IMPROVING UPTAKE OF LA-ARVS AMONG POPULATIONS MOST LIKELY TO BENEFIT

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Caroline Derrick, PharmD, BCPS, AAHIVP
Infectious Diseases Clinical Pharmacist
ID Ambulatory Pharmacy Supervisor

Big Data Health Science Center

UNIVERSITY OF SOUTH CAROLINA

OUTLINE

- R25 mentorship
- Skills development
- Hands on research and proposal development
- Future plan

PROFESSIONAL INTERESTS

- Clinician
- Interprofessional Education (IPE)
  - IPE – HIV, Infection Prevention (Project Firstline- CDC)
- Telehealth
  - Southeast Viral Interactive Case Conference (SVICC)
  - Yelverton et al. The Future of Telehealth in Human Immunodeficiency Virus Care: A Qualitative Study of Patient and Provider Perspectives in South Carolina
- Clinical Implementation (Rapid Start for HIV, LAI ART Clinic)
  - Workflow, feasibility, outcomes (Derrick et al. AJHP. Acceptance pending)
  - Preferences (Ostermann, Derrick et al. Value Health. 2020 Jul; 23(7): 851–861.)
- Improving uptake of LA-ARVs among populations most likely to benefit
  - Understanding preferences and trade-offs among patients and providers in the Southern US
  - *Re-submission pending*

R25 MENTORSHIP

- Invaluable one-on-one mentorship (enrollment: August 2023)
  - Dr. Jiajia Zhang, PhD, Professor at Department of Epidemiology and Biostatistics
    - Biostatistical support, mentorship, and direction
  - Dr. Weissman, MD, Clinical Professor, Chair of Internal Medicine
    - Mentor, Clinician, Researcher
  - Dr. Xueying Yang, previous R25 Trainee
    - Peer mentor
- Biweekly/Weekly meeting with mentors
- Allows for data science bridge

LEARNING CONTRACT

- Individualized Learning Contract
  - Scheduled mentorship meetings
  - Workshop on Data Science Ethics
  - Grant Writing Seminars: ID Week 2023, Boston MA
  - Bios 710 (Efficient Data Management for Public Health)
  - HIV/STI Conference, October 2023
  - IRB/CITI Training
  - Journal Clubs: Expanded Multivariable Models to Assist Patient Selection for Long-Acting Cabotegravir+Rilpivirine Treatment: Clinical Utility of a Combination of Patient, Drug Concentration, and Viral Factors Associated With Virologic Failure. Orkin et al. Clin Infect Dis. 2023 Jun 21.

DATA SCIENCE BRIDGE

- Big picture patient record review
- Interpretation of electronic health record
- Generate ideas for professional interests
- Shape future directions

HANDS ON RESEARCH

- Publications supporting preliminary work with BDG
  - 1 previously published, 1 pending revisions, 2 in preparation
    - One Size Does Not Fit All. Hetreogeneous Patient Preferences and Tradeoffs For Antiretroviral Therapy. Results of a Discrete Choice Experiment. Value in Health. 21. S12-S13. 10.1016.
    - Telehealth or in-person HIV care? Qualitative study findings on telehealth use and decision-making from people living with HIV and HIV care providers in South Carolina during the COVID-19 pandemic. *(accepted pending revisions to AIDS and Behavior)*
    - Tenofovir alafenamide associated weight change in persons living with HIV. Pending Submission.
    - Process evaluation and early outcomes of real-world implementation of a pharmacist-driven cabotegravir/rilpivirine long-acting injectable initiative (PDCI). Pending Submission.

GRANT PROPOSALS

- NIH R21
  - **An implementation science exploratory study to comprehensively advance our understanding regarding the preparedness and readiness of implementing LA-ART in Ryan White clinics in South Carolina (SC) (Co-I)**
  - **Improving uptake of LA-ARVs among populations most likely to benefit: Understanding preferences and trade-offs among patients and providers in the Southern US (resubmission pending 5/2024)**

