



LAAI 2026

2ND INTERNATIONAL
WORKSHOP ON
LONG-ACTING
ANTI-INFECTIVES

ABSTRACT BOOK

2nd International Workshop on Long-Acting Anti-Infectives
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ORAL ABSTRACT PRESENTATIONS

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1

PrEP-naïve Lenacapavir Initiators More Likely to be Assigned Female Sex at Birth in a Real-World Cohort

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Background: HIV pre-exposure prophylaxis (PrEP) uptake has remained low among women, who account for 23% of HIV cases but make up only 9% of PrEP users in the United States. Furthermore, there is very limited data about PrEP use among those assigned female at birth (AFAB) who identify as transgender or gender diverse. We hypothesize that lenacapavir (LEN), a twice-yearly injectable capsid inhibitor, will facilitate uptake among PrEP naïve AFAB persons who may have lower HIV risk perception and thus be more accepting of a PrEP formulation with a lower burden of commitment.

Methods: We conducted a multicenter retrospective cohort study of individuals who received at least one LEN injection for HIV prevention from June 18 to December 31, 2025 across 17 large academic and community-based PrEP programs in the United States. Demographic and clinical characteristics were abstracted from electronic health records. We compared characteristics among those who were PrEP naïve

to the total cohort. Factors associated with new PrEP initiation were evaluated using univariate logistic regression and Fisher's exact tests, as appropriate. All tests were 2-sided with a significance threshold of $p < 0.05$. Analyses were performed using Stata version 19.5 (StataCorp).

Results: Across 17 clinical programs, 501 individuals initiated LEN during the first 6.5 months following FDA approval, including 54 (10.8%) who were PrEP naïve. Among the entire cohort, 82 (16.4%) were AFAB, while among the new starts, 31 (57.4%) were AFAB (22 cisgender women, 5 transgender men, and 4 gender diverse). Among the overall cohort, 326 (65.1%) were gay/lesbian, 79 (15.8%) were bisexual, and 51 (10.2%) were heterosexual. Among the new starts, 15 (27.8%) were gay/lesbian, 18 (33.3%) were bisexual, and 15 (27.8%) were heterosexual. Among the entire cohort, 296 (59.1%) identified as White, 123 (24.6%) as Black, and 132 (26.3%) as Hispanic, while among the new starts, 29 (53.7%) identified as White, 20 (37.0%) as Black, and 7 (13.0%) as Hispanic. Predictors of initiating LEN without prior PrEP use included female sex (AFAB) (odds ratio [OR] 10.46, 95% CI 5.66-19.32, $p < 0.0001$), identifying as heterosexual (OR 4.39, 95% CI 2.21-8.72, $p < 0.0001$) or bisexual (OR 3.16, 95% CI 1.69-5.92, $p = 0.0003$),

Conclusion: In this multicenter cohort of early LEN initiators, more than 10% of individuals had never previously used PrEP. PrEP-naïve early adopters of LEN were significantly more likely to be AFAB and to identify as heterosexual or bisexual. These findings suggest that twice-yearly LEN may expand PrEP uptake among populations historically underrepresented in HIV prevention, helping broaden access beyond traditional PrEP user groups.



2

The Use of PBPK Modelling to Assess the Need for Simultaneous Oral Initiation with Long-Acting Cabotegravir and Rilpivirine in the Setting of Post-exposure Prophylaxis (PEP)

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Background: HIV post-exposure prophylaxis (PEP) is most effective when started within 24 hours, yet adherence to standard oral PEP is poor, especially among sexual assault survivors. Long-acting injectable (LAI) cabotegravir (CAB) plus rilpivirine (RPV), is effective in maintaining suppression in people living with HIV, and could improve uptake and reduce pill-related stigma for PEP. However, LAIs alone might not elicit rapid attainment of therapeutic concentrations, needed for PEP to be effective. We used PBPK modelling tailored to the Atlanta population to simulate exposures and evaluate initiation strategies. We modelled a single oral dose plus IM LAI on day 1 (D1) versus LAI alone to assess sufficiency for rapid attainment of PEP target exposures.

Material and Methods: PBPK models were implemented in Julia to simulate 100 adult (50% female) African American (AA) with body mass index (BMI) 25–40 kg/m² (based on reported AA BMIs for Atlanta, 2024). For CAB, UGT1A1 mediated intrinsic clearance was reduced by ~10% versus European Americans (EA); for RPV, no AA–EA difference in CYP3A4 clearance has been reported. LAI depot release kinetics were taken from published population PK models: CAB as a single first order release depot; RPV as two first order release fractions (fast and slow). Models were qualified against reported clinical pre

exposure prophylaxis (PrEP) IM regimens with oral lead in in overweight (BMI 25–30 kg/m²) and obese (BMI 30–40 kg/m²) cohorts. Models were considered valid if the absolute average fold error (AAFE) was within 2 fold of observed mean exposures. Verified models simulated a PEP regimen of single oral 30 mg + 600 mg IM CAB and single oral 25 mg + 900 mg IM RPV, both on D1. Target concentration was defined as 4× the invitro protein adjusted 90% inhibitory concentration (4×PAIC₉₀): CAB 664 ng/mL and RPV 48 ng/mL.

Results: Successfully qualification against observed PrEP data was achieved prior to predictive simulations, with mean AAFE 1.24 for CAB and 1.00 for RPV. Simulations of LAI PEP showed therapeutic concentrations in almost all AA patients on D1 when an oral initiation dose was employed, but not when the LAI was given alone. CAB plasma concentration was estimated to remain above 4×PAIC₉₀ for 28 days (mean 1,370 ng/mL at D28). RPV was estimated to drop below the 4×PAIC₉₀ on D18 (mean 49 ng/mL at D17). However, predicted concentrations for the simulated regimen at D28 for both RPV and CAB were similar to those reported after the first dose when this regimen is used in treatment of virologically suppressed patients.

Conclusions: Whole body PBPK simulations in healthy adults (BMI 25–40 kg/m²) support administration of a single oral initiating dose simultaneously with IM CAB and RPV at LAI PEP initiation to ensure rapid attainment of therapeutic concentrations. This conclusion remains consistent when accounting for physiological differences associated with overweight/obesity and AA population characteristics. The proposed dosing scheme should provide rapid therapeutic levels and sustained exposure without challenges of daily adherence, prospective clinical trials are justified to evaluate pharmacokinetics and effectiveness, and to inform dosing and implementation strategies.



3

Adherence to Oral versus Long-acting Injectable HIV Preexposure Prophylaxis among Women Who Inject Drugs

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Background: Women who inject drugs (WWID) have had limited access and adherence to oral HIV preexposure prophylaxis (PrEP). In 2022, the largest syringe services program in Philadelphia integrated long-acting injectable cabotegravir (CAB-LA) into its PrEP services. This study compares adherence to oral vs. injectable PrEP among WWID enrolled in an ongoing randomized controlled trial (RCT) evaluating a trauma-informed writing intervention combined with contingency management for stimulant/opioid non-use and PrEP adherence, taking place within this harm reduction setting.

Methods: We analyzed clinical and study records to characterize adherence among WWID initiating PrEP and the RCT between June 2022 and November 2024. Next, we used Kaplan-Meier survival curves to assess time-to-loss of protection for oral vs. CAB-LA over 6-months of follow-up per participant. We defined sufficient PrEP protection as 4 or more oral doses per week or receiving CAB-LA injections within 6 weeks of target dates (i.e., prior to estimated loss-of-protection based on prior pharmacologic studies).

Results: Of 144 WWID enrolled and initiating PrEP, the mean age was 41 years, 75% were unhoused, 73% injected substances daily (vs. less frequently), and 52% had >1 sex partner; 7% initiated oral PrEP and 93% initiated CAB-LA. The proportion of women with uninterrupted PrEP protection dropped to 0% by 60 days after initiation in the oral PrEP group. By contrast, uninterrupted PrEP protection for CAB-LA was 100% at 60 days after

initiation, 76% at 120 days, and 53% at 180 days. The proportion of WWID with any lapse in protection during follow-up was 48% with CAB-LA and 100% with oral PrEP. Among women who had any lapse in protection, reinitiation was 66% for CAB-LA and 70% for oral PrEP; 50% initiating oral PrEP eventually received at least one dose of CAB-LA. No new HIV diagnoses were observed.

