-3100.

Results

Between February 1, 2021, and April 15, 2022, providers referred 132 patients, of whom 51 were started on injections. Reasons for not starting included: referral in process (n=35), on hold due to patient or provider preference (n=24), awaiting initial injection (n=13), ineligible due to rilpivirine-associated resistance mutations (n=5), subsequently declined (n=2), and transferred care (n=2). Of 51 patients receiving injections between June 2021-April 2022, our analytic sample with at least two follow-up injections consisted of 39 patients (Table 1). Median age was 46 years (IQR 39-55 years); there were 3 cisgender women and one transgender woman and 24 (61%) had non-White race/ethnicity, 16 (41%) were experiencing unstable housing or homelessness, and 20 (54%) endorsed current stimulant use. Three patients were monolingual Spanish speakers. One patient had a N155H resistance mutation at baseline. Five patients were receiving other long-acting injections (antipsychotics n=4, naltrexone n=1).

Of 24 patients initiating CAB/RPV-LA with viral suppression (median CD4 cell count 706 cells/mm^3), 19 (79%) direct-to-inject, with median 6 injections (range 2-8 injections), 100% (95% CI -86-100%) maintained viral suppression after starting injections. One patient successfully transferred care to another clinic and another patient had unplanned travel to his home country but took oral therapy in the interim and was found to have viral suppression when he returned 83 days after his last injection. Of 15 patients starting with detectable viremia, (median CD4 cell count 99 cells/mm^3, mean log10 viral load 4.67 SD 1.16), all direct-to-inject, with median 6 injections (range 3-11 injections), 12 (80%; 95% CI 55-93%) have achieved and maintained viral suppression, including the patient with the baseline N155H mutation. For the 3 patients who have not yet achieved viral suppression, all had a 2-log decline by a median of 22 days (Figure 1). No patient decided to discontinue CAB/RPV-LA due to side effects. In

general, injection site reactions were mild to moderate; one patient developed cellulitis at the injection site and received oral antibiotics. No cases of hepatitis B viremia were observed with discontinuation of tenofovir/emtricitabine containing regimens, although we did not systematically measure hepatitis B DNA levels in our cohort.

Thirty-four patients (87%; 95% CI 73-94%) had on-time injection attendance, with one patient late for one injection and two patients late for two injections each. Two episodes of lateness required re-induction with CAB600mg/RPV 900mg dosing. All of these patients were documented to have viral suppression after the delayed visits. At the time of database closure, one additional patient was 7 days late for his injection and had not yet presented to the clinic; this patient had viral suppression at his last injection. Two patients in our cohort experiencing homelessness received injections in community locations (a harm reduction mobile van and a community clinic) in collaboration with street-based nursing services.

Discussion

This study describes the first demonstration project to our knowledge to use CBV/RPV-LA in patients with challenges adhering to oral ART. Our data demonstrate preliminary short-term effectiveness of using every 4-week CAB/RPV-LA in patients with and without viral suppression in a diverse urban clinic serving publicly insured patients with high levels of marginal housing and stimulant use. Consistent with clinical trial populations, those who initiated injections with viral suppression maintained suppression. A more striking finding is that those who began injections with detectable viremia successfully achieved viral suppression or had a two-log decline in viral load within a month of their first injection. Two of these patients, who had been living with HIV for over ten years, had never previously been virally suppressed, including the patient with the baseline N155H mutation, who has now demonstrated >8 months of viral suppression. The program allowed this patient to enroll because clinical trial participants on every 4-week dosing who developed CVF failed with rilpivirine in addition to INSTI mutations, rather than a single INSTI mutation alone. Achieving viral suppression in those who have

never been suppressed spotlights the key role LA-ART can play in benefitting those with challenges adhering to oral ART.

We note that the majority of patients in our cohort were from priority populations in EHE efforts i.e. Black, Hispanic (including monolingual Spanish-speaking PLWH), and those currently using stimulants, highlighting the potential of CAB/RPV-LA to reach groups of interest. However, we had no patients under age 30 and only a small number of women among these early adopters of CAB/RPV-LA, illuminating the need for exploration of awareness and preferences in these groups. Importantly, a small subset of patients in our program were receiving other long-acting injections, i.e., anti-psychotics, highlighting the promise of leveraging attendance at other injections to deliver CAB/RPV-LA in those with psychiatric conditions. Nearly all injections were "on-time," and no patient had viral rebound after a late injection. In-person outreach was deployed twice for patients with unplanned missed injections. The case of the patient who went to his home country emphasizes the importance of a supply of oral ART in the event of an unplanned missed injection. No patients discontinued injections due to injection site reactions. While patients were willing to regularly attend injection appointments, some had difficulty with the recommended lab monitoring schedule. Small incentives, e.g. $10 grocery store vouchers, are one strategy to encourage blood draws that our program has utilized with success.