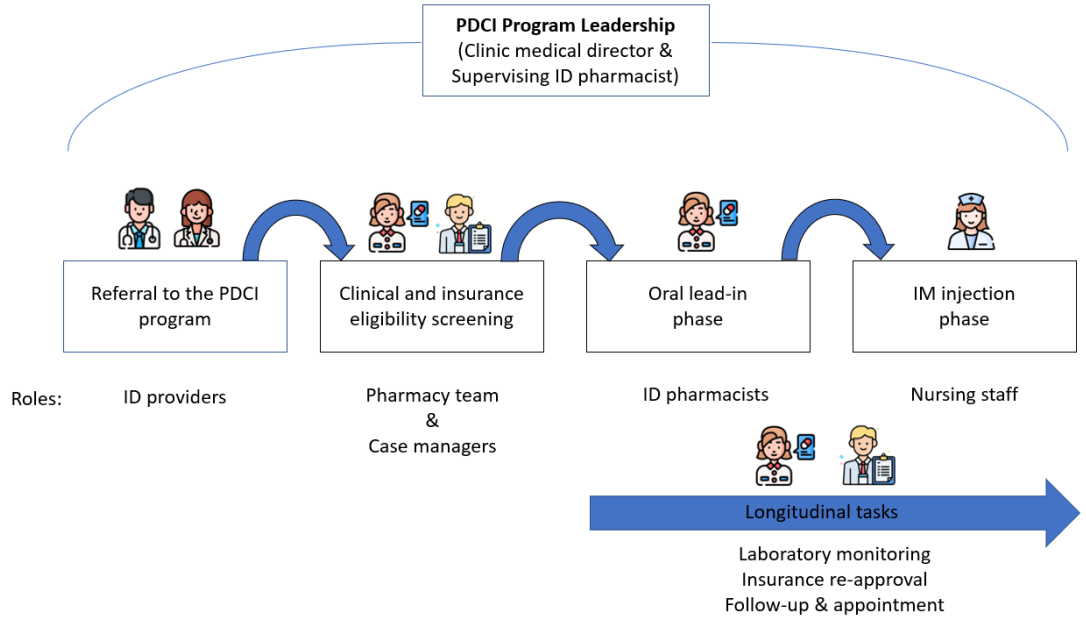
BACKGROUND

- Long-acting antiretrovirals (LA-ARVs) have significant potential to improve the health outcomes of people living with HIV (PWH) by improving treatment adherence.
- To realize this potential, LA-ARVs must be available and accessible to PWH and their characteristics must match the preferences of the intended target population.
- In a prior DCE, we demonstrated the feasibility of the DCE-based elicitation of ARV treatment preferences and identified significant preference heterogeneity with respect to ARV characteristics and interest in switching to LA-ARVs.

PURPOSE

PharmD Visit	Oral Lead In (Day 0)	• Lab orders for the following listed below at IM doses 1,3, & 4
	30 days	
Nurse Practitioner-giving injection	IM Dose #1	• HIV Viral Load, CMP
	4 weeks (+/- 7 days)	
Nursing Staff	IM Dose #2	• No labs needed
	8 weeks (+/- 7 days)	
Nursing Staff	IM Dose #3	• HIV Viral Load, CMP
	8 weeks (+/- 7 days)	
Original Provider	IM Dose #4	• HIV Viral Load, CMP, **CD4, Lipid Panel**

After IM dose #4, patient has completed 6 months of therapy, lab ordering per provider discretion



RESEARCH AIMS

- Aim 1: Qualitative formative work, including focus groups with PWH and in-depth interviews with their providers to characterize LA-ARV decision-making and ***identify structural, social, and individual-level barriers, facilitators, and preference-relevant features that impact feasibility, acceptability, and scalability of LA-ARVs.***
- Aim 2: **Traditional quantitative surveys and DCE preference surveys** to elicit LA-ARV-related preferences and **uptake barriers** from 300 PWH residing in the Southern US, including 6 of 7 Ending the HIV Epidemic (EHE) priority states and 19 of 49 EHE priority counties.
- Aim 3: Combine qualitative information on patient-level and provider-level barriers and quantitative information on LA-ARV related preferences to identify a limited number of feasible, preference-concordant LA-ARV **strategies that hold potential to broadly increase LA-ARV uptake** among PWH in the Southern US.

METHODOLOGY

- Recruitment from outlying, rural partner clinics to ensure the adequate representation of rural providers and patients.
- The goal is to represent the diversity of PWH with respect to distance to care, gender, race/ethnicity, and treatment experience, as well as sociodemographic characteristics that may impact treatment choices and adherence.
- FGD participants will be asked to **rank LA-ARV characteristics** with respect to their likely impact on uptake. Provider IDI participants will be asked to **rank implementation challenges** at the level of the clinic or health system.

Figure 4. DCE-based elicitation of treatment preferences in ESPRIT

Please consider treatment options A, B, and C. Which option would you prefer most?

A	B	C
You take **1 pill twice daily**	You take **1 pill once daily**	You take **1 pill once daily**
The pills are **Small** but you must take them **with a meal**	The pills are **Large** but you can take them **with or without a meal**	The pills are **Small** and you can take them **with or without a meal**
You have **No depression**	You have **No depression**	You feel **Depressed** most days of the week and some people consider suicide
15 out of 100 patients will develop **High blood sugar** (Higher risk) 15	15 out of 100 patients will develop **High blood sugar** (Higher risk) 15	15 out of 100 patients will develop **High blood sugar** (Higher risk) 15

MEASURES

- We will use Ngene software to identify a *d*-efficient design that has good attribute level balance to ensure that each respondent will see most or all attribute levels. To incorporate preference heterogeneity, the design will be optimized for mixed multinomial logit analysis
- Linear and logistic regression models, respectively, will estimate correlates of class membership and correlates of awareness, attitudes, and willingness to adopt LA-ARVs

FUTURE DIRECTIONS

- Continue professional collaborations utilizing different skillsets I’ve gained over this course
  - HIV and aging/polypharmacy
- Complete publishable manuscripts
- Resubmission of pending R21
- Present at national/international conferences

QUESTIONS?