Conclusion: In this sample of WWID at an urban syringe services program, nearly all participants chose CAB-LA over oral PrEP. More than half of women initiating CAB-LA had continuous coverage over a 6-month period as compared to none of the women using oral PrEP. These findings highlight the public health importance of expanding access to and the prescribing of CAB-LA for WWID.



4

Early Patient-Reported Outcomes and Planned Persistence with Lenacapavir for HIV Pre-Exposure Prophylaxis in Routine Clinical Care

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Background: Long-acting injectable pre-exposure prophylaxis (PrEP) has the potential to overcome adherence challenges associated with daily oral PrEP. Lenacapavir (LEN), a first-in-class capsid inhibitor administered subcutaneously every six months, recently demonstrated high efficacy for HIV prevention in registrational trials, with favorable safety profiles and high continuation rates. However, real-world patient experience with LEN and anticipated persistence outside of clinical trial settings remain poorly characterized. Early patient-reported outcomes (PROs) may provide insight into acceptability, tolerability, and potential barriers to sustained use during initial implementation. We therefore evaluated early real-world PROs among individuals initiating LEN for PrEP across four U.S. clinical sites.

Methods: We analyzed data from a standardized survey administered to individuals who initiated LEN for HIV PrEP at four large community-based PrEP programs in the United States following FDA approval. Surveys were completed after receipt of the initial injection and assessed motivations for choosing LEN, counseling regarding drug–drug interactions, adherence to oral loading doses, injection-site reactions (ISRs), and anticipated continuation of injections. Descriptive statistics were used to summarize responses.

Results: A total of 58 individuals completed the survey. Convenience-related factors predominated in decisions to initiate LEN. The most commonly cited reason for choosing LEN was reduced dosing frequency (48/58, 82.8%), followed by difficulty

remembering daily oral PrEP (19/58, 32.8%). Direct recommendation by health care provider was reported by 8 participants (13.8%).

Most respondents reported receiving counseling prior to initiation regarding potential drug–drug interactions (53/58, 91.4%). Adherence to oral loading dose was high (57/58; 98.2%); only one participant reported delaying the second oral loading dose, which occurred two days after injection.

ISRs were common, 45 participants (77.5%) reported at least one injection-site symptom. The most frequently reported reactions included pain (26/45, 57.8%), swelling (20/45, 44.4%), and nodules (17/45, 37.8%). Most participants reported minimal interference with daily activities related to injection-site symptoms.

Seven participants (12.1%) reported that they did not plan to continue subsequent LEN injections; no patient-reported factors were significantly associated with plans to discontinue. When asked what factors might influence discontinuation of LEN, open-text responses identified injection-site reactions as the most common concern (9/21, 43%), particularly persistent nodules and pain. Other themes included unanticipated insurance/access barriers, interest in longer-acting PrEP options, medication interactions, and reduced perceived HIV vulnerability.

Conclusions: In early real-world implementation across four U.S. PrEP programs, LEN was perceived as highly convenient and generally well tolerated despite frequent ISRs. However, a notable proportion of participants reported plans not to continue injections, and ISRs emerged as the most commonly cited concern influencing potential discontinuation. These findings suggest that persistence with LEN for PrEP in routine clinical care may differ from continuation patterns observed in clinical trials. Ongoing monitoring of real-world persistence and patient-centered implementation strategies will be critical to maximize the impact of long-acting PrEP.



5

Long-Acting Injectable Treatment for Tuberculosis: Multi-Country Cross-Sectional Study to Examine Preferences, Acceptability, and Trade-Offs

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Background: Development of long-acting injectable (LAI) tuberculosis (TB) drugs could transform global TB management. We first conducted a pilot study in the Philippines, followed by an expansion to a global study in Indonesia, South Africa, and Tanzania. In each setting, we assess the acceptability of and preferences for three potential LAI TB treatment scenarios and seven product-specific attributes among TB patients and survivors, TB clinicians, and other key program stakeholders.

Methods: Pilot study: For the pilot study, a two-stage mixed-method study was conducted in Manila and Cavite, the Philippines. Stage 1 included semi-structured interviews with key informants (KIs) including public health organizations, government, and clinical practice. Stage 2 entailed a face-to-face survey and discrete choice experiment (DCE) of 3 scenarios (below) with TB health providers, adult TB patients, and adult TB survivors.

Scenario 1: 4 injections in a one-time treatment

Scenario 2: 2 injections per visit over a 4-month period

Scenario 3: 1 month daily oral run-in, followed by 2 injections that are 3 months apart

Global study: For the global study in Indonesia, South Africa, and Tanzania, learnings from the pilot study in the Philippines were incorporated into the choice of key informants (Stage 1) and survey design (Stage 2). In each country of the global study, tablet-based face-to-face surveys will

be conducted with TB patients, survivors, and healthcare providers, with a target of n=1050 participants per country (n=150 providers, n=150 TB survivors, n=750 active TB patients).

Results: Pilot study: Through 15 KI interviews in Stage 1, we identified common themes including goals of minimizing treatment burden, maximizing adherence and efficacy, preference for a primary care setting, and the ability to monitor response. In Stage 2, 352 survey respondents included 247 active TB patients, 54 TB survivors and 51 TB clinicians. Most participants reported the LAI TB treatment scenarios were acceptable relative to the current oral standard-of-care, with Scenarios 1, 2, and 3 deemed acceptable by 59.1%, 78.1% and 78.7% of participants, respectively. The DCE identified differences in preferences for LAI attributes between TB patients, survivors, clinicians, and locations. Body placement of the injection was a driving characteristic of treatment choice for patients; preference for LAI treatment delivered through a primary care setting was reported as positively influencing treatment choice across respondent types.

Global study: At the time of abstract submission, all Stage 1 consultations in Indonesia have been completed, along with completion of approximately 1050 surveys of TB patients, survivors, and clinicians. The Stage 2 survey sites in Indonesia includes Jakarta (urban), Medan (peri-urban), and Bandung (rural). Data analysis is underway and will be shared as available. Stage 1 and Stage 2 activities are ongoing in South Africa and Tanzania.

Conclusion: In summary, our results indicate broad interest in LAI TB treatment, despite concerns over injection site pain and the potential need for delivering multiple injections at a single visit. Efforts to support the development of LAI TB treatment should continue to be guided by stakeholder input to understand acceptable product characteristics.



6

A Regulatory Strategy for Long-Acting Injectable Regimens for Tuberculosis

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Background: The success of long-acting injectables (LAI) in HIV and other therapeutic areas has established that LAIs can deliver adherence-independent, durable efficacy with an acceptable safety profile. Regulatory frameworks increasingly support incorporation of model-informed drug development (MIDD) strategies; a MIDD approach to LAIs for tuberculosis (TB) underpinned by pharmacokinetic/pharmacodynamic (PK/PD) target attainment analyses, route-specific toxicology, and robust risk management, is proposed. LAI regimens could transform TB treatment by reducing adherence burden and enabling sustained therapeutic exposures.

Methods: We propose a product-agnostic regulatory strategy in which efficacy and systemic safety of a multidrug LAI combination (2–4 agents) are established primarily through PK/PD bridging to an oral regimen, replacing a traditional Phase 2 LAI dose-finding trial and a large LAI pivotal trial powered for efficacy. Regulatory guidances supporting MIDD, including the International Council for Harmonisation M15 Guideline, encourage the use of mechanistic models in regulatory submissions to assess comparability between formulations. The European Medicines Agency Guideline on pharmacokinetic and clinical evaluation of modified release dosage forms also recognizes integration of physiological, PK/PD considerations in development of modified release formulations. Regulatory approvals for alternative routes of administration have similarly relied on PK bridging with targeted safety assessment, particularly in anti-psychotic and HIV LAIs: approvals of LAIs or new regimen initiation options underpinned by PK characterization and exposure-response translation. These precedents support oral to LAI bridging using a safety-first sequence (oral followed by LAI).

Expected Outcomes: The proposed strategy leverages exposure-response relationships characterized during oral regimen full clinical development. For each drug component, efficacy-supporting (AUC, C_{avg}, C_{min}) and safety-limiting (C_{max}, AUC) exposure thresholds would be defined using population PK (PopPK) and exposure-response modeling. LAI doses would be selected using simulation to achieve systemic exposures within predefined therapeutic acceptance bands derived from oral data.