We acknowledge several program features as facilitators of implementation. At the provider level, centralization of insurance authorization, injection initiation, and injection visit monitoring in the pharmacy team have encouraged provider referrals. At the patient level, availability of a direct-to-inject strategy removed a significant obstacle for those patients who already had demonstrated challenges to adherence. The importance of minimizing the need for adherence to oral ART prior to initiation of injections is reflected in changes made to the protocol of the ongoing AIDS Clinical Trial Group 5359 LATITUDE study in order to increase enrollment of PLWH with adherence challenges, shortening the required period on oral ART from 24 to 12 weeks and allowing a direct-to-inject option for those achieving viral suppression. In addition, allowing patients to drop-in at Ward 86 on a designated injection day with flexibility on the exact time has supported retention for difficult-to-engage patients. A bilingual

pharmacy technician facilitates communication with monolingual Spanish-speaking patients. Finally, partnering with community programs to deliver injections in the field has enabled the offer of injections to some of the highest-risk patients in the clinic POP-UP program, which serves PLWH experiencing homelessness or marginal housing who require low-barrier care. For example, one POP-UP patient with detectable viremia at baseline received injections and most viral load monitoring at a mobile harm reduction van in partnership with street-based nursing staff from the San Francisco Department of Public Health. Building on these partnerships to increase access to CAB/RPV-LA is essential to reach PLWH unable to achieve viral suppression on oral ART due to homelessness, substance use, or severe mental illness.

At the policy level, an important feature of the local context that has facilitated CAB/RPV-LA initiation is that all of the patients in our safety-net clinic had government-based insurance or benefits, which in California saw rapid availability of CAB/RPV-LA on formularies (May 2021 for Medicaid and October 2021 for the AIDS Drug Assistance Program) with relatively streamlined processes for acquiring the drugs. Prior authorization processes for commercial insurance can be more challenging.[40] Of these government-based programs, only Medicare has had co-pays, which for most patients were covered by ADAP. The pharmacy technician refers patients whose income is too high to qualify for ADAP to private foundations for co-pay coverage. CAB/RPV-LA is billed as pharmacy rather than a medical benefit, which facilitates community-based injections rather than requiring administration in a health care facility.

Limitations of our analysis are that it evaluates a small cohort of patients at a single clinical site during the first year of the CAB/RPV-LA rollout. In addition, early adopters of CAB/RPV-LA may be among the most highly motivated PLWH to uptake and persist with injections and as such may not be representative of those who initiate CAB/RPV-LA at later points in time. Our findings may not be transferable to rural areas or jurisdictions with different insurance formulary requirements. Nevertheless, we believe our experience provides important knowledge about the use of CAB/RPV-LA outside of clinical trial settings.

In summary, this small demonstration project found that patients with detectable viremia due to challenges adhering to oral ART can be successfully started on CAB/RPV-LA. Our data show early success in suppressing this group of patients on CAB/RPV-LA and in keeping patients with viral suppression suppressed. A longer period of follow-up and a larger cohort, along with other demonstration projects examining the use of CAB/RPV-LA in hard-to-reach populations and qualitative assessments of acceptability, are needed.

NOTES

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Potential Conflicts of Interest Dr. Christopoulos has received investigator-initiated research support from Gilead Sciences and has been a medical advisory board member for Gilead Sciences. Dr. Imbert reports personal fees from WebMD. Dr. Havlir has received non-financial support from Gilead Sciences and Abbott Diagnostics. All other authors report no potential conflicts of interest.

