

PA

POSITIVELY AWARE

THE HIV TREATMENT JOURNAL OF TEST POSITIVE AWARE NETWORK
MAY+JUNE 2015

WHAT ABOUT CONDOMS?

CONFERENCE UPDATE:
THE CROI REPORT

WHY I RIDE:
OUT AND OPEN IN THE
RIDE FOR AIDS CHICAGO

THE BIGGEST CHANGES IN 20 YEARS ARE COMING

RETHINKING HIV

- NEW APPROACHES TO TREATMENT
- CHASING THE CURE
- 3D ANIMATION OF HIV



TRIUMEQ is a once-a-day pill used to treat HIV-1. TRIUMEQ should not be used by itself in some people. Take TRIUMEQ exactly as your healthcare provider tells you.

Is it time for you? Ask your doctor.

APPROVED USES

TRIUMEQ is a prescription medicine used to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults. HIV-1 is the virus that causes AIDS. It is not known if TRIUMEQ is safe or effective in children under the age of 18. TRIUMEQ is not for use by itself in people who have or have had resistance to abacavir, dolutegravir, or lamivudine.

TRIUMEQ does not cure HIV-1 or AIDS. You must stay on continuous HIV-1 therapy to control HIV-1 infection and decrease HIV-related illness.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about TRIUMEQ?

- **Serious allergic reaction (hypersensitivity reaction).** TRIUMEQ contains abacavir. Patients taking TRIUMEQ may have a serious allergic reaction to abacavir that can cause death. Your risk is much higher if you have a gene variation called HLA-B*5701. Your healthcare provider can determine with a blood test if you have this gene variation. **If you get symptoms from 2 or more of the following groups while taking TRIUMEQ, call your healthcare provider right away: 1. fever; 2. rash; 3. nausea, vomiting, diarrhea, or stomach pain; 4. generally ill feeling, extreme tiredness, or achiness; 5. shortness of breath, cough, or sore throat.** Your pharmacist will give you a Warning Card with a list of these symptoms. **Carry this Warning Card with you at all times.**

If you stop taking TRIUMEQ because of an allergic reaction, never take TRIUMEQ or any other medicine that contains abacavir or dolutegravir again. If you take TRIUMEQ or any other abacavir-containing medicine again after you have had an allergic reaction, **within hours** you may get **life-threatening symptoms** that may include **very low blood pressure or death.** If you stop TRIUMEQ for any other reason, even for a few days, and you are not allergic to TRIUMEQ, talk with your healthcare provider before taking it again. Taking TRIUMEQ again can cause a serious allergic or life-threatening reaction, even if you never had an allergic reaction to it before. **If your healthcare provider tells you that you can take TRIUMEQ again, start taking it when you are around medical help or people who can call a healthcare provider if you need one.**

- **A buildup of acid in your blood (lactic acidosis).** Lactic acidosis can happen in some people who take TRIUMEQ. This serious medical emergency can cause death. Call your healthcare provider right away if you feel very weak or tired; have unusual muscle pain; have trouble breathing; have stomach pain with nausea and vomiting; feel cold, especially in your arms and legs; feel dizzy/light-headed; or have a fast/irregular heartbeat.
- **Severe liver problems.** Severe liver problems can happen in people who take TRIUMEQ. In some cases, these severe liver problems can lead to death. You may be more likely to get lactic acidosis or serious liver problems if you are female, very overweight, or have been taking nucleoside analogue medicines for a long time. Call your healthcare provider right away if you get any of the following signs or symptoms:

- yellow skin, or the white part of the eyes turns yellow; dark urine; light-colored stools; nausea; itching; or stomach-area pain.
- **Worsening of hepatitis B virus in people who have HIV-1 infection.** If you have HIV-1 and hepatitis B virus infections, your hepatitis virus infection may get worse if you stop taking TRIUMEQ. Do not stop taking TRIUMEQ without first talking to your healthcare provider, so he or she can monitor your health.
- **Resistant hepatitis B virus.** If you have HIV-1 and hepatitis B, the hepatitis B virus can change (mutate) during your treatment with TRIUMEQ and become harder to treat (resistant).
- **Use with interferon and ribavirin-based regimens.** If you're taking TRIUMEQ and interferon, with or without ribavirin, tell your healthcare provider about any new symptoms. Liver disease might get worse in patients who are taking HIV-1 medicines and interferon.

Who should not take TRIUMEQ?

- **Do not take TRIUMEQ if you:**
 - have the HLA-B*5701 gene variation
 - have ever had an allergic reaction to abacavir, dolutegravir, or lamivudine
 - take dofetilide (Tikosyn®)
 - have certain liver problems

What are other possible side effects of TRIUMEQ?

- People with a history of hepatitis B or C virus may have an increased risk of developing new or worsening changes in certain liver tests during treatment with TRIUMEQ. Your healthcare provider may do tests to check your liver function before and during treatment with TRIUMEQ.
- When you start taking HIV-1 medicines, your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.
- Changes in body fat can happen in people who take HIV-1 medicines.
- Some HIV-1 medicines, including TRIUMEQ, may increase your risk of heart attack.

The most common side effects of TRIUMEQ include: trouble sleeping, headache, and tiredness.

These are not all the possible side effects of TRIUMEQ. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Important Safety Information continued on next page.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Please see brief summary of Prescribing Information for TRIUMEQ on the following pages.



If you don't have prescription coverage and can't afford your medicines, visit GSKforYou.com or call the ViiV Healthcare Response Center 1-877-844-8872



“I have the
Courage
to start **HIV**
treatment.
It’s Time.”



Not an actual patient. Testimonial is based on a collection of real patient experiences.

What should I tell my healthcare provider before taking TRIUMEQ?

- **Before you take TRIUMEQ, tell your healthcare provider if you:**
 - have been tested and know whether or not you have a gene variation called HLA-B*5701.
 - have or had liver problems, including hepatitis B or C infection; have kidney problems; have heart problems, smoke, or have diseases that increase your risk of heart disease such as high blood pressure, high cholesterol, or diabetes; drink alcoholic beverages; or have any other medical condition.
 - are pregnant or plan to become pregnant. It is not known if TRIUMEQ will harm your unborn baby.
 - are breastfeeding or plan to breastfeed. Do not breastfeed if you take TRIUMEQ.
- **You should not take TRIUMEQ if you also take:**
 - abacavir (EPZICOM, TRIZIVIR, or ZIAGEN)
 - lamivudine (COMBIVIR®, EPIVIR, EPIVIR-HBV®, EPZICOM, or TRIZIVIR)
 - emtricitabine (EMTRIVA®, ATRIPLA®, COMPLERA®, STRIBILD®, TRUVADA®)
- **Tell your healthcare provider about all the medicines you take**, including prescription and nonprescription medicines (for example, antacids; laxatives; vitamins such as iron or calcium supplements; anti-seizure medicines; other medicines to treat HIV-1, hepatitis, or tuberculosis; metformin; and methadone) and herbal supplements (for example, St. John’s wort). TRIUMEQ may affect the way they work, and they may affect how TRIUMEQ works.

 **Triumeq**[®]
abacavir 600 mg/dolutegravir 50 mg/
lamivudine 300 mg tablets

It’s Time.

BRIEF SUMMARY

TRIUMEQ® (TRI-u-meck)

(abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg) tablets

Read this Medication Guide before you start taking TRIUMEQ and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. Be sure to carry your TRIUMEQ Warning Card with you at all times.

