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I ANTI-HIV AGENTS

A. Some HIV drugs in development

Effective combination HIV treatment was introduced in the mid-1990s in North America. For the first time in the history of the HIV pandemic, treatment was able to reduce the risk of serious AIDS-related complications. In that era, treatment was complex, often involving a fistful of pills at least two and sometimes three times daily, in many cases with food and water requirements. What's more, treatment back then had many side effects.

Since that time, pharmaceutical companies have developed more effective and simpler regimens. In many cases an entire regimen (two or three potent drugs) can be packed into one pill taken once daily.

Another advance has been the creation of long-acting medicines. In the year 2020, regulatory authorities in Canada approved the first long-acting HIV treatment. This was a combination of two drugs—cabotegravir + rilpivirine (sold as Cabenuva). The combination is injected deep into the buttocks, where it is slowly released into the bloodstream. Clinical trials have found that after monthly injections for two consecutive months, Cabenuva only needs to be injected every two months. Several other long-acting therapies are in development.

Modern HIV treatment (ART) has been so transformative that researchers expect that many ART users will have near-normal life expectancy. However, as people with HIV age, they may need to change their regimens for a number of reasons—for example, if they develop drug-resistant virus or are dealing with side effects or want to simplify their regimen. As a result, the pharmaceutical

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industry is developing new drugs. In this issue of *TreatmentUpdate*, we summarize HIV drugs that are coming to clinics in the future.

Lenacapavir

Another anti-HIV drug called lenacapavir has recently been approved in Canada. Lenacapavir works in a way that is different from other HIV drugs—by interfering with an HIV protein called the capsid. The initial approval of lenacapavir will be for people with limited treatment options due to drug-resistant HIV (this population is sometimes referred to as "heavily treatment-experienced patients" by researchers). Lenacapavir is meant to first be taken as a pill three times over the course of eight days. About a week after the third (and final) oral dose, nurses administer two subcutaneous (just under the skin) injections of lenacapavir in the belly. After these initial injections, additional injections are administered every 26 weeks (roughly every six months). For now, lenacapavir will need to be taken with other HIV drugs (as daily pills). However, it is possible in several years that there will be other drugs equally as long acting as lenacapavir. This could remove the need for daily pill-taking in the long term. Lenacapavir is also under development for the prevention of HIV—pre-exposure prophylaxis (PrEP). We have more information on lenacapavir later in this issue of *TreatmentUpdate*.

Islatravir

Another emerging HIV drug is islatravir, which is being tested as part of dual combination therapy with another drug called doravirine (Pifeltro and in Delstrigo). Islatravir has long-acting potential and will hopefully be tested in clinical trials with lenacapavir.

Maturation inhibitor

The experimental drug GSK 3640254 is set to enter clinical trials sometime in 2023. This HIV drug belongs to an emerging class of medicines called maturation inhibitors. It will be tested in combination with other anti-HIV drugs.

Lenacapavir is the first of the three drugs previously mentioned to be approved in Canada. If all goes well, the two other drugs (Islatravir and GSK 3640254) will hopefully be approved in several years.

B. Islatravir returns to clinical trials

In late 2021, the pharmaceutical company Merck announced that it had suspended many clinical trials with the experimental anti-HIV drug islatravir. This suspension arose because interim data analyses from clinical trials had found that some people who were given relatively large doses of this drug (0.75 mg and 2.25 mg per day) developed lower-than-normal levels of a certain group of cells in their blood.

The cells in question are called lymphocytes (T-cells, B-cells and natural killer cells). These cells are needed to contain infections and tumours and regulate the immune system. Fortunately, none of the people who took relatively high doses of islatravir and who developed low lymphocyte levels became ill.

The reductions in lymphocyte levels occurred during the first year of use of high-dose islatravir and then stabilized. That is, no further decreases occurred while people were taking high-dose islatravir. This is reassuring and suggests that no permanent injury occurred. Furthermore, once people stopped taking high-dose islatravir or were switched to a lower dose (0.25 mg per day), recovery of lymphocyte levels gradually ensued. In some people this recovery took longer than six months. Researchers are continuing to monitor all people who took high-dose islatravir.