Caroline Derrick, PharmD, BCPS, AAHIVP
Caroline.Derrick@prismahealth.org
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CURRENT SUBMISSION

- **<u>Improving uptake</u> of LA-ARVs among populations most likely to benefit: Understanding preferences and trade-offs among patients and providers in the Southern US**
  - **Impact Score:45 Percentile:44 +**
- This application proposes to use qualitative methods, survey methods, and Discrete Choice Experiment (DCE) methods to understand the preferences of 300 people living with HIV for long-acting antiretrovirals and to identify strategies for increasing the uptake of long-acting antiretrovirals in 14 states in the southern part of the US. In addition, in-depth interviews will also be conducted with up to 20 providers to identify provider-level barriers to and facilitators of long-acting antiretrovirals.
- Positive: Collect additional qualitative data from providers and patients to inform the DCE
- Feedback: Dissemination plan

Prevalence of Cabotegravir and Rilpivirine Resistance Associated Mutations Among Treatment Experienced Patients in a South Carolina Outpatient Clinic

Y. Vivian Tsai, PharmD[1,2]; Morgan Pizzuti, PharmD[1,2]; Michael Deaney, PharmD Candidate[2]; P. Brandon Bookstaver, PharmD[1,2]; Divya Ahuja, MD[1,3]; Caroline Derrick, PharmD[1,3]

1 Prisma Health Richland, 2 University of South Carolina College of Pharmacy, 3 University of South Carolina School of Medicine

Poster# 2069

BACKGROUND

- Cabotegravir/Rilpivirine (CAB/RPV) was approved in January 2021 as the first long-acting injectable treatment for people living with human immunodeficiency virus (PLWHIV).
- CAB/RPV is indicated as a switch therapy for PLWHIV who have been virologically suppressed and clinically stable on their current combination antiretroviral therapy (cART).
- One key consideration prior to switching to CAB/RPV therapy is to evaluate patients' cumulative history of mutation genotype(s) to decrease the risk for virologic failure.
- The primary objective of this study was to characterize the proportion of individuals with resistance associated mutations (RAMs) to CAB and/or RPV.

METHODS

Study Design	• Retrospective, observational cohort study
Study Inclusion	• PLWHIV who were referred to pharmacist and screened for eligibility to transition to CAB/RPV therapy between April 1, 2021 and August 31, 2022 at Prisma Health Immunology Center
Key Definitions	• The Stanford University HIV Drug Resistance Database was used to evaluate the inferred resistance level for reverse transcriptase (RT), integrase strand transfer inhibitor (INSTI), and protease inhibitor (PI) sequences
Statistical Analysis	• Descriptive statistics

REFERENCES

1. CABENUVA [package insert]. Research Triangle Park, NC: ViiV Healthcare;2021.
2. Swindells S, et al. N Engl J Med 2020; 382(12):1112
3. Orkin C, et al. N Engl J Med 2020;382(12):1124
4. Howe ZW, et al. Pharmacotherapy 2021;41(8):686
5. Overtone ET, et al. Lancet 2021;396(10267):1994

DISCLOSURES

The authors of this presentation have no disclosures concerning possible financial or personal relationships with commerical entities that may have a direct or indirect interest in the subject matter of this presentation

C. Derrick is now affliated with Janssen Pharmaceuticals

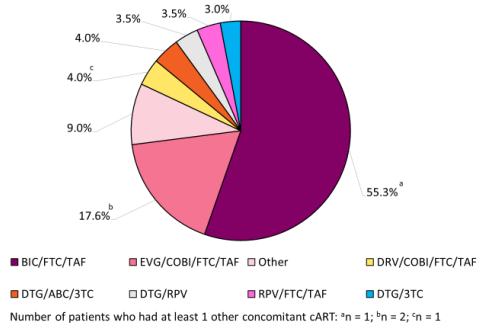
RESULTS

Table 1. Baseline Characteristics

Characteristics	N = 199
Age, years, median (min, max)	38 (17-72)
Gender, n (%)	
Male	132 (66.3)
Female	65 (32.7)
Transgender	2 (1.0)
Race, n (%)	
Asian	2 (1.0)
Black or African American	163 (81.9)
Native Hawaiian or Other Pacific Islander	1 (0.5)
White or Caucasian	29 (14.6)
Hispanic or Latino	4 (2.0)
Charlson Comorbidity Index, mean (SD)	1.4 (2.1)
BMI (kg/m^2), median (min, max)	28.6 (16.5, 74.1)
Genotype Report Availability, n (%)	
Any	147 (73.9)
NRTIs	144 (72.4)
NNRTIs	144 (72.4)
PIs	143 (71.9)
INSTIs	36 (18.1)
Number of Genotype Reports, median (min, max)	1 (1-11)