What is the most important information I should know about TRIUMEQ?

• **Serious allergic reaction (hypersensitivity reaction).** TRIUMEQ contains abacavir (also contained in EPZICOM®, TRIZIVIR®, and ZIAGEN®). Patients taking TRIUMEQ may have a serious allergic reaction (hypersensitivity reaction) that can cause death. Your risk of this allergic reaction to abacavir is much higher if you have a gene variation called HLA-B*5701. Your healthcare provider can determine with a blood test if you have this gene variation.

If you get a symptom from 2 or more of the following groups while taking TRIUMEQ, call your healthcare provider right away to find out if you should stop taking TRIUMEQ.

	Symptom(s)
Group 1	Fever
Group 2	Rash
Group 3	Nausea, vomiting, diarrhea, abdominal (stomach area) pain
Group 4	Generally ill feeling, extreme tiredness, or achiness
Group 5	Shortness of breath, cough, sore throat

A list of these symptoms is on the Warning Card your pharmacist gives you. **Carry this Warning Card with you at all times.**

If you stop TRIUMEQ because of an allergic reaction, never take TRIUMEQ or any other medicines that contain abacavir or dolutegravir (EPZICOM, ZIAGEN, TRIZIVIR, or TIVICAY®) again. If you take TRIUMEQ or any other abacavir-containing medicine again after you have had an allergic reaction, **within hours** you may get **life-threatening symptoms** that may include **very low blood pressure** or **death**. If you stop TRIUMEQ for any other reason, even for a few days, and you are not allergic to TRIUMEQ, talk with your healthcare provider before taking it again. Taking TRIUMEQ again can cause a serious allergic or life-threatening reaction, even if you never had an allergic reaction to it before.

If your healthcare provider tells you that you can take TRIUMEQ again, start taking it when you are around medical help or people who can call a healthcare provider if you need one.

• **Build-up of acid in your blood (lactic acidosis).** Lactic acidosis can happen in some people who take TRIUMEQ. Lactic acidosis is a serious medical emergency that can lead to death.

Lactic acidosis can be hard to identify early, because the symptoms could seem like symptoms of other health problems.

Call your healthcare provider right away if you get the following symptoms that could be signs of lactic acidosis:

- feel very weak or tired
- have unusual (not normal) muscle pain
- have trouble breathing
- have stomach pain with nausea and vomiting
- feel cold, especially in your arms and legs
- feel dizzy or light-headed
- have a fast or irregular heartbeat

• **Severe liver problems.** Severe liver problems can happen in people who take TRIUMEQ. In some cases these severe liver problems can lead to death. Your liver may become large (hepatomegaly) and you may develop fat in your liver (steatosis).

Call your healthcare provider right away if you get any of the following signs or symptoms of liver problems:

- your skin or the white part of your eyes turns yellow
- dark “tea-colored” urine
- light colored stools (bowel movements)
- nausea
- itching
- stomach-area pain

You may be more likely to get lactic acidosis or serious liver problems if you are female, very overweight, or have been taking nucleoside analogue medicines for a long time.

• **Worsening of hepatitis B virus in people who have HIV-1 infection.**

If you have HIV-1 and hepatitis B virus infections, your hepatitis virus infection may get worse if you stop taking TRIUMEQ. To help avoid this: Take TRIUMEQ exactly as prescribed.

- Do not run out of TRIUMEQ.
- Do not stop TRIUMEQ without talking to your healthcare provider.
- Your healthcare provider should monitor your health and do regular blood tests to check your liver for at least several months if you stop taking TRIUMEQ.

• **Resistant Hepatitis B Virus (HBV).** If you have HIV-1 and hepatitis B, the hepatitis B virus can change (mutate) during your treatment with TRIUMEQ and become harder to treat (resistant).

• **Use with interferon and ribavirin-based regimens.** Worsening of liver disease has happened in people infected with HIV-1 and hepatitis C virus who are taking anti-HIV medicines and are also being treated for hepatitis C with interferon with or without ribavirin. If you are taking TRIUMEQ and interferon with or without ribavirin, tell your healthcare provider if you have any new symptoms.

What is TRIUMEQ?

TRIUMEQ is a prescription medicine used to treat HIV-1 (Human Immunodeficiency Virus-type 1) infection. TRIUMEQ contains 3 prescription medicines: abacavir (ZIAGEN), dolutegravir (TIVICAY), and lamivudine (EPIVIR®).

- TRIUMEQ is not for use by itself in people who have or have had resistance to abacavir, dolutegravir, or lamivudine.

It is not known if TRIUMEQ is safe and effective in children.

TRIUMEQ may help:

- reduce the amount of HIV-1 in your blood. This is called “viral load”.
- increase the number of white blood cells called CD4+ (T) cells in your blood, which help fight off other infections.

Reducing the amount of HIV-1 and increasing the CD4+ (T) cells in your blood may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak (opportunistic infections).

TRIUMEQ does not cure HIV-1 infection or AIDS. You must stay on continuous HIV-1 therapy to control HIV-1 infection and decrease HIV-related illnesses.

Avoid doing things that can spread HIV-1 infection to others.

- Do not share or re-use needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

Ask your healthcare provider if you have any questions about how to prevent passing HIV to other people.

(continued on the next page)

BRIEF SUMMARY (cont'd)

TRIUMEQ® (abacavir, dolutegravir, and lamivudine) tablets

Who should not take TRIUIMEQ?

Do not take TRIUIMEQ if you:

- have a certain type of gene variation called the HLA-B*5701 allele. Your healthcare provider will test you for this before prescribing treatment with TRIUIMEQ.
- have ever had an allergic reaction to abacavir, dolutegravir, or lamivudine
- take dofetilide (TIKOSYN®). Taking TRIUIMEQ and dofetilide (TIKOSYN) can cause side effects that may be life-threatening.
- have certain liver problems

What should I tell my healthcare provider before taking TRIUIMEQ?

Before you take TRIUIMEQ, tell your healthcare provider if you:

- have been tested and know whether or not you have a particular gene variation called HLA-B*5701
- have or had liver problems, including hepatitis B or C virus infection
- have kidney problems
- have heart problems, smoke, or have diseases that increase your risk of heart disease such as high blood pressure, high cholesterol, or diabetes
- drink alcoholic beverages
- have any other medical condition
- are pregnant or plan to become pregnant. It is not known if TRIUIMEQ will harm your unborn baby. Tell your healthcare provider if you become pregnant while taking TRIUIMEQ.

Pregnancy Registry. There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of the registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.

- **are breastfeeding or plan to breastfeed. Do not breastfeed if you take TRIUIMEQ.** You should not breastfeed because of the risk of passing HIV-1 to your baby. It is not known if abacavir or dolutegravir passes into your breast milk. Lamivudine can pass into your breast milk and may harm your baby. Talk to your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TRIUIMEQ may affect the way other medicines work, and other medicines may affect how TRIUIMEQ works.

