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887. Implementation of Long-acting Injectable Cabotegravir/Rilpivirine for HIV-1 Treatment at a Ryan White-funded Clinic in the U.S. South

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Session: P-51. HIV: Treatment

Background. In January 2021, the first ever long-acting injectable (LAI) antiretroviral therapy (ART), cabotegravir/rilpivirine (CAB/RPV), was approved for maintenance HIV-1 treatment in select patients with virologic suppression. LAI-ART has the potential to improve ART adherence, reduce HIV stigma, and promote equity in care outcomes, however, implementation in real-world settings has yet to be evaluated.

Methods. We launched a pilot LAI-ART program at the largest Ryan White-funded HIV clinic in the Southeast. From 4/14/21 to 5/14/21, providers referred patients interested and willing to switch to LAI-CAB/RPV who met screening criteria. Our interdisciplinary LAI team (Clinician-Pharmacy-Nursing) verified clinical eligibility (HIV-1 < 200 c/ml ≥6 months and no history of virologic failure, resistance to either drug, or chronic HBV infection) and pursued medication access for 28-day oral lead-in and monthly injectable CAB/RPV. We describe demographic and clinical variables of referred PWH and early outcomes in accessing LAI-ART.

Results. Among 42 referrals, median age was 40.5 (Q1-Q3, 32-52) years, 83% were men, and 76% Black. Payor source distribution was 26% Private, 19% Medicare, 10% Medicaid, and 45% ADAP. At the time of referral, median CD4 count was 583 (Q1-Q3, 422-742) cells/mm^3 and median sustained HIV-1 RNA < 200 c/ml was 1427 (Q1-Q3, 961-2534) days. A total of 35 patients (74%) met clinical eligibility for LAI-CAB/RPV, including 4 patients who required a transition off proton pump inhibitor therapy to accommodate oral RPV. Ineligible PWH were excluded due to evidence of RPV resistance (n=5), possible RPV hypersensitivity (n=1), and HIV non-suppression (n=1). The table summarizes the process of pursuing LAI-ART access for the initial 10 enrollees by insurance status.

Table. Summary of medication access pursuit for patients enrolled in long-acting injectable (LAI) cabotegravir/rilpivirine (CAB/RPV) pilot program for HIV-1 treatment.

Patient	Prescription drug coverage	Initial insurance claim disposition	If initial claim rejected, PA disposition	If PA denied, appeal disposition	Additional comments	Time since medication access pursued to current disposition	Current disposition
1	Private	Approved	- - -	- - -	Pending insurance verification by ViiV, given patient required to pay entire cost out-of-pocket	29 days+	CAB/RPV not started
2	Private	Rejected	Denied (same day)	Denied (9d later)	Benefit investigation submitted and awaiting response from ViiV (16 days+)	29 days+	CAB/RPV not started
3	Private	Rejected	Denied (same day)	Pending (29 days+)	N/A	29 days+	CAB/RPV not started
4	Private	Rejected	Denied (6d later)	Pending (14 days+)	N/A	29 days+	CAB/RPV not started
5	Medicare	Approved	- - -	- - -	PAP required for oral lead-in approved by ViiV (14d later)	15 days	CAB/RPV oral lead-in day 15/28
6	Medicare	Approved	- - -	- - -	PAP required for oral lead-in submitted and awaiting response from ViiV (9 days+)	16 days+	CAB/RPV not started
7	Medicare	Approved	- - -	- - -	PAP required for oral lead-in submitted and awaiting response from ViiV (1 days+)	5 days+	CAB/RPV not started
8	Medicaid	Rejected	Pending (for 5d+)	- - -	N/A	5 days+	CAB/RPV not started
9	ADAP	CAB/RPV not covered; PAP required			PAP required for oral lead-in and injectable submitted and awaiting response from ViiV (9 days+)	16 days+	CAB/RPV not started
10	ADAP	CAB/RPV not covered; PAP required			PAP required for oral lead-in and injectable submitted and awaiting response from (9 days+)	14 days+	CAB/RPV not started

(+) = status still pending at time of abstract submission
Abbreviations: ADAP = AIDS Drug Assistance Program; d = days; PA = Prior Authorization; PAP = Patient Assistance Program

Conclusion. Our experience implementing LAI-ART at a Ryan White-funded HIV clinic in the Southern U.S. has been challenged by substantial human resource capital to attain drug, delayed therapy initiation due to insurance denials, and patient ineligibility primarily due to concern for potential RPV resistance. These barriers may perpetuate disparities in ART access and virologic suppression among PWH and need to be urgently addressed so that LAI-ART can be offered equitably.

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888. *In Vitro* Forgiveness of INSTI-Containing Regimens at Drug Concentrations Simulating Variable Adherence

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Session: P-51. HIV: Treatment

Background. The integrase strand transfer inhibitor (INSTI)-based regimens bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF), dolutegravir (DTG)+FTC/TAF, DTG/lamivudine (3TC), and DTG/rilpivirine (RPV) are all used for treatment of HIV-infected patients. Here, relative time to *in vitro* viral breakthrough (VB) and resistance barrier using simulated human drug exposures at either full or suboptimal treatment adherence to each regimen were compared.

Methods. Wild-type HIV-1 (IIIb)-infected MT-2 cells were exposed to the combinations of BIC+FTC+TAF, DTG+FTC+TAF, DTG+3TC, or DTG+RPV for up to 35 days or until VB. Fixed drug concentrations were the human plasma-free adjusted clinical trough concentrations (C_{min}) or fixed at simulated C_{min} after missing 1 to 4 consecutive doses (C_{min}-1 to -4), with many replicates. Drug resistance was studied by next-generation sequencing at ≥2% frequency.