A stepwise development framework is proposed:

1. Establish oral exposure-response relationships for each regimen component.
2. Define quantitative PK criteria to support oral-to-LAI bridging.
3. Conduct Phase 1 LAI trials (single-agent and combination) in healthy participants and people with TB to characterize PK and injection-site reactions.
4. Develop and refine LAI PopPK models incorporating absorption characteristics and covariates.
5. Conduct pivotal LAI trial focused on PK target attainment and safety, with efficacy assessed descriptively rather than powered for noninferiority.

Under this framework, LAI regimens would be expected to maintain C_{min} and AUC above efficacy thresholds throughout the dosing interval while keeping C_{max} and overall AUC within established safety margins at the population level. The pivotal LAI trial would confirm PK targets attainment and evaluate route-specific safety. The evidence generated with this approach is proposed to meet regulatory requirements for demonstration of positive benefit vs risk assessment for LAI TB regimens.

Conclusions: We propose that a PK/PD-anchored regulatory pathway, grounded in robust oral exposure-response characterization and supported by MIDD principles, could enable extrapolation of efficacy from oral to LAI TB regimens. If endorsed by regulators, this strategy could shorten development timelines by ≥ 2–4 years while maintaining evidentiary rigor and patient safety.



7

Clinician Attitudes toward and Utilization of Long-Acting Injectable Cabotegravir/Rilpivirine for Pregnant Persons Living with HIV

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Background: Long-acting injectable cabotegravir/rilpivirine (LAI-CAB/RPV) offers an effective alternative to daily oral antiretroviral therapy, with demonstrated benefits for adherence and viral suppression in non-pregnant people living with HIV (PLWH). However, pregnancy-specific safety, pharmacokinetic (PK), and efficacy data remain limited. In the absence of definitive guidelines, clinical decision-making regarding LAI-CAB/RPV in pregnancy is left to individual clinicians. Clinician attitudes and perceptions play a critical role in counseling and access to this therapy. The objective of our study was to assess clinician knowledge, attitudes, and self-efficacy regarding LAI-CAB/RPV use in persons of childbearing age and pregnant PLWH; to characterize clinical practices when pregnancy occurs in patients receiving LAI-CAB/RPV; and to evaluate willingness to use LAI-CAB/RPV in the setting of adherence challenges during pregnancy.

Methods: We conducted a cross-sectional, web-based survey of front-line HIV clinicians who provide care to PLWH who are pregnant or of childbearing age. Participants were recruited through national clinician networks, including the American Academy of HIV Medicine (AAHIVM) and the National Clinician Consultation Center Reproductive Infectious Disease (ReproID) Listserv. The 30-item survey assessed demographics, clinical experience, knowledge of LAI-CAB/RPV, perceived risks and benefits, prescribing practices, and responses to clinical scenarios. Consent was implied by completion and no compensation was provided. Data was collected via Research Electronic Data Capture (REDCap) and analyzed using descriptive statistics.

Results: A total of 101 survey responses were received and 70 were eligible. Demographics of survey respondents varied, but a majority of respondents were physicians (70.0%), worked at a large (11+ provider) practice (58.6%), worked in an academic health center/hospital based clinic (81.4%), in an urban environment (78.6%), and had 10+ years of experience working with PLWH (74.6%). Clinicians reported high comfort in prescribing LAI-CAB/RPV with a mean comfort score of 8.94 (SD 2.07) out of 10. Comfort remained high in prescribing LAI-CAB/RPV to PLWH of childbearing age (mean 8.84(1.64)) but was significantly lower for prescribing LAI-CAB/RPV to pregnant PLWH (mean 5.92(3.25)). Chief concerns in pregnancy included lack of real-world data (76.2%), PK data (63.5%), safety data (54.0%), and lack of clinical guidelines (52.4%). Variability in clinicians' comfort level existed, with a majority (73.0%) indicating they have continued LAI-CAB/RPV in PLWH who became pregnant on it. Chief benefits to continuing LAI-CAB/RPV in pregnancy included improved adherence (98.4%) and avoiding changes in ARV regimens (57.1%). Clinical decisions in these scenarios, such as adjusting dosing schedules or adding additional drugs to the regimen, varied among providers but were most often guided by existing PK modeling data.

Conclusions: Although many clinicians desire to have the option of LAI-CAB/RPV in pregnancy due to perceived benefits including improved adherence, comfort in prescribing or initiating therapy during pregnancy is low due to lack of safety data and guidelines. This disconnect has led to significant variability in prescription practices. Further data on the safety of these regimens in pregnancy, and subsequent inclusion in national guidelines, is important in supporting clinical decision making for this important population and ultimately in ensuring equitable access to this novel treatment regimen for all pregnant PLWH.



8

PREFER-LA: Improved Adherence and Viral Control in Real-World Study of People with HIV in the United States with Adherence Challenges on Oral Antiretroviral Therapy Switching to Long-Acting Cabotegravir + Rilpivirine

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Background: Long-acting cabotegravir + rilpivirine (CAB+RPV LA) has demonstrated superior efficacy when compared to oral therapy in a randomized controlled trial of people with HIV with adherence challenges (LATITUDE). Real-world adherence and clinical outcomes from PREFER-LA (Perspectives on Treatment with CAB+RPV LA Injectable Therapy from PWH in the US with Prior Adherence Challenges to Oral ART) are presented.

Materials and Methods: PREFER-LA was an observational real-world US study of people with HIV receiving CAB+RPV LA for ≥ 6 months to ≤ 18 months with documented adherence challenges on prior oral antiretroviral therapy (ART). The study consisted of: (1) cross-sectional survey of people with HIV to evaluate experiences of historical oral ART use and perspectives of treatment with CAB+RPV LA, (2) corresponding retrospective medical chart review (eCRF) to establish treatment history and clinical outcomes, and (3) cross-sectional survey of healthcare providers (HCPs) from each site.

Results: Median age of the 159 participants was 39 years and median time since HIV diagnosis was 11.7 years. The participants received a median of 2 ART regimens prior to CAB+RPV LA and had been

receiving CAB+RPV LA for a median of 12 months. Healthcare providers identified the type of sub-optimal adherence—categorized as situational non-adherence, sub-optimal adherence, intermittent adherence, or non-adherence—for each person with HIV for study eligibility. Healthcare providers reported forgetfulness (64%) as the most common factor impacting daily oral ART adherence. From the perspective of people with HIV, remembering to take oral ART was the most common adherence challenge (84%). For nearly 70% of people with HIV, CAB+RPV LA was at least their third ART regimen. Over 90% of people with HIV switched from a single tablet oral ART; bicitegravir/tenofovir alafenamide/emtricitabine (59%) was the most common prior single tablet oral ART. No resistance data were available at time of switch for 38% of people with HIV. Nearly one-quarter (23%) of people with HIV had a viral load >50 copies/mL at time of switch. At the time of evaluation, median follow-up time on CAB+RPV LA was 1 year, and viral load <200 copies/mL was achieved/maintained in over 98% of people with HIV. Missed/skipped/delayed CAB+RPV LA injections were uncommon (13%).

Conclusions: In this cohort of people with HIV with documented adherence challenges to oral ART, virological control was achieved/maintained by most after switching to CAB+RPV LA. These real-world findings complement existing clinical trial and real-world evidence regarding use of CAB+RPV LA in people with HIV with identified adherence challenges on prior oral ART.



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Rethinking Eligibility: Long-Acting Cabotegravir/Rilpivirine Achieves Suppression in Viremic Individuals: From the Midway Cohort

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Background: Long acting cabotegravir/rilpivirine (LA CAB/RPV) is approved for maintenance therapy in people with HIV (PWH) who are virologically suppressed. Data on its use in viremic patients are limited, and the real-world effectiveness of Cabenuva in achieving viral suppression in this population remains unclear. Understanding time to suppression and long-term outcomes in viremic patients is critical for informing treatment strategies and expanding access to long-acting antiretroviral therapy.

Materials and Methods: We conducted a retrospective analysis of PWH in the Midway Cohort who were viremic (HIV-1 RNA > 50 copies/mL) at the time of LA CAB/RPV initiation (start date August 2021 through December 2025). Demographic and clinical data were collected from electronic health records. The primary outcomes were time to viral suppression (HIV RNA <50 copies/mL) and current viral suppression rates. Incidence of viral blips and low level viremia are also reported. Descriptive statistics were used for baseline characteristics and study outcomes.

