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COMMENTARY

Experiences to date with the logistical management of long-acting cabotegravir and rilpivirine

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Abstract

The logistical management of an injectable therapy for the treatment of HIV can be expensive, time consuming, frustrating and riddled with barriers. In this Commentary, we describe our experiences to date with acquiring, storing, handling, administering and billing for long-acting cabotegravir and rilpivirine through four scenarios, each of which have presented their own unique obstacles and learning curves. At the time of writing, we have successfully transitioned four patients from the CUSTOMIZE trial to long-acting cabotegravir and rilpivirine. In doing so, we encountered a variety of barriers to acquiring, handling and administering the medication for both insured and uninsured patients; it is expensive, on a limited number of insurance formularies, and often requires a prior authorization from the provider. Cold-chain handling of the injectable therapy, along with individual patient characteristics, present barriers to management and administration of this therapy. Whilst a seemingly very attractive option for the treatment of HIV-1 infection in adults, long-acting cabotegravir and rilpivirine present a variety of challenges to pharmacists, providers and clinic staff on how to obtain it for and administer it to the patient. We plan to continue documenting our experiences, progress and successes, or lack thereof, in order to fine-tune our process and share with others.

Keywords: antiretroviral agents, antiretroviral therapy, clinical management, highly active, HIV, long-acting antiretroviral, practice management.

Citation

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Introduction

Antiretroviral therapy (ART) has reduced the burden of HIV-associated illness and the number of deaths over all stages of HIV infection, and can effectively reduce the viral load in a person living with HIV to below the level of detection, thereby preventing the transmission of HIV to an individual who is HIV negative. Effective and sustained suppression of plasma virus levels can help prevent the development of drug-resistance mutations and can improve CD4 T lymphocyte levels and overall immune function.[1]

In general, HIV is most often treated by using three different drugs from two or more classes of antiretroviral drug classes, with the goal of suppressing the HIV viral load to below the level of detection. When the viral load fails to become suppressed or cannot be maintained, the regimen must often be changed to a new regimen containing at least two active drugs. Factors that favour successful suppression of the virus include the potency of antiretroviral agents, convenient dosing and patient tolerability.[1]

Inconsistent adherence to ART may result in suboptimal treatment response and may be due to complicated medication regimens, patient-specific factors (such as substance abuse, depression, adverse effects) and healthcare issues, which may include disruptions in access to medication therapy and inadequate education and support. Barriers to adherence should be minimized before and after initiation of ART.[1]

Current first-line ARTs, or those initial regimens for most people with HIV, are oral medications that must be taken daily and for the rest of the patient's life, which may prove challenging for some patients, affecting adherence and increasing the risk for treatment failure.[2–4] Evidence suggests that there is a great deal of interest amongst those living with HIV for therapy options that are dosed less frequently.[5,6] Ongoing research involving ART has focused on simplifying regimens to improve patient satisfaction and adherence. The development of long-acting injectable therapies will also help address the factors that play into virological success.[6–8]

CABENUVA* (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension), copackaged for intramuscular use, was approved by the FDA on January 21, 2021.[9,10] The long-acting injectable portion of this treatment consists of two parts: an initiation dose for 1 month followed by the continuation dose monthly thereafter. The initiation dose is 600 mg (3 mL) of cabotegravir and 900 mg (3 mL) of rilpivirine, each of which is given in the gluteal muscle on opposite sides of the body or 2 cm apart on the same side. The continuation dose is 400 mg (2 mL) of cabotegravir and 600 mg (2 mL) of rilpivirine also given in the gluteal muscle on opposite sides of the body or 2 cm apart on the same side. The injections are administered in the healthcare practitioner's office.[10]

Long-acting cabotegravir and rilpivirine are indicated as a full and complete regimen for the treatment of HIV-1 infection in adults to replace the current regimen in those whose viral load is suppressed (HIV-1 RNA less than 50 copies per mL) on a stable regimen without evidence of treatment failure and with no known or suspected resistance to either medication. Prior to initiating treatment with long-acting cabotegravir and rilpivirine, an oral lead-in dose of cabotegravir 30-mg and rilpivirine 25-mg oral tablets should be used for at least 28 days to assess tolerability of both medications.[10]

HIV treatment has evolved from inconvenient regimens that were quite difficult to adhere to due to high pill burden, dosing frequency, intolerable toxicities, food requirements, drug interactions, insufficient viral suppression and higher risks for drug resistance, to much more manageable one- to two-tablet, once-daily regimens.[11] Now, with the advent of long-acting injectable ART, HIV treatment may become even more convenient for many patients.

Commentary

Patient excitement around this treatment is palpable; there is no pill burden after the first month, stigma may be reduced by not being reminded daily of the condition by the act of taking a pill, and privacy is enhanced as it will not be necessary to hide medication from friends and family. Provider excitement is high as well with the anticipation of improved patient satisfaction, increased medication therapy adherence and sustained HIV viral load suppression.

As a clinical trial site for long-acting cabotegravir and rilpivirine, KC CARE Health Center (KC CARE) experienced a sneak peek of what to expect once it received full FDA approval in terms of patient response and adherence to injectable treatment for HIV. Whilst it has been thrilling to anticipate the transition of patients from oral ART to injectable therapies, and ultimately increase adherence and improve outcomes, what the clinical trial did not prepare providers for were the piles of denied insurance claims, appeal letters, clinician burnout and workflow that does not necessarily 'flow'.

At KC CARE, many patients are underinsured or uninsured and it would be cost prohibitive for them to access long-acting cabotegravir and rilpivirine for the treatment of HIV. Through their ViiVConnect Patient Assistance Program (ViiVConnect PAP), ViiV Healthcare (the manufacturer of long-acting cabotegravir and rilpivirine) offers these medicines at no cost to patients who qualify based on financial or other criteria. Below, we describe a variety of scenarios regarding the access, storage, administration, and billing for long-acting cabotegravir and rilpivirine that we have encountered thus far.