A safer, lower dose of islatravir

Scientists at Merck have since undertaken in-depth analyses of different doses of islatravir in lab experiments with cells and animals and other experiments with people. Their analyses suggest that using a lower dose of islatravir (0.25 mg per day) is likely much safer. So far, no decrease in lymphocyte levels have been found in people who have used this lower dose. The 0.25 mg per day dose will be used in several clinical trials that are planned to start in the first half of 2023.

In some trials Merck will be testing a combination of low-dose islatravir with another anti-HIV drug called doravirine (Pifeltro). This latter drug is already approved for HIV treatment. The approach with reduced-dose islatravir for clinical trials has been approved by regulatory authorities in the U.S. (the Food and Drug Administration) and other

high-income countries. Merck will test low-dose islatravir in the following populations:

- people with HIV who have not previously taken treatment
- people with HIV who are taking treatment and have a suppressed viral load and who will change to an islatravir-based regimen

Merck is cooperating with another company called Gilead Sciences to develop a combination of islatravir + lenacapavir (the latter is made by Gilead). Both companies will test a combination of two drugs: lenacapavir (mentioned in detail later in this issue of *TreatmentUpdate*) and low-dose islatravir.

PrEP

Merck was testing islatravir taken once monthly for its ability to reduce the risk of HIV infection. Using drugs to reduce the risk of getting HIV is called pre-exposure prophylaxis (PrEP). However, due to previously mentioned issues with high-dose islatravir, this trial was halted. Merck does not plan to resume testing once-monthly islatravir with a lower dose of this drug.

Islatravir as a model for new drugs

Islatravir belongs to a new class of drugs called HIV reverse transcriptase translocation inhibitors (RT translocation inhibitors). This class of drugs interferes with the functioning of a vital viral enzyme called RT, which is needed to help HIV infect cells. Translocation inhibitors also interfere with HIV's ability to take over a cell and hijack its functions. It is possible that translocation inhibitors have other actions against HIV that are less well understood. Islatravir is a model of the first translocation inhibitor to enter clinical trials.

A new drug

Merck has also developed another experimental anti-HIV drug with the code name MK-8527. It is also a translocation inhibitor acting against RT. It is likely that this drug has potential for long-acting therapy. However, at this time, the focus of the study of MK-8527 is safety and to determine how long the drug remains in the body.

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C. Lenacapavir – an emerging drug for HIV treatment and hopefully prevention

Lenacapavir is an emerging anti-HIV drug. It works by interfering with an HIV protein called the capsid. Lenacapavir therefore belongs to an emerging group of HIV drugs called capsid inhibitors.

Lenacapavir was first approved for use by authorities in the European Union and has recently been approved by Health Canada. Lenacapavir is meant to be used as part of combination therapy for people who have HIV that is resistant to many treatments. Researchers refer to this group of people as "heavily treatment-experienced."

Lenacapavir is meant to first be taken as a pill three times over the course of eight days. About a week after the third (and final) oral dose, nurses administer two subcutaneous (just under the skin) injections of lenacapavir in the belly. After these initial injections, additional injections are administered every 26 weeks (roughly every six months). Lenacapavir is meant to be taken as part of combination treatment, so people using it will also have to take other HIV drugs (as daily pills). Lenacapavir must be taken with other anti-HIV drugs to have maximal effect against the virus.

Lenacapavir has been tested in a clinical trial with 72 people who had HIV with extensive resistance to other treatments. Prior to using lenacapavir, and while taking other HIV treatments, many of these people had detectable viral loads (on average around 15,000 copies/mL). Fourteen people had a viral load greater than 100,000 copies/mL. Prior to the participants taking lenacapavir, technicians performed resistance test analyses of their blood samples. This was done to assess the degree of HIV's ability to resist the effect of treatment. Based on the

results of resistance testing, participants' regimens were adjusted and lenacapavir was added.

After six months, 82% of participants achieved and maintained a suppressed viral load. Limited data suggested that viral suppression persisted for many people in the study after one year.

