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ABSTRACT BOOK

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ORAL ABSTRACT PRESENTATIONS

1st International Workshop on Long Acting Anti-Infectives (LAAI) 2025

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Proof-of-Concept Study of Oral VH4004280, a New HIV-1 Capsid Inhibitor

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Background: To expand antiretroviral therapy (ART) and pre-exposure prophylaxis choices for people affected by HIV-1, there is a need for additional antiretrovirals with long-acting potential and a range of administration options. VH4004280 (VH-280) is a new HIV-1 capsid inhibitor with a multimodal mechanism of action that has demonstrated highly potent in vitro antiviral activity. In a first-time-in-human study in adults without HIV, VH-280 was well tolerated, did not inhibit or induce CYP3A4, and had a long oral half-life of 146 to 208 hours (~6 to 9 days). Here, we present antiviral effect, pharmacokinetics, safety, and tolerability data for VH-280 from a proof-of-concept, phase 2a trial in people with HIV-1.

Material and Methods: This was a randomized, double-blind, placebo-controlled study evaluating oral VH-280 monotherapy in adults naive to ART with HIV-1 RNA ≥3000 c/mL and CD4+ cell count ≥200 cells/mm³. For the 10-day monotherapy period, participants received a single oral dose of VH-280 100, 300, or 600 mg or placebo on Day 1 (baseline). On Day 11, after the monotherapy period, participants initiated locally sourced, open-label, standard-of-care ART. The primary endpoint was maximum change from baseline in plasma HIV-1 RNA through Day 11, and secondary endpoints included pharmacokinetics, exposure-response relationship, safety, and tolerability. No formal hypothesis testing was conducted, and data were summarized descriptively.

Results: Twenty-one participants were enrolled (VH-280, n=18; placebo, n=3); median (range) age was 32 (18-58) years, 86% were assigned male sex at birth, 76% identified as White race, and 71% identified as Hispanic or Latin American ethnicity. Dose-dependent reductions in plasma HIV-1 RNA were observed over the 10-day monotherapy period after a single dose of VH-280 100, 300, or 600 mg on Day 1. The VH-280 600 mg dose group had the greatest mean (SD) maximum change in HIV-1 RNA from baseline to Day 11 (−1.98 [0.22] $\log_{10}$ c/mL) compared with the 100 mg (−1.06 [0.46] $\log_{10}$ c/mL) and 300 mg dose groups (−1.39 [0.70] $\log_{10}$ c/mL). Increasing VH-280 Day 11 exposures were associated with higher viral load declines. During the monotherapy period, all adverse events (AEs) were grade 1 or 2 in severity, with no observable trends in types of AEs across VH-280 dose groups. Each drug-related AE was only reported once, and no AEs leading to withdrawal, serious AEs, or deaths occurred. There were no clinically meaningful changes in electrocardiograms, vital signs, or laboratory parameters, including lipids and liver biochemistry.

Conclusions: After a single oral dose in people with HIV-1, VH-280 monotherapy was well tolerated and had a favorable safety profile. VH-280 demonstrated potent antiviral activity in people with HIV-1, with up to a mean maximum 1.98 $\log_{10}$ c/mL decrease in HIV-1 RNA over 10 days. These results, in combination with first-time-in-human pharmacokinetic data supporting long-acting dosing schedules, provide further support for the development of new capsid inhibitors for the treatment and prevention of HIV-1.

2

Utilization and Effectiveness of Cabotegravir + Rilpivirine in People with HIV (PWH) with Viremia at Treatment Initiation

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Background: Cabotegravir + Rilpivirine (CAB+RPV) is the first complete regimen of long-acting (LA) injectable antiretroviral therapy (ART) for the treatment of HIV for ART-experienced PWH with undetectable viral load (VL <50 copies/mL [c/mL]). This analysis examined utilization and effectiveness of CAB+RPV LA among viremic individuals at initiation (VL ≥50 c/mL) in US clinical settings.

Material and Methods: ART-experienced adults with viremia receiving ≥1 CAB+RPV LA injection between Feb 2021-Mar 2024 were identified from electronic health records in the Trio Health Cohort. Discontinuation of CAB+RPV LA was defined as 2 consecutive missed injections or ART regimen switch, while confirmed virologic failure (CVF) was defined as 2 consecutive VLs ≥200 c/mL or 1 VL ≥200 c/mL with discontinuation within 4 months of elevated VL; delayed injections were defined as occurring >7 days after target injection date. Emergent resistance associated mutations (RAMs) were analyzed using the Stanford HIVdb algorithm for those with HIV genotype results prior to initiation and after CVF. Results are stratified by low-level viremia (LLV: VL 50-199 c/mL) and higher-level viremia (HLV: VL ≥200 c/mL) at baseline.

Results: Analysis included 111 PWH who initiated CAB+RPV LA (57 LLV; 54 HLV); median age was 44 years (IQR: 34-57), 65% were male, 55% of Black race, and 58% treated in the US South. Median follow-up after initiation was 9 months (IQR: 3-13); 34 (31%) had ≥12 months follow-up. HLV group had median VL of 3.6 log10 c/mL (IQR: 2.30-5.77).

Pre-initiation HIV genotype results were available in 45 (41%) of the cohort (LLV: 21 [37%]; HLV: 24 [44%]). No INSTI resistance was identified; intermediate/high NNRTI resistance was identified in 8 (18%) (LLV: 3 [14%]; HLV: 5 [21%]), with low-level RPV resistance in 4 (9%) (LLV: 0 [0%]; HLV: 4 [17%]).

At analysis, 90 (81%) individuals remained on CAB+RPV LA (LLV: 45 [79%]; HLV: 45 [83%]), with 55/86 (64%) individuals with continuation injections having all injections administered on time (LLV: 30/44 [68%]; HLV: 25/42 [60%]).

At least 1 follow-up VL was available in 81 individuals (73%) (LLV: 43 [75%]; HLV: 38 [70%]). Among those, 72 (89%) achieved suppression (VL <50 c/mL) during follow-up (LLV: 40 [93%]; HLV: 32 [84%]), with last VL suppressed in 68 (84%) (LLV: 39 [91%]; HLV: 29 [76%]). Of 9 who did not suppress, 5 (56%) reached VL <200 c/mL, the remaining 4 (44%) discontinued CAB+RPV (all HLV).

CVF was observed in 2 who suppressed to VL <50 during follow-up (both HLV). The first individual had VL 1210 c/mL and switched from bimonthly to monthly CAB+RPV, re-suppressing before rebounding to VL 4160 c/mL (HIV genotypes unavailable). The second individual had VL 44,800 c/mL and switched to DRV/c/FTC/TAF, re-suppressing in 6 weeks. Low-level RPV resistance was identified pre-initiation (V179D), with emergent NNRTI RAMs (L100I+K101E) and no emergent INSTI RAMs.

Conclusions: High rates of viral suppression with low virologic failure were observed among PWH initiating CAB+RPV LA with VL ≥50 c/mL at initiation, including those with prior NNRTI resistance. Most individuals were adherent to the dosing schedule and were able to remain on CAB+RPV.

3

Novel Ultra-Long-Acting Injectable Formulations of Bictegravir

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Background: Bictegravir (BIC), an integrase strand transfer inhibitor (INSTI) which blocks the action of integrase, a viral enzyme that inserts the viral genome into the DNA of the host cell, has been clinically proved effective for HIV treatment. However, the challenges from the current therapy remain. These include suboptimal adherence, adverse events, and viral resistance. To address these unmet clinical needs, developing ultra-long-acting (ULA) formulations with extended action duration is of significant importance. Herein, we present two ultra-long-acting injectable formulations of BIC that displayed sustained therapeutic concentrations in rats. The ultimate goal is to create once to twice annually ULA BIC injectable formulations, providing an alternative to the current once daily oral medication, which may be used as single or combination therapy with other ULA HIV drugs for the treatment of HIV.

Material and Methods: Formulation 1: A BIC injectable microparticle formulation was created and subsequently injected through intra-muscular route into Sprague Dawley rats (n = 6, 240 mg/kg). Formulation 2: Another BIC injectable formulation was developed with one of our proprietary long acting injectable technologies, followed by a subcutaneously injection into Sprague Dawley rats (n = 6, 240 mg/kg).
The plasma BIC concentrations from both formulations were monitored over 210 days.

Results: Plasma BIC concentrations in both groups exceeded 4 × PA-IC_{95} (protein-adjusted 95% inhibitory concentration, 162 ng/mL) within 30 minutes of administration and remains well above this threshold over a period of 210 days. Furthermore, the profile of Formulation 2 demonstrated a second upward trend in drug concentration after 138 days of administration. The ultimate therapeutic effective window for our ULA BIC injectable formulations is kept being monitored. No adverse events were encountered and no visible injection-site reactions were observed over the period of study in either group.

In addition, we noticed that Formulation 1 peaked on Day 11 with 489-fold PA-IC_{95}, which may contribute more risk of adverse events than necessary efficacy. On the other hand, however, Formulation 2 demonstrated much smaller peak-to-trough ratio with Cmax equals 123-fold PA-IC_{95}, which is sufficient to inhibit the virus without excess drug exposure. Although no adverse events were observed in this study, our model does provide a possible solution to overdosing without compromising long action of drug.

Conclusions: Our lead ULA BIC injectable formulations demonstrate the potential for once to twice annually dosing interval.

Furthermore, the formulation utilizing our proprietary long acting injectable technology suggests significant advantages over microparticle formulation by maintaining plasma BIC concentrations at levels sufficient to potentially enable once to twice annually dosing interval while keeping low peak-to-trough ratio. We see the potential wide usage of our model particularly on drugs with narrower therapeutic windows by effectively inhibiting virus while minimizing the drug exposure and, ultimately, benefiting people living with HIV.

4

Facilitators and Barriers to Long-Acting Injectable Antiretroviral Therapy Uptake Among Youth Living with HIV in Cape Town, South Africa: A COM-B Analysis

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Background: Youth living with HIV in South Africa face treatment adherence and retention challenges with unmet needs even in 2025. Long-acting injectable antiretroviral therapy (LAI-ART) represents an emerging option to mitigate treatment challenges. This study qualitatively examined contextual facilitators and barriers to LAI-ART implementation among youth living with HIV in South Africa.

Material and Methods: From May 2023-May 2024, in-depth interviews were conducted with youth living with HIV 12-29 years (n=16) and caregivers (n=8) in Cape Town, and key stakeholders including providers and governing officials (n=8). Semi-structured guides based on the Consolidated Framework for Implementation Research (CFIR) 2.0 were used. Youth and caregivers were recruited using maximum variation sampling, while stakeholders were purposively sampled. Transcripts were deductively coded using ATLAS.ti. The Capability, Opportunity, and Motivation influencing Behaviour (COM-B) model, integrated into the individual domain of the CFIR 2.0 was used to assess youth engagement with LAI-ART.

Results: Youth and stakeholders described potential challenges and enablers to LAI-ART uptake and persistence, corresponding with COM-B subcomponents. Barriers aligned with physical capability, psychological capability, physical opportunity, and reflective motivation. Traveling, relocation, school as a competing priority, and lower socioeconomic status were reported as potential challenges for youth's physical capability and opportunity to maintain adherence to LAI-ART. Lack of Prior knowledge of LAI-ART including anticipated side effects lowered youth's motivation to initiate. Facilitators aligned with psychological capability, physical opportunity, social opportunity, reflective motivation, and automatic motivation. Youth and stakeholders reported adolescent-tailored services, incentives, and being free from the daily pill burden and associated stigma as enablers to youth LAI-ART uptake. Achieving viral suppression was reported as a motivator among youth for LAI-ART use and social support from families, providers, and counsellors was emphasized as critical for youth's treatment adherence.