You should not take TRIUIMEQ if you also take:

- abacavir (EPZICOM, TRIZIVIR, or ZIAGEN)
- lamivudine (COMBIVIR®, EPIVIR, EPIVIR-HBV®, EPZICOM, or TRIZIVIR)
- emtricitabine (EMTRIVA®, ATRIPLA®, COMPLERA®, STRIBILD®, TRUVADA®)

Tell your healthcare provider if you take:

- antacids, laxatives, or other medicines that contain aluminum, magnesium, sucralfate (CARAFATE®), or buffered medicines. TRIUIMEQ should be taken at least 2 hours before or 6 hours after you take these medicines.
- anti-seizure medicines:
 - oxcarbazepine (TRILEPTAL®)
 - phenytoin (DILANTIN®, DILANTIN®-125, PHENYTEK®)
 - phenobarbital
 - carbamazepine (CARBATROL®, EQUETRO®, TEGRETOL®, TEGRETOL®-XR, TERIL®, EPITOL®)
- any other medicine to treat HIV-1
- iron or calcium supplements taken by mouth. Supplements containing calcium or iron may be taken at the same time with TRIUIMEQ if taken with food. Otherwise, TRIUIMEQ should be taken at least 2 hours before or 6 hours after you take these medicines.

- medicines used to treat hepatitis virus infections, such as interferon or ribavirin
- a medicine that contains metformin
- methadone
- rifampin (RIFATER®, RIFAMATE®, RIMACTANE®, RIFADIN®)
- St. John's wort (*Hypericum perforatum*)

Know the medicines you take. Keep a list of your medicines with you to show to your healthcare provider and pharmacist when you get a new medicine. Ask your healthcare provider or pharmacist if you are not sure if you take one of the medicines listed above.

How should I take TRIUIMEQ?

- **Take TRIUIMEQ exactly as your healthcare provider tells you.**
- Do not change your dose or stop taking TRIUIMEQ without talking with your healthcare provider.
- Stay under the care of a healthcare provider while taking TRIUIMEQ.
- You can take TRIUIMEQ with or without food.
- If you miss a dose of TRIUIMEQ, take it as soon as you remember. If it is within 4 hours of your next dose, skip the missed dose and take the next dose at your regular time. Do not take 2 doses at the same time. If you are not sure about your dosing, call your healthcare provider.
- Do not run out of TRIUIMEQ. The virus in your blood may become resistant to other HIV-1 medicines if TRIUIMEQ is stopped for even a short time. When your supply starts to run low, get more from your healthcare provider or pharmacy.
- If you take too much TRIUIMEQ, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of TRIUIMEQ?

TRIUIMEQ can cause serious side effects including:

- **See “What is the most important information I should know about TRIUIMEQ?”**
- **Changes in liver tests.** People with a history of hepatitis B or C virus may have an increased risk of developing new or worsening changes in certain liver tests during treatment with TRIUIMEQ. Your healthcare provider may do tests to check your liver function before and during treatment with TRIUIMEQ.
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.
- **Changes in body fat (fat redistribution)** can happen in people who take HIV-1 medicines. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these problems are not known.
- **Heart attack (myocardial infarction).** Some HIV medicines including TRIUIMEQ may increase your risk of heart attack.

The most common side effects of TRIUIMEQ include:

- trouble sleeping
- headache
- tiredness

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of TRIUIMEQ. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

(continued on the next page)

BRIEF SUMMARY (cont'd)

TRIUMEQ® (abacavir, dolutegravir, and lamivudine) tablets

How should I store TRIUMEQ?

- Store TRIUMEQ at room temperature between 68°F to 77°F (20°C to 25°C).
- Store TRIUMEQ in the original bottle.
- Keep the bottle of TRIUMEQ tightly closed and protect from moisture.
- The bottle of TRIUMEQ contains a desiccant packet to help keep your medicine dry (protect it from moisture). Keep the desiccant packet in the bottle. Do not remove the desiccant packet.

Keep TRIUMEQ and all medicines out of the reach of children.

General information about the safe and effective use of TRIUMEQ

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TRIUMEQ for a condition for which it was not prescribed. Do not give TRIUMEQ to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about TRIUMEQ. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about TRIUMEQ that is written for health professionals.

For more information go to www.TRIUMEQ.com or call 1-877-844-8872.

What are the ingredients in TRIUMEQ?

Active ingredients: abacavir, dolutegravir, and lamivudine

Inactive ingredients: D-mannitol, magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate. The tablet film-coating contains iron oxide black, iron oxide red, macrogol/PEG, polyvinyl alcohol-part hydrolyzed, talc, and titanium oxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:



ViiV Healthcare
Research Triangle Park, NC 27709

by:



GlaxoSmithKline
Research Triangle Park, NC 27709

Lamivudine is manufactured under agreement from

Shire Pharmaceuticals Group plc

Basingstoke, UK

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Issued: August 2014

TRM:1MG

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TO END
DISPARITIES!



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POSITIVELY AWARE

MAY+JUNE 2015 | VOLUME 27 NUMBER 3



EMERALD CITY
SEATTLE WAS THE CENTER OF HIV NEWS AS RESEARCHERS GATHERED FOR THE ANNUAL CROI MEETING.

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RETHINKING HIV
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AND ADAM ANDREW.

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TELL IT TO ENID

Damon L. Jacobs on the psychology of PrEP.



JOURNALISM. INTEGRITY. HOPE.

JEFF BERRY

EDITOR-IN-CHIEF

@PAeditor

“Rethinking HIV’ is about how HIV research and treatment is evolving, and how radical shifts in our perspective are necessary for us to continue to make progress.”

ENID VÁZQUEZ

ASSOCIATE EDITOR

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“More good news on PrEP—spread the word.”

RICK GUASCO

CREATIVE DIRECTOR

@rickguasco

“For many of us living with HIV, the long-term strategy has been to stay alive for the next advance in treatment. It’s pretty heady to think we’re on the brink of the next revolution.”

JASON LANCASTER

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SUBSCRIPTION SERVICES
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SINCE 1989. PUBLISHED BY



SUITE 300

5050 N. BROADWAY ST.

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SAVE THE DATE: JUNE 19, 2015 CHICAGO

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THE REUNION PROJECT

**A one-day summit for long-term survivors of HIV/AIDS
to share their stories and identify strategies for successful
living—today and into the future.**

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THIS PROGRAM IS SUPPORTED BY AN UNRESTRICTED
EDUCATIONAL GRANT FROM BRISTOL-MYERS SQUIBB.

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REINVENTION

HOW DO YOU REINVENT YOURSELF?

MADONNA HAS DONE IT numerous times over the years. Her Re-Invention World Tour in 2004 was the highest grossing U.S. tour that year. IBM, Apple, and National Geographic have all reinvented themselves by adapting to the changing times, and embracing new technology. Stagnation and resistance to change can spell trouble for businesses and brands that get too comfortable with their own success, if they don't take the time to reassess and reevaluate what got them there in the first place.

It can also often stand in the way of our own personal development and growth.

This issue of POSITIVELY AWARE, "Rethinking HIV," is about how HIV research and treatment is evolving, and how radical shifts in our perspective are necessary for us to continue to make progress. Researchers and physicians are building upon the successes of the past while tackling new approaches in how we treat HIV, recognizing the possibilities and challenges that lie ahead not only for treatment, but even perhaps a lifelong remission of HIV without antiretroviral therapy.

It's these kinds of profound new ways of conducting research and business that are shaking up the field of HIV. It was only a few years ago when we were still seeing companies bringing to market "me-too" drugs. Today companies and researchers have become much more focused on only developing drugs that will provide a distinct advantage to patients, or that bring some added benefit on top of what's currently available, because the old model and way of thinking are no longer feasible.