Lenacapavir and islatravir

Lenacapavir will be tested in a clinical trial with the experimental drug islatravir (mentioned earlier in this issue of *TreatmentUpdate*). In that trial both drugs will be given once weekly.

Lenacapavir as PrEP

Lenacapavir is also being tested in large studies to assess its effectiveness for the prevention of HIV—pre-exposure prophylaxis (PrEP). If the trials show that lenacapavir is highly effective, its developer, Gilead Sciences, will hopefully seek to have it approved for PrEP. Such approval is first likely in the U.S. As the trials are still underway, lenacapavir may not be approved for PrEP until 2025.

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D. Maturation inhibitor advances into clinical trials

Approved anti-HIV drugs can be grouped into different classes depending on how they work. These drugs target different parts of HIV-infected cells and interfere with their ability to make new copies of HIV. The following proteins or enzymes inside HIV-infected cells are affected by the following drugs:

- RT (reverse transcriptase) – tenofovir, 3TC, FTC, efavirenz, rilpivirine
- protease – darunavir (Prezista and in Prezcobix), atazanavir (Reyataz)
- integrase – bictegravir (in Biktarvy), cabotegravir (in Cabenuva), dolutegravir (Tivicay and in Dovato and Triumeq), raltegravir (Isentress)

As mentioned earlier in this issue of *TreatmentUpdate*, an emerging class of drugs is called capsid inhibitors. The first capsid inhibitor—lenacapavir—is developed by Gilead Sciences. Another company, ViiV Healthcare, also has a capsid inhibitor but it is in very early stages of development.

Maturation inhibitors

ViiV is also developing another class of anti-HIV drugs called maturation inhibitors. As the name suggests, maturation inhibitors affect the final stage of virus production inside infected cells. These drugs prevent new copies of HIV from maturing and render them non-infectious.

GSK '254

ViiV is developing a maturation inhibitor code-named GSK 3640254 (we will shorten this to compound '254). In clinical trials, when compound '254 was the only anti-HIV drug given to participants, no resistance to the drug appeared up to seven days of dosing. However, when it was used as the only anti-HIV drug for 10 days, resistance did appear. Therefore, in the future, compound '254 will need to be used as part of a combination of anti-HIV drugs in order to minimize the risk of resistance developing. In that clinical trial of 34 people with HIV, researchers tested different doses of compound '254. Depending on the dose used, viral load fell between 10- and 100-fold over the course of the study (seven to 10 days).

The researchers stated that nine participants (26%) reported 14 drug-related side effects. According to the researchers, the most common side effects were "diarrhea, abdominal pain, and vomiting." They also stated that these side effects were "mild to moderate in intensity."

No one prematurely left the study or died because of drug-related side effects.

Other research

Researchers have done small and short studies to assess how combinations of compound ’254 might affect other drugs (and vice versa). The combinations tested included the following:

- compound ’254 and dolutegravir
- compound ’254 and the combination of TAF + FTC (sold in a pill called Descovy)
- compound ’254 and oral contraceptives

In all cases, there were no significant interactions.

For the future

ViiV will likely put compound ’254 into larger and longer clinical trials with other anti-HIV drugs to assess its safety and effectiveness.

As with other relatively new drugs, such as the long-acting injectable Cabenuva (cabotegravir + rilpivirine), it is plausible that ViiV will eventually develop and test both oral and injectable formulations of compound ’254. Clinical trials will be needed to assess the safety and effectiveness of long-acting formulations of compound ’254, and this will take time. Therefore, it may be several years before compound ’254 is approved in Canada and other high-income countries as a new option for HIV treatment.