Conclusions: Future strategies should focus on reducing logistical barriers to clinic access, particularly if more frequent clinical visits will be necessitated compared to multi-month dispensing for daily oral pills, providing youth-centered counseling, and strengthening available support systems. These approaches will help optimize LAI-ART implementation, improving treatment adherence and retention outcomes and overall well-being for youth living with HIV in South Africa.

5

Cabotegravir and Rilpivirine in Pregnancy: A Multi-Center Study Evaluating HIV Viral Suppression, Perinatal and Neonatal Outcomes

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Background: Long-acting cabotegravir and rilpivirine (LA-CAB/RPV) is a novel injectable antiretroviral therapy approved for virologically suppressed individuals with HIV-1. Data on the safety, efficacy, and outcomes for individuals receiving LA-CAB/RPV during pregnancy are limited. We evaluated HIV viral suppression, perinatal, and neonatal outcomes in pregnant persons with HIV-1 receiving LA-CAB/RPV. This is the first case series to evaluate these outcomes, offering new insight into the use of LA-CAB/RPV during pregnancy.

Material and Methods: We performed a multi-center retrospective chart review of pregnant persons prescribed LA-CAB/RPV between January 2021 and October 2024. Patient demographics, HIV RNA throughout pregnancy, and key perinatal and neonatal outcomes, including birth weight, gestational age, and rates of viral suppression at delivery were collected.

Results: Twenty-two pregnant persons receiving LA-CAB/RPV were included. Baseline demographics are presented in Table 1. Sixteen (73%) initiated LA-CAB/RPV prior to pregnancy and 6 (27%) switched to LA-CAB/RPV during pregnancy. Among those who remained on LA-CAB/RPV for the remainder of pregnancy, 90% maintained HIV RNA <200 copies/mL. The majority had vaginal deliveries; caesarean deliveries were performed for obstetric indications only. Most neonates were born at term, with a median birth weight of 2,390 grams (interquartile range: 2,144, 2,816). Additionally, 81% (n=17) of the newborns received zidovudine only post-delivery. There were no cases of vertical transmission. Three cases of congenital anomalies occurred (ventriculomegaly, fetal pyelectasis, and Trisomy 21) which were not attributed to LA-CAB/RPV by an independent Maternal Fetal Medicine consultant.

Conclusions: The results of this multi-center retrospective cohort suggest that LA-CAB/RPV is associated with high percentage of viral suppression in pregnant persons with HIV-1. Given the small sample size, it was not possible to conduct a meaningful analysis of any associations between perinatal outcomes and the use of LA-CAB/RPV during pregnancy. Our findings support the consideration of LA-CAB/RPV as a viable treatment option during pregnancy, though further research with larger cohorts is needed to validate these findings and ensure long-term safety.

6

Development of Long-Acting Telacebec (Q203) for Treatment of M. Tuberculosis, M. Ulcerans and M. Leprae.

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Background: Telacebec (Q203) is a new anti-mycobacterial imidazopyridine that interfere with ATP synthesis and causes bacterial cell death regardless of the replication status of the bacteria. It is currently in the phase 2 clinical trial for drug susceptible pulmonary tuberculosis caused by Mycobacterium tuberculosis and showed high efficacy in pre-clinical models of Buruli ulcers caused by Mycobacterium ulcerans and leprosy caused by Mycobacterium leprae.
Adherence to medication is essential for treatment success. Long-acting injectable (LAI) formulations with sustained drug release for weeks or months can reduce frequency of drug administration, simplify drug regimen, and improve adherence to medication. Here we developed LAI formulations of telacebec using two different technologies.

Material and Methods: Q203 ditosylate was formulated to an In Situ Forming Implant formulation (Q203-ISFI) and an aqueous crystalline suspension (Q203-IM). ISFI formulations are composed of biodegradable polymer, biocompatible solvent, and drug. They are injectable and solidify after administration. Drug is released from ISFI by diffusion and biodegradation of the polymer matrix and the release can be modulated by composition of the formulation. A suspension with 40 and 70 mg/mL based upon Q203 ditosylate was milled in a dual centrifuge using a media milling approach using zirconium beads. The suspension was stabilized with 3% poloxamer 338, isotonicity adjusted with mannitol and pH adjusted to 4.0 in a 25 mM citric acid buffer. The mean particle size of the two suspensions was 3.20 and 4,17 µm, respectively. Both formulations were optimized to release drug at least for 1 month and evaluated in vitro and in vivo in Sprague Dawley rats.
Each Q203 formulation was administered subcutaneously (Q203-ISFI) or intramuscularly (Q203-IM) to 21 female Sprague Dawley rats at nominal doses of 0, 15.8, and 47.4 mg/animal for Q203-ISFI and of 0, 8.13, and 14.1 mg/animal for Q203-IM. Blood was collected from all groups over a 12-week duration and plasma samples were analyzed for concentration of Q203 using an appropriate LC-MS/MS method (BASP-0030).

Results: Subcutaneous administration of Q203 ISFI resulted in peak concentrations (Cmax) 199 and 382 ng/mL following the 15.8 mg/animal and 47.4 mg/animal dose, respectively. Mean AUClast values for SC administered Q203 were 70,700 ng.hr/mL for 15.8 mg/animal and 195,000 ng.hr/mL for 47.4 mg/animal dose. Dose comparisons of AUClast between the two dose levels indicated a dose proportional increase in AUClast.
After intramuscular administration of Q203-IM, mean Cmax was 250 and 427 ng/mL for 8.13, and 14.1 mg/animal doses, respectively. Mean AUClast values were 114,000 ng·hr/mL for 8.13mg/animal dose and 179,000 ng·hr/mL for 14.1 mg/animal dose and were approximately dose proportional.

Conclusions: We successfully developed two LAI formulations of telacebec that provide sustained drug release in vivo exceeding 12 weeks post administration in female Sprague Dawley rats. Data presented here support further formulation development.

7

First in Human Dose Prediction Scaled from Preclinical Pharmacokinetics for LAI Rifabutin

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Background: A previously reported long-acting in-situ forming implant of rifabutin (RFB) showed consistent drug release for 18 weeks following a single subcutaneous (SC) injection in mice. The current work describes a pharmacometric assessment of the preclinical depot release (from available in vitro and in vivo data) and its deployment to inform human dose estimates.

Material and Methods: In vitro data was fitted with a biexponential model where release was partitioned into slow and fast fractions, yielding estimates of two 1st order in vitro release rate constants: KAslow and KAfast. Mouse in vivo pharmacokinetic (PK) data was fitted with a 1-compartment disposition model with three 1st order depot release input fractions (fast, medium and slow).The 2nd fraction was delayed with a lag time and a transit compartment. Human simulations used a 2-compartment disposition model with parameters obtained from a fitting to a human oral PK study, with a known absolute bioavailability of 20%. Human simulations were then undertaken with depot release inputs to the human disposition model from 1) direct use of in vitro KAslow and KAfast values, or 2) Allometric scaling of mouse release model rate constants by body size according to the formula: KA (human, pred) ≈ KA (mouse) x (70 kg/0.02 kg)-0.25. Trough concentrations (Cmin) and maximum concentrations (Cmax) following clinically approved oral RFB doses of 150 and 450 mg, and RFB minimum inhibitory concentration (MIC) were used as target references to inform first-in-human (FIH) dose expectations, reflecting an acceptable RFB therapeutic window. Given that bioavailability (F) is unknown for novel LAIs and varies for approved LAIs, profiles were simulated assuming 50, 75 and 100% F.

Results: PK simulations for FIH dose predictions using depot release allometrically scaled from mice suggest a 2200 mg dose every 4 weeks may provide a suitable exposure profile - this dose being ~75% lower than the cumulative oral dose of 300 mg daily over 4 weeks; however, this may require up to 2 x 4mL injections at current formulation drug loading. Simulations using in vitro release directly imply weekly injections of 740 mg may be suitable. In the optimal case, with 100% F, a 2200mg single dose is predicted to yield Cmax, C28d and AUC0-28d of 71, 64 ng/mL and 44 µg.h/mL, respectively. In vitro data proved to be unsuitable for prediction of in vivo performance.

Conclusions: Assessment of preclinical data provided an initial human dose estimate based on allometric scaling of in vivo release parameters. Despite much faster metabolism of RFB in humans relative to mice, the simulations support continued development of the RFB in-situ forming implant. Higher drug loading may be possible to minimise injection volume, but additional work is needed to better predict F and thereby improve scaling from preclinical to clinical PK.

8

LAPaL: Your Free Digital Compass in the Evolving Long-Acting Therapeutics Landscape

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Background: With the first marketed injectables for HIV treatment and prevention on the market, and an ever-richer pipeline of long-acting (LA) products across multiple health areas, it becomes challenging to keep tabs on the exciting developments in LA therapeutics and their potential applications. LAPaL, the Long-Acting Therapeutics Patents and Licences database is a free online, access-oriented platfrom, containing expertly curated information on long-acting therapeutics and technology platforms, including their intellectual property landscape, global clinical development and regulatory approvals.

Material and Methods: LAPaL is the first and only database tracking the clinical development and regulatory status of long-acting therapeutics. Priority is given to therapeutics with current or potential application for indications of global health importance, including in the fields of HIV, malaria, viral hepatitis and tuberculosis. Information is collected from publicly accessible sources, including peer-reviewed journal articles, patents, conference proceedings and commercial press releases. Clinical trial information is sourced directly from trial sponsors websites and online registries. Regulatory approval data is compiled from national formularies, drug registries, and approved drug databases maintained by individual countries.

LAPaL also features interactive dashboards of clinical trials and regulatory data, providing a one-stop shop for users seeking an overview of the long-acting therapeutics landscape.
A dynamic search and filter tool can be used to look-up technologies based on their features such as their target health areas, route of administration, associated medicine(s), development stage and intended target population. Users can also generate visual comparisons based on the technologies' and compounds characteristics.

Results: A total 34 long-acting technologies and 38 long-acting compounds and formulations have been published on LAPaL as of February 2025. Primary routes of administration for curated technologies include subcutaneous (66%), intramuscular (25%), and topical (27%) administration routes. Supported dosing frequencies include monthly (n = 17), weekly (n = 14), bi-yearly (n = 7) and yearly (n = 4). Interestingly, most technologies (n=18) could accomodate at least two co-formulated compounds, offering potential for full regimens or multi-purpose formulations. Clinical development stages of the curated compounds include Preclinical (29%), Phase I (4%), Phase I/II (4%), Phase II (33%) and Phase III (21%). Some trends were observed in the LAPaL collection. For example, among the long-acting therapeutics for infectious diseases, marketed products were more likely to have been filed for regulatory approval in higher income countries, than in low- and lower income countries. Another observation is related to the eligibility for HIV treatment trials across LAPaL entries, which was highest for adults at 96% of studies, and lowest for children and adolescents, at 7% of the trials tracked.

Conclusions: Early engagement and multisectorial collaboration on long-acting therapeutics is key to foster innovations and achieve greater impact. LAPaL brings together innovators, advocates, pharmaceutical companies, manufacturers, healthcare professionals, funding agencies and national health programs to increase information sharing, foster partnerships and accelerate innovation in the LA therapeutics' space, with access, affordability and inclusivity in mind. LAPaL's objective is to create a favourable environment to facilitate access to these innovations globally, and reducing time to market in low- and middle income countries.