REFERENCES

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed on May 4, 2022.
2. Group ISS, Lundgren JD, Babiker AG, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *N Engl J Med.* 2015;373(9):795-807.
3. Strategies for Management of Antiretroviral Therapy Study G, El-Sadr WM, Lundgren J, et al. CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med.* 2006;355(22):2283-2296.
4. Strategies for Management of Antiretroviral Therapy Study G, Lundgren JD, Babiker A, et al. Inferior clinical outcome of the CD4+ cell count-guided antiretroviral treatment interruption strategy in the SMART study: role of CD4+ Cell counts and HIV RNA levels during follow-up. *J Infect Dis.* 2008;197(8):1145-1155.
5. Eisinger RW, Dieffenbach CW, Fauci AS. HIV Viral Load and Transmissibility of HIV Infection: Undetectable Equals Untransmittable. *JAMA.* 2019;321(5):451-452.
6. Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. Ending the HIV Epidemic: A Plan for the United States. *JAMA.* 2019;321(9):844-845.
7. Cihlar T, Fordyce M. Current status and prospects of HIV treatment. *Current Opinion in Virology.* 2016;18:50-56.
8. Gandhi M, Gandhi RT. Single-Pill Combination Regimens for Treatment of HIV-1 Infection. *New England Journal of Medicine.* 2014;371(3):248-259.
9. Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2018 Cycle (June 2018–May 2019). HIV Surveillance Special Report 25. https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published May 2020. Accessed May 18, 2022.
10. Beer L, Bradley H, Mattson CL, et al. Trends in Racial and Ethnic Disparities in Antiretroviral Therapy Prescription and Viral Suppression in the United States, 2009-2013. *J Acquir Immune Defic Syndr.* 2016;73(4):446-453.
11. Lesko CR, Hutton HE, Fojo AT, Shen NM, Moore RD, Chander G. Depression and HIV viral nonsuppression among people engaged in HIV care in an urban clinic, 2014-2019. *Aids.* 2021;35(12):2017-2024.
12. Wohl AR, Benbow N, Tejero J, et al. Antiretroviral Prescription and Viral Suppression in a Representative Sample of HIV-Infected Persons in Care in 4 Large Metropolitan Areas of the United States, Medical Monitoring Project, 2011-2013. *J Acquir Immune Defic Syndr.* 2017;76(2):158-170.
13. Menza TW, Hixson LK, Lipira L, Drach L. Social Determinants of Health and Care Outcomes Among People With HIV in the United States. *Open Forum Infect Dis.* 2021;8(7):ofab330.
14. Dandachi D, May SB, Davila JA, et al. The Association of Unmet Needs With Subsequent Retention in Care and HIV Suppression Among Hospitalized Patients With HIV Who Are Out of Care. *J Acquir Immune Defic Syndr.* 2019;80(1):64-72.
15. Clemenzi-Allen A, Geng E, Christopoulos K, et al. Degree of Housing Instability Shows Independent "Dose-Response" With Virologic Suppression Rates Among People Living With Human Immunodeficiency Virus. *Open Forum Infect Dis.* 2018;5(3):ofy035.

16. Christopoulos KA, Neilands TB, Dilworth S, et al. Internalized HIV stigma predicts subsequent viremia in US HIV patients through depressive symptoms and antiretroviral therapy adherence. *AIDS.* 2020;34(11):1665-1671.
17. Rajabiun S, Rumptz MH, Felizzola J, et al. The impact of acculturation on Latinos' perceived barriers to HIV primary care. *Ethn Dis.* 2008;18(4):403-408.
18. Dale SK, Bogart LM, Wagner GJ, Galvan FH, Klein DJ. Medical mistrust is related to lower longitudinal medication adherence among African-American males with HIV. *J Health Psychol.* 2016;21(7):1311-1321.
19. Duthely LM, Sanchez-Covarrubias AP, Prabhakar V, et al. Medical Mistrust and Adherence to Care Among a Heterogeneous Cohort of Women Living with HIV, Followed in a Large, U.S. Safety Net Clinic. *Health equity.* 2021;5(1):681-687.
20. Doshi RK, Bowleg L, Blankenship KM. Tying Structural Racism to Human Immunodeficiency Virus Viral Suppression. *Clin Infect Dis.* 2021;72(10):e646-e648.
21. Scarsi KK, Swindells S. The Promise of Improved Adherence With Long-Acting Antiretroviral Therapy: What Are the Data? *J Int Assoc Provid AIDS Care.* 2021;20:23259582211009011.
22. Kanazawa JT, Saberi P, Sauceda JA, Dubé K. The LAIs Are Coming! Implementation Science Considerations for Long-Acting Injectable Antiretroviral Therapy in the United States: A Scoping Review. *AIDS Res Hum Retroviruses.* 2021;37(2):75-88.
23. Orkin C, Arasteh K, Gorgolas Hernandez-Mora M, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection. *N Engl J Med.* 2020;382(12):1124-1135.
24. Swindells S, Andrade-Villanueva JF, Richmond GJ, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression. *N Engl J Med.* 2020;382(12):1112-1123.
25. Overton ET, Richmond G, Rizzardini G, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. *The Lancet.* 2020;396(10267):1994-2005.
26. Spinelli MA, Le Tourneau N, Glidden DV, et al. Impact of Multi-Component Support Strategies on HIV Virologic Suppression Rates during COVID-19: An Interrupted Time Series Analysis. *Clin Infect Dis.* 2022.
27. Christopoulos KA, Hartogensis W, Glidden DV, Pilcher CD, Gandhi M, Geng EH. The Lorenz curve: a novel method for understanding viral load distribution at the population level. *AIDS.* 2017;31(2):309-310.
28. Hickey MD, Imbert E, Glidden DV, et al. Viral suppression during COVID-19 among people with HIV experiencing homelessness in a low-barrier clinic-based program. *AIDS.* 2021;35(3):517-519.
29. Christopoulos KA, Riley ED, Carrico AW, et al. A Randomized Controlled Trial of a Text Messaging Intervention to Promote Virologic Suppression and Retention in Care in an Urban Safety-Net HIV Clinic: The Connect4Care (C4C) Trial. *Clin Infect Dis.* 2018.
30. Imbert E, Hickey MD, Clemenzi-Allen A, et al. Evaluation of the POP-UP programme: a multicomponent model of care for people living with HIV with homelessness or unstable housing. *AIDS.* 2021;35(8):1241-1246.
31. 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(9):1333-1342.
32. Rizzardini G, Overton ET, Orkin C, et al. Long-Acting Injectable Cabotegravir + Rilpivirine for HIV Maintenance Therapy: Week 48 Pooled Analysis of Phase 3 ATLAS and FLAIR Trials. *J Acquir Immune Defic Syndr.* 2020;85(4):498-506.
33. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf.