Abbreviations: NRTIs, nucleoside reverse transcriptase inhibitors; NNRTIs, non-nucleoside reverse transcriptase inhibitors; PIs, protease inhibitors; INSTIs, integrase strand transfer inhibitors

Figure 1. Baseline cART Regimen at the Time of CAB/RPV Eligibility Screening



Number of patients who had at least 1 other concomitant cART: ^{a}n = 1; ^{b}n = 2; ^{c}n = 1

Figure 2. Prevalence of RAMs to CAB or RPV

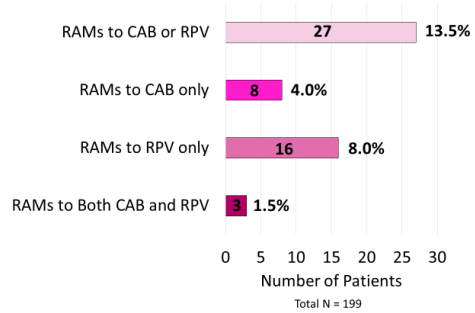


Table 2. Types of RAMs to CAB and RPV

CAB, n		RPV, n
• E138K: 2	• S147G: 2	• E138A/K: 5
• E92Q: 3	• S230R: 2	• K101E: 2
• G140S: 1	• T66I: 1	• L1001: 1
• N155H: 1	• T94A: 1	• V179D/E: 2
• Q148H/R: 2		• Y181C/I: 10

Total individual, unique copies of RAMs to CAB and RPV, n = 36

Figure 3. Prevalence of RAMs and Exposure History to cART

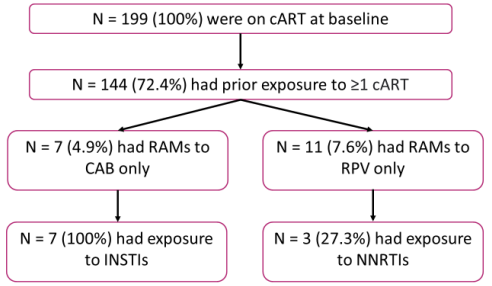
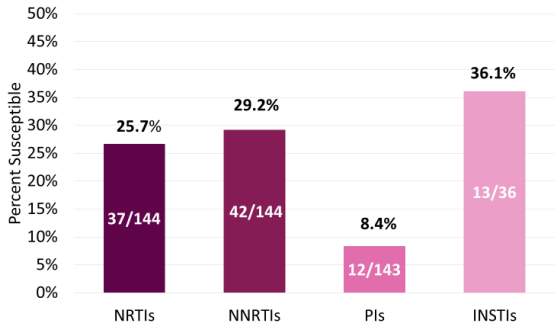


Figure 4. Prevalence of RAMs to NRTIs, NNRTIs, PIs, and INSTIs



CONCLUSIONS

RAMs
- The high prevalence of RAMs to CAB or RPV suggest increased risk for virologic failure when transition to CAB/RPV therapy

Exposure
- Findings suggest relationship between prevalence of RAMs to CAB and exposure history to cART, whereas prevalence of RAMs to RPV could be transmitted

Practice Implications
- Genotype assessment is pertinent for determining patient specific mutations to decrease risk of virologic failure when considering transition to CAB/RPV therapy

What would you choose?

Q30.

Several new HIV medicines are being developed that could be taken less frequently than currently available options. Compared with your current HIV medicines, how interested would you be in switching to a new treatment that...

	Not at all interested in switching		Somewhat interested in switching		Very interested in switching
	1	2	3	4	5
... is a single pill taken once a week?	O	O	O	O	O
... is two shots given in clinic every other month?	O	O	O	O	O
... involves implanting and removing two small plastic rods (about the size of matchsticks) in each forearm every six months?	O	O	O	O	O

Emerging data shows the process of accumulation of VL failures→

Method of delivery→

Complexities of patient care
- ADME

harmacokinetics/dynami
s

Non-obese	Obese	Severely obese	Morbidly obese
(BMI <29.9 kg/m^2)	(BMI 30-34.9 kg/m^2)	(BMI 35-39.9 kg/m^2)	(BMI ≥40 kg/m^2)
N = 32	**N = 12**	**N = 19**	**N = 9**

Oral Lead In
CAB 30 mg + RPV 25 mg PO daily

IM Load x 2
IM Load CAB 600 mg + RPV 900 mg

Every Two Month Dosing
IM Maintenance CAB 600 mg + RPV 900 mg