9

VH3810109 (N6LS) Efficacy and Safety in Adults Who Are Virologically Suppressed: The EMBRACE Study

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Background: VH3810109 (N6LS) is a broadly neutralizing CD4-binding site antibody being developed for long-acting HIV-1 therapy. N6LS was well tolerated and efficacious in participants with HIV-1 naive to treatment when administered intravenously (IV) or subcutaneously (SC) in the proof-of-concept phase 2a BANNER study. In the phase 1 SPAN study, single-dose N6LS given IV (60 mg/kg) or SC (3000 mg) with recombinant human hyaluronidase PH20 (rHuPH20) showed a good safety profile in adults without HIV. Using the same doses from SPAN, the EMBRACE study evaluated the efficacy, safety, and tolerability of N6LS every 4 months + long-acting intramuscular cabotegravir (CAB LA) monthly for maintenance of HIV-1 suppression.

Material and Methods: EMBRACE is a phase 2b, randomized, open-label, multicenter study (45 sites; US and Puerto Rico) in adults with screening HIV-1 RNA <50 c/mL and phenotypic sensitivity to N6LS (90% inhibitory concentration [IC_{90}] ≤2.0 µg/mL). Participants were randomized 2:2:1 to N6LS 60 mg/kg IV + CAB LA, N6LS 3000 mg + rHuPH20 SC + CAB LA, or to continue their pre-baseline standard-of-care (SOC) regimen. The primary endpoint was plasma HIV-1 RNA ≥50 c/mL at Month 6 (FDA Snapshot algorithm).

Results: Of 125 participants randomized, median (range) age was 53 (22-69) years and 83% were male; 63% identified as White, 28% as Black or African American, and 43% as Hispanic or Latin American. At Month 6, proportions with HIV-1 RNA ≥50 c/mL were 2/50 (4%) with N6LS 60 mg/kg IV, 3/49 (6%) with N6LS 3000 mg SC + rHuPH20, and 0/26 (0%) with SOC, and proportions with HIV-1 RNA <50 c/mL were 48/50 (96%) with N6LS IV, 43/49 (88%) with N6LS SC + rHuPH20, and 25/26 (96%) with SOC. Through Month 6, confirmed virologic failure (CVF) occurred in 2 participants receiving N6LS 60 mg/kg IV, 2 receiving N6LS 3000 mg SC + rHuPH20, and 0 receiving SOC. Of 3 participants with data available at CVF, 1 had N6LS IC_{90} >2 µg/mL and none had integrase resistance mutations. N6LS was well tolerated when given IV or SC + rHuPH20, with AEs leading to withdrawal only occurring in the N6LS SC + rHuPH20 group (3/49; 6%) and no N6LS/CAB-related serious AEs reported. N6LS/CAB-related AEs occurred in 32/50 (64%) participants in the IV group and 32/49 (65%) in the SC + rHuPH20 group; 8/49 (16%) participants in the SC + rHuPH20 group experienced grade 3 or 4 N6LS/CAB-related AEs. Infusion site reactions (ISRs) were reported in 4/50 (8%) participants in the IV group and 25/49 (51%) in the SC + rHuPH20 group, with grade ≥3 N6LS-related ISRs reported in 0/50 (0%) participants receiving N6LS IV and 7/49 (14%) receiving N6LS SC + rHuPH20. Mean (SD) duration of all ISRs was 2.0 (0.8) and 6.4 (5.2) days with N6LS dosed IV or SC + rHuPH20, respectively.

Conclusions: N6LS administered IV or SC + rHuPH20 every 4 months in combination with monthly CAB LA maintained viral suppression in most adults who were sensitive to N6LS at baseline, with tolerability favoring IV N6LS.

LB-#1

What Do Early Adopters of Long-Acting Injectable Cabotegravir-Rilpivirine Think About It?

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Background: Little is known about experiences with long-acting injectable cabotegravir/rilpivirine (LA-CAB/RPV) in underserved people with HIV (PWH), particularly PWH initiating with viremia due to adherence challenges.

Material and Methods: In a cross-sectional survey of PWH with ≥3 injections at Ward 86 (San Francisco), Grady Ponce de Leon (Atlanta), and the University of Chicago, we assessed treatment satisfaction (HIVTSQs12/c12), burden compared to oral ART, and interest in alternate delivery locations and modalities. We summarized responses overall and stratified by viral load (VL) < vs. ≥50 copies/mL at LA-CAB/RPV initiation, using chi-square tests to assess for differences by viremic status. Multivariable logistic regression investigated characteristics of PWH who experienced reduction in effort to remember to take LA-CAB/RPV vs. oral ART (reduction from somewhat/very/extremely difficult to not/a little bit difficult).

Results: From 9/2023–7/2024, we surveyed 206 PWH (30% initiating with viremia) with median age 46, 23% cis/trans women, 47% Black, 21% Latine, 36% with housing instability, and 22% with substance use. Median number of injections was 9 (IQR 5,14). Mean (SD) satisfaction using LA-CAB/RPV was 61.5/66 (5.3), and 74% reported mental well-being as better with LA-CAB/RPV. Worry about inadvertent HIV disclosure existed for 66% on oral ART compared to 13% with LA-CAB/RPV. While 35% found remembering both treatment modalities low effort, 62% experienced a substantial reduction in effort with LA-CAB/RPV. In adjusted analyses, unstable housing (AOR = 2.33, 95% CI 1.18, 4.60) and substance use (AOR = 2.42, 95% CI 1.13, 5.19) were associated with reduced effort. Among all PWH surveyed, only 4% found clinic visits more of a problem with LA-CAB/RPV. Preferences for injection location (not mutually exclusive) were their HIV clinic (91%), place where they sleep (32%), community pharmacy (19%), mobile clinic (15%), and community organization (12%). A majority (63%) were at least moderately interested in self-injection and 55% at least moderately interested in injection from someone in their personal life. About half (47%) would prefer another LA modality, e.g. oral, patch. Results were similar stratified by VL at initiation.

Conclusions: In a diverse sample of early LA-CAB/RPV adopters, satisfaction was high and treatment burden reduced compared to oral ART, particularly among PWH with unstable housing or substance use. The HIV clinic was the preferred location. However, ~50% would opt for a different LA modality.

LB-#2

Twice-Yearly Lenacapavir PrEP in Cisgender Gay Men, Transgender Women and Men, and Gender-Diverse People (PURPOSE 2)

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Background: Twice-yearly subcutaneous lenacapavir (LEN) has been shown to be safe and efficacious for HIV prevention in cisgender women. We evaluated LEN for pre-exposure prophylaxis (PrEP) in cisgender gay, bisexual and other men who have sex with men and gender-diverse populations who are disproportionately affected by HIV.

Materials and Methods: PURPOSE 2 (NCT04925752) is a Phase 3, double-blind, active-controlled, randomised trial evaluating HIV prevention efficacy of twice-yearly subcutaneous LEN among cisgender gay, bisexual and other men, transgender women, transgender men and non-binary people who have sex with partners assigned male at birth from the Americas, Africa and Asia. Participants were randomised 2:1 to receive subcutaneous LEN every 26 weeks or daily oral emtricitabine-tenofovir disoproxil fumarate (F/TDF), with corresponding placebos. The primary efficacy endpoint compared HIV incidence in the LEN group with background HIV incidence in the screened cohort, and the secondary analysis compared HIV incidence between LEN and F/TDF groups. LEN adherence was defined as administration within 28 weeks of prior injection; oral F/TDF adherence was evaluated by dried blood spot (DBS) assessment of tenofovir diphosphate levels in a randomly preselected 10% of participants' study visits.

Results: Among 3267 participants who were initially HIV negative, two incident HIV infections occurred in the LEN group (0.10/100 person-years; 95% CI: 0.01-0.37) versus nine infections in the F/TDF group (0.93/100 person-years; 95% CI: 0.43-1.77). HIV incidence in the screened cohort was 2.37/100 person-years (95% CI: 1.65-3.41; N=4637). LEN significantly reduced HIV incidence versus background incidence (incidence rate ratio [IRR]: 0.04; 95% CI: 0.01-0.18) and F/TDF (IRR: 0.11; 95% CI: 0.02-0.51). LEN and placebo injection adherence was high (91% on time). No new or significant safety concerns with LEN were reported. Injection-site reactions were more frequent in the LEN group (83.2%) versus the placebo injection group (69.5%), but discontinuations due to these reactions were low (1.2%). The lenacapavir plasma concentrations for the two participants who acquired HIV were within range of the overall lenacapavir concentrations in the PK cohort. For both participants, the N74D capsid resistance mutation was found on the date of their HIV diagnosis. In the F/TDF PK cohort, adherence was high (consistent with >/= 4 doses/week) in 67% at 26 weeks and 62% at 52 weeks.

Conclusions: Twice-yearly subcutaneous LEN showed superior efficacy to daily oral F/TDF in preventing HIV and was safe and well tolerated among cisgender men and trans and gender-diverse people.

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LB-#3

Clinical Development of Long-Acting Formulations for TB Treatment and Prevention: Insights from the Bedaquiline Long-Acting TMC207TBC1006 Phase 1 Trial

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Background: Tuberculosis (TB) remains the leading infectious cause of mortality worldwide, underscoring the urgent need for innovative prevention and treatment strategies. Long-acting (LA) therapies have shown promise in enhancing adherence, improving patient satisfaction and resultant treatment outcomes in a broad range of health conditions to date. To effectively meet TB global health challenges, it is important for long-acting TB regimens and formulations to align with target multidrug-regimen profiles (TRP) and individual target product profiles (TPP).

Materials and Methods: The TMC207TBC1006 study is an open-label, parallel-group, single ascending dose Phase 1 first-in-human trial to assess the pharmacokinetics (PK), safety, and tolerability of an intramuscular (IM) injection(s) of long-acting bedaquiline (BDQ). The trial is currently enrolling the final dosing group and interim analysis of PK and safety data is expected in the third quarter of 2025. The PK sampling strategy is intended to capture intra- and inter-subject variability in PK and inform PK/PD modeling to establish the human dose. Safety monitoring includes adverse events, notably injection site reactions, as well as visual analog pain scale reporting at scheduled timepoints after injection(s). Probable characteristics of LA TB compounds were compared against the current World Health Organization (WHO) TRP for oral TB treatment and TPP for oral TB prevention. Based on the insights gained from TMC207TBC1006 as well as from the evolving landscape of LA formulations, critical considerations for future LA TB TRP and TPP development are proposed.

Results: Initial experience from TMC207TBC1006 indicate that future TB LA TRP/TPP development should consider two key LAI characteristics: the volume and number of injections required for TB treatment or prevention, and the time necessary for LA injectable drugs to achieve steady-state concentrations promptly. For TB treatment, minimum suggested TRP requirements include: indications for drug-resistant TB (RR-TB) in both adults and children; non-inferior efficacy and safety compared to standard of care regimens; consideration of time windows to make up for missed injections ; a regimen with 3 to 4 LA drugs that includes an intensive oral/LA lead-in phase followed by an LA continuation phase and an overall treatment duration of maximally? 3-4 months. For TB prevention, the minimum requirements suggested include: a pan-tuberculosis preventive therapy (PAN-TPT) indication for high-risk populations; a single dosing instance with 1-2 LA injections during one clinic visit; non -inferior efficacy compared to SOC and an acceptable safety profile.

Conclusions: Bedaquiline LA is the first long-acting TB drug to undergo evaluation in a Phase 1 clinical trial. The insights obtained from this study are crucial for developing target regimen and product profiles that consider realistic expectations for what may be achieved with individual LA compounds in development, as well as their combination into multidrug regimens for the treatment of TB disease.