34. 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(11):e668-e678.
35. Overton ET, Richmond G, Rizzardini G, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. *Lancet.* 2021;396(10267):1994-2005.
36. 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(11):e679-e689.
37. Roseenu S, Neyens M, Van Solingen-Ristea R, et. al. Population PK Modeling of Every 2 Months IM RPV LA For Managing Dosing Interruptions in HIV-1 Patients. Abstract 1189, Conference on Retroviruses and Opportunitistic Infections, Boston USA, March 6-10, 2021. .
38. Han K, Baker M, Spreen W, et. al. Cabotegravir Population Pharmacokinetic (PPK) Simulation to Inform Q2M Strategies Following Dosing Interruptions. Abstract 1327, Conference on Retroviruses and Opportunistic Infections, Boston USA, March 6-10, 2021. .
39. Brown L.D., Cai T.T. and Dasgupta A. (2001) Interval estimation for a binomial proportion Statistical Science, 16(2), pp. 101-133.
40. Collins LF, Corbin-Johnson D, Asrat M, et al. 887. Implementation of Long-acting Injectable Cabotegravir/Rilpivirine for HIV-1 Treatment at a Ryan White-funded Clinic in the U.S. South. *Open Forum Infectious Diseases.* 2021;8(Supplement_1):S535-S535.

Table 1. Characteristics of Patients Initiating Long-Acting Injectable Cabotegravir and Rilpivirine With At Least Two Follow-up Injections (n=39)

Characteristic	N (%)
Age, Median (IQR, range)	46 (39-55, 31-68)
Gender	
Cis-Gender Man	35 (89.7)
Cis-Gender Woman	3 (7.7)
Transgender Woman	1 (2.6)
Race/Ethnicity	
Black	8 (20.5)
Hispanic	10 (25.6)
White	15 (38.5)
Multiracial/Other	6 (15.4)
Housing	
Stable	23 (59.0)
Unstable	13 (33.3)
Homeless	3 (7.7)
Insurance	
Medicare	25 (64.1)
Medicaid	13 (33.3)
Healthy San Francisco (Uninsured)	1 (2.6)
Current Stimulant Use	20 (54.1)
ART Regimen at Referral	
TAF/FTC/BIC	15 (38.5)
TAF/FTC/DRV-c	12 (30.8)
ABC/3TC/DTG	4 (10.3)
Other DTG-containing regimen*	4 (10.3)
TDF/3TC/DOR	2 (5.1)
ELV-c containing regimen**	2 (5.1)
HIV Viral Load ≥30 copies RNA/mL at time of referral	18 (46.2)
HIV Viral Load ≥30 copies RNA/mL proximal to first injection	15 (38.0)
Log10 HIV Viral Load of those with ≥30 copies RNA/mL at first injection *Mean (StD)*	4.67 (1.16)
CD4 cell count/mm^{3+} *Median (IQR)*	
Those with VL ≥30 copies/mL	99 (51,299)
Those with VL <30 copies/mL	732 (364, 883)
Attended a primary care visit in each 6-month period of the year prior to 1st injection	
Those with VL ≥30 copies/mL‡	14 (93.3)
Those with VL <30 copies/mL	20 (83.3)

*Includes DRV-c/DTG, 3TC/DTG, 3TC/DOR/DTG, and TAF/FTC/RPV/DTG

**Includes TAF/FTC/ELV-c and TAF/FTC/DRV/ELV-c

$^{+}$CD4 cell count defined using measurements up to one year prior to and up 28 days after 1st injection; there were nine patients without measurements in this time frame due to a history of stable CD4 cell counts >200 cells/mm^{3}.

