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BRIEF REPORT

Long-acting Injectable Cabotegravir/Rilpivirine Effective in a Small Patient Cohort With Virologic Failure on Oral Antiretroviral Therapy

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We report 12 patients with persistent viremia on oral antiretroviral therapy who were initiated on injectable cabotegravir/rilpivirine (iCAB/RPV) without oral lead-in. All patients achieved viral suppression without any virologic rebound. iCAB/RPV may be considered as an option for patients unable to maintain suppression on oral antiretroviral therapy.

Keywords. HIV; therapeutics.

Long-acting injectable cabotegravir-rilpivirine (iCAB/RPV) is approved for virologically suppressed people with human immunodeficiency virus (HIV) without cabotegravir- or rilpivirine-associated mutations as a switch strategy [1]. iCAB/RPV has subsequently received approval for administration every 2 months, and the oral lead-in phase has been relegated to optional, greatly improving convenience of this regimen [2, 3]. However, the group of patients in greatest need of long-acting antiretroviral therapy (ART) may be those unable to achieve virologic suppression on oral therapy who are currently not candidates due to lack of evidence to support its use in this group [4]. Experience with this combination in a viremic patient was first demonstrated in a single patient case report in 2022 [5]. Subsequently, a single-center cohort of 133 patients (57 of whom were viremic) demonstrated virologic suppression in 54 of 57 viremic patients [6]. Beginning February 2022, the Adult Special Care Clinic, a Ryan White–funded HIV clinic at the University of Mississippi Medical Center in Jackson, Mississippi, began offering iCAB/RPV as a salvage option for patients with poor virologic outcomes (viremic at multiple time points) despite ART optimization and intensive case management strategies. Over the following year, 12 patients with viremia were started on iCAB/RPV.

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Table 1. Baseline Demographics

Characteristic	Patients ($N = 12$)
Age (years, median)	42 (range 28–61)
Race (n)	
Black/African American	11
Native American	1
White	0
Ethnicity (n)	
Not Hispanic/Latinx	12
Hispanic/Latinx	0
Gender (n)	
Cis-female	7
Cis-male	5
BMI (kg/m^2, mean)	25.2 (range 17.9–39.9)
Payor (n)	
Medicaid	9
Medicare	2
Commercial	1
No insurance	0
Pill burden (mean)	
All medications	6.1 (range 2–14)
Antiretrovirals	1.5 (range 1–3)
Viral load (copies/mL, mean)	152 657 (range 2410–566 000)
Absolute CD4 (cells/μL, mean)	233 (range 131–475)
Baseline resistance-associated mutations (n)	
NNRTI	
K103N	2
V106I	1
P225H	1
INSTI	
D232N	1
N155H	1
E157Q	3

Abbreviations: BMI, body mass index; INSTI, integrase strand transfer inhibitor; NNRTI. non-nucleoside reverse transcriptase inhibitor.

Between February/2022 and June 2023, 12 patients initiated iCAB/RPV. Baseline demographics are listed in Table 1. The median age was 42 years (range 28–61). Seven patients were cisgender females, and 5 were cisgender males. Eleven patients were Black/African-American, 1 patient was Native American, and no patients were Latinx. Mean baseline body mass index (BMI) was 25.1 kg/m^2 (range 17.9–39.9). Nine patients had Medicaid as a primary payor, 2 had Medicare, and 1 had a commercial payor. Three patients had substance use disorder, including alcohol, methamphetamine, and cocaine. No patients reported injection drug use. No patients had hepatitis B coinfection. One patient had housing instability. Three patients had major depressive disorder, and 1 patient had paranoid schizophrenia. Before starting iCAB/RPV, the mean number of total pills prescribed was 6.1 (range 2–14), and the mean number of ART pills was 1.5 (range 1–3).

Baseline historical resistance-associated mutations were common, present in 83% (10 of 12) of patients. Non-nucleoside reverse transcriptase inhibitor- (NNRTI) associated mutations noted in the cohort included K103N (2), V106I (1), and P225H (1). Integrase strand transfer inhibitor (INSTI) mutations included D232N (1), N155H (1), and E157Q (3). Among patients initiated directly to Q2M dosing, 1 had an E157Q mutation, 1 had K103N and P225H mutations, and the other 4 had no INSTI- or NNRTI-associated mutations.