LB-#4

Global Perspectives of People Living with Hepatitis B on Long-Acting Antivirals: Survey Results

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Background: Currently, daily oral long-term antiviral therapy is the only available treatment option for chronic hepatitis B – the world's most common liver infection worldwide. With the development of new potential treatments—such as long-acting antivirals (LAA) – it is essential to understand how people living with hepatitis B (PLWHB) perceive these emerging options, including anticipated challenges, concerns, and enablers. This study aimed to document global patient perspectives, preferences, and values regarding novel hepatitis B LAA therapies.

Material and Methods: We conducted a mixed methods study of adults ≥ 18 years who self-reported as PLWHB. A global online survey, available in five languages (English, Mandarin, Arabic, Tagalog, and Spanish), was open for four months and comprised four main sections developed in consultation with subject matter experts and reviewed by community partners. We also held a focus group discussion with six participants from five countries. This abstract reports findings from the survey only. The study was IRB approved, and all participants provided online consent. This work was supported by the NIH (LEAP, R24AI118397) and the Hepatitis B Foundation.

Results: The survey received over 1,000 responses from 81 countries. Respondents were mostly between the ages of 26–45 (55%) years old, male (70%), and 43% identified as Black. HBV long-acting injectables were the most preferred option compared to daily pills (67%), while microneedle patches were least preferred, with only 53% favoring patches over daily pills. When asked to rank all four formats, long-acting injectables were favored most (51%), followed by pill (25%), microneedle patch (13%), and implant (11%). Willingness to join HBV clinical trials was highest for injectables (68%) versus implants or patches (both 47%).

Conclusions: Early engagement of PLWHB is critical to ensure their perspectives and preferences inform the development and rollout of new treatment modalities. Tailored patient education will be particularly important for novel options like microneedle patches, which may be unfamiliar or counterintuitive despite their non-invasive nature. These findings underscore the importance of including patient perspectives early in the HBV treatment development process.

POSTER ABSTRACT PRESENTATIONS

1st International Workshop on Long Acting Anti-Infectives (LAAI) 2025

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Black Transgender and Cisgender Women's Experiences With PrEP and Reasons for Choosing Injectable PrEP

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Background: Black women account for ~50% of new HIV diagnoses among cisgender and transgender women in the United States. Notably, HIV PrEP uptake has been low among Black women; therefore, understanding their motivation for initiation is key to improving engagement. We present differences in PrEP perceptions and reasons for choosing long-acting injectable cabotegravir (CAB LA) in Black cisgender and transgender women before initiation.

Materials and Methods: EBONI is the first industry-led, gender-concordant, Phase 4 hybrid implementation study evaluating implementation of CAB LA delivery to Black cisgender and transgender women across US "Ending the HIV Epidemic" jurisdictions. From November 2022 to September 2024, 151 women enrolled from 20 clinics and completed baseline surveys. A purposive sample of 40 women completed interviews that were transcribed. Descriptive statistics and representative quotes are presented.

Results: Overall, 111 (74%) participants were cisgender women; 40 (26%) were transgender women; 6 (4%) were Hispanic. Mean age was 36 years (standard deviation [SD]: 10.3). Additionally, 75% (transgender women: 95% vs. cisgender women: 68%) and 52% (transgender women: 63% vs. cisgender women: 49%) had heard of oral PrEP and CAB LA, respectively; 36% (transgender women: 10% vs. cisgender women: 46%) had never taken PrEP. Overall, 26% of women were unaware of their partner's HIV status. A lower proportion of cisgender women perceived positive community attitudes toward PrEP compared with transgender women (40% vs. 87%). Two common reasons reported for choosing CAB LA were wanting a more convenient prevention option (transgender women: 45%; cisgender women: 42%; "It's a great match for me. I'm a business owner, I have a family…And also I had a son who had a medical issue…switching to long-acting PrEP has really made my peace of mind just a lot better…I can make time to schedule to do that, versus having to do something daily." [cisgender woman]) and often forgetting to take pills (transgender women: 43%; cisgender women: 37%; "and you maybe forgot your pills, but once you know you got that shot in you, it's a great feeling to know that you didn't miss that one pill a day." [transgender woman]). Key differences in motivations by gender identity included having never tried PrEP but wanting protection from HIV (transgender women: 20% vs. cisgender women: 43%), not having to worry about HIV every day (transgender women: 20% vs. cisgender women: 32%), and CAB LA being suggested by their doctor (transgender women: 30% vs. cisgender women: 15%). Most women (87%) reported having no concerns about CAB LA and found it appropriate (mean/total possible score [SD]: 4.4/5.0 [0.73]) and feasible (mean/total possible score [SD]: 4.4/5.0 [0.69]).

Conclusions: A total of 36% of Black women were newly using PrEP, suggesting CAB PrEP is expanding prevention coverage among this population. At initiation, cisgender and transgender women believed CAB LA was appropriate and feasible for them. There were notable differences in community attitudes towards PrEP, PrEP awareness, and reasons for choosing CAB LA by gender identity. Equipping providers with gender identity–sensitive PrEP discussion strategies could support PrEP uptake among Black women.

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PILLAR Month 12 Clinical Results: Zero HIV Acquisition and High Persistence with CAB LA for PrEP

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Background: In 2022, men who have sex with men (MSM) and transgender men (TGM) accounted for 67% and <1% of new US HIV diagnoses, respectively. Additionally, an estimated 15% of MSM, and 3% of TGM, were estimated to be living with HIV in the US. Long-acting (LA) cabotegravir (CAB) administered every 2 months via intramuscular injection is the first and only approved LA medication for HIV-1 pre-exposure prophylaxis (PrEP). We present clinical outcomes through Month (M) 12 with CAB LA in the PILLAR (NCT05374525) study.

Material and Methods: PILLAR is a phase 4 gender-concordant implementation science trial assessing integration of CAB LA at 17 clinics for MSM and TGM. Clinical assessments included HIV incidence, HIV diagnostic testing, persistence (duration for which an individual continued to receive injections), and safety and tolerability.

Results: From May 2022 to August 2023, 201 participants enrolled and initiated CAB LA; 6% were TGM, median age (interquartile range) was 35 (29–44) years, 26% were Black, and 38% were Hispanic. Most (78%) had taken oral PrEP in the last 6 months prior to CAB LA initiation. There were no cases of HIV acquisition through M12. At M6 and M12, persistence on CAB LA was 85% (n=171/201) and 72% (n=142/196; excludes 5 participants who completed the study post data cutoff), respectively. A total of 27 (13%; n=26 MSM, n=1 TGM) participants acquired a sexually transmitted infection that was identified through last on-study visit (gonorrhea, n=14; chlamydia, n=12; syphilis, n=7). Most study sites used HIV-1 antigen/antibody (Ag/Ab) testing during screening (94%; n=16/17), 71% (n=12/17) used HIV-1 RNA testing, and 65% (n=11/17) of clinics utilized both HIV-1 Ag/Ab and HIV-1 RNA testing. Overall, 70% (n=141/201) of participants completed all injections within the study. Five (2%) participants missed an injection and received oral CAB (n=1) or alternative PrEP (n=4). Adverse events (AEs) related to CAB LA were rare, with injection site pain the most frequently reported (3%; n=6). A total of 11 (5%) participants had AEs leading to discontinuation, most commonly due to injection site pain (n=6).

Conclusions: These real-world data obtained from a diverse population support CAB LA as an effective PrEP option associated with high persistence. No cases of HIV acquisition were observed through 12 months irrespective of the testing method(s) used, potentially suggesting a less prescriptive testing guideline.

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Feasibility of Delivering Long-Acting Antiretroviral Injectables to Key Populations in Uganda: Lessons from HIV Prevention Programs

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Background: Long-acting antiretroviral injectables (LAAIs) are a promising innovation in HIV treatment and prevention, especially for key populations. Despite their potential, unique barriers such as stigma, limited access, and healthcare infrastructure challenges hinder their delivery in resource-limited settings. This study evaluates the feasibility of LAAI delivery in Uganda, focusing on lessons from existing HIV prevention programs.

Material and Methods: Data were drawn from three HIV prevention initiatives in Uganda targeting key populations: the Twakke Project, the Social Media HIV Prevention Campaign, and the YOUCAN Project. Mixed methods were used, including quantitative metrics (adherence rates and uptake data) and qualitative interviews with 240 participants and 15 healthcare providers between 2023 and 2024. Key outcomes assessed included patient preferences, adherence levels, and healthcare provider insights on LAAI implementation.

Results: Seventy-five percent of participants expressed a preference for LAAIs due to reduced stigma and convenience compared to daily oral medications. Adherence rates improved by 20% in programs incorporating treatment literacy sessions. However, significant challenges included inadequate healthcare provider training (reported by 60% of providers) and infrastructure gaps, such as cold-chain storage. Stakeholder feedback highlighted the need for community sensitization to address misconceptions about LAAIs.

Conclusions: This study demonstrates the feasibility of delivering LAAIs to key populations in Uganda, emphasizing the importance of addressing structural barriers and enhancing community awareness. Tailored interventions, including provider training and targeted outreach campaigns, are essential for scaling up LAAI delivery and improving outcomes for key populations.

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Long-Acting PrEP Awareness and Interest among Black and Hispanic Men in the US

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Background: Recent data continue to highlight the inequities in HIV pre-exposure prophylaxis (PrEP) among Black and Hispanic people in the US, as PrEP coverage remains low in these groups while overall PrEP use has increased over the past decade. New PrEP options, such as long-acting (LA) PrEP, may help bridge this gap, especially in areas targeted by the Ending the HIV Epidemic (EHE) initiative. This study assesses PrEP preferences and use among Black and Hispanic men living in predominately EHE jurisdictions.

Material and Methods: Cisgender men were recruited to participate in an in-person survey covering demographics, healthcare access, sexual health, and PrEP use. Eligible participants were: age 18+ years, self-reported Black race and/or Hispanic ethnicity, penetrative sex in the past six months, and unknown or negative HIV status. Participants were also asked about their interest in various PrEP options if available for free from their healthcare provider (HCP). Descriptive analyses were conducted using SAS v9.4.

Results: 157 men completed the survey (median age: 31; Black, non-Hispanic: 34%; Hispanic: 66%; living in an EHE jurisdiction: 96%; single/dating: 69%); almost two-thirds (63%, n=99) were aware prior to the survey of oral PrEP for HIV prevention, while one-third (32%, n=50) had heard of LA PrEP. One-third (32%, n=51) were currently taking PrEP, of whom the vast majority (86%) were taking daily oral (DO) PrEP, while a small percentage (10%) reported on-demand (OD) PrEP use. When asked about starting various forms of PrEP, 43% of all participants expressed interest in starting LA PrEP if offered by their HCP; among participants not currently taking DO PrEP (n=108), 41% (n=44) expressed interest in starting LA PrEP, and among those not currently taking OD PrEP (n=152), 38% (n=58) expressed interest in starting LA PrEP. Among participants interested in LA PrEP (n=67), primary reasons were effectiveness in preventing HIV (79%, n=53) and ease of use (49%, n=33). When asked about switching to another form of PrEP, about half (49%, n=25) of current PrEP users expressed interest in switching to LA PrEP. Among men unaware of LA PrEP prior to the survey (n=107), 38% (n=41) stated that they would start LA PrEP in the next 3 months if it were available.

Conclusions: There was considerable interest in LA PrEP among Black and Hispanic men, demonstrating promise that LA PrEP may be an effective tool to reduce existing racial and ethnic inequities in PrEP use, especially in priority areas in the US.