ǂOne patient had two visits in the six-month period prior to 1st injection.
Note: Housing status and stimulant use (methamphetamines, cocaine) were reported by providers in the referral form. Unstable housing was defined as single room occupancy/hotel, temporarily staying with friends/family, or treatment/transitional program.

Figure 1. HIV Viral Loads Over Time for Patients Initiating Injections with Detectable Viremia

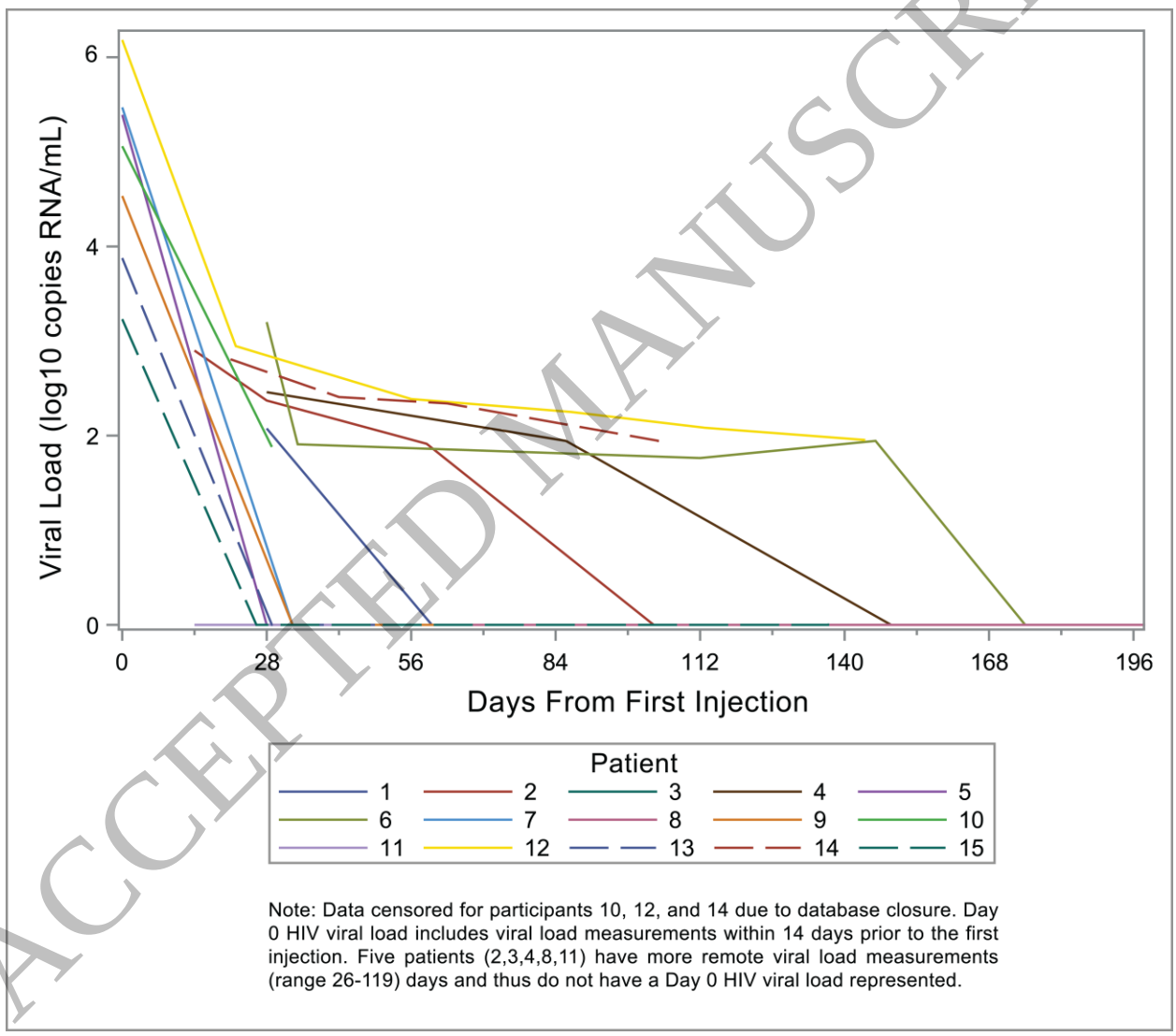

Figure 1
165x144 mm (.73 x DPI)