Results: A total of 31 patients were included in the analysis. The median age was 50 years (range, 22 – 93). 58% identified as cisgender male (18), while 42% identified as cisgender female (13). 64.5% were predominantly Black (20) and 35.5% identifying as White (11). 87% non-Latine (27) and 13% identified as Latine (4).

The most common reason for initiation of long-acting cabotegravir/rilpivirine (LA CAB/RPV) was patient preference (32.3%), followed by adherence issues (16.1%) and pill fatigue (9.7%); the indication was unknown in the remaining 41.9%. The median duration of therapy was 410 days

(range, 28 – 1547). Baseline HIV-1 RNA levels were heterogeneous. Sixteen patients (51.6%) had HIV-1 RNA levels of 50–199 copies/mL, four (13.0%) had 200–999 copies/mL, and seven (22.6%) had 1,000–49,999 copies/mL. Higher baseline viral loads were observed in a smaller proportion of patients: one (3.2%) had 50,000–99,999 copies/mL, two (6.4%) had 100,000–500,000 copies/mL, and one (3.2%) had ≥500,001 copies/mL.

The median time to viral suppression (HIV-1 RNA <50 copies/mL) was 130 days (range, 5–758). At most recent follow-up, 24 patients (77.4%) achieved viral suppression <50 copies/mL, and all patients (31, 100%) had HIV-1 RNA <200 copies/mL. Viral blips (HIV-1 RNA >50 but <200 copies/mL) occurred in 4 patients (13.0%). Low-level viremia (LLV; defined as two consecutive HIV-1 RNA values >50 but <200 copies/mL) was observed in 7 patients (22.6%). Of these, 3 cases resolved with subsequent viral suppression, while 4 patients continued to experience LLV; all 4 had a history of LLV on prior antiretroviral therapy (BIC/F/TAF). One patient with persistent LLV had lenacapavir added to LA CAB/RPV. At the time of analysis, 26 patients (83.9%) remained on LA CAB/RPV, 1 (3.2%) discontinued due to insurance coverage issues, 3 (9.7%) were lost to follow-up, and 1 (3.2%) relocated.

Conclusion: In this real-world cohort of viremic PWH, LA CAB/RPV achieved high rates of viral suppression, with all patients reaching HIV-1 RNA <200 copies/mL and most achieving <50 copies/mL. These findings support its effectiveness as a treatment strategy beyond virologically suppressed populations.



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How Long-Acting Anti-Infective mAbs Can Catalyze Global mAb Pharmaco-equity

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After more than fifty years of development and over 200 approvals in high-income countries, monoclonal antibodies have created a \$200+ billion global market—even extending to veterinary applications for cats and dogs. Yet this extraordinary class of drugs remains largely inaccessible across ~100 countries, including thirty-year-old mAbs for cancer and inflammatory diseases included in the WHO Essential Medicines List (EML). This paradox reflects a vicious cycle: few mAbs achieve EML inclusion because they appear too expensive, while generic development stagnates because products lack EML status so that manufacturers can plan and invest.

Current approaches treat each mAb as an isolated therapeutic rather than components of a unified class requiring combined volume for affordable manufacturing. Pembrolizumab costs almost \$6,000 per cycle in India despite local manufacturing capacity because individual disease markets cannot justify dedicated production to reduce costs. This fragmentation exemplifies the core problem.

Long-acting anti-infective mAbs, starting with nirsevimab for RSV prevention, offer unique potential to break the impasse by serving as the volume catalyst needed for system-wide transformation. WHO EML mAbs targeting cancer and autoimmune diseases require ~35-52 tons annually for global unmet need—insufficient volume for commodity manufacturing. When combined with infectious disease applications such as RSV, malaria, HIV, and pandemic preparedness, the unified mAb class generates 130-1,300 tons annual demand—a 10-60x volume multiplier enabling cost reduction.

Long-acting anti-infective mAbs provide uniquely large volume contributions through population-level prevention. Nirsevimab exemplifies this principle: 140 million infants requiring annual RSV protection generates 7-14 tons, representing the critical "connector" between WHO EML mAbs and commodity-scale manufacturing.

We can learn from history: The delay in ART access to LMICs resulted in an estimated 12 million preventable deaths. We risk repeating this failure: nirsevimab could prevent 100,000 infant deaths annually (99% of RSV deaths happen in countries without access); malaria prevention mAbs could save hundreds of thousands every year.

The HIV treatment precedent from the 2000s demonstrates feasibility. Coordinated advocacy and political will drove antiretroviral costs from \$10,000 to <\$100 annually between 2000 and 2008. Indian generic production at scale was a key driver in reducing costs. The same approach can work for mAbs.

Long-acting anti-infective mAbs represent the missing catalyst that shifts the narrative from "How can we afford mAbs for cancer?" to "How do we build manufacturing infrastructure for the entire mAb class?" Long-acting anti-infectives for RSV, malaria, HIV, and pandemic preparedness represent essential infrastructure for global mAb equity—catalysts for transformation benefiting all applications worldwide.



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ACC085, a Novel HIV-1 Capsid Function Inhibitor, Exhibits Human Pharmacokinetics Predicted from Nonclinical Data Using a PBPK Model, Supporting Its Long-Acting Potential in Humans

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Background and Objectives: ACC085, a novel HIV-1 capsid function inhibitor, is being developed for pre-exposure prophylaxis (PrEP) against HIV. This article presents the nonclinical pharmacokinetic profiles of ACC085 and describes the use of physiologically based pharmacokinetic (PBPK) modeling to predict its human plasma concentrations based on preclinical data.

Methods: Standard in vitro methods were employed to characterize the physicochemical properties of ACC085, including lipophilicity (LogP), dissociation constant (pKa) and solubility, as well as plasma protein binding in rats, beagle dogs, and humans. The pharmacokinetic parameters of ACC085 were evaluated in rats and dogs following intravenous (IV) administration (1 mg/kg) and subcutaneous (SC) administration (10 mg/kg, 30 mg/kg, and 100 mg/kg). A PBPK model for ACC085 was developed using PK-Sim[®] 12 to predict plasma concentration profiles in humans following SC dosing. This was informed by preclinical PBPK modelling in rats and beagle dogs for both IV and SC routes. The Poulin and Theil method was employed to predict the volume of distribution at steady state, and an allometric scaling model was used to predict human clearance. A first-order absorption process (preclinical $t_{1/2} = 400$ h and clinical $t_{1/2} = 800$ h, assuming that the human SC release rate is twice as slow as in nonclinical species) was used to characterize SC absorption.

Results: In. ACC085 is highly lipophilic (LogP = 4.84) with an apparent solubility below 5 mg/mL and a pKa of 6.65. Its predicted clearance is low, at 0.057 L/h/kg. Following single SC administration, the pharmacokinetics of ACC085 in rats and dogs were characterized by slow absorption and elimination of the drug. The predicted plasma concentration-time profiles of ACC085 after IV administration in rats and dogs and after SC administration at all dose levels were consistent with observed values. When extrapolated to humans, a single SC dose of 972 mg (the clinically projected dose) maintained plasma concentrations above four times the human plasma protein binding-adjusted EC95 (4*EC95: 13.88 ng/mL) for up to six months.

Conclusion: The nonclinical data from ACC085 in animals, along with the favorable comparative projections of human plasma concentrations and antiviral activity, will support its continued development as a PrEP.



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Leveraging Pharmacists and Pharmacy Technicians to Optimize Long-Acting Injectable Antiretroviral Therapy Access, Adherence, and Clinical Outcomes

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Background: While PWH and provider enthusiasm for long-acting injectable cabotegravir-rilpivirine (LA-CAB/RPV) is high, implementation barriers exist due to operational challenges related to drug procurement and the need to monitor for on-time injections. Delivery models that utilize pharmacists and pharmacy technicians have allowed clinics to launch and sustain successful programs that support access, adherence, and clinical outcomes. We sought to identify the implementation strategies that make pharmacy teams effective.

Methods: We conducted two rounds of focus group discussions and semi-structured interviews (12/22-5/23 and 12/24-3/25) with staff and prescribing providers (Round 1 n=36, Round 2 n=31) in three Ryan White-funded academic HIV clinics. This analysis focuses on the two clinics that utilized pharmacists and pharmacy technicians in key roles for LA-CAB/RPV delivery: Ward 86 in San Francisco, where the pharmacist and pharmacy technician were based in the clinic, and University of Chicago, where they were staff of the affiliated hospital specialty pharmacy. We identified transcript excerpts related to tasks performed by pharmacist or pharmacy technician, coded these excerpts according to inner setting constructs from the Consolidated Framework for Implementation Research 2.0, and then mapped pharmacy team activities to implementation strategies from the Expert Recommendations for Implementing Change compendium.