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E. Northern Alberta researchers study Biktarvy and mutations in HIV

Resistance to anti-HIV drugs can be a concern for doctors treating some people with HIV, particularly people who have been taking HIV treatment (ART) for decades. In the early years of HIV, treatment was typically one drug used on its own (monotherapy). In the early 1990s, it became two drugs. The drugs in common use in that era were nucleoside analogues (nukes). By themselves or even in combination with other nukes, these drugs are unable to suppress HIV for long. As a result, some people developed strains of HIV that were partially or wholly resistant to other anti-HIV drugs (usually other nukes). It was not until about 1996 that regimens became more effective with the addition of other classes of drugs—particularly protease inhibitors and non-nucleosides (non-nukes). Today, HIV treatment regimens are much more robust than those that were used in the late 1990s or early 2000s. The robustness of these regimens is usually due to the presence of an integrase inhibitor. Examples of integrase inhibitors include bictegravir (in Biktarvy), dolutegravir (Tivicay and in Dovato, Juluca and Triumeq) and raltegravir (Isentress).

Back to nukes

Examples of nukes that are used today include the following:

- 3TC
- abacavir
- FTC

- tenofovir; this comes in two formulations – tenofovir DF and tenofovir alafenamide (TAF)

Nukes are sometimes combined into one pill (co-formulated):

- tenofovir DF + FTC – sold as Truvada and available in generic combinations
- TAF + FTC – sold as Descovy

However, as mentioned earlier, nukes on their own are insufficient to suppress HIV. Therefore, some nukes are coformulated with other more potent drugs—usually integrase inhibitors or non-nukes (such as doravirine or rilpivirine)—to form a complete regimen in one pill. Here are some examples of that:

- bictegravir + TAF + FTC — sold as Biktarvy
- dolutegravir + 3TC – sold as Dovato
- dolutegravir + 3TC + abacavir – sold as Triumeq
- doravirine + tenofovir DF + 3TC – sold as Delstrigo
- rilpivirine + TAF + FTC – sold as Odefsey

Northern Alberta

For their study on the potency of Biktarvy, researchers at the University of Alberta in Edmonton scoured medical records of HIV-positive people to find information about people who were taking Biktarvy. They found 779 records; 50 of these people had drug resistance testing done at some point in the past (prior to initiating Biktarvy) when their viral loads were detectable.

The Northern Alberta researchers focused on resistance testing that identified mutations, or changes, in HIV's genetic material that were associated with resistance to nukes. None of the participants had HIV that was resistant to integrase inhibitors (Biktarvy contains the integrase inhibitor bictegravir). All 50 participants had at least one mutation associated with resistance to nukes. A total of 29 participants had just one such mutation. The remaining 21 participants had two or more mutations that were associated with resistance to nukes. Despite this finding, 48 out of 50 participants had a viral load less than 50 copies/mL an average of 18 months after initiating treatment with Biktarvy.

The Alberta study confirms the usefulness of triple therapy anchored by an integrase inhibitor—in this case, bictegravir.

Study details

Researchers collected health-related information between May 2020 and January 2022. Viral load testing could have been done at any time in the past when participants had a detectable viral load. In most cases, this was before they switched to another regimen, and well before they subsequently began to take Biktarvy.

The average profile of the 50 participants prior to initiating Biktarvy was as follows:

- age – 54 years
- 64% men, 36% women
- CD4+ count – 609 cells/mm^3

Results

Shortly before initiating Biktarvy, four people had a detectable viral load, distributed as follows:

- two people who had never previously taken ART but had become infected with HIV that was resistant to some nukes – one of them had a viral load of almost 1,800 copies/mL, while the other had a viral load of 62,000 copies/mL
- two people who had previously used ART – one of them decided to stop ART two months before initiating Biktarvy. Their viral load was 68,000 copies/mL. This person had HIV with mutations that were associated with resistance to some nukes and protease inhibitors.
  The other person had a viral load close to 1,000 copies/mL and doctors suspected that he had problems with adherence.

Before the 50 people initiated Biktarvy, the most common regimen used was anchored by a boosted protease inhibitor.

Distribution of mutations associated with resistance to nukes

A total of 29 participants had just one mutation associated with resistance to nukes. The remaining 21 participants had two or more such mutations, distributed as follows:

- two nuke resistance mutations – nine people
- three nuke resistance mutations – three people
- four nuke resistance mutations – four people
- five nuke resistance mutations – two people
- six nuke resistance mutations – one person
- seven nuke resistance mutations – one person
- eight nuke resistance mutations – one person

Deaths

Two people died during the study period; both died 10 months after initiating Biktarvy. One person died from unspecified trauma and the other person died from complications caused by tumours that had spread from the liver. These deaths were unrelated to Biktarvy.