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Evaluation of Patient Experience and Treatment Tolerability in the Phase 2b Study of VH3810109 (N6LS) and Cabotegravir Long-Acting Injections for HIV Treatment

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Background: Clinical outcome assessments (COAs) are crucial for evaluating the effectiveness and patient experience of new treatments. This study examines COAs in a phase 2b randomized open-label study of VH3810109 (N6LS) combined with cabotegravir (CAB) long-acting injections for HIV treatment.

Material and Methods: The study involved 125 participants aged 18 to 70 with HIV, divided into three groups: VH3810109 administered intravenously (IV) (N=50), VH3810109 administered subcutaneously (SC) with recombinant human hyaluronidase (rHuPH20) (N=49), and a standard of care (SOC) oral group (N=26). Both VH3810109 groups received monthly CAB intramuscular (IM) injections. Primary endpoints were efficacy, safety, pharmacokinetics (PK), and tolerability, with COAs as exploratory endpoints. COAs included the Acceptability (ACCEPT) Questionnaire, Numeric Rating Scale (NRS) for injection site reaction, HIV Treatment Satisfaction Questionnaire (HIVTSQ), EQ-5D-3L for quality of life (QoL), and the Perception of Injection (PIN) for bothersomeness. Participants completed COAs electronically via a secure app. Injection site pain and acceptability were assessed at Day 1 and Month 4, while other COAs were completed at Day 1 and Month 6. Missing values were imputed by carrying forward the most recent post-Day 1 value, if available.

Results: Participants in both VH3810109 + CAB groups reported favorable scores on the 'Bother of Injection Site Reactions (ISRs),' 'Physical Impact,' 'Sleep,' and 'Acceptability' domains of the PIN. Over 90% were minimally bothered by pain, redness, swelling, itching, or bruising at the injection site at Day 1, with no physical impact or sleep disruption, and found the reactions and pain 'totally or very acceptable.' These results were consistent at Month 4 (over 90%). Satisfaction with the injection system was high at both Day 1 and Month 4, with participants expressing willingness to continue the treatment outside the trial. Mean NRS scores for pain were low at Day 1 and remained low at Month 4, indicating good tolerability. On Day 1, the 'Acceptance/General' dimension score of ACCEPT was high across all three study arms. At Month 4 and Month 6, the scores for both VH3810109 + CAB treatment arms were relatively stable. Mean values for HIVTSQ total treatment satisfaction scores remained high from Day 1 to Month 6 for all treatment groups. The HIVTSQ change score indicated improved satisfaction over time in both treatment groups, with mean scores of 26.5 for both VH3810109 treatment groups, compared to 19.4 in the oral group. On the EQ-5D-3L, over 75% of participants at Day 1 and over 80% of participants at Month 6 in both VH3810109 treatment groups reported 'no problems' across the five dimensions.

Conclusions: Both VH3810109 IV + CAB and VH3810109 + rHuPH20 SC + CAB treatments were well tolerated. Quality of life showed some improvement by Month 6 for the treatment arms. There was little difference in COAs between the IV and SC groups. Treatment satisfaction was high across all groups at both Day 1 and Month 6, with high acceptance of the treatment. Patient experience of both the SC and IV treatment arms was excellent.

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Higher Real-World Adherence and Persistence with Long-Acting Cabotegravir Plus Rilpivirine (CAB+RPV LA) Compared to Oral Antiretroviral Therapy (ART) among People with HIV (PWH) in the US: the ABOVE Study

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Background: CAB+RPV LA is the only complete long-acting regimen for treatment of virologically suppressed people with HIV and may alleviate adherence challenges with daily oral therapy. Treatment adherence and persistence are critical for the long-term success of HIV treatment. The ABOVE study evaluated real-world adherence and persistence to CAB+RPV LA versus remaining on oral ART regimens.

Material and Methods: ABOVE was a retrospective US cohort study using Symphony Health Solutions Integrated Dataverse administrative claims database from 01/01/2020 to 8/31/2023. people with HIV ≥12 years of age on stable guideline-recommended oral ART were categorized into those initiating CAB+RPV LA and those remaining on oral ART. Index date was defined as first injection between 01/01/2021 and 03/01/2023 (CAB+RPV LA cohort) or imputed for the oral ART cohort. People with HIV were required to have ≥12 months of follow-up after index. Standardized mortality ratio (SMR) weights were generated based on propensity scores to balance baseline characteristics between cohorts. Adherence (percentage of people with HIV with proportion of days covered (PDC) ≥0.9 over 12-months following index) and persistence (days from index to the earliest of treatment discontinuation or end of follow-up) to the index regimen were compared. Doubly robust logistic regression model was used to estimate the adjusted odds ratio (aOR) and 95% confidence interval (CI) for adherence.

Results: 442,091 people with HIV were identified during the study period. After applying eligibility criteria, 1,245 in the CAB+RPV LA cohort (mean age 47 years, 24% females) and 58,644 in the oral ART cohort (mean age 50 years, 23% females) were included. Majority of CAB+RPV LA dosing was every 2 months only (58%) or switched from monthly to every 2 months (29%). After SMR weighting, key baseline characteristics were balanced. In the weighted sample, a higher proportion of people with HIV in the CAB+RPV LA cohort was adherent (74% vs 30%, p<0.001; median [IQR] PDC: 1.00 [0.89, 1.00] vs. 0.80 [0.51, 0.92]) and had higher persistence (median [IQR]: 424 [201, 537] vs. 393 [174, 431] days, p<0.001) compared with the oral ART cohort. People with HIV in the CAB+RPV LA cohort had significantly higher odds of being adherent over 12 months compared with the oral ART cohort (aOR: 8.06, 95% CI: 6.62, 9.81, p<0.001).

Conclusions: These data demonstrate that, among US people with HIV previously on stable oral ART, switching to long-acting ART resulted in significantly higher 12-month adherence and persistence over the follow-up compared with remaining on oral ART.

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Similar Virologic Outcomes and Isolated Viremic Event (Blips, Low-Level Viremia, Suspected Virologic Failure) Frequency Between Oral and Long-Acting Antiretroviral Therapy: Pooled Analysis of Phase 3/3b Cabotegravir + Rilpivirine Long-Acting Studies

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Background: The definition and management of viral blips vary across clinical guidelines. Long-acting (LA) antiretroviral therapy (ART) may present different management considerations for healthcare providers. In phase 3/3b studies, viral blips (single viral load [VL] between 50 and <200 c/mL with adjacent values <50 c/mL) with cabotegravir + rilpivirine LA (CAB+RPV LA) were not associated with confirmed virologic failure (CVF; 2 consecutive VLs ≥200 c/mL) through up to 152 weeks of follow-up. We present a pooled post hoc analysis assessing virologic outcomes following viral blips, low-level viremia (LLV; ≥2 consecutive VLs between 50 and <200 c/mL), and isolated suspected virologic failure (SVF; single plasma VL ≥200 c/mL with the subsequent value <200 c/mL), through 1 year in CAB+RPV LA phase 3/3b studies.

Material and Methods: Viral blips, LLV and VLs meeting isolated SVF criterion were analyzed across the phase 3/3b FLAIR, ATLAS, ATLAS-2M (through Week 48) and SOLAR (through Month 12) studies. Isolated SVF was divided into 3 categories: (1) single VL ≥200 to <500 c/mL; (2) single VL ≥500 to <1000 c/mL; (3) single VL ≥1000 c/mL, all with the subsequent adjacent VL <200 c/mL. SVFs that became CVF at next VL testing were excluded. Plasma samples were analyzed for HIV-1 RNA VL using the Abbott RealTime HIV-1 assay.

Results: Overall, 2506 participants were included (CAB+RPV LA, n=1692; comparator oral ART, n=814). The proportion of participants experiencing viral blips was 6% (n=97/1692) and 7% (n=61/814) with LA and oral ART, respectively; <2% had LLV or isolated SVF in both arms. SVFs by magnitude of VL elevation were low and similar between arms (category 1: LA, n=9/1692 [<1%], oral, n=4/814 [<1%]; category 2: LA, n=3/1692 [<1%], oral, n=5/814 [<1%]; category 3: LA, n=0/1692, oral, n=4/814 [<1%]). CVF occurred in <1% of participants (LA arm, n=16/1692; oral, n=7/814). The number of participants with previous viral blips or LLV experiencing CVF was low across both arms (LA, n=0/97 and n=1/18, respectively; oral, n=1/61 and n=0/10, respectively). In the LA arm, 25% (n=3/12) of participants with isolated SVF had subsequent CVF vs. 23% (n=3/13) in the oral ART arm.

Conclusions: In this pooled analysis through 1 year, CVF rates were low and similar between oral and LA ART. Viral blips and LLV were similarly infrequent with LA and oral ART and were not associated with CVF. Isolated SVF events were rare, with similar rates of subsequent CVF with LA and comparator oral ART. These data suggest similar outcomes after isolated viremic events with both LA and oral ART.

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Patient Preferences for Long Acting Injectable and Oral ART: A Discrete Choice Experiment in the US

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Background: Antiretroviral therapy (ART) advancements have expanded treatment options for people with HIV, now including both daily oral therapies and newer long-acting injectables (LAIs). While oral ART remains the standard of care, long-acting formulations offer potential benefits like improved adherence, reduced treatment fatigue, and greater convenience. Understanding patient preferences is crucial for guiding treatment development and regulatory decision-making. This study evaluates preferences for ART regimen attributes in the US.

Material and Methods: We employed a discrete choice experiment (DCE)-based survey, where people with HIV chose between hypothetical ART regimens, with varying attributes: administration mode (weekly oral vs. LAIs as intramuscular, subcutaneous, intravenous), administration setting (healthcare provider [HCP] vs. self-administered), administration frequency (weekly, every 2, 3, 4, or 6 months), injection-related side effects (injection site pain, redness/swelling, nodule formation) and general side effects (0%, 5%, or 10% probability). Participants were presented with a choice between two LAI and one weekly oral ART. If oral was chosen, they then had to select between the two injectable treatments. Oral treatments varied only by general side effects, while administration mode (self-administered), frequency (weekly), pain and injection-related side effects (none) remained constant.
Participants were recruited online and through HCP referrals. Eligible participants were ≥18 years, diagnosed with HIV, and currently receiving ART. The final survey included 16 choice tasks structured using a fractional factorial experiment design to optimize statistical efficiency. A multinomial model was used to estimate preference weights. Conditional relative importance (CRI) scores were derived to quantify the significance of each attribute in patient decision-making.

Results: Overall, 201 people responded to the online survey (71.6% male, 47.3% men who have sex with men, 48.8% Black or African American). When comparing oral and injectable ART, if the weekly oral treatment presented with 0% side effects, it was preferred over injectables presented with a higher risk (5% or 10%) in 56.1% of choices. When the weekly oral treatment was associated with a 5% or 10% probability of side effects, it was preferred 47% to 49% of times. CRI analysis identified "Treatment administration frequency" (43.7%) and "Injection site pain" (26.0%) as the most influential factors. The remaining five attributes each contributed 5% to 7%. Multinomial model results indicated preference for longer intervals between injections (two months: r=-0.872, p<0.0001; 6 months: r=0.797, p<0.0001), and reduced injection site pain (mild: r=0.491, p<0.0001; severe: r=-0.502, p<0.001). That is, negative coefficients for the two-month interval suggest that participants perceive shorter intervals as less preferable. Positive coefficients for the six-month interval indicate that longer intervals are preferred. There was no significant preference for injection types, except for subcutaneous, with higher preference for HCP administration (r=-0.126, p=0.003).

Conclusions: When considering LAI, people with HIV showed strong preferences for longer intervals between treatments, and minimal injection site pain. Treatment administration frequency and injection site pain are the primary decision-making factors. Future ART developments should prioritize these attributes to enhance adherence and satisfaction. Understanding these preferences is crucial for guiding treatment development and regulatory decisions, ultimately improving quality of life for people with HIV.