Results: The pharmacist and pharmacy technician were involved in nearly all steps of LA-CAB/RPV delivery: verifying eligibility, patient education and

counseling, writing prescriptions, ensuring payer coverage, obtaining and storing the medication, tracking injection appointments, following up on late injections, ordering and following up on viral load testing, communicating results to providers, maintaining contact information, managing late injections, ensuring safe discontinuations, and documenting management decisions. As one MD reported, "We refer and then they take it from there, in terms of getting the drug procured and starting. Having that level of support is indispensable. I couldn't do this without (them)." We identified five salient inner setting constructs in participant descriptions of reasons why pharmacist and pharmacy technician participation was effective: relational connections, communication, recipient-centeredness, mission alignment, and relative priority. A cross-cutting example in one setting was the decision to have the pharmacy technician perform reminder calls and follow-up late injections, and more generally, function as the point of contact for questions from PWH, as opposed to front desk staff. "Creating a relationship with all the patients that are coming in for injectables probably helps a lot...they have the same person reaching out to them...she knows every single one." We also identified five key implementation strategies: creating new clinical teams, creating an implementation blueprint in the form of a protocol, network weaving by cultivating relationships with specialty pharmacies, facilitating relay of clinical data to providers, e.g., prompt feedback on viral load results, and coalition-building via regular multidisciplinary meetings. As one staff member noted, "The pairing of the pharmacy team and the nursing team is an effective, beautiful pair. All about it is cohesion...the seamlessness of it."

Conclusions: Pharmacy-team based models of LA-CAB/RPV delivery can overcome multi-level barriers to LA-CAB/RPV delivery and provide person-centered care that supports treatment engagement.



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On-time Injection Adherence and Persistence among People with HIV on Long-Acting Cabotegravir/Rilpivirine

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Background: Long acting cabotegravir–rilpivirine (LA CAB/RPV) may help people with HIV (PWH) overcome adherence challenges to daily oral antiretroviral therapy. LA-CAB/RPV implementation requires intensive pharmacy and nursing support and frequent clinic visits. Real world data describing adherence to on time injections and persistence on therapy remain limited.

Methods: We conducted a retrospective cohort study using chart review of adults with HIV receiving ≥ 1 LA CAB/RPV loading injection as part of routine care at Weill Cornell Medicine between April 2022 and October 2024. Follow up began at first loading injection and ended at LA CAB/RPV discontinuation, last visit, or April 2025. On time injections were defined as those administered within ± 7 days of the target date (28 days after the previous injection for loading and Q4W dosing; 56 days for Q8W dosing). We calculated the proportion of injections administered on time, the proportion of patients receiving all injections on time, and discontinuation rates. Multivariable logistic regression identified predictors of late injections and LA CAB/RPV discontinuation. Viral suppression (HIV 1 RNA < 50 copies/mL) was assessed at last follow up or discontinuation.

Results: A total of 139 patients met study criteria; median age was 48 years (IQR 38–58), 81% were male, 41% non-Hispanic Black, and 94% had baseline HIV 1 RNA < 50 copies/mL. Patients received a median of 10 injections (IQR 5–16) over a median 17.6 months (IQR 8.8–27.5). Thirty-five patients (25.2%) discontinued LA CAB/RPV, most commonly due to adverse effects or missed injection appointments. Of 1401 total injections administered, 1370 (97.8%) were on time. Among 134 patients with ≥ 1 follow up injection, 106 (79.1%) had all injections administered on time, while 28 (20.1%) had ≥ 1 late injection. In adjusted

analyses, late injections were associated with non-Hispanic Black race (aOR 3.70, 95% CI 1.02–13.35) and a history of missed medical appointments in the 12 months prior to LA-CAB/RPV initiation (aOR 2.64, 95% CI 1.04–6.71). Discontinuation of LA CAB/RPV was associated with Hispanic ethnicity (aOR 3.47, 95% CI 1.13–10.65) and age 18–29 years (aOR 97.74, 95% CI 6.65–1436.27). At last measurement, 129 patients (92.8%) remained virally suppressed; among 31 late injection events, 90.3% had documented bridging with oral ART.

Conclusion: In this real-world cohort, adherence to on time LA CAB/RPV injections and maintenance of viral suppression were high. Patients with a history of missed appointments were more likely to receive late injections and may benefit from targeted adherence support. Nearly one quarter of patients discontinued LA CAB/RPV within 18 months, with younger age strongly associated with discontinuation, highlighting the need for tailored retention strategies for specific subgroups.



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In-Country Evaluation of Compact Prefilled Autodisable Devices for Delivery of Long-Acting Medicines in Uganda and Zambia

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Background: PATH and BD developed the Uniject™ injection system, a compact prefilled autodisable (CPAD) device that combines a needle, a syringe, and a single dose of a pharmaceutical for safer, easier injections. CPAD devices enable task-shifting to lower-trained health care workers or self-administration (e.g., of contraceptives) and can reduce the cost of goods sold and total cost of delivery of long-acting injectable medications compared with vials or standard prefilled syringes. For decades, Uniject devices have delivered hepatitis B vaccine birth doses in Indonesia and more than 20 million doses of self-injectable long-acting hormonal contraceptives for women in sub-Saharan Africa. To advance long-acting products intended for low- and middle-income countries, PATH is partnering with developers to evaluate the technical, cost, and programmatic suitability of novel, lower-cost CPAD devices for delivery of long-acting therapeutics. PATH conducted a human factors evaluation in Uganda and Zambia to assess the usability, acceptability, and programmatic fit of the Injecto CPAD device [1] compared with the Uniject CPAD device [2].

Materials and Methods: A mixed-methods usability study was conducted in rural and urban areas in Uganda and Zambia. Study participants included service providers (36), relevant district staff (2), and self-injection-naive clients (40). The evaluation included simulated use and a semi-structured interview to capture feedback on the use experience and acceptability of the devices. For the simulated use activity, the device used first was alternated. Participants were first trained on the selected device and then asked to deliver a placebo into an injection aid. This process was repeated for the second device.

Results: Overall, participants in both countries identified the advantages of a prefilled device and were willing to use the CPAD devices. Participants highlighted that the devices were easy to learn and use, easy to transport, could reduce waste, and are time saving. On average, over 90% of users completed the necessary steps to deliver a dose. Almost 90% of providers and staff described the Injecto device as easy to use. Injection-naive clients had more difficulties, with 75% describing the device as easy to use. Participants noted that with a new device, education and sensitization are needed to ensure uptake. Stakeholders stated that CPAD devices could increase injection safety and ensure uniform dose delivery and offered suggestions to improve the design, packaging, and labeling.

Conclusions: CPAD devices offer significant benefits over traditional prefilled syringes and vial presentations for administration of long-acting therapeutics. CPAD devices were highly acceptable to potential end users and stakeholders in Zambia and Uganda. Ongoing work seeks to evaluate an additional novel CPAD device and the design modifications necessary to administer larger doses required for certain long-acting therapeutics. Future work for specific use cases will be required for regulatory approval and country introduction of long-acting therapeutics in CPAD devices.

1. <http://injecto.eu/auto-disable-devices>
2. <https://www.bd.com/en-us/products-and-solutions/products/product-families/uniject-auto-disable-pre-fillable-injection-system>



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A Novel Islatravir Prodrug Formulated as a Long-Acting Nanosuspension for HIV Treatment

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Background: Antiretroviral agents (ARV) have significantly reduced new HIV transmission and improved survival and quality of life for people living with HIV (PLWH). However, the lack of a cure and ongoing challenges with medication and medical care adherence highlight the need for long-acting formulations for long-term treatment. Islatravir (EFdA) in its 5'-triphosphate form (EFdA-TP) is a highly potent, sub-nanomolar HIV-1 nucleoside reverse transcriptase translocation inhibitor currently in Phase 3 development by Merck for HIV-1 prevention and treatment. Low-dose studies demonstrated safety and efficacy in PLWH. Its high potency and long intracellular half-life of its active metabolite, EFdA-TP, make it well-suited for long-acting regimens. However, the hydrophilicity of EFdA limits sustained release without the use of large amounts of excipients. We developed a long-acting injectable (LAI) formulation of EFdA using a prodrug strategy to eliminate excipients and extend drug release. This approach aims to extend the dosing interval from daily to quarterly or longer, improving adherence in both treatment and prophylaxis.