In her article "Rethinking HIV Treatment," Melanie Thompson talks about some of the transformations in treatment that we can expect to see in the next 10–15 years. Dr. Thompson looks at not only the kinds of drugs that we'll see, but also how they are administered and delivered. Long-acting injectables have garnered quite a bit of interest in the last few years, and are gaining momentum as research moves forward. But we'll have to make sure we have working systems in place, to ensure these new technologies actually get to those who need them.

As someone who takes a lot of pills in addition to my HIV meds (such as vitamins, blood pressure medication, etc.), I've often said that an injectable wouldn't make much difference to someone like me. But as I've given it more thought, I'm not so sure. Just as going from twice a day to once a day made a big difference to me in my quality of life, once a week or once a month might actually be quite nice! Of course the shots will have to be given in a provider setting, as they can't be self-administered. New delivery systems will need to be created to help keep down costs (such as office co-pays) and support adherence, which will become even more critical if and when therapy is dosed at less than once daily.

More baby steps are also being taken in the effort to eradicate HIV once and for all, or at least put it into remission. Treatment Action Group's Richard Jefferys gives a fantastic overview of the current data, some of the obstacles ahead, and the exciting work that's ongoing in the field.

Also in this issue, leading PrEP advocate and educator Damon Jacobs challenges us to take another look at the reasons behind why people may choose not to use condoms. Our report back from the 19th Conference on Retroviruses and Opportunistic Infections (CROI) looks at different ways of using PrEP that may be more in line with "real-world" use; an investigational drug in a new class that will be useful for those with multi-drug resistance; and a newer version of an older drug that could have the potential to alter the landscape of HIV treatment.

So what does all this mean for you and me? The good news is, there are those out there who are developing innovative and improved treatment options that will help us live longer, healthier lives. But it's up to us as individuals to continue to work on ourselves, perhaps reinvent our own lives, or change our perspectives and shift our priorities. For me that's meant another change in my regimen due to side effects, but I'm undetectable as of yesterday! I've also gone back into therapy, and rediscovered yoga (which has been amazing). If we don't take care of ourselves, no treatment is going to save us. Sometimes we are our own worst enemy.

Whether you're newly diagnosed or a long-term survivor, positive or negative, a healthcare provider or case-worker, we all definitely have one thing in common. We always have a choice. And when it comes to life with or without HIV, we can choose to stay in our comfort zone, or maybe try to think outside the box. Challenge yourself to look forward, instead of holding back.

Take care of yourself, and each other.

The good news is, there are those out there who are developing innovative and improved treatment options that will help us live longer, healthier lives. But it's up to us as individuals to continue to work on ourselves, perhaps reinventing our own lives.

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Briefly

BY ENID VÁZQUEZ

Viekira Pak for hep C

The FDA in December 2014 approved Viekira Pak for the treatment of hepatitis C virus (HCV), genotype 1, including patients who have cirrhosis. Viekira Pak consists of three new hep C drugs (ombitasvir, paritaprevir, and dasabuvir) along with the older medication ritonavir, used to boost blood levels of the paritaprevir. The treatment can be taken with or without ribavirin, but is not recommended for those whose liver doesn't function properly (decompensated cirrhosis). In studies, 91% of the participants taking it were cured at week 12 (experienced a sustained virologic response, or SVR). The dose is one dasabuvir tablet twice daily plus two tablets once daily that contain the three other meds in them. The most common side effects in research were itching, nausea, trouble sleeping, lack of energy, and feeling tired or weak.

Truvada 2.0 closer to approval

On April 7, Gilead Sciences applied for a New Drug Application from the FDA for a new version of its bestselling Truvada. Instead of using the tenofovir DF (TDF) found in Truvada, the new fixed-dose pill combines tenofovir alafenamide (TAF) with the other medication in Truvada, emtricitabine. The new drug will come in two doses: 200 mg of emtricitabine with either 10 mg TAF or 25 mg TAF. TAF has shown high efficacy at a smaller dose than TDF, and with less bone and renal toxicity. The smaller 10 mg dose is for use with protease inhibitors or regimens containing ritonavir (Norvir, also found in Kaletra) or cobicistat (Tybost, also found in EvoTaz, Prexcobix, and Stribild). Read more about TAF on page 30.

Sovaldi, Harvoni drug interaction found

The hepatitis C medication sofosbuvir appears to have a negative interaction with the heart medication amiodarone (brand name Cordarone). Some patients developed abnormally slow heartbeats and one died of cardiac arrest. Three patients needed to have a pacemaker inserted. The others recovered after discontinuing medication.

According to the FDA, anyone combining these medications should seek immediate medical attention if they experience fainting or near fainting; dizziness or light-headedness; malaise (general ill feeling); weakness; excessive tiredness; shortness of breath; chest pains; or confusion or memory problems.

"The U.S. Food and Drug Administration (FDA) is warning that serious slowing of the heart rate can occur when the antiarrhythmic drug amiodarone [Cordarone] is taken together with either the hepatitis C drug Harvoni (ledipasvir/sofosbuvir) or with Sovaldi (sofosbuvir) taken in combination with another direct-acting antiviral for the treatment of hepatitis C infection [such as Olysio or daclatasvir]," the agency reported in March. "We are adding information about serious slowing of the heart rate, known as symptomatic bradycardia, to the Harvoni and Sovaldi labels."

The FDA also reported that, "Health care professionals should not prescribe either Harvoni or Sovaldi combined with another direct-acting antiviral drug with amiodarone. However, in cases where alternative treatment options are unavailable, we recommend heart monitoring in an inpatient hospital setting for the first 48 hours. Subsequently, monitoring in a doctor's office or self-monitoring of the heart rate should be done every day through at least the first 2 weeks of treatment."

DHHS updates HIV treatment guidelines

On April 8, the Department of Health and Human Services (DHHS) updated its HIV treatment guidelines. Atripla is no longer on the "recommended" list, but considered an "alternative" drug, based on a high rate of central nervous system (CNS) side effects and a possible association with suicidality. Reyataz, with a Norvir booster dose plus Truvada, is also no longer recommended but alternative, based on a higher discontinuation rate due to side effects in one large study comparing it to two other recommended regimens. The Reyataz side effect was not harmful to health, but cosmetic (yellowing of the eyes and skin).

Three other regimens were downgraded from "recommended" to "alternative": Complera; Sustiva plus Epzicom; and boosted Reyataz plus Epzicom. A caveat remains—that they be used only in people with less than 100,000 viral load and more than 200 T-cells.

For patients who cannot take either abacavir (Ziagen, found in Epzicom) or tenofovir DF (Viread, found in Truvada, Atripla, Stribild, and Complera), there are now two regimens listed as "other": Kaletra plus Epivir and Prezista boosted by Norvir or Tybost (Prezista/Tybost is also available in the fixed-dose tablet Prezcobix) plus Isentress.

"How effective are condoms for gay men?" Read the informative report on a recently published CDC study at thebodypro.com. While condoms used consistently during anal sex can reduce the risk of HIV by 70%, "Notably, the study observed low rates of consistent condom use. Only 16% of participants reported 'always' using condoms during anal sex with male partners (of any HIV status) throughout the entire study period, despite having received sustained behavioral interventions." Go to thebodypro.com/content/75349/cdc-analysis-puts-numbers-on-condom-effectiveness-.html?ic=700100.