The follow-up period for this cohort ranged 1–17 months. Six patients have at least 12 months of clinical follow-up. Six patients were initially started on injections every month (Q1M) but were transitioned to every 2 months (Q2M). Virologic kinetics of patients initiated on Q1M demonstrated achievement of viral load <200 by 2 months in 5 of 6 patients and by month 3 in 1 of 6 patients. This experience, along with maintenance of suppression in all 6 Q1M participants, supported implementation of direct-to-Q2M injections in the remainder of the cohort, who received loading doses at months 0 and 1 prior to transition to every other month. Despite historical poor adherence to oral therapy in this patient cohort, adherence to injection visits was very good with 5 of 82 injection visits occurring after the scheduled injection window period. These late injection visits were addressed by repeating a loading dose within a month. Despite no oral bridging, none of these late injection visits resulted in virologic failure. There have been no discontinuations due to attrition, virologic failure, or adverse effects.

Virologic outcomes of this cohort were excellent. The mean viral load was 152 657 copies/mL (range 2410–566 000) at baseline. All patients achieved viral load <50 copies/mL within 3 months of initiation of iCAB/RPV, and virologic rebound (viral load ≥200 copies/mL) has not been observed to date.

Immunologic outcomes in this cohort were positive in all but 1 participant. At baseline, 5 patients had a current AIDS diagnosis with prior diagnoses of *Candida* esophagitis (3), cryptococcal meningitis (1), and *Pneumocystis* pneumonia (1). Baseline absolute CD4 count mean was 233 cells/μL (range 131–475). Mean CD4 increase was 184 cells/μL (range 26–414), and patients with CD4 <200 cells/μL at baseline had a mean absolute CD4 increase of 308% (range 64%–844%) during this short follow-up period. Among the 3 patients with evidence of wasting at baseline, weight gain ranged from 2.6 to 6.9 kg during follow-up.

Implementation of this program has required close collaboration of clinicians, case management, and pharmacists. iCAB/RPV has been included in the Mississippi Medicaid preferred drug list without viral suppression restrictions. However, obtaining initial approval through other payors has required peer-to-peer discussions after initial denials on prior authorization. Successful peer-to-peer discussions included mention of any prior failing oral regimens and that this regimen is being utilized as salvage in high-risk patients. Case management of patients on iCAB/RPV requires regular telephone follow-up, appointment reminders, transportation assistance, and proactive rescheduling of missed injection visits. Adult Special Care Clinic's (ASCC's) injectable ART program has grown to a full-time RN for case management and injection administration, which may not be reproducible outside resource-rich clinical settings. Barriers to care were common, including lack of transportation and inconsistent phone service. Reasons for missing injection visits were not always ascertainable, but lapses in phone coverage were common to all missed visits. One patient had conflicts with thrice-weekly dialysis and a hospitalization.

In summary, this cohort further supports the use of iCAB/RPV in patients with viremia. This regimen has been utilized in our practice as a salvage option for people with long-standing viremia and often advanced disease, where the potential benefits of virologic suppression far outweigh the risks of treatment emergent resistance. Directly observed therapy through Q2M injections provides a much-needed therapeutic option for thousands of people in the United States who have not achieved virologic suppression. Although this cohort has not demonstrated virologic failure to date, there was a 4-fold increase in virologic failure in Q2M dosing compared to Q1M dosing in the ATLAS 2M trial (8/522 vs 2/523), and the convenience of direct-to-Q2M dosing in salvage should be weighed against a concern for higher potential for virologic failure and development of further resistance-associated mutations. Up to 10% of the ASCC patient cohort has not achieved virologic suppression at any time point with durable virologic suppression even more difficult to maintain. This is despite intensive case management and social support services offered to our patients in a resource-rich clinical setting. Unfortunately, rilpivirine- and cabotegravir-associated mutations are common in the cohort of patients in our practice with inconsistent or no virologic suppression. Reassuringly, 3 patients with minor INSTI mutations with minimal effect on CAB achieved virologic suppression with follow-up data up to 1 year for 3 patients. Long-term outcomes of this growing cohort will continue to be collected and reported as experience with this treatment strategy accumulates, and additional long-acting ART formulations are greatly needed to expand the toolkit in the effort to reach 100% virologic suppression.

Notes

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