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Clinical Outcomes at Month 12 After Initiation of Cabotegravir and Rilpivirine Long Acting (CAB+RPV LA) in an Observational Real-World Study (BEYOND)

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Background: CAB+RPV LA is the first complete long-acting regimen for virologically suppressed people with HIV administered by a healthcare provider (HCP). The BEYOND real-world study describes the month 12 (M12) clinical outcomes of patients initiating CAB+RPV LA in the United States.

Material and Methods: BEYOND is a 2-year observational study of utilization, outcomes, and experience of people with HIV initiating CAB+RPV LA (monthly or every 2 months) across 30 US sites. HCPs completed an electronic case report form (eCRF) at baseline, M6, and M12 to capture demographics, medical and treatment history, and clinical outcomes.

Results: A total of 308 people with HIV were enrolled between Sep 2021-Jul 2022 and initiated CAB+RPV LA. Mean age of participants was 46 years, 39% were ≥50 years, 13% were female assigned at birth, with 44% White, 33% Black, and 23% other races. By M6, 36/308 (12%) participants discontinued the study. This M12 analysis (data cutoff Sep 2023) included 272 people with HIV: 245 remained on treatment at M12, 8 (3%) additional people with HIV were reported as having discontinued CAB+RPV LA since M6, and 19 (7%) had unknown treatment status. The most common reason for discontinuation was medication cost/access issues (3/8 people with HIV). At M12, 97% were receiving CAB+RPV LA every 2 months and 3% were on monthly dosing. Of people with HIV with viral load <50 c/mL at baseline, 97% (181/187) had a most recent viral load of <50 c/mL at M12. Of people with HIV with viral load >50 c/mL at baseline, 100% (13/13) had a viral load of <50 c/mL at M12. Confirmed virologic failure (CVF; defined as 2 consecutive HIV-1 RNA viral loads ≥200 c/mL or 1 HIV-1 RNA viral load ≥200 c/mL followed by regimen discontinuation within 3 months of viral load ≥200 c/mL) with resistance was reported in 1/272 (0.4%) PWH between M6 and M12.

Conclusions: The M12 results from real-world initiation of CAB+RPV LA in the United States are consistent with the phase 3/3b clinical trials with high rates of virologic suppression, low rates of CVFs with treatment emergent resistance, and no new discontinuations due to intolerance.

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Comparison of Treatment-Emergent Resistance Associated Mutations among Single Tablet Regimens and Cabotegravir+Rilpivirine for the Treatment of Virologically Suppressed People with HIV: A Systematic Literature Review and Network Meta-Analysis

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Background: Treatment emergent resistance associated mutations (TE-RAMs), including dual-class resistance, are developing in people with HIV (PWH) adherent to the injection schedule for cabotegravir+rilpivirine (CAB+RPV). TE-RAMs have not been observed in people adherent to HIV guideline recommended single tablet regimens (STRs) with a high barrier to resistance. This study compared the risk of TE-RAMs among STRs and CAB+RPV in virologically suppressed (VS) PWH.

Material and Methods: Randomised controlled trials (RCTs) investigating switching to any STR or CAB+RPV in VS PWH with > 48 weeks of follow-up in both arms, and published 2003-March 2024, were retrieved from PubMed, Embase, Cochrane CENTRAL and EBSCO Open Dissertation. Arms comprised of multi-tablet regimens were included only if the intervention arm was an STR. For studies with multiple regimens in the comparison arm, the regimen with the most participants was used. Risk ratios (RR) with 95% confidence intervals were estimated using a random-effects model. Surface under the cumulative ranking curves (SUCRA) were used to rank interventions to prevent TE-RAMs. SUCRA scores signal the probability a treatment has of being among the best options in the network. Higher scores represent better ranking.

Results: Nineteen RCTs (10760 participants) were included. At 48 weeks, risk of TE-RAMs with B/F/TAF and DTG/ABC/3TC is potentially 80% lower than CAB+RPV Q8W [RR 0.20 (0.02, 1.83) and 0.20 (0.002, 16.67), respectively], and tended to be lower than CAB+RPV Q4W and all two- and three-drug STRs. Risk of TE-RAMs with CAB+RPV Q4W appears 56% lower than Q8W [RR 0.44 (0.16, 1.22)]. CAB+RPV Q8W showed a trend toward a higher risk of TE-RAMs and a lower probability of preventing TE-RAMs than all INSTI- and PI-based STRs. Based on SUCRA scores, B/F/TAF (74.3%) ranked highest and EFV/FTC/TDF (22.7%) ranked lowest for probability of preventing TE-RAMs.

Conclusions: In VS PWH, B/F/TAF has the highest probability of preventing TE-RAMs and tended to have the lowest risk of TE-RAMs, whereas CAB+RPV Q8W performed similar to STRs with lower barriers to resistance. Since treatment is lifelong, and resistance impacts current and future treatment options, clinicians should include the differential risk of TE-RAMs in shared-decision making discussions when switching ART in stable, suppressed individuals.

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High and Comparable Efficacy between CAB+RPV LA and Oral ART Across a Range Cardiovascular Risk Profiles and Statin Use: A Post Hoc Analysis of CAB+RPV LA Phase 3/3b Studies

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Background: People with HIV (PWH) are at increased risk of cardiovascular disease (CVD). An elevated body mass index (BMI) contributes to CVD risk and is a risk factor for virologic failure (when present in combination with other factors) with long-acting cabotegravir+rilpivirine (CAB+RPV LA). Guidelines recommend initiating statins to reduce CVD risk in PWH aged ≥40 years with an American Heart Association atherosclerotic CVD (ASCVD) risk score of ≥5% and may be considered for those with an ASCVD score <5%. CAB+RPV LA offers unique benefits for PWH, reducing pill burden in those with comorbidities and, as a two-drug regimen, reducing potential toxicities from nucleoside reverse transcriptase inhibitors. We describe BMI, virologic outcomes, and statin use across CVD risk profiles in Phase 3/3b CAB+RPV LA studies.

Material and Methods: This post hoc analysis includes pooled data from the Phase 3/3b FLAIR, ATLAS, ATLAS-2M (through Week [W] 48), and SOLAR (through Month [M] 12) studies. Characteristics for CVD risk calculation include age, gender, total and high-density lipoprotein cholesterol, antihypertensive use, and systolic blood pressure. Framingham CVD risk score (FRS) was calculated for all participants with data available. ASCVD was calculated for participants aged ≥40 years. BMI (baseline) and virologic outcomes (through W48/M12) were described by CVD risk profiles (FRS: <10% and ≥10%; ASCVD: 0–<5%, ≥5%–<10%, ≥10–<15%, and ≥15%). Prevalent and incident statin use were described.

Results: Overall, 2491 participants were included (CAB+RPV LA, n=1685; oral ART, n=806). At baseline, 81% (n=2025/2491) had an FRS <10% and 18% (n=437/2491) had an FRS ≥10% (n=29 missing data). The proportion of participants with an FRS ≥10% was similar between CAB+RPV LA (18% [n=296/1663]) and oral ART (18% [n=141/799]). More participants had a BMI ≥30 kg/m² in higher CVD risk groups for FRS (<10%: 17% [n=338/2025]; ≥10%: 26% [n=114/437]) and ASCVD (0–<5%: 22% [n=149/685]; ≥5%–<10%: 21% [n=54/263]; ≥10–<15%: 26% [n=25/98]; ≥15%: 33% [n=20/60]). Viral suppression rates at W48/M12 were similar with CAB+RPV LA and oral ART across FRS groups (<10%: 92% [n=1254/1367] vs. 95% [n=623/658]; ≥10%: 95% [n=280/296] vs. 93% [n=131/141]). In participants aged ≥40 years, with available data, FRS correlated with ASCVD. Virologic suppression rates were similar across ASCVD categories (0–<5%: 95% [n=651/685]; ≥5%–<10%: 94% [n=247/263]; ≥10–<15%: 95% [n=93/98]; ≥15%: 93% [n=56/60]). Baseline statin use with: (1) FRS <10% was 4% (n=52/1367) and 2% (n=15/658); (2) FRS ≥10% was 18% (n=53/296) and 11% (n=16/141), in the CAB+RPV LA and oral ART arms, respectively. Incident statin use with: (1) FRS <10% was 2% (n=26/1367) and 1% (n=9/658); (2) FRS ≥10% was 6% (n=19/296) and 4% (n=6/141), in the CAB+RPV LA and oral ART arms, respectively. Serious adverse events (SAEs) reported in participants with concurrent statin use receiving CAB+RPV LA did not identify any new safety concerns.

Conclusions: HIV treatment guidelines recommend primary prevention of CVD with statins. This analysis demonstrates the efficacy of CAB+RPV LA in PWH with moderate and elevated CVD risk, despite elevated BMI, with an expected SAE profile in participants receiving CAB+RPV LA using and initiating statins.

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Evaluation of the Interest of Cameroonian Adolescents Living with HIV/AIDS to Long-Acting Antiretroviral Treatment: the CIPHER-ADOLA Study

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Background: Long-acting injectable antiretroviral therapy (LAI-ART) might be a potential game-changer in the treatment of adolescents living with HIV (ALWH). We aimed at delineating the profile of Cameroonians ALWH regarding their interest in receiving LAI-ART.

Material and Methods: A cross-sectional study was performed in ALWH 10-19 years receiving tenofovir/lamivudine/dolutegravir (TLD) in four paediatric HIV treatment centres in Cameroon. Data were collected using medical records and questionnaires. Uni-multivariate logistic regression was performed to identify factors associated with interest of ALWH to LAI-ART.

Results: We enrolled 236 ALWH (male: 51.7%; median [IQR] age: 15 [13-17] years) mainly treated in urban-settings (84.3%), with a median-BMI of 19.3 (17.3-21.8); overweight: 10.6%; and underweight: 7.2%. Majority lived with their biological parents [60.6%] and HIV status was partially/fully disclosed in 76.7%; stigmatised and non-injectable drug-users represented 3.0% and 5.9%, respectively. About 77.5% were in a multi-month ARV-dispensing differentiated service delivery model (M-DSD) and only 34.3% self-reported no missed ARV-dose since 30-days. About 30.9% were knowledgeable on LAI-ART; and 73.1%, 15.8% and 11.1% had respectively no-, moderate- and high-fear of injection/needle. About 71.6% and 72.5% respectively had a VL<50 copies/mL and CD4≥500 cells/mm3. Globally, 92.4% (n=218) were LAI-ART interested. Compared to non-LAI-ART interested ALWH, they had a higher median-age (15 [13-17]) vs. 13 [11-15], p=0.010); higher BMI (19.4 [17.4-21.9] vs. 17.9 [16.7-19.3], p=0.041), mainly living with their biological-parent (62.4% vs. 38.9%, p=0.096), mainly non-injection/needle fearing (74.5% vs. 55.6%, p=0.058), and knowledgeable on LAI-ART (32.6% vs. 11.1%, p=0.075). Sex, immuno-virological status, ART-adherence and living in urban-settings were not significantly associated with interest in LAI-ART. In multivariate model, only injection/needle fear independently predicted LAI-ART interest. Compared to ALWH with high fear, those without fear were about four-folds more interested (OR [95% CI]: 4.243 [1.089-16.527], p=0.037). Finally, concerning the preference between LAI-ART and M-DSD, 74.8%, 20.9% and 4.3% respectively preferred LAI-ART, M-DSD and no preference.