Five regimens remain recommended for people taking HIV meds for the first time: the protease inhibitor drug Prezista boosted by Norvir plus Truvada and four integrase inhibitors (INIs)-based regimens—Stribild, Triumeq, Isentress/Truvada, and Tivicay/Epzicom.

There is also new information and clinician guidance on such topics as HIV-2, drug interactions, treatment of people with hepatitis C virus, persistently low T-cells, and initial therapy in various clinical scenarios. Go to aidsinfo.nih.gov.

Updated kidney disease guidelines in HIV

The 2005 version of “Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected with HIV” has been updated. “These guidelines recommend ART for all HIV-infected patients with kidney disease—a group that is frequently undertreated because of uncertainties regarding appropriate drug selection and dosing,” according to Meghan E. Sise, MD, MS, and Rajesh T. Gandhi, MD, writing for the *NEJM Journal Watch/Infectious Diseases*. The HIV Medicine Association (HIVMA) and Infectious Diseases Society of America (IDSA) produce the guidance.

HIV-positive people needed for ANCHOR anal cancer study

Anal cancer is more prevalent in HIV-positive people whether gay or straight, male or female, with or without having anal sex. Yet doctors still don’t know the best way to screen, prevent, or treat problems that can progress to cancer. An important new study is set to help change that.

“No one knew that cervical cancer was preventable before the use of Pap smears became widespread in the 1960s and cut the incidence of disease by 80%,” said Joel Palefsky, MD, principal investigator of the ANCHOR study.

According to the study’s website, “Anal cancer rates are rising among people living with HIV. The goal of the ANCHOR study is to find the best way to prevent anal cancer among HIV-positive men and women. During

Update on HCV sexual transmission

New data on the sexual transmission of the hepatitis C virus (HCV) have emerged since our article on the topic (“Can hepatitis C be sexually transmitted?” in the November+December 2014 issue). In the March 1st issue of the *Journal of Infectious Diseases* (JID), researchers reported finding HCV in the semen of gay males and other men who have sex with men (MSM) whether they were HIV-positive or -negative, or had acute (recent) or chronic HCV. They reported that this could affect sexual transmission of HCV, “but other factors, including high-risk behaviors, may be the main drivers for HCV transmission in HIV-infected individuals.” In the February 18 online edition of *Clinical Infectious Diseases*, Kaiser Permanente reported on two PrEP patients who remained HIV-negative, but had acquired HCV. Neither of the two men reported any injection drug use, tattoos or occupational exposures to blood while taking PrEP, but both were diagnosed and treated with multiple rectal STIs and condomless receptive anal sex with partners whose HCV status they did not know. This is a small sample—two out of 485 PrEP patients—but still significant enough to monitor. And at this year’s CROI (see page 28), there was a poster presentation from MOSAIC, the largest case-control study focusing on transmission of HCV in HIV-positive MSM. Risk factors associated with HCV transmission in HIV-positive MSM included receptive anal sex without a condom, ulcerative STIs, unprotected (no gloves) fisting, and shared sex toys. Additional non-sexual factors include sharing of straws for snorting drugs and having a lower CD4 cell count. In contrast to past results, there was no relationship with the number of sex partners, group sex participation, or rectal bleeding. These are still worth considering as potential risk factors going forward. Additionally the authors called for further research on the role of CD4 count as a potential driver for HCV infection. These results further support the recommendation that sexually active MSM and those who do not use injection drugs should be routinely screened for HCV as a component of their sexual health and wellness. —ANDREW REYNOLDS, PROJECT INFORM

a screening visit, you will be screened for precancerous anal lesions. If lesions are found, you will be enrolled and randomized to either have the lesions treated or monitored every six months. Both groups will be followed for a minimum of five years. You will be compensated \$100 for the screening visit.”

Screening consists of an anal Pap smear, a swipe with a medical cotton swab. Despite the growing risk of anal cancer, the procedure is not yet widely practiced in medical care.

For more details, go to anchorstudy.org. There are 12 sites throughout the country, including Chicago, at the Anal Dysplasia Clinic Midwest, headed by Gary Bucher, MD, a longtime specialist in the disease.

Chicago PrEP clinic opens

The Core Center (2020 W. Harrison St., in the Medical District) has opened a PrEP clinic for the prevention of HIV in anyone

at risk of infection, age 18 and up. People can be seen whether or not they have insurance, and the clinic will help patients obtain benefits such as co-pay assistance or free medicine. Research opportunities are also available (free medicine and care). Clinic hours are currently being held on the first and third Friday afternoon of the month; appointments must be made. Call (312) 572-4500. Walk-ins, however, can be seen for screening and preliminary labs Mondays through Thursdays; ask for a Health Educator. Adolescents younger than 18 will be referred to a different clinic nearby. Read more about PrEP on page 28.

HIV-related heart attack risk reversible

Kaiser Permanente has found a decline in heart attacks in its HIV-positive patients. “Our findings lend support to the concept

Briefly

that increased heart attack risk for HIV patients is largely reversible with continued emphasis on primary prevention in combination with early initiation of anti-retroviral therapy to preserve immune function," said lead study author Daniel B. Klein, MD, in a press release. Read the press release at prnewswire.com/news-releases/dramatic-decline-in-risk-for-heart-attacks-among-hiv-positive-members-of-kaiser-permanente-in-california-300021887.html.

Annual long-term survivors day

The second annual National HIV/AIDS Long-Term Survivors Awareness Day (NHATSAD) is Friday, June 5th. The organization Let's Kick ASS (AIDS Survival Syndrome) created the awareness day last year to recognize and honor those living longest with HIV. According to a press release, this year's

event "spotlights the present-day intricacies of survival while aging with HIV. It also stresses the importance of keeping those older adults without HIV from acquiring it.

"This year's theme is 'Every Survivor Counts,' because many long-term survivors feel forgotten and invisible," the release continued. To learn more, go to LetsKickASS.org and NHATSAD.org.

Illinois ADAP drugs list sees significant expansion

The Illinois ADAP (AIDS Drugs Assistance Program) list of drugs issued on February 3rd shows an astounding growth in coverage. The formulary not only includes a new HIV medication approved by the FDA in January, Prezcoibix, but for the first time also includes psychotropic medications, such as the anti-depressants Cymbalta, Paxil, and Wellbutrin,

along with other drugs not specifically for HIV but frequently used by people living with the virus, including testosterone.

NASTAD leadership changes

Julie Scofield, executive director of the National Alliance of State and Territorial AIDS Directors (NASTAD), has stepped down after 22 years. In a blog Scofield noted that, "The decision to step down feels right for the organization at this time and for me. ...The good news is that I am passing the baton to an extraordinary leader who is eager to lead the organization into the future and the challenges we all know are ahead." Deputy executive director Murray Penner, an expert in the treatment of both HIV and hepatitis C who joined NASTAD in 2001, stepped up into the executive director's job in April.