Materials and Methods: Five EFdA prodrugs were synthesized and evaluated for anti-HIV activity in primary human lymphocytes, with cytotoxicity assessed in PBM, CEM, Vero, and Huh-7 cells. Metabolic stability was determined in human plasma and liver microsomes. One of the EFdA prodrugs (named DISL-5) was selected for pharmacokinetic (PK) evaluation in CD-1 mice, administered subcutaneously (sc) as an aqueous suspension, alongside EFdA.

Results: All five EFdA prodrugs demonstrated potent anti-HIV activity in human PBM cells. Four prodrugs exhibited no cytotoxicity up to 100 μ M. Their half-lives in human plasma and liver microsomes ranged from less than 5 min to more than 240 min. For compound DISL-5, approximately 6.5% of EFdA was released after 4 h incubation in human plasma, while 22% was released in human liver microsomes, suggesting a slow and sustained release profile. Under a transmission electron microscope (TEM), the aqueous suspension of DISL-5 exhibited needle-shaped crystals measuring 200-1,400 nm ($D_{90} < 950$ nm). Following a single sc administration at an EFdA-equivalent dose of 20 mg/kg in mice, DISL-5 maintained plasma concentration above 1 nM (Coverage in human with 0.25 mg daily dose) for over 12 weeks, markedly longer than EFdA itself.

Conclusions: Compound DISL-5 exhibited anti-HIV activity comparable to EFdA, with a significantly improved cytotoxicity profile. This prodrug design enhanced EFdA's hydrophobicity, slowed metabolic degradation and system clearance, and promoted depot formation, resulting in improved PK and sustained drug release from the LAI. The markedly prolonged release observed following a single sc injection of DISL-5 aqueous suspension demonstrates the feasibility of this prodrug strategy and highlights its potential to enable long-acting formulations capable of extending dosing interval from daily to quarterly or longer. These findings warrant further optimization of formulation parameters to maximize therapeutic performance.



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Pharmacokinetics and Evaluation of Potential Dosing Regimens for Long-Acting VH4524184

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Background: VH4524184 (VH-184) is a third-generation integrase strand transfer inhibitor (INSTI) that has an enhanced in vitro resistance profile versus second-generation INSTIs. In a prior proof-of-concept study of people with human immunodeficiency virus type 1 (HIV-1), oral VH-184 demonstrated potent antiviral activity. We report data from the first-time-in-human study of injectable VH-184 formulations in adults without HIV to assess the feasibility of long-acting dosing with VH-184.

Materials and Methods: This is an ongoing phase 1, randomized, double-blind, placebo-controlled study (ClinicalTrials.gov, NCT06310551). We are evaluating the safety, tolerability, and pharmacokinetics (PK) of parenterally administered VH-184 in adults without HIV for up to 52 weeks. PK data were obtained after escalating doses of VH-184 administered subcutaneously (SC) or intramuscularly (IM). Observed PK data were incorporated into a population PK (PopPK) model, which was used to simulate regimens of monthly (Q1M), every 2 months (Q2M), every 4 months (Q4M), and every 6 months (Q6M) dosing.

Results: Across the first 7 study cohorts, 39 participants (33 male) received a single dose of 1 of 2 formulations (A and B). Most injection site reactions (ISRs) were grade 1, grade 2 ISRs occurred less frequently, and 2 grade 3 ISRs were reported. Erythema, pain, and nodules were the most commonly observed ISRs. For formulation A, median time to maximum plasma concentration (C_{max}) was 3 days after SC or IM injection, and the median terminal half-life after SC dosing was 7 weeks. Formulation B demonstrated a wider time range to reach C_{max}, consistent with slow absorption, and maintained a flat PK profile

through Month 7; the median terminal half-life after SC dosing was 20 weeks. The PopPK model adequately characterized the observed PK profile of both formulations. Results from the simulations demonstrated that VH-184 long-acting injectable (LAI) formulations have the potential to maintain VH-184 PK above clinically effective concentrations. For formulation A, this includes Q1M or Q2M dosing, whereas formulation B allows Q4M or Q6M dosing.

Conclusions: LAI formulations of VH-184 were well tolerated and demonstrated a favorable PK profile. Both formulations A and B showed an extended half-life, which supports future long-acting dosing. The emerging safety profile of VH-184 is consistent with that of INSTIs currently on the market. Data from the ongoing study and the PopPK model will be used to further optimize dosing regimens and inform the phase 2b LAI VH-184 study design.



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Injectable HIV-1 Capsid Inhibitor VH4011499 (VH-499) Formulation Supports Twice-Yearly Dosing

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Background: VH4011499 (VH-499) is an investigational HIV-1 capsid inhibitor currently in development as a long-acting antiretroviral for HIV-1. Previously, oral VH-499 demonstrated rapid and potent antiviral activity in people with HIV-1 and was well tolerated in a proof-of-concept study. Here, we present safety and pharmacokinetic (PK) results from a first-time-in-human study evaluating the ultra-long-acting (ULA) potential of an injectable formulation of VH-499.

Materials and Methods: This is an ongoing phase 1, double-blind (sponsor-unblinded) study (NCT06724640). Participants without HIV-1 were randomized to receive single ascending intramuscular (IM) or subcutaneous (SC) doses of VH-499 (100, 200, 400, or 800 mg evaluated herein) or placebo. Safety and PK data were collected post dose. Single-dose PK parameters using available data were evaluated by non-compartmental analyses.

Results: A total of 65 participants received VH-499 or placebo as an IM (n=33) or SC (n=32) injection. Overall, median age was 36 years, most (92%) participants were male, and 51% identified as White. Across all treatment groups, the majority of adverse events (AEs) had a maximum severity grade of 1. VH-499-related AEs were mainly injection site reactions (ISRs), with injection-site pain being the most common ISR (38/47; 81%). The median duration of ISRs ranged from 1 to 4 days across all cohorts. VH-499-related ISRs were more frequently observed in SC vs IM treatment groups (83%-100% vs 33%-100%). No participants withdrew due to safety reasons, and no serious

AEs were reported. Preliminary PK analysis showed that median time to maximum VH-499 concentration (t_{max}) was approximately 7 days after IM dosing and approximately 42-63 days after SC dosing. The mean half-life of VH-499 after IM was approximately 11 weeks. Based on available data, the SC half-life appears longer, but additional long-term PK data are still needed.

Conclusions: Single-dose injections of both IM and SC VH-499 were well tolerated and demonstrated slower absorption through SC vs IM administration in people without HIV-1. These data suggest that long-acting injectable formulations of VH-499 may support ULA (i.e., 6-month) dosing intervals. The emerging PK and safety data from this study will support model-informed drug development approaches and help guide future clinical development of VH-499.



POSTER ABSTRACT PRESENTATIONS

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Injection Site Reactions More Common and Bothersome with Single Doses of Lenacapavir vs Cabotegravir

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Background: Differences in injection site reaction (ISR) profiles are an important consideration when choosing long-acting injectable (LAI) antiretrovirals. Nodules and indurations are of interest given their potential for long-lasting inflammatory effects and inadvertent disclosure of therapy if visible, yet data remains lacking on their characteristics. The CLARITY study (NCT06970223) provides detailed evaluation of ISRs after a single-dose each of cabotegravir IM (CAB) and lenacapavir SC (LEN) injections.

Materials and Methods: CLARITY is an open-label, randomized crossover study (CAB IM and LEN SC, 1 dose each) in 63 adults without HIV. The primary endpoint was ISR acceptability 7 days after injection using the Perception of Injection (PIN) questionnaire. Secondary endpoints evaluate participant preference and ISR incidence, severity and duration through 6-month follow-up. Size and inflammatory components of ISRs are assessed using a combination of 2D photography and 3D ultrasound. Here we report detailed visible/palpable ISR events of interest up to 190 days after administration of each drug.