Conclusions: Cameroonian ALWH have many challenges to overcome during their therapeutic pathway. Despite their low knowledge of LAI-ART, they express a high interest in LAI-ART, particularly predicted by the absence of injections/needles fear. Providing data on their eligibility to this new strategy is essential to guide decision-making.

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Patient Experiences at Month 6 After Initiation of Cabotegravir Long-Acting (CAB LA) for PrEP in the First Male Gender Concordant Implementation Science Trial (PILLAR) in the US

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Background: Little is known outside of registrational clinical trials about patient experiences on CAB LA, the first long-acting injectable regimen for HIV prevention. We report real-world experiences and outcomes of men at month 6 (M6) after initiating CAB LA in the US.

Material and Methods: PILLAR is a Phase 4 gender-concordant implementation science trial assessing integrating CAB LA at 17 clinics for men who have sex with men and transgender men. Men who have sex with men and transgender men completed surveys at baseline (BL) and M6 on experiences and implementation outcomes. A purposeful sample of men completed interviews about their experiences.

Results: 201 men enrolled and initiated CAB LA from May 2022-August 2023, 186 (93%) and 159 (79%) completed BL and M6 surveys, respectively; of these, 45 men completed interviews at M6. The majority of participants were aged 26-49 years (n=146; 72.6%) and identified as cisgender (n=189; 94.0%), White (n=124; 61.7%), and not Hispanic or Latino (n=120; 59.7%); 70.6% (142/186) reported using oral PrEP in the last 6 months. At BL,15-29% of men reported experiencing stigma and anxiety on oral PrEP. At M6, 0-1% of individuals using CAB LA reported stigma and anxiety concerns. At BL, 53-54% of individuals using oral PrEP reported concerns about forgetting to take and running out of PrEP. At M6, 2-7% of individuals using CAB LA concerns were forgetting or missing injection visits. Interviewees noted CAB LA reduced stress and fear of missing PrEP, while offering confidence of protection. High acceptability of CAB LA increased from BL to M6 [mean acceptability: 4.4 (SD: 0.69) vs. 4.6 (SD: 0.61)] and feasibility remained high [mean feasibility: 4.4 (SD: 0.74) vs 4.4 (SD: 0.75)]. Interviewees noted CAB LA was convenient for their life. Though 45% reported injection site reactions, the majority (86%) returned to daily activities the same day. Few were bothered by injection pain (8%) and reported that pain decreased over subsequent injections. At M6, 80-92% of survey respondents reported flexible scheduling by clinics as useful to supporting CAB LA use, which was also expressed by most interviewees. Among men who received transportation to visits, had injection reminders and had virtual appointments, over 80% rated them useful.

Conclusions: M6 results show that men who have sex with men and transgender men report no to little PrEP stigma and anxiety concerns while on CAB LA and that it is feasible and acceptable in their lives. Flexible and virtual appointments and transportation support are helpful while on injectable PrEP.

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Comparative Analysis of Screening and Preventative Measures and Healthcare Resource Utilization among People with HIV Receiving Long-Acting Cabotegravir Plus Rilpivirine or Oral Antiretroviral Therapy in the US: the ABOVE Study

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Background: Clinic visits for administration of cabotegravir plus rilpivirine long-acting (CAB+RPV LA) may provide additional preventative healthcare opportunities for people with HIV. This retrospective study (ABOVE) compared rates of screening and preventative measures and healthcare resource utilization between people with HIV receiving CAB+RPV LA or oral antiretroviral therapy (ART).

Material and Methods: People with HIV on stable daily oral ART or initiating CAB+RPV LA were identified using administrative claims from Symphony Health Solutions (01/01/2020 - 8/31/2023). Index date was first CAB+RPV LA injection (01/01/2021 - 03/01/2023) or imputed for the oral ART cohort. Baseline characteristics were balanced using standardized mortality ratio (SMR) weighting. Rates of vaccinations, cancer and STI screenings, bone density tests, viral load and antiretroviral resistance testing, all-cause and HIV-related hospitalizations and outpatient visits (excluding those associated with CAB+RPV LA administration) were compared during follow-up. Rate ratios (RR) and 95% confidence intervals (CI) were estimated using a doubly robust generalized linear model with a negative binomial distribution.

Results: The study included 1,245 PWH in the CAB+RPV LA cohort and 58,644 (1,275 after weighting) in the oral ART cohort. Baseline characteristics were balanced after weighting (mean age 47 years, 24% females). Median follow-up was 392 days for CAB+RPV LA and 371 days for oral ART cohorts. While rates of preventative measures were generally low in both cohorts, the CAB+RPV LA cohort had higher rates of vaccinations (RR 1.25 [95% CI 1.18,1.33]), cancer screenings (RR 1.17 [95% CI 1.07, 1.28]), STI screenings (RR 1.24 [95% CI 1.09, 1.40]), and bone density tests (RR 2.37 [95% CI 1.64, 3.42]) compared to the oral ART cohort (all p<0.001). Viral load and resistance testing rates were similar between cohorts. The CAB+RPV LA cohort had higher rates of all-cause (RR 1.08 [95% CI 1.02, 1.16]) and HIV-related (RR 1.38 [95% CI 1.23, 1.54]) outpatient visits (p<0.001), but lower rates of all-cause (RR 0.37 [95% CI 0.22, 0.63]) and HIV-related (RR 0.40 [95% CI 0.19, 0.86]) hospitalizations compared to the oral ART cohort (p<0.001).

Conclusions: People with HIV switching from stable oral ART to long-acting ART had higher rates of key preventative measures, compared to those remaining on oral ART. Despite more frequent outpatient visit rates in the CAB+RPV LA cohort, hospitalization rates were lower, suggesting that more healthcare interactions likely improve outcomes for people with HIV. These data highlight the benefits of increased medical engagement for CAB+RPV LA.

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Feasibility, Fidelity, and Effectiveness of Administering CABENUVA in Infusion Centers

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Background: Administering intramuscular CABENUVA at infusion centers (ICs) offers a convenient alternative for people with HIV-1 to receive treatment. Giving Long Acting CABENUVA in Infusion centERs (GLACIER) examined feasibility and fidelity of delivering monthly and every 2-monthly CABENUVA at ICs from the perspective of patient study participants (PSPs) over 8 months.

Material and Methods: Study data include clinical data and questionnaires to examine PSPs' experiences receiving CABENUVA in IC routine care. Quantitative questionnaires include the Feasibility of Intervention Measure (FIM), the Acceptability of Intervention Measure (AIM), and implementation questions. Qualitative interviews were completed with a subset of PSPs.

Results: Enrolled participants (n=44) had a mean age of 46.8 years, 20.5% were assigned female at birth, and 51.2% had not previously received CABENUVA. Overall, 96.4% (187/194) of injections were within the treatment window. No study withdrawals or treatment discontinuations were due to adverse events (AEs). There were 16 injection site reaction AEs in 12 participants and 19 treatment-related AEs in 13 participants; most were mild (grade 1) or moderate (grade 2). Injection site discomfort (14%) and pain (14%) were cited most frequently. No serious AEs were reported. At Month 8, IC administration was highly feasible (FIM: M=4.41) and acceptable (AIM: M=4.51). Advantages of ICs reported by PSPs at baseline, Month 3, and Month 8 included ease of parking (baseline, 21/43 [48.8%]; Month 3, 19/36 [52.8%]; Month 8, 24/37 [64.9%]), convenient location (baseline, 22/43 [51.2%]; Month 3, 20/36 [55.6%]; Month 8, 22/37 [59.5%]), ease of scheduling/rescheduling (baseline, not applicable; Month 3, 17/36 [47.2%]; Month 8, 21/37 [56.8%]), privacy (baseline, 19/43 [44.2%]; Month 3, 17/36 [47.2%]; Month 8, 18/37 [48.6%]), others not knowing what medication they received (baseline, 12/43 [27.9%]; Month 3, 12/36 [33.3%]; Month 8, 18/37 [48.6%]), and reduced stigma (baseline, 13/43 [30.2%]; Month 3, 10/36 [27.8%]; Month 8, 16/37 [43.2%]). At Month 8, 94.6% of PSPs reported being very or extremely satisfied with the care they received at the ICs. Qualitative interviews highlighted positive views of IC administration, including staff relationships and continuity in care as key acceptability factors.

Conclusions: CABENUVA administration at ICs was safe, effective, and convenient. High levels of adherence to the treatment window, acceptability, and feasibility were reported. Rapport with IC staff, continuity in care, reduction in logistical barriers, and the perception of decreased stigma highlight that ICs can be a valuable alternative site of care for CABENUVA administration. ICs should be considered to improve convenience of treatment administration and when healthcare provider offices have limited capacity.

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Abstract number 25 has been withdrawn.

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Impact of Introduction of Long-Acting Injectable Antiretroviral on Viral Suppression Among People with HIV and Adherence Challenges in a Low-Barrier, Support-Intensive Program

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Background: Low-barrier, support-intensive programs for people with HIV (PWH) who have adherence/engagement challenges have been shown to improve antiretroviral therapy (ART) adherence and viral suppression. The Denver Health Direct Access to Care Environment (DACE) clinic is such a program which launched in January 2023 and currently serves 55 PWH. In January 2024 we introduced long-acting injectable (LAI) cabotegravir/rilpivirine for PWH in the DACE program. This analysis describes LAI outcomes and compares overall viral suppression in the program before and after the introduction of LAI- ART.

Material and Methods: The DACE clinic is located within the Denver Health Infectious Disease clinic, a moderate-sized, urban HIV clinic in Denver, Colorado. DACE enrolled adult PWH with ≥ 1 episode of HIV-1 RNA >200 copies/mL in the 12 months prior to program enrollment. Core program components include person-centered care and drop-in services such as intensive case management, primary medical care, and adherence support, as well as offering incentives for viral suppression. We conducted a retrospective review of DACE clients on oral- or LAI-ART with at least 3 months of follow-up and ≥1 program encounter after program enrollment. LAI-ART was started after ≥1 month of DACE engagement. Outcomes include viral suppression (HIV-1 RNA <200 copies/mL) and on-time LAI-ART (scheduled injection date +/- 7 days). Descriptive statistics was used, and a t-test was employed for comparison.

Results: Over 22 months, 47 people were enrolled in DACE and included in the current analysis: 7 (15%) female- and 40 (85%) male-identifying. Eighteen (38%) identified as Hispanic/Latino, 18 (38%) non-Hispanic White, and 11 (23%) as non-Hispanic African American. At baseline, 45 individuals (96%) reported active substance use and 31 (66%) were unhoused or unstably housed. Viral suppression at enrollment was 35%.

In total, 12 people (26%) were started on LAI-ART during follow up including 2 (17%) female and 10 (83%) male identifying individuals. Eleven (92%) reported substance use and 11 (92%) were unstably housed. Viral suppression at first injection was present in 6 (50%), and 6 (50%) were initiated on LAI-ART while viremic. Median baseline viral load in viremic individuals who initiated LAI-ART was 74,265 cps/mL (IQR 8,518-207,829 cps/mL) and absolute CD4 was 187 cells/uL (IQR 66-211 cell/uL). Eleven individuals (92%) achieved and have sustained viral suppression. One person had virologic failure with previously unknown baseline rilpivirine resistance and development of integrase resistance at time of virologic failure. Out of 46 injections over 13 months among 12 PWH on LAI-ART in the DACE program, there have been no late injections.

Prior to the introduction of LAI-ART, 56% of people (19/34) achieved viral suppression compared to 77% (36/47) after the introduction of LAI-ART ($p<0.05$).