Scenario 1

The patient is uninsured and meets income requirements for the ViiVConnect PAP.

- **Solution:** Nursing and pharmacy staff help complete the ViiVConnect PAP application for long-acting cabotegravir and rilpivirine on behalf of patients. Patient placed on ViiVConnect PAP.
- **Concern:** The ViivConnect PAP could end and then the patient may need to transition back to oral medication, creating confusion and frustration for the patient. This scenario is unlikely but not impossible.

This scenario is surprisingly the easiest process and the best bet from an administrative standpoint. If patients meet the income requirements, ViiV Healthcare ships the medications from a pharmacy of their choice to the provider's office. Staff can then schedule the patient for an appointment for their injection.

Scenario 2

The patient is insured, but long-acting cabotegravir and rilpivirine are not covered by insurer.

- **Solution:** The ViiVConnect PAP currently provides a bridge programme for approximately 1 year.
- **Concern:** If, after 1 year, long-acting cabotegravir and rilpivirine are not on the patient's insurance formulary, the patient may need to transition back to oral medications, again creating confusion and frustration for the patient.

This scenario is feasible, but the approval process can be a nightmare. We have experienced pharmacy benefits managers (PBMs) not wanting to share information about coverage with ViiVConnect, resulting in having to work directly with the PBM, which presents complications. One of the largest PBMs was not even aware of the oral therapy lead-in period. For one patient, we spent an hour on the phone with the PBM only to obtain a denial. The aim of completing the ViiVConnect PAP form was to limit the leg work to obtain approval. In this case,

*Research Triangle Park, NC: ViiV Healthcare; 2021.

we completed twice the amount of paperwork and still had zero medicine in hand. We are currently still waiting on bridge approval for this patient.

Scenario 3

Long-acting cabotegravir and rilpivirine are only covered through the patient's medical benefit.

- **Solution:** 'Buy-and-bill' – the patient's doctor buys the medication and has it delivered to their office to inject and then bills the patient's insurance for the medication and administration. We have had one patient where this has worked, and the patient was ultimately responsible for a US$600.00 co-pay.
- **Concern:** This can be quite cost prohibitive for organizations to invest money upfront to carry this inventory whilst there is little to no reimbursement for product, and the administrative cost can be higher than reimbursement for administration.

This scenario is not really an option for us at our Federally Qualified Health Center. Financial constraints make it precarious to purchase this multithousand-dollar medication up front and keep stocked without the reassurance of reimbursement. Doctors' offices often do not even want to stock vaccines because of the convenience that pharmacies offer. Pharmacies are accustomed to managing inventory and inventory cost and are more than capable of administering the injection. Whilst providers are capable of Buy-and-Bill, it may not be feasible for providers to increase staff, clinical services and refrigerator space to provide monthly injections to patients they are currently accustomed to seeing only once or twice per year. Currently, some after-market studies are looking at administering long-acting cabotegravir and rilpivirine injections every 2 months; however, that is still more than double the number of appointments for a single patient in 1 year following current standards of practice.

Scenario 4

Long-acting cabotegravir and rilpivirine are covered through the patient's pharmacy benefit plan but require prior authorization.

- **Solution:** Complete prior authorization on behalf of the patient.
- **Concern:** Insurance may deny the medication due to lack of medical necessity and the medication can only be dispensed by a limited number of pharmacies. Additionally, pharmacies need to be able to manage the cold-chain handling of these products — the medication is kept refrigerated, lending itself to a limited shelf life. Additionally, licensure limitations on if or how a pharmacist may administer the medication to the patient can vary by state, with most patients needing to receive their injection by a nurse, physician or another provider at a medical office visit.

This scenario is the game changer from the authors' point of view, with pharmacists anticipating and advocating for provider status.

Discussion

Most of what has been described here has been worked out by and is second nature to specialty pharmacy teams and can be performed at the community pharmacy level. Pharmacists started performing COVID-19 testing in community pharmacy drive-through lanes and administering COVID-19 vaccines in community pharmacies in less than a year. The challenges seen here are no different than when any new medication hits the market; it is expensive, on limited formularies and requires prior authorization. As pharmacists, we hope that coverage will be expanded because it is the right thing to do for patients living with HIV. However, getting the medication to the medical office securely, timely and within its temperature constraints presents new challenges in the world of HIV treatment. Aside from the monthly visits and additional workflow measures mentioned in Scenario 3, what also needs to be considered and can complicate workflow is what happens when the patient falls out of care and the medication needs to be returned to stock so that insurance companies are not on the hook paying for a medication that was not used. We cannot return the drug to the pharmacy; it has already been dispensed; this is wasteful healthcare spending. Additionally, PBMs could deny future refills if they observe non-compliance upon review of fill history. We experienced this with hepatitis C treatment, and we were required to complete additional prior authorizations when the patient returned to care.

Ideally, we would dispense the oral lead-in medication and the injection at the community pharmacy level and allow pharmacists to provide the injection on site. This would be a novel form of delivery for pharmacists because, historically, we have not been injecting into the gluteal muscle at the community pharmacy level; however, we are more than capable. Yes, there will still be prior authorizations and price overrides but that is beyond the scope of this article. This option mitigates additional visits to the medical office and places the management of patient medications and dispensing back into the hands of the pharmacist.

As of the writing of this article, we successfully have four patients on treatment following their completion of the clinical trial. We have experienced each scenario described earlier and, whilst the learning curve has been steep, it has been a rewarding experience to see patients receive this treatment.

The authors of this article plan to continue to document our experiences, progress and obstacles encountered along the way and hope to share that information in the near future.

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