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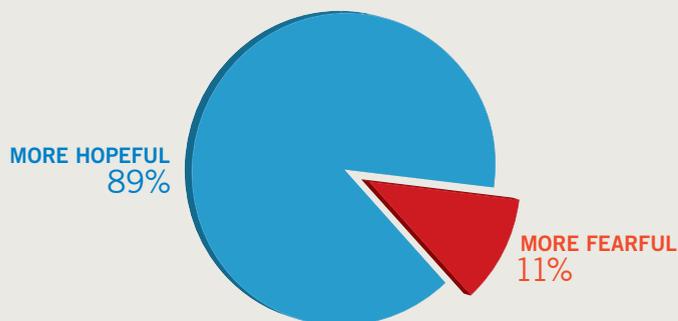
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READERS POLL

IN THE MARCH+APRIL ISSUE WE ASKED

Does news of HIV medical developments make you feel more fearful or more hopeful?



THIS ISSUE'S QUESTION

How often do you use condoms?

VOTE AT POSITIVELYAWARE.COM.

LONG-TERM SURVIVAL

I just finished reading the January+February issue. Thank you [Jeff Berry] for educating me. Thank you for reducing stigma. Thank you for saying uncomfortable things and asking uncomfortable questions. Thank you for your advocacy.

—KRISTIN FREEMAN,
HEALTH EDUCATOR
PLANNED PARENTHOOD
DAYTON, OH

I am also a longtime survivor and I am still kicking ass (January+February 2015, Let's Kick ASS). I tested positive in 1990 when I was 22. Three weeks after donating blood, the Palm Beach County Blood Bank called me to come and see them. Driving up there my thoughts were: Why do these people want to see me? What is wrong with my blood? My first stage was shock. I could not believe I was being handed a death sentence (back then). I was so young. I did not know what to say to my family and friends. I began a suicide mission. My second stage was denial. I went to many places to get tested again, just hoping one test would come back negative. That never happened. I became angry. It took me a long time, many years, to come to acceptance. I'm able to tell people, to talk about HIV, to not feel ashamed anymore, and to take in as much knowledge as I could about this

virus. I go to support groups and face my fears, I forgive and stop asking why. Today I am 47 years old. My last CD4 count was 1,034 and viral load was undetectable. I am a survivor, a strong, healthy person living with HIV. The why was to tell my story.

—LEA FIORINI
DELRAY BEACH, FL

DRUG GUIDE INTERACTION

I just got through reading the March+April issue. Your drug guide is always improving. Kudos!

—EDUARDO PEREZ
VIA THE INTERNET

I'm 45 years old and I was diagnosed in January of 1994. I was prescribed AZT because it was the only medication available. After taking it for two or three months, I tossed the bottle of AZT into the trash and refused to go back to my doctor. In 2003 I came down with pneumonia and my T-cells dropped to 168 and I was officially diagnosed with AIDS. A doctor



started me on Combivir and Sustiva. Since I started on medications, I've remained undetectable and my CD4 count has remained within normal ranges. With protease, integrase, and entry inhibitors still available to me for future use, my answer to the March+April poll question is I definitely feel more hopeful! The only issue about HIV/AIDS that still saddens me is the secrecy of HIV status disclosure.

—SHAWN A. SIMMONS
ORIGINALLY FROM KANSAS CITY, MO

HEP C IN PRISON

As a subscriber to POSITIVELY AWARE, and an individual who is co-infected with HIV and hepatitis C, I read with great interest Andrew Reynolds' article (HIV/HCV Co-Infection News from the 2014 Liver Meeting, January+February 2015). I am a 49-year-old male who is confined in an Illinois Department of Corrections facility. I was diagnosed with HIV in 1992, came into the system in 1995, and diagnosed with HCV 15 years ago. The treatment I have been receiving for HIV has been quite adequate; I have an undetectable viral load and between 700 and 900 T-cells. This has been my average for several years and I have no complaints with the treatment. In 2009, I was treated for the hep C with interferon. I was advised that this drug has a 30% chance of success, but after 40 weeks it was determined that it had failed. Since then, a new class of drugs have been released (Sovaldi and Harvoni), and they apparently have a 90% success rate. I discussed the possibility of being prescribed either

of these medications and was informed that I was a good candidate, but that due to their expense, it was unlikely that I would be approved for either. I find it difficult to understand how I can be denied the opportunity to possibly secure a cure for my hepatitis C, simply because I am incarcerated.

—NAME WITHHELD
GALESBURG, IL

LET'S CONNECT

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NEW APPROACHES TO TREATMENT

THE BIGGEST CHANGES IN 20 YEARS ARE COMING

BY MELANIE THOMPSON, MD



THE DECADE OF THE 2020s will see the biggest change in HIV treatment paradigms since the birth of HAART two decades ago. Newer regimens will emphasize tolerability and adherence, without sacrificing potency, and long-acting injectables will debut. Yet while we contemplate the exciting new drugs that may emerge, there must be equal emphasis on how we deliver care. Even the most stunning advances in treatment will disappoint if we do not solve the harder challenges around care linkage, continuous care engagement, and uninterrupted access to ART for both prevention and therapy.

ANTIRETROVIRAL THERAPY

Since March 1987, FDA has approved over 40 drugs for the treatment of HIV, including

a few extended release formulations. Yet our armamentarium is less robust than the numbers suggest, as three are no longer marketed, and 11 are no longer recommended

by guidelines from the Department of Health and Human Services (DHHS). Others have simply stepped aside as alternatives to more potent, forgiving, and tolerable therapies. As cross-resistance rapidly eliminates entire classes and limits treatment options, we still find ourselves at the end of the line all too quickly. Today's pipeline however is robust, and licensure for its drugs will take us well into the Roaring '20s.

An entire group of drugs likely to win FDA approval* over the next two to three years is the tenofovir alafenamide (TAF) family of fixed-dose compounds:

- **elvitegravir/cobicistat/FTC/TAF** (expected November 2015),
- **FTC/TAF** (expected 2016),
- **rilpivirine/FTC/TAF** (expected 2017), and
- **darunavir/cobicistat/FTC/TAF** (2016–17).

These will cannibalize Stribild, Truvada,

* APPROVAL DATES ARE BASED ON EDUCATED GUESSES ABOUT WHEN STUDIES ARE PROJECTED TO END, OR ON ASSUMPTIONS THAT COULD CHANGE.

Complera, and Atripla, and provide the first single-tablet regimen (STR) containing a boosted protease inhibitor (PI). The tenofovir prodrug TAF concentrates in cells rather than plasma, causing less renal and bone toxicity compared to tenofovir DF (TDF; Viread), and may have an advantage in potency and resistance. The decrease in total and LDL cholesterol associated with TDF (Randell, 2010), however, appears to be lost with TAF.

Following TAF, NRTIs will be expected to have high potency, exceptionally low toxicity, daily or less frequent dosing potential, and high resistance barriers in order to play. Only time will tell whether EFda, one of the few current NRTI candidates, will live up to its promise of potency and resistance advantage in the hands of Merck. If so, FDA approval might occur in the mid-20s.

The current NNRTI pipeline is thin, but Merck's doravirine (MK-1439) is in Phase 3, having exhibited potency and low central nervous system (CNS) toxicity (Gatell, 2014) and could reach pharmacy shelves in 2017–18. On a similar course is fixed-dose doravirine/TDF/3TC, a compound that could potentially take advantage of generic 3TC (available now) and generic TDF (expected 2018).