Regardless of previous treatment, the vast majority of participants (48 out of 50) had a viral load less than 50 copies/mL an average of 18 months after initiating Biktarvy. One person had a viral load that was greater than 50 copies but less than 100 copies/mL. The other person was not taking Biktarvy as directed.

Technical note

Researchers found that one particular mutation was common—M184V. This mutation is associated with resistance to the nukes 3TC and FTC and partial resistance to the nuke abacavir.

Bear in mind

Although the study relied on data that was collected in the past for one purpose and subsequently analyzed for another purpose, its findings are in line with larger studies.

The researchers stated: "We had limited numbers of patients with three or more [mutations associated with nucleoside resistance], which could be due to the low prevalence of such patients but could also be explained by patient selection bias." That is, doctors may be reluctant to treat such patients with Biktarvy alone. Instead, doctors in northern Alberta may have given such patients more complex, multi-pill regimens.

The researchers reviewed key studies and stated that in many cases nuke resistance mutations "do not appear to impair the virological response to triple therapy with two [nukes] combined with a boosted protease inhibitor, or dolutegravir or bictegravir…provided that there is no resistance to the protease inhibitor, dolutegravir or bictegravir. Our study provides further evidence that this is true of [Biktarvy] specifically."

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F. Long-acting HIV treatment in people with multiple challenges

When effective HIV treatment (ART) first became available, it involved taking a fistful of pills at least twice daily, often with food and water requirements. Although these early treatments were life-saving, they had many side effects. About 18 years ago, pharmaceutical companies created the first regimen in an entire pill—sold as Atripla. In addition to packing an entire regimen into one pill, Atripla needed to be taken just once daily. Subsequently, other once-daily regimens in a pill were developed. This ensured that for many people with HIV, treatment could be as simple as one pill taken once daily. This development of treatment simplification greatly enhanced adherence for many people.

For ART to be effective, treatment has to be taken daily as directed. According to a team of researchers in San Francisco, daily pill-taking can be difficult for some people for at least the following reasons:

- over the long-term people may become frustrated at having to take pills
- taking pills can remind people that they have HIV
- if pill-taking is observed by others, they can inadvertently disclose that a person has HIV
- some people may not have a place to store pills safely

The first long-acting treatment

In 2020 Health Canada approved a long-acting formulation of ART. This formulation is called

Cabenuva and consists of two drugs—cabotegravir + rilpivirine. Cabenuva is meant to replace an existing treatment regimen in people whose viral loads are suppressed. Cabenuva is administered by a healthcare practitioner (usually a nurse) as one injection deep into each buttock (for a total of two injections) monthly for two consecutive months. After this time, it can be injected every two months or once a month.

Cabenuva has the potential to address many of the issues that some people with HIV can face with daily pill-taking. Note that Cabenuva is meant to be used by people who have HIV that is not resistant to it.

Cabenuva does not treat hepatitis B virus (HBV); some people are co-infected with both HIV and HBV. Co-infected people require a daily pill to help keep HBV suppressed. Doctors usually use one of the following pills for this purpose:

- tenofovir DF + FTC – sold as Truvada and available in generic formulations
- tenofovir alafenamide (TAF) + FTC – sold as Descovy

In the everyday world

Cabenuva has been tested in more than 1,000 people with HIV in clinical trials. As with many other studies, the people in clinical trials of Cabenuva were carefully selected. They did not have issues that could affect daily pill-taking, they were willing to undergo the deep intramuscular injections that are required, and they could keep clinic appointments, particularly for repeated injections, and laboratory visits for blood tests.

Researchers at San Francisco General Hospital conducted a small demonstration project to explore the effect of Cabenuva in people with complex lives and adherence issues. They enrolled 39 people with HIV who had adherence challenges due to mental illness, stimulant use and/or insecure housing.