Conclusions: LAI-ART is a promising treatment modality for people with adherence challenges including PWH who use substances and have unstable housing. The flexibility and support of a low-barrier, support-intensive program such as the Denver Health DACE clinic can successfully provide LAI-ART to people with adherence challenges. Future work will include a qualitative evaluation of patient and key informant perspectives on this program.

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Cost-Effectiveness of Cabotegravir Long-Acting for HIV Pre-Exposure Prophylaxis (PrEP): A Systematic Review of Modelling Studies

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Background: Cabotegravir long-acting (CAB-LA) is a promising HIV prevention strategy; however, its cost-effectiveness compared to oral pre-exposure prophylaxis (PrEP) varies across settings. This systematic review examines the economic viability of CAB-LA interventions using modelling studies in diverse populations.

Material and Methods: We searched literature databases for modelling studies on the cost-effectiveness of CAB-LA in various settings. The search was executed in PubMed, Web of Science, Scopus, and the Cochrane Library. The search was conducted in January, 2025, and was limited to English studies; but there was no limitation on year of publication. Quality assessment was based on the 2022 CHEERS checklist for economic evaluation studies. A narrative synthesis was conducted to summarize the findings. Key outcomes to be extracted included study characteristics and design, incremental cost-effectiveness ratios (ICERs), adherence rates, and willingness-to-pay (WTP) thresholds.

Results: The search retrieved 19 results, but only six modeling studies meeting predefined inclusion criteria were included. These studies evaluated CAB-LA among various populations, including heterosexual men, women at high risk of HIV, men who have sex with men (MSM), transgender women (TGW), and large simulated cohorts. The studies employed static epidemiological models, deterministic compartmental models, and Markov cohort models to evaluate CAB-LA alongside oral PrEP. Quality assessment results show that studies were of moderate and high quality. CAB-LA demonstrated potential cost-effectiveness under specific conditions. In Sub-Saharan Africa, CAB-LA achieved ICERs below $1,000 per disability-adjusted life year (DALY) averted at adherence rates exceeding 75%. In high-income settings, ICERs for CAB-LA remained below $98,000 per quality-adjusted life year (QALY) when drug costs were reduced to $4,100/year. Low-income settings required annual costs below $16 for cost-effectiveness. Epidemiological benefits included a 30%-40% reduction in HIV incidence with optimal adherence. Drug pricing, adherence, and quarterly monitoring were identified as key determinants of cost-effectiveness. Comparisons with oral PrEP indicated that CAB-LA could be more cost-effective in populations with low adherence to oral regimens.

Conclusions: CAB-LA is a cost-effective HIV prevention intervention under specific economic and adherence scenarios. Reducing drug costs and enhancing adherence strategies are critical to optimizing its economic and epidemiological impact.

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Maintained Virologic Suppression with Cabotegravir-Rilpivirine in PLWH on Dialysis

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Background: End-stage renal disease (ESRD) presents significant challenges for people living with HIV (PLWH). Long-acting injectable (LAI) ART, particularly cabotegravir and rilpivirine (CAB/RPV LA), has shown efficacy in PLWH who experience difficulties with daily dosing, such as pill fatigue and stigma, that may result in non-adherence or treatment discontinuation. However, PLWH with ESRD are typically excluded from clinical trials, resulting in a paucity of data on the use of LAI ART in this population. Here, we present real-world efficacy outcomes of CAB/RPV LA in PLWH on dialysis.

Material and Methods: This retrospective case series includes PLWH on renal replacement therapy (hemodialysis (HD) or peritoneal dialysis (PD)), who initiated CAB/RPV LA between January 2021 and November 2024 from several clinics in Florida. Data extracted from electronic medical records included demographic characteristics, duration since HIV diagnosis, dialysis modality, comorbidities, prior ART regimen before initiation of CAB/RPV, duration of prior ART, HIV-1 viral load, absolute and percentage CD4 counts, resistance-associated mutations (RAMs), and adverse events at baseline (date of CAB/RPV initiation) and current (most recent follow-up). We used descriptive statistics to describe clinical outcomes in this cohort of PLWH with ESRD on CAB/RPV LA.

Results: Among 7,516 PLWH, 419 individuals (5.6%) were prescribed CAB/RPV LA, and 9 individuals (2.1%) were on dialysis (8 on HD, 1 on PD). All 9 individuals were of Black race, 1 Hispanic; 7 males, 2 females. Median age was 44 years. PLWH in this cohort were diagnosed with HIV a median of 10 years and 67% were on ART for more than 1 year prior to switching to CAB/RPV LA. CAB/RPV LA duration ranged from 0.7-2.8 years (4 over 114 weeks and 4 up to 55 weeks). One individual with vertical transmission was prescribed lenacapavir with CAB/RPV LA, which was stopped after the patient demonstrated immune recovery. One patient underwent a renal transplant. All individuals remained virologically suppressed with no missed doses and transitioned to LAI therapy due to challenges with oral ART, such as pill burden and medication fatigue. No emergent resistance-associated mutations (RAMs), adverse events, virologic failures, or treatment discontinuations were reported.

Conclusions: This case series demonstrates sustained virologic suppression and excellent tolerability in PLWH on dialysis treated with CAB/RPV LA. The findings highlight the regimen's efficacy in addressing adherence challenges associated with oral ART. CAB/RPV LA can be considered as a treatment option for PLWH with ESRD.

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How Do Injection Site Reactions Influence Preferences for Long-Acting Injectable HIV Treatment?

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Background: Long-acting injectable (LAI) antiretrovirals (ARVs) represent a new paradigm for HIV-1 prevention and treatment, with potential benefits of better adherence and satisfaction by reducing daily pill burden. As HIV care evolves from daily oral to LAI therapies, it is essential to understand the views of people living with HIV on acceptability of injection site reactions (ISRs) to inform the development of LAI ARVs and support clinician-patient treatment decisions. We assessed the attitudes and perception of people living with HIV in the US towards ISRs in the context of self-administered LAI ARVs.

Material and Methods: This primary market research study included in-depth interviews and ethnographic research (video diaries [3 weeks], focus groups). Participants were given illustrative images/materials (3D-printed auto-injector, red sports tape, blister plasters) for use to simulate and illustrate potential ISR profiles (redness, nodule, pain). Participants were asked to rate the acceptability of ISRs based upon their frequency, size/intensity and duration, and about preference for subcutaneous vs. intramuscular administration routes. Level of interest in LAI ARVs and acceptability of potential ISR profiles were assessed using Likert scales and qualitative thematic analysis of in-depth interviews, video diaries and focus groups.

Results: In-depth interviews of n=30 people living with HIV were undertaken (83% male, 14% female, 3% non-binary); ethnicity included White/European/Middle Eastern (37%), Black/African (37%), Hispanic/Latino (10%), Asian (10%), and Mixed/Other (6%). 57% had been on ARV therapy for >10 years, 17% had experience with LAI ARVs and 20% with non-ARV self-administered injectables. For ethnographic research, 16 participants were recruited (60% male, 40% female), one was lost to follow-up.

Overall, participants had high interest in self-administered LAIs (average score 5.9 out of 7-point Likert scale), recognizing the benefits of LAIs vs. daily pills. Regarding ISR acceptability:
• Erythema size: 70% considered ≤ credit card size acceptable, 17% ≤ coin-sized and 13% ≤ palm-sized
• Erythema duration: 70% considered ≤7–10 days acceptable, 20% ≤1–3 days and 10% ≤2 weeks
• Nodule size: 77% considered ≤ pea-sized nodule acceptable, 3% ≤ grape-sized and 20% preferred no nodule
• Nodule duration: 67% considered ≤1 month acceptable, 23% ≤1–2 days and 10% ≤2–3 months
• Pain intensity: 70% considered pain ≤3–4 on a 0–10 Likert scale acceptable, 27% preferred none and 3% accepted an intensity >4
• Pain duration: 53% considered duration ≤1–2 days acceptable, while 47% accepted ≤8 days
From the ethnographic research, subcutaneous injections were preferred versus intramuscular by 60% (9/15) of participants, however preference for route of administration was influenced by ISR profile. All participants (n=15) expected severity of ISRs to reduce over time with subsequent injections and reported perceived tolerance to ISRs would improve with provision of information/education.

Conclusions: People living with HIV value the potential benefits of self-administered LAI therapies, with ISRs being a manageable consideration. These data suggest that frequency, severity, visibility and duration of ISRs may affect acceptability of LAI ARVs, with participants expecting ISRs to decrease over time. Proper patient education and realistic expectations can enhance adherence and overall patient experience of LAI ARVs.

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Expanding the Use of Long-Acting HIV Treatment: Will Hepatitis B Have a Field Day?

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Background: Hepatitis B virus (HBV) remains a global health concern, with 1.2 million new infections and 1.1 million deaths in 2022, primarily due to liver cirrhosis and hepatocellular carcinoma[1]. Although childhood HBV vaccination programs were implemented between 2000 and 2010[2], vaccination rates and disease burden still vary widely between regions. HBV surface antigen (HBsAg) seroprevalence is 8.8% in Africa, and 22.4% in South Sudan, correlating with vaccination disparities[345].

Long-acting antiretroviral therapy (LA-ART) has the potential to transform HIV management, enhancing adherence and treatment satisfaction in people living with HIV. However, as opposed to oral regimens[6], the currently available regimen of long-acting cabotegravir/rilpivirine (CAB/RPV), lacks HBV activity, raising concerns about HBV infection or reactivation. We evaluated this risk through a literature review.

Methods and Results: A literature search was conducted via PubMed on 26-01-2025, focusing on English-language publications. Additionally, registrational trial papers and supplementary appendices were reviewed, identifying eight relevant studies. The review identified five cases of acute HBV from registrational trials (out of 2,076 participants, 0.2%), one additional acute HBV case report, one probable HBV reactivation, and three instances of low-level HBV viremia that may represent reactivation. All data originated from high-income countries where pre-switch HBV serology is routinely performed.

The registrational trials[78910] excluded participants with positive HBsAg, positive hepatitis B core antibody (anti-HBc), detectable HBV DNA, and no immunity (negative anti-HBs). However, detailed HBV serology was unavailable for four of the five acute HBV cases, limiting immune status interpretation. The fifth case involved an individual who did not respond to vaccination[11]. Another acute HBV case occurred in a vaccinated individual (anti-HBs 14.5 mIU/mL), who developed hepatitis four months post-switch (HBV DNA 52,000 IU/mL)[12]. This individual had multiple sexual partners and a recent piercing.

An individual with presumed resolved HBV (anti-HBs 8 mIU/mL, negative HBV DNA, HBsAg, and anti-HBc) experienced likely reactivation[13]. Four months after switching, ALT rose to 104 IU/L, HBsAg and HBV DNA became detectable again, and anti-HBs declined to nearly zero.

A retrospective study of 149 PLWH on LA-ART found 38 (25.5%) were anti-HBc positive but HBsAg negative[14]. Three (7.9%) developed low-level HBV viremia (14-101 IU/mL) without elevated liver enzymes.

Discussion: LA-ART is a welcome breakthrough in the treatment of HIV. Our findings identify a small but clinically significant risk of HBV infection or reactivation when switching to LA-ART. This highlights the need for a thorough HBV risk assessment including exposure risk, HBV serology, immunity status, and administration of vaccination when the history is unclear before initiation of LA-ART. The available data is from low HBV prevalence, high income or clinical trial settings where individuals with prior HBV infection had been excluded, so our findings could underestimate the risk in public health settings where access to HBV serology is limited.
Given that detailed serologic testing is not widely available or implementable in public health settings, development of long-acting agents with anti-HBV activity for use in developing countries is an essential priority for the future.