Protease inhibitor development has slowed as companies have focused instead on incorporating cobicistat into FDCs, or fixed-dose combinations (EvoTaz, Prezcofix). TaiMed, though, is chasing the holy grail of a potent unboosted PI with TMB-607 (formerly from Ambrilla). This nanoformulation is active in the lab against PI resistance mutations and aims for monthly or quarterly dosing. This is the kind of innovation that will be required of future PIs. We may indeed see the boosted PIs find a new niche as tertiary therapy in the '20s.

Integrase inhibitors (INIs) have stolen the spotlight lately, largely due to the high potency and tolerability and favorable resistance profile of dolutegravir, the first INI for daily dosing without a booster. Reformulated once-daily raltegravir is in trials and, if successful, headed toward possible approval in 2016. Of newer INIs in development, the most advanced is once-daily GS-9883, which also doesn't require boosting. Now in Phase 2, successful trials could lead toward FDA approval by the end of the decade.

Earlier in development are the LEDGINS whose mechanism of action differs from the currently licensed strand transfer inhibitors, opening the possibility of combination INI strategies in the mid '20s.

LONG-ACTING MEDS

The promise of long-acting nanoformulation injectables for both treatment and prevention is the most riveting story to emerge in decades. Dolutegravir's longer acting cousin, cabotegravir (GSK12657744, or 744, CAB), and long-acting rilpivirine are being studied together as monthly maintenance injections for treatment (and cabotegravir as a quarterly injection for PrEP). Meanwhile, an oral dolutegravir/rilpivirine co-formulation is planned for use as two-drug maintenance (as a switch for those who have achieved viral suppression on an initial three-drug regimen and have no history of viral resistance), based on LATTE results (Margolis, 2015). Oral cabotegravir will be developed as well, but used only as part of an initial regimen in persons who are transitioning to maintenance with injectable CAB/RPV.

If the nanos are safe and effective for maintenance, FDA approval could come by the turn of the decade. But success is not a slam-dunk. There are potential pitfalls to long-acting injectables such as the risk of incremental toxicity that cannot be halted by stopping drug, and resistance due to a long "pharmacologic tail" that could expose the virus to lengthy intervals of suboptimal dosing if repeated injections are not delivered on time. Barriers to safety monitoring and drug delivery must be identified and addressed, including exploration of new distribution systems such as designated pharmacy partners and home health options. Clearly, the 744/rilpivirine adventure is being closely watched by biopharmas itching to embrace nanotechnology and explore the acceptability of non-oral therapies.

Fusion inhibitors could get new life if albuvirtide, a better-looking cousin of enfuvirtide (T-20), can capitalize on its 11-day half-life, potentially allowing weekly dosing by injection. PRO-140, a monoclonal CCR5 antagonist (administered weekly or biweekly), and the monthly anti-CD4 monoclonal antibody TMB-360 (second generation ibalizumab) are moving (slowly) in clinical trials. The anti-HIV neutralizing antibody 3BNC117 showed promise in an early human trial. This new direction toward injectables could make the '20s very interesting indeed.

Bristol-Myers Squibb (BMS) is attacking two new targets that could also change the treatment paradigm. An attachment inhibitor (AI), fostemsavir (BMS-663068), is in Phase 3, but only for highly treatment-experienced

patients, as twice-daily dosing complicates use in initial therapy. Meanwhile, BMS-955176, a maturation inhibitor (MI), disrupts a late stage in viral replication and is entering Phase 2 for both treatment-naïve and experienced patients. If successful, FDA approval for the AI could come in late 2017–early 2018, and for the MI in 2020–21. Other AIs and MIs will surely emerge in the late teens and early '20s and could provide options for treatment of multidrug-resistant virus as well as displace the NRTI class as first-line therapy.

Gene therapies, including the Sangamo zinc-finger nuclease approach, continue to make slow progress (Wang, 2015). While therapeutic vaccines have missed the sweet spot to date, newer vector-based gene immunotherapy raises hope of spanning the treatment and prevention realms (Gardner, 2010).

Finally, chronic inflammation contributes to excess non-AIDS morbidity and mortality in spite of viral suppression. Two potential approaches to controlling inflammation are in clinical trials, and this line of research is sure to expand in the next decade. Cenicriviroc blocks CCR2 and affects surrogate markers of inflammation, in addition to its CCR5-mediated antiviral effect. It is now under study for fatty liver (non-alcoholic hepatic steatosis; NASH). The NIH REPRIEVE trial will look at the impact of pitavastatin on cardiac outcomes over five years, with results in the '20s (reprivetrials.org).

WHAT ABOUT GENERICS?

Generic ARVs have had little impact on overall treatment cost, as most drugs have been rendered obsolete prior to becoming generic. This is due to the rapid pace of HIV drug development combined with a 20-year patent life plus additional years of marketing protections (called "exclusivity"). Of the seven generic ARVs, only lamivudine (3TC) and abacavir are still recommended for use by DHHS and IAS-USA guidelines. Eclipsed by INIs, efavirenz and atazanavir are no longer recommended as first-line therapy, but they are due to become generic in 2017–18. By the time TDF becomes generic in 2018, it will be seen as the ugly stepmother of TAF, although it is likely to be incorporated into multiple generic formulations and continued to be used in prevention until TAF is further studied for use in PrEP.

It is through the coupling of generics in

SOME OF OUR BIGGEST CHALLENGES IN THE LATE TEENS AND 2020s
will be those of implementing strategies to help patients stay consistently engaged in care, with continuous access to therapy.

A ROSE BY ANY OTHER NAME

Below are some of the drug abbreviations and acronyms used in this article. Names for the FDA-approved drugs are listed in alphabetical order by the generic name.

abacavir (ABC)	Ziagen; also found in Epzicom and Triumeq
atazanavir (ATV)	Reyataz; also found in EvoTaz
cobicistat (COBI)	Tybost; also found in EvoTaz, Prezcoibix, and Stribild
darunavir (DRV)	Prezista, also found in Prezcoibix
dolutegravir (DTG)	Tivicay; also found in Triumeq
efavirenz (EFV)	Sustiva; also found in Atripla
elvitegravir (EVG)	Vitekta, also found in Stribild
emtricitabine (FTC)	Emtriva
enfuvirtide (T-20)	Fuzeon
lamivudine (3TC)	Epivir, also found in Combivir, Epzicom, and Triumeq
lopinavir (LPV)	Kaletra (lopinavir/ritonavir)
raltegravir (RAL)	Isentress
rilpivirine (RPV)	Edurant; also found in Complera
ritonavir (r)	Norvir (booster dose); also found in Kaletra

DRUG CLASSES

NRTI	nucleoside/nucleotide reverse transcriptase inhibitor
NNRTI	non-nucleoside reverse transcriptase inhibitor
PI	protease inhibitor
INI	integrase inhibitor

FDCs with branded drugs that a cost-benefit could first be realized. Lopinavir/ritonavir/lamivudine is approved in Europe and twice-daily raltegravir/lamivudine could be an incremental advance. ViiV Healthcare has the opportunity to pair generic abacavir/lamivudine with dolutegravir to bring down the high price of Triumeq. One study projects first-year cost savings nearing a billion dollars using a partially generic efavirenz-based regimen (Walensky, 2013).