The researchers developed what they called a "patient-centred [Cabenuva] care delivery program in an academic HIV clinic that serves urban [patients] with high levels of psychosocial and economic vulnerability." Some of these patients had a detectable viral load before initiating Cabenuva. However, over the course of a year, a majority of the 39 patients achieved or maintained a suppressed viral load while on Cabenuva.

The study's findings are promising and should stimulate other researchers to conduct larger and longer demonstration studies in vulnerable populations. Such studies will require adequate funding to provide the array of services needed by these populations.

Study details

The researchers developed a program to support patients and their care providers and promote adherence to Cabenuva injections.

Researchers did not enroll patients who had mutations, or changes, in HIV's genetic material that allowed the virus to resist the effect of rilpivirine (this drug is a non-nuke and one of the two medicines in Cabenuva). People who had no or only one mutation associated with resistance to integrase inhibitors (cabotegravir, the other drug in Cabenuva, is an integrase inhibitor) were allowed to enter the program. This is because modern integrase inhibitors are robust drugs that usually require several mutations before HIV can wholly resist them.

People who were co-infected with HBV and who were willing to take HBV treatment were allowed to be considered for entry into the program.

Potential participants were referred to a team pharmacist who checked their lab test results, particularly to ensure that HIV was not resistant to the drugs in Cabenuva. The pharmacist also reviewed other medicines that the patient was taking to ensure that there were likely no unfavourable drug interactions once Cabenuva was injected. As well, the pharmacist also checked their HBV infection status and, if necessary, HBV treatment was initiated or maintained.

Direct to injection

When Cabenuva was initially approved in 2020, patients first had to take several weeks of the oral formulations of cabotegravir and rilpivirine (the drugs in Cabenuva). Once they completed this, and there were no issues, they could then switch to the injectable formulation.

In the past several years, ViiV Healthcare, the developer of Cabenuva, has tested a different approach called "direct to injection." That is, people whose viral loads were suppressed on oral formulations (of drugs other than cabotegravir or rilpivirine) could simply switch from their oral regimen and go directly to injections of Cabenuva. This direct-to-injection approach has proved successful. Therefore, direct to injection of Cabenuva has been approved as an option for patients by regulatory authorities in Canada, the European Union and the U.S.

The program in San Francisco favoured the direct-to-injection approach. The researchers stated that they felt this approach was necessary because they were concerned about potential problems with pill taking by patients.

The study team developed individualized plans to help patients return to the clinic for future injections of Cabenuva. Such plans included:

- identifying community-based support, such as case managers, nursing services that were available for people at home or for those who were experiencing homelessness, and harm reduction sites
- providing small financial incentives to encourage return visits to the clinic or lab

Every two weeks a multidisciplinary team consisting of a doctor, nurse and pharmacist would meet to review the progress of patients in the program.

During the first week after people had their first injection, pharmacy staff would phone the patient to enquire about their health and any side effects they may have experienced. Subsequently, staff would send reminders about future appointments via text or phone call.

People who entered the study with a detectable viral load underwent viral load testing every four weeks until they developed an undetectable viral load (this is called viral suppression). For this study, an undetectable viral load was less than 30 copies/mL. In cases where the viral load remained detectable, resistance testing was done after the second clinic visit.

Although care providers referred 132 people in the first year of the program, only 51 people initiated Cabenuva injections. In many cases this was because the referral procedure was incomplete or the patients (or their care providers) decided to delay initiation of Cabenuva. Some of the 51 people only had two injections of Cabenuva at the time the report on the study was written. This left the researchers with data on 39 people who had at least several injections of Cabenuva. The researchers decided to focus on these 39 people, as they could provide a fuller report of their experience with multiple injections of Cabenuva.

