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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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Session: P-51. HIV: Treatment

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

therapy, 22% started DTG-based therapy and 24% started BIC/F/TAF. 36 discontinued INSTI-based therapy early yielding an incidence rate of 0.17 DCs per person-years (PPY) among RAL patients, 0.14 DCs PPY among EVG/c patients, 0.22 DCs PPY among DTG patients, and 0 DCs PPY among BIC patients, p=0.006. Treatment-related AEs occurred in 27% of RAL patients, 42% of EVG/c patients, 50% of DTG patients, and 43% of BIC patients p=0.607; and were responsible for early DC rates of 0.022 in 3 EVG/c patients and 0.075 in 5 DTG patients. No treatment-related early DCs occurred among RAL or BIC patients. No evaluated factor was significantly associated with early INSTI DC, however DTG use was significantly associated with treatment-related AEs (aOR 3.46, 95% confidence interval: [1.20; 10.82]).

Table 1. Risk factors for early integrase inhibitor discontinuation and treatment-related adverse events

Characteristic	Early INSTI DCs (n=36) N (%)	Unadjusted OR for early INSTI DC (CI)	Adjusted OR for early INSTI DC (CI)	Treatment-related AEs (n=141) N (%)	Unadjusted OR for treatment-related AE (CI)	Adjusted OR for treatment-related AE (CI)
Age	N/A*	1.01 (0.98; 1.04)	0.99 (0.96; 1.03)	N/A*	1.01 (0.99; 1.03)	1.01 (0.99; 1.04)
Gender						
Male	30/285 (11)	Ref	Ref	128/294 (44)	Ref	Ref
Female	6/37 (16)	1.64 (0.58; 4.03)	1.62 (0.52; 4.58)	13/37 (35)	0.70 (0.34; 1.41)	0.59 (0.27; 1.23)
INSTI						
RAL	4/26 (15)	Ref	Ref	7/26 (27)	Ref	Ref
EVG/c	18/149 (12)	0.76 (0.25; 2.80)	1.26 (0.38; 5.06)	63/151 (42)	1.94 (0.80; 5.23)	2.48 (0.94; 7.16)
DTG	14/74 (19)	1.28 (0.41; 4.90)	1.98 (0.53; 8.57)	37/74 (50)	**2.71 (1.06; 7.66)**	**3.46 (1.20; 10.82)**
BIC	0/73 (0)	NA	NA	34/80 (42)	2.01 (0.78; 5.63)	2.76 (0.9; 9.08))
NRTI Backbone						
F/TDF	21/120 (18)	**2.64 (1.31; 5.45)**	1.64 (0.72; 3.78)	50/120 (42)	0.94 (0.60; 1.48)	1.02 (0.57; 1.80)
F/TAF	15/202 (7)	Ref	Ref	91/211 (43)	Ref	Ref
Baseline HIV-1 RNA (copies/mL)						
<100,000 copies/mL	18/210 (9)	Ref	Ref	82/216 (38)	Ref	Ref
≥100,000 copies/mL	18/111 (16)	**2.08 (1.02; 4.17)**	1.62 (0.71; 3.68)	58/114 (51)	**1.69 (1.07; 2.68)**	1.57 (0.93; 2.65)
Baseline CD4⁺ count (cells/mm³)						
≥200 cells/mm³	19/230 (8)	**0.39 (0.19; 0.80)**	0.82 (0.07; 11.37)	94/237 (40)	0.64 (0.39; 1.04)	1.06 (0.18; 6.11)
<200 cells/mm³	17/91 (19)	Ref	Ref	47/93 (51)	Ref	Ref
HIV Disease Status						
Asymptomatic	14/193 (7)	Ref	Ref	77/198 (39)	Ref	Ref
Symptomatic	5/40 (12)	1.83 (0.56; 5.12)	1.19 (0.35; 3.49)	18/41 (44)	1.23 (0.62; 2.42)	1.38 (0.67; 2.83)
AIDS	17/89 (19)	**3.02 (1.42; 6.54)**	1.54 (0.13; 20.75)	46/91 (51)	1.61 (0.97; 2.66)	1.31 (0.23; 7.61)

Note. Significant p-values (<0.05) have been **bolded** for ease of interpretation
Abbreviations. OR, odds ratio; INSTI, integrase strand transfer inhibitor; DC, discontinuation; CI, confidence interval; AE, adverse event; RAL, raltegravir; EVG, elvitegravir; c, cobicistat; DTG, dolutegravir; NRTI, nucleoside reverse transcriptase inhibitor; F/TDF, emtricitabine/tenofovir disoproxil fumarate; F/TAF, emtricitabine/tenofovir alafenamide
*Age was analyzed as a continuous variable

Conclusion. In this cohort, early DCs occurred in 11% initiating INSTI-based therapy, however of these only 2% were treatment-related. These data support use of INSTI-based regimens as preferred options for treatment-naïve patients living with HIV due to their favorable safety and tolerability profiles.