Results. At drug concentrations corresponding to full adherence and 1 missed dose (C_{min} and C_{min}-1), no VB occurred with any regimen (Table). At C_{min}-2, only DTG+3TC had VB, with some emergent resistance to both drugs. At C_{min}-3, all regimens had VB: by day 12, 100% of DTG+3TC wells had VB; for BIC+FTC+TAF, DTG+FTC+TAF, and DTG+RPV, < 15% of wells had VB which began after day 14. Emergent RT or IN resistance was seen for DTG+RPV and DTG+3TC but not for BIC+FTC+TAF or DTG+FTC+TAF. At C_{min}-4, all DTG+3TC and DTG+FTC+TAF wells had VB by day 12, while DTG+RPV had 94% VB by day 25 and BIC+FTC+TAF had 50% VB by day 35. Emergent C_{min}-4 drug resistance was seen for all regimens but at differing frequencies; DTG+RPV had the most wells with resistance. Cumulatively, emergent RT and/or IN resistance was found in 1.3% BIC+FTC+TAF, 2.5% DTG+FTC+TAF, 7.9% DTG+3TC, and 8.8% DTG+RPV cultures.

Summary of Forgiveness and Barrier to Resistance of INSTI-Containing Regimens

In Vitro Drug Concentration	Breakthrough Frequency (Resistance Development)							
	BIC+FTC+TAF		DTG+FTC+TAF		DTG+3TC		DTG+RPV	
	VB (n/N; %) [first day of VB]	With Resistance, n[a]	VB (n/N; %) [first day of VB]	With Resistance, n[a]	VB (n/N; %) [first day of VB]	With Resistance, n[a]	VB (n/N; %) [first day of VB]	With Resistance, n[a]
C_{min}	0/60; 0 [na]	0	0/48; 0 [na]	0	0/60; 0 [na]	0	0/48; 0 [na]	0
C_{min}-1	0/36; 0 [na]	0	0/48; 0 [na]	0	0/36; 0 [na]	0	0/48; 0 [na]	0
C_{min}-2	0/60; 0 [na]	0	0/48; 0 [na]	0	41/60; 68 [14]	13; RT: M184V/I (4), V75I (3) *IN: G140E/R (2), E157K (2), L74M (1), S153F (1)*	0/48; 0 [na]	0
C_{min}-3	3/36; 8 [21]	0	1/48; 2 [25]	0	36/36; 100 [7]	3; RT: None *IN: L74M (2), V72A (1), S153F (1)*	7/48; 15 [14]	1; RT: M230I *IN: None*
C_{min}-4	18/36; 50 [15]	3; RT: M184I (2) *IN: G163R (1)*	48/48; 100 [11]	6; RT: M184V (1), K219R (1) *IN: Q148R (2), Q95R (1), H51Y (1), S153F (1)*	36/36; 100 [5]	2; RT: None *IN: R263K (2), L74M (1)*	45/48; 94 [8]	20; RT: E138K (8), K101E (3), M230I (2), V90I (2), V106I (1), Y181C (1), H221Y (1) *IN: H51Y (2), R263K (1), M50I (1), Q95R (1), A128T (1), S153F (1), G163R (1)*

na = not applicable
a. Reverse transcriptase (RT) substitutions are shown in plain text. *Integrase (IN) substitutions are shown in italics.*

Conclusion. Regimen forgiveness and resistance barrier are important factors in long term treatment. These INSTI-based regimens had high *in vitro* forgiveness and resistance barriers with concentrations simulating high adherence. When multiple missed doses were simulated *in vitro*, BIC+FTC+TAF had the highest forgiveness and barrier to resistance. When compared to DTG+3TC and DTG+FTC+TAF, DTG+RPV had higher forgiveness but lower resistance barrier after several simulated missed doses.

Disclosures. **Rima K. Acosta, BS**, **Gilead Sciences, Inc.** (Employee, Shareholder) **Andrew Mulato, BS, MBA**, **Gilead Sciences, Inc.** (Employee, Shareholder) **Michelle L. D'Antoni, PhD**, **Gilead Sciences** (Employee, Shareholder)**Gilead Sciences, Inc** (Employee, Shareholder) **Stephen R. Yant, PhD**, **Gilead Sciences, Inc.** (Employee, Shareholder) **Tomas Cihlar, PhD**, **Gilead Sciences, Inc.** (Employee, Shareholder) **Kirsten L. White, PhD**, **Gilead Sciences, Inc** (Employee, Shareholder)

889. Early Discontinuations and Adverse Events Among Treatment-Naïve Patients Initiating Integrase Inhibitors in a Real-world Setting

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Background. Cohort studies suggest higher rates of discontinuations (DCs) and adverse events (AEs) with integrase inhibitors (INSTIs) than is reported in clinical trials. Here, we assess DC of different INSTIs in combination with one of two tenofovir prodrugs in the first year following initiation defined as "early DC" in a real-world cohort of treatment-naïve patients.

Methods. This analysis evaluated treatment-naïve patients at a single center initiating raltegravir (RAL), elvitegravir/cobicistat (EVG/c), dolutegravir (DTG) or bictegravir (BIC) in combination with emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) between 10/2007-1/2020. Eligible patients had a minimum follow-up of 1 year. The primary endpoint was incidence of early INSTI DC. Secondary endpoints included AEs and risk factors for early INSTI DC and treatment-related AEs.

Results. 331 patients were included. Median age was 32 years, 89% were male, 43% were non-White, 8% started RAL-based therapy, 46% started EVG/c-based