The average profile of people who initiated Cabenuva was as follows:

- age – 46 years
- 35 were cisgender men, three were cisgender women, and one was a transgender woman
- major ethno-racial groups: White – 39%; Hispanic – 26%; Black – 21%
- 40% had unstable housing or were experiencing homelessness
- 54% were currently using stimulants
- CD4+ counts – among people with detectable viral loads, the CD4+ count was 99 cells/mm^3; among people with viral suppression, the CD4+ count was 732 cells/mm^3
- five people were also taking long-acting medicines unrelated to HIV, including antipsychotics (four people) and naltrexone (one person)

Commonly used HIV drugs prior to switching to Cabenuva included the following (in decreasing frequency of use):

- Biktarvy – bictegravir + TAF + FTC
- darunavir + cobicistat + TAF + FTC
- Triumeq – dolutegravir + 3TC + abacavir
- Delstrigo – doravirine + TDF + 3TC

Results

Among 24 people who entered the program with an undetectable viral load (prior to initiating Cabenuva), 19 people (almost 80%) subsequently maintained an undetectable viral load over an average of six injections.

There were 15 people who entered the program with a detectable viral load (around 50,000 copies/mL) and a very low CD4+ count (around 99 cells/mm^3). In this group, 12 out of 15 people (80%) achieved and maintained an undetectable viral load over an average of six injections. Among the three

people who did not achieve this milestone, their viral load fell 100-fold 22 days after they initiated Cabenuva. Data collection from these three people is ongoing, and researchers expect that they will eventually achieve an undetectable viral load.

Side effects

Reactions at the site of injections were generally mild to moderate. None of the participants quit Cabenuva because of such reactions. One person developed a bacterial skin infection at the Cabenuva injection site. This person received oral antibiotics and recovered.

Adherence to clinic visits

Returning to the clinic for continued injections is important so that levels of cabotegravir and rilpivirine remain high in the blood and are able to suppress and keep HIV suppressed. According to ViiV Healthcare, "the date of the first initiation injection becomes the target treatment date going forward. The dose can be given up to 7 days before or 7 days after the target treatment date."

Thus, there is a window of seven days before and after the appointment for the next dose within which the next injection for Cabenuva must occur—or else levels of the drug can fall below an acceptable level. In cases when people miss this window period (we refer to this as late appointments), they need to switch to oral formulations to ensure that their drug levels are maintained. After a few weeks of oral formulations, they can return to injections. However, repeated missed appointments for injections may flag that there are issues that require attention from patients and their care providers.

Researchers designated certain days at the clinic as "injection days," whereby patients could drop into the clinic at a time convenient to them to receive their injections.

Thirty-four people (87%) attended the clinic in a timely manner. One person was late for one injection and two others were late for two injections each.

In two cases of late visits for injections, patients had to temporarily take oral formulations of Cabenuva to quickly raise their levels of cabotegravir and rilpivirine in their blood and minimize the chances of HIV developing resistance.

Two other people who were experiencing homelessness had help from street-based nurses and received their Cabenuva injections at a mobile harm reduction van or at a community clinic. Researchers noted that one person even received viral load monitoring through the harm reduction van.

Bear in mind

The present study has found that Cabenuva can be successfully deployed in a patient population experiencing challenges. The researchers found it "striking" that people with detectable viral loads were able to achieve an undetectable viral load once on Cabenuva. In some cases, viral suppression occurred for the first time in their lives.

The researchers cooperated with organizations in the community (nursing services, clinics, harm reduction sites) so that Cabenuva injections could occur, if necessary, outside of the main study clinic. Such cooperation would be essential in the future if Cabenuva can be successfully expanded to people who use drugs or people who are experiencing mental health issues and/or homelessness. Studies of Cabenuva are also needed in rural areas.

The study did not have people who were under the age of 30 and there were a small number of women. The study itself was small, but that is often the case with demonstration projects.

Still, the study's findings are promising and pave the way for future demonstration projects with larger numbers of people for longer periods. Such studies are important because pharmaceutical companies are developing other long-acting formulations of ART.

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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CATIE is Canada's source for up-to-date, unbiased information about HIV and hepatitis C. We connect people living with HIV or hepatitis C, at-risk communities, healthcare providers and community organizations with the knowledge, resources and expertise to reduce transmission and improve quality of life.

For more than 20 years, CATIE has been there to provide information that enables people to make informed choices about their health and enhances the ability of healthcare providers and other frontline organizations to respond to their clients' needs.

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