Results: A diverse group of 63 participants were enrolled including 33% Female, 38% Hispanic, and 29% Black. Previously this study showed higher ISR acceptability and preference for a single dose of CAB over LEN. Frequency (LEN, n=642 vs CAB, n=150) and grade (\geq grade 2: LEN, 52% vs CAB, 30%) of ISRs were higher with LEN compared to CAB injections. Participants experienced more visible/palpable ISRs of interest with LEN vs CAB, with induration reported in 87% (54/62) vs 20%

(12/61) and nodules in 100% (62/62) vs 57% (35/61), respectively. After 190 days, the number of visible nodules (CAB, 5 vs LEN, 78) and indurations (CAB, 10 vs LEN, 84) was also higher with LEN injections. By modified DAIDS grading criteria (by assigning nodules to equivalent induration DAIDS grading criteria in which ISRs $<$ 2.5 cm in diameter or $<$ 6.25 cm² in surface area were also classified as grade 1 to allow size comparison), 33 CAB and 98 LEN nodules were grade 1, while 2 CAB and 26 LEN nodules were grade 2. Of indurations, 10 were grade 1 and 2 were grade 2 after CAB injections, and 92 were grade 1 and 2 were grade 2 after LEN injections. Across all PIN domains (ie, bother, movement, sleep, acceptability) and individual item assessments (ie, anxiety before/after injection, pain, satisfaction, willingness to continue), participants reported better scores for CAB vs LEN.

Conclusions: The CLARITY study found significant differences in ISRs between CAB and LEN injections after a single dose of each, including more long-lasting, visible, and bothersome ISRs with LEN. These data are critical for informing individuals and their providers regarding LAI antiretrovirals.



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Community-Led Implementation Pathways for Long-Acting Anti-Infective Therapies among HIV-Positive Adolescent Girls and Young Women Experiencing Sexual and Gender-Based Violence in Low-Resource Settings

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Adolescent girls and young women living with HIV who have experienced sexual and gender-based violence represent a key population with persistent challenges in antiretroviral therapy adherence and viral suppression across low-resource settings. These challenges are driven by intersecting structural, psychological, and socioeconomic determinants including trauma, stigma, poverty, unstable housing, and disrupted social support systems that undermine consistent engagement with daily oral treatment regimens. Frequent treatment interruptions, loss to follow-up, and heightened risk of drug resistance remain common within this vulnerable group.

Recent advances in long-acting anti-infective therapies offer promising alternatives to daily adherence-dependent models of care. However, practical pathways for delivering these innovations to marginalized key populations remain insufficiently explored. This abstract examines community-led, trauma-informed implementation insights drawn from Eneza Imani Community Shelter and Rescue Centre in Kenya, a grassroots organization providing shelter, psychosocial care, adherence counseling, peer mentorship, and reintegration support for HIV-positive adolescent girls and young women surviving sexual and gender-based violence and extreme poverty.

Programmatic observations indicate that even within supportive shelter environments, daily medication routines remain psychologically burdensome due to trauma triggers, fear of

disclosure, and competing survival priorities. Upon reintegration into unstable community settings, adherence frequently declines, demonstrating the limitations of behavior-dependent treatment models. These patterns highlight significant opportunities for long-acting injectable antiretrovirals, monoclonal antibodies, and extended-duration preventive formulations to reduce daily adherence demands while improving retention in care.

Community shelters emerged as feasible delivery platforms because of established trust, structured follow-up, and integrated psychosocial services. Implementation considerations identified include consent complexities for minors and survivors, cold-chain and storage realities in low-resource facilities, stigma-sensitive service delivery, and task-shifting to trained community health workers. Integration of long-acting therapy administration with trauma-informed psychosocial care was identified as essential for acceptability and continuity.

These real-world insights suggest that biomedical innovation must be embedded within trusted community systems to achieve equitable access and sustained treatment outcomes. Positioning shelters as novel platforms for long-acting anti-infective delivery reframes implementation science for highly marginalized populations. This model demonstrates how survivor-centered environments can reduce loss to follow-up, mitigate resistance risk, and improve viral suppression trajectories. It further emphasizes the importance of regulatory flexibility, end-user engagement, and context-responsive delivery strategies.

Findings contribute practical evidence to ongoing discussions on scaling long-acting anti-infective therapies across HIV care in resource-limited settings. They underscore that addressing adherence requires not only pharmacological advancement but also community-embedded, trauma-informed implementation pathways. Adopting such approaches may improve long-term outcomes for adolescent girls and young women living with HIV who experience sexual and gender-based violence.

Future research should evaluate acceptability, feasibility, and effectiveness of shelter-based delivery models through implementation studies and pilot programs. Partnerships between community organizations, clinicians, researchers, and policymakers will be critical for translating



these insights into scalable practice. Such collaboration can ensure that long-acting innovations reach those most affected by structural inequities and treatment disruption. Ultimately, aligning biomedical advances with grassroots delivery platforms offers a pathway toward dignified, consistent, and effective HIV care for vulnerable adolescent populations in low-resource environments globally, sustainably, and equitably, today, and tomorrow, throughout communities, everywhere.



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Early Switch to CAB+RPV LA in Treatment-Naive Adults with HIV-1: Month 11 Outcomes from VOLITION

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Background: Long-acting cabotegravir + rilpivirine (CAB+RPV LA) and daily oral dolutegravir/lamivudine (DTG/3TC) are integrase strand transfer inhibitor–based, antiretroviral therapy (ART) regimens with different indications, modalities, and dosing schedules. VOLITION (NCT05917509) is the first study to evaluate an optional CAB+RPV LA switch based on participant choice immediately after attaining virologic suppression with DTG/3TC in adults with HIV-1 who are naive to ART. Median time to suppression on DTG/3TC was 4.1 weeks (95% CI: 4.1–4.3). We present VOLITION Month 11 (M11) outcomes for participants opting for a switch to CAB+RPV LA.

Materials and Methods: VOLITION, a phase 3b, multicenter, non-randomized, open-label study, enrolled adults naive to ART with plasma HIV-1 RNA ≥ 1000 copies/mL receiving DTG/3TC during a suppression phase of up to 16 weeks. After reaching virologic suppression (HIV-1 RNA <50 copies/mL) anytime from Week 4 to 16, eligible participants were offered the choice to switch to CAB+RPV LA Q2M, at the next study visit (Day of Choice [DoC]) or to continue DTG/3TC. A co-primary endpoint was the proportion with HIV-1

RNA <50 copies/mL per Snapshot algorithm at M11 with CAB+RPV LA. Participant experience and safety were assessed.

Results: At DoC, 129/151 (85%) participants switched to CAB+RPV LA, among whom 51% were Hispanic/Latinx, 33% were Black or African American, and 26% were women. At M11, 113 (88%) had HIV-1 RNA <50 copies/mL, six (5%) had HIV-1 RNA ≥ 50 copies/mL, and 10 (8%) had no virologic data per the modified Snapshot algorithm. The observed virologic suppression rate at M11 was 95% (n=113/119 with available virologic data in-window). One (<1%) participant had confirmed virologic failure (CVF) with integrase strand transfer inhibitor and non-nucleoside reverse transcriptase inhibitor resistance. Top reasons for switching were avoiding missed doses (n=103, 80%), not needing pills for travel (n=88, 68%), and convenience (n=82, 64%). Moreover, the participants reported high treatment satisfaction (HIV Treatment Satisfaction Questionnaire score of 57.6 at DoC; 62.5 at M11). Long-acting CAB+RPV was well tolerated and no new safety signals were identified; drug-related adverse events (excluding injection site reactions) occurred in 13 (10%) participants.

Conclusions: Most participants who were ART-naive switched to CAB+RPV LA after achieving virologic suppression on daily oral therapy, demonstrating the importance of choice in addressing individualized needs. Empowering people to choose their preferred treatment through shared decision-making can enable treatment success, as shown by high rates of virologic suppression, low rates of CVF with resistance, and high treatment satisfaction at M11 with CAB+RPV LA.



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Chemistry, Manufacturing, and Control (CMC) Considerations for Tuberculosis Long-Acting Injectable Products for Low-Middle Income Countries

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Background: Tuberculosis (TB) therapy requires prolonged multidrug oral regimens, creating adherence barriers that can contribute to treatment failure and drug resistance. Long-acting injectables (LAIs) could reduce dosing frequency and support implementation in low- and middle-income countries (LMICs), but feasibility depends on CMC strategies that enable high drug loading, acceptable injectability, robust manufacturability, and consistent release.