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890. Evaluation of Association Among Integrase Inhibitors for HIV Treatment, Weight Gain, and Body Image

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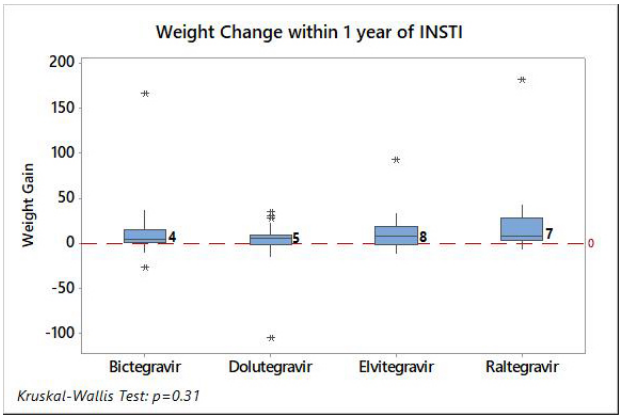
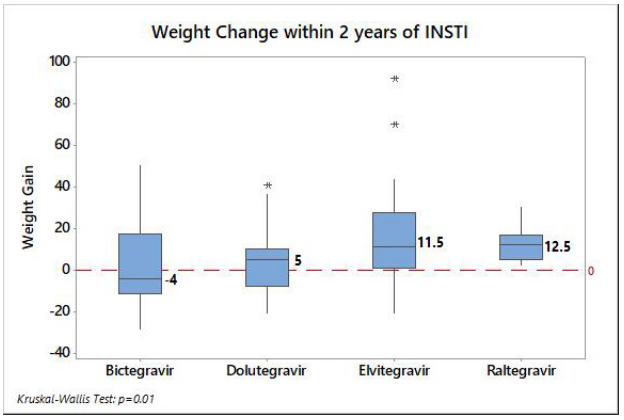
Session: P-51. HIV: Treatment

Background. Integrase inhibitors (INSTIs) are preferred antiretroviral agents for people living with HIV (PLWH). Recent studies suggest that INSTIs may contribute to weight gain and the development of metabolic syndrome. A lack of knowledge remains about how INSTIs affect metabolic parameters that contribute to weight gain as well as the impact of weight gain on medication adherence and body image in PLWH.

Methods. We conducted a retrospective chart review along with a real time survey of PLWH who are receiving HIV care at UConn Health. Participants who were switched to or added an INSTI to their ART regimen between 2012 - 2020 were included (n=204). Patient weight was recorded in 3-month intervals for two years prior to and two years after INSTI initiation. Lipid profile parameters and hemoglobin A1c were noted pre and post INSTI switch. A survey was administered to rate perception of weight gain, body appearance, and medication adherence on a five-point Likert scale. Statistical methods included Chi-square test and Fisher's Exact test for categorical data, and T-test or Kruskal-Wallis test for continuous data.

Results. Patients started on or switched to any INSTI regimen experienced a mean weight gain of 5 and 7 pounds at 12 and 24 months, respectively ($p < 0.001$). Weight gain was greatest with raltegravir and elvitegravir (Figure 1,2). Bictegravir regimens resulted in a 4 pound weight loss at 24 months. An INSTI switch increased cholesterol by a mean of of 7.9mg/dL (p=0.05), with no effect on other parameters. A switch to Bictegravir increased HDL by 4mg/dL (p=0.04) and decreased triglycerides by 35mg/dL (p=0.04). Survey results showed that 100% of patients denied missing ART doses despite 69% mentioning weight gain due to ART. 97% of patients were satisfied with their ART regimen, with the majority disagreeing that their body image was negatively affected.





Conclusion. We demonstrate a link between INSTI use and weight gain up to two years following INSTI initiation, with the most weight gained within the first 12 months. Elvitegravir and raltegravir are associated with greater weight gain whereas bictegravir demonstrates weight loss and beneficial effects on lipid profile. Despite weight gain, most patients remained adherent and satisfied with their medication and denied negative perceptions of body image.

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891. Minimum Manufacturing Costs and National Prices for Weight Loss Treatments, as Potential Mitigation for Anti-Retroviral Related Weight Gain in HIV

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Session: P-51. HIV: Treatment

Background. Weight gain is being observed for a wide range of antiretroviral treatments. Weight gains are higher for people taking first-line integrase inhibitor based treatments, especially those including TAF/FTC. Weight gains are higher for women and people of colour. Clinical obesity increases the risks of cardiovascular disease, diabetes, adverse birth outcomes and could lower survival rates. Anti-obesity treatments are needed to supplement lifestyle interventions and counteract progressive weight gains, but are not routinely provided as part of HIV care.

Methods. Costs of production for FDA-recommended weight loss treatments and anti-diabetic medications (orlistat, naltrexone-bupropion, topiramate, phentermine, semaglutide, liraglutide and metformin) were estimated using an established and published methodology based on costs of active pharmaceutical ingredients (API), extracted from the global shipping records database Panjiva. This was compared with national drug list price data from a range of low, medium, and high-income countries.