Methods: A risk-based CMC framework was applied to align the target product profile (route, dose/volume, and release duration) with quality target product profile elements and critical quality attributes (CQAs), focusing on particle size distribution (PSD), suspension performance (sedimentation/redispersion), syringeability (25G), and stability. A low-solubility crystalline candidate drug was used as a case study and formulated as a micronized aqueous suspension depot. Jet milling conditions were varied to reduce API PSD to a suitable range, followed by excipient/vehicle screening and prototype characterization (appearance, PSD, optical microscopy, assay, in vitro release, resuspendibility/sedimentation, syringeability). Select formulations were evaluated in rats after subcutaneous (SC) or intramuscular (IM) dosing with plasma pharmacokinetics (PK) and local tolerability assessment.

Results: Jet milling reduced the drug substance from aggregated, large-particle material (Dv90 ~200 µm) to a micronized material with a narrow PSD range, improving suspension behavior (lower sedimentation, improved redispersion without vial-wall adherence) and enabling 25G syringeability relative to non-micronized suspensions. Formulation concentration strongly

impacted performance: prototype formulations met syringeability criteria, while highly concentrated formulations showed aggregation with bimodal PSD and failed syringeability assessment. Initial PK profiles will be shown.

Conclusions: For TB LAIs intended for LMIC use, micronized aqueous suspensions are an attractive, scalable, high-drug-loading platform when PSD, aggregation control, and syringeability are treated as primary CQAs. In this case study, micronization enabled practical injectability, while higher concentration increased aggregation and delivery risk; route selection also influenced tolerability (IM favored over SC). These findings illustrate how an integrated CMC strategy linking particle engineering to suspension performance and in vivo outcomes can accelerate selection of feasible TB LAI candidates for resource-limited settings.



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Real-World Effectiveness and Tolerability of Cabotegravir + Rilpivirine Long-Acting in People Living with HIV-1: A Meta-Analysis of Real-World Evidence

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Background: Long-acting cabotegravir plus rilpivirine (CAB+RPV LA) is approved for the maintenance of viral suppression in people with HIV-1. Benefits of CAB+RPV LA include less frequent dosing, increased discretion, and freedom from the daily reminder of HIV status. In real-world cohorts, CAB+RPV LA has demonstrated long-term effectiveness with low virologic failure rates across diverse populations, consistent with clinical trial outcomes. We present a meta-analysis of real-world effectiveness and tolerability outcomes.

Materials and Methods: A systematic literature review (SLR) of abstracts, posters, and articles published between January 2020 and July 2024 identified real-world observational cohort studies of CAB+RPV LA. A single-arm meta-analysis was used to produce point-estimates at Month (M) 12 for the proportion of individuals maintaining viral suppression, experiencing virologic failure, and discontinuing treatment, as well as the proportion of injections administered within the dosing window. Estimates were calculated using both a random-effects model and a fixed-effects model. Sensitivity analyses were conducted to assess the impact of consistency in endpoint definitions and in the observation window.

Results: The meta-analysis consisted of 16 studies eligible for inclusion, including 2,264 virologically suppressed participants who had received CAB+RPV LA QM, Q2M, or mixed. At M12, the

proportion of participants maintaining virologic suppression was high (92% in the fixed-effects model and 95% in the random-effects model), with low rates of virologic failure (<1% in both models). Rates of discontinuation were low (11% in both models) through M12 and most injections (92% and 94% in the fixed-effects and random-effects models, respectively) were administered within the ± 7 -day dosing window. Results were robust across sensitivity analyses.

Conclusions: Among diverse people with HIV-1 in real-world clinical settings, CAB+RPV LA maintained high rates of virologic suppression and low rates of virologic failure through 12 months following switch. Rates of discontinuations were low, and most injections were administered within the ± 7 -day injection window. These data reinforce the efficacy and tolerability seen in phase 3/3b trials and further support CAB+RPV LA as an effective and well-tolerated treatment option.



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HVTN 206/HPTN 114: A Randomized, Double-Blind, Controlled Phase 2 Trial Evaluating a Broadly Neutralizing Antibody Combination in Adults without HIV to Inform Future HIV Prevention Efficacy Studies

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Background: The HIV epidemic requires innovative prevention tools to complement existing strategies. The Antibody-Mediated Prevention (AMP, HVTN 703/HPTN 081 and HVTN 704/HPTN 085) trials demonstrated protective efficacy of a single broadly neutralizing antibody (bnAb), VRC01, against sensitive HIV strains, highlighting the need for bnAb combinations to improve breadth and overall protection. HVTN 206/HPTN 114 is the first phase 2 study to evaluate a triple-bnAb combination—VRC07-523LS, PGT121.BIJ414.LS, and PGDM1400LS—sequentially administered intravenously to adults without HIV.

Materials and Methods: The HVTN 206/HPTN 114 design was informed by AMP and six subsequent phase 1 trials of next-generation bnAbs. These studies showed that LS-modified bnAbs, alone and in combination, are safe, well tolerated, and maintain pharmacokinetics (PK) and neutralization activity for at least six months, with no bnAb interference or clinically relevant anti-drug antibodies (ADA), and that fixed-dose regimens were comparable to weight-based.

Results: HVTN 206/HPTN 114 is a randomized, double-blind, controlled phase 2 trial conducted at 18 clinical research sites in Brazil, Peru, and the United States. A total of 190 participants, aged 18–65 years and without HIV, will receive two intravenous infusions six months apart and be followed for 24 weeks after their last study product administration. Participants are

randomized to either a lower-dose group (400 mg of each bnAb per infusion) or a higher-dose group (3200 mg VRC07-523LS, 1600 mg PGT121.BIJ414.LS, and 1600 mg PGDM1400LS per infusion). From March 2025 to March 2026, 168 participants have been enrolled of which 60 have received their second infusion. The study is ongoing and still blinded. Outcomes include safety, serum PK, neutralization activity, and ADA, with subgroup analyses by age, sex, and weight.

Conclusions: HVTN 206/HPTN 114 represents a critical step toward long-acting HIV immunoprophylaxis, building on robust data from the AMP efficacy trials and extensive phase 1 experience with next-generation bnAbs, including prior studies of this same triple-bnAb combination. Results will inform the design of forthcoming combo-AMP efficacy trials and may establish bnAb-based passive immunization as a complementary, long-acting option within global HIV prevention programs.



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Engaging Aging PLHIV in Preparing for Long-Acting HIV Therapies: Lessons From Community Platforms in Botswana

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Background: As long-acting HIV therapies advance into implementation phases, limited attention has been given to preparing aging populations of people living with HIV (PLHIV) in high-burden African settings. In Botswana, over 50% of PLHIV are now aged 50 years and older, reflecting the success of long-term treatment and the growing reality of aging with HIV. Many long-term survivors experience multimorbidity, polypharmacy, and renal impairment. Community engagement is essential to ensure safe, equitable, and acceptable rollout of long-acting therapies in this demographic.

Methods: This abstract draws from structured community engagement activities conducted through community advisory boards (CABs), treatment literacy workshops, and patient support platforms in Botswana. Discussions focused on awareness of long-acting therapies, perceived benefits and risks, inclusion of older adults in clinical trials, eligibility considerations, and concerns related to comorbidities and long-term safety.

Results: Older PLHIV expressed strong interest in reduced pill burden and decreased stigma associated with long-acting options. However, key concerns included management of adverse events during the pharmacokinetic tail, drug–drug interactions in the context of polypharmacy, monitoring of renal function, and equitable access within public health systems. Participants also raised questions regarding eligibility criteria, particularly the potential exclusion of individuals

with hepatitis B virus (HBV) co-infection from certain long-acting regimens that do not provide HBV coverage. Concerns were expressed about the risks of HBV reactivation, treatment interruption, and the need for clear clinical guidance in co-infected populations. Participants emphasized the importance of transparent safety data, age-inclusive trial design, and structured education prior to rollout.

Conclusions: Community platforms are essential for preparing aging PLHIV for the safe and equitable introduction of long-acting HIV therapies. Proactive engagement addressing renal health, multimorbidity, polypharmacy, hepatitis B co-infection considerations, and eligibility criteria will be critical to minimizing unintended harms. Age-inclusive clinical trial design and clear implementation guidance are necessary to ensure that older adults are not systematically excluded from innovation. Integrating aging and comorbidity perspectives into rollout strategies can strengthen informed decision-making, improve uptake, and support sustainable long-term outcomes in high-burden African settings.