Concerns about the potential adherence consequences of decoupling FDCs deserve study to ensure that outcomes are preserved while money is saved. The fear that insurance companies could mandate use of obsolete generics has not yet materialized, but this must be closely watched into the next decade as prior authorizations and drug tiering with high cost sharing are other ways to

steer patients toward outdated generics and limit access to the best new drugs. There is likely to be increased attention to cost implications as incremental benefits influence the ranking of preferred therapies by guidelines. Some fear that inequality in standards of care could emerge as a trade-off for treating larger volumes of patients, mirroring the use of obsolete drugs in low-resource countries for the sake of cost. We will need to systematically evaluate treatment outcomes to assure that cost pressure does not compromise health.

IMPROVING THE CARE CONTINUUM

Inventing drugs is just the beginning. It is equally, if not more, challenging to reinvent our healthcare system to increase care access, provide better support for care linkage and retention, and improve services for mental health, substance use, housing assistance, incarceration transition, and other essential needs. The care continuum consistently shows our failings in care retention and viral suppression.

Some of our biggest challenges in the late teens and '20s will be those of implementing strategies to help patients stay consistently engaged in care, with continuous access to therapy. One structural intervention, the Health Information Exchange (HIE), has proven effective in identifying persons who are out of HIV care as they seek non-HIV medical services at clinics and hospitals, and achieving high rates of reengagement in care (Herwehe, 2012). Building HIEs for HIV and other medical purposes should be a national priority over the next decade.

The Affordable Care Act has the potential to greatly improve the care of people with HIV, but early implementation has been hampered by lack of Medicaid expansion, especially in states with the highest HIV rates. Among the insured, drug affordability is compromised by plans that place HIV meds on unaffordable tiers in apparent violation of anti-discrimination provisions of the ACA. High cost sharing puts patients at risk for inconsistent drug access and viral resistance. Additionally, traditional insurance plans generally do not offer adequate coverage for mental health and substance use services, transportation, or case management to assist with housing and other critical social needs of people with HIV.

Ryan White programs have been called upon to supplement the ACA in providing

access to these so-called “wrap-around” services, assistance with care engagement, and support for high out-of-pocket costs. Yet clinics in non-expansion states now are straining to care for newly diagnosed uninsured patients. Over time, without substantially increased funding, waiting lists will emerge both for clinical care and drug access through the AIDS Drug Assistance Program (ADAP). Medicaid expansion and preservation (perhaps re-invention) of Ryan White must be priorities in the coming decade.

Other priorities entail exploring novel options for care delivery, including telemedicine visits, use of non-traditional venues for delivery of injectables and PrEP, and judicious use of non-clinicians (especially pharmacists) to supplement the waning clinical workforce.

Finally, we must push for structural changes to better integrate prevention and care, as biomedical prevention through both treatment and PrEP stretches the boundaries of traditional systems. Federal funding streams across agencies (HRSA, CDC, SAMHSA) must be aggressively reevaluated and harmonized. And while each of the Bad Bugs (HIV, STIs, viral hepatitis, and TB) brings its own science and epidemiology to the table, and deserves to have separate attention and strategies, successful translation of science amid increasing economic constraints require us to eliminate artificial silos of funding that create duplicative infrastructures and waste. Program Coordination and Service Integration (PCSI) has been a CDC buzzword for a decade, yet not enough has been done at the federal level to make it a reality in the field.

The 2020s may be an exuberant time for treatment paradigms, and a roller-coaster time for treatment provision. Ever mindful of the progress we have made, we will be further challenged to extend those successes to the largest number of people possible. Time to get to work—the Roaring '20s are on the way! 🇺🇸

DR. MELANIE THOMPSON is Principal Investigator of the AIDS Research Consortium of Atlanta (ARCA) where she has conducted over 400 studies of HIV, STDs, and viral hepatitis. She is a member of the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents and provided the doctor's comments for the POSITIVELY AWARE 2015 HIV Drug Guide.

CHASING THE CURE

THE STATE OF THE SEARCH IN 2015
BY RICHARD JEFFERYS

OVER THE PAST DECADE, the pursuit of a cure for HIV infection has gained significant momentum. At one time, the word *cure* was used rarely and cautiously, for fear of raising false hopes. The immediate focus after the discovery of HIV in 1983 was on treatments capable of suppressing the virus, which arrived in the form of combination antiretroviral therapy (ART) in the mid-1990s, transforming a fatal viral infection into one that now, for many people, is likely to have little or no impact on life expectancy.

But ART is imperfect, with potential toxicities and regular dosing that can negatively impact quality of life. Scientific advances and the availability of new technologies have conspired to create optimism that another step forward is possible. A major research effort, not just in the U.S. but internationally, is now working toward that goal.

To anyone who reads the news, the high profile of cure research has been evident in relatively frequent headlines—not always accurate, unfortunately—about various aspects of the science and newly presented or published studies.

A great deal of attention has focused on the inspiring case of Timothy Ray Brown, who has lacked any sign of active HIV for eight years now and is the first individual considered cured of the infection. Amidst all the media coverage, it can be difficult to ascertain exactly where the research stands and whether or not a broadly effective cure is on the horizon. This article will attempt to offer a brief guide to the state of the field in the spring of 2015, and some of the challenges that lie ahead.

THE LONE CURED MAN

The **circumstances** that led to a cure in Timothy Brown have been extensively documented. Brown had been living with HIV for many years when the occurrence of a life-threatening cancer—acute myelogenous leukemia (AML)—necessitated not one but two stem cell transplants as part of a complex series of treatments. The purpose of the stem cell transplant procedure is to create



a new immune system in the recipient, generated by stem cells received from a genetically matched donor.

Brown's cancer doctor, Gero Hütter, successfully searched for a donor homozygous for the CCR5-Delta32 mutation, which causes immune cells to lack the CCR5 co-receptor that most HIV variants use to infect cells. When Brown ultimately interrupted ART after receiving the transplants, his viral load did not rebound.

With extraordinary altruism, Brown has volunteered samples from just about every possible tissue and while a few times a trace amount of HIV genetic material has been detected, no sign of virus capable of replicating has emerged. He remains off ART today.

Brown's experience suggests that it is not impossible to cure HIV. But it can't be applied to most HIV-positive people, because stem cell transplantation is extremely risky, and can lead to death in around one fifth of cases. Part of the risk is attributable to the cell-killing drugs that are typically given to wipe out the existing immune system and make room for the transplanted cells. There is also a potentially fatal complication called graft-versus-host disease (GVHD), in which donated cells are recognized as foreign and attacked by the recipient's body.

Researchers are investigating whether it might be possible to repeat the HIV cure achieved in Brown in other HIV-positive individuals who require stem cell transplants to treat life-threatening cancers, but to date there have been no reported successes. Gero Hütter recently wrote a letter to the *New England Journal of Medicine* reviewing the results of all six known cases where HIV-positive individuals received stem cell transplants from donors homozygous for CCR5-Delta32, and sadly the news was not good: all have died either due to the underlying cancer or complications from the procedure. One of the individuals displayed a rebound of viral load due to the presence of an HIV variant capable of using an alternative receptor to CCR5 (named CXCR4), indicating that even if the cancer had been cured, HIV would not have been.

MORE PRACTICAL APPROACHES

A number of alternative approaches are being developed and tested, including gene therapies and a therapeutic vaccine or vaccine-like strategies.

Scientists are also attempting to find

methods for depleting the body of the HIV that persists despite ART, so that there'll be less virus for the immune system to deal with when ART is withdrawn. Or, even better, no intact HIV left at all.

To delve into the depletion approaches first, the population of HIV-infected cells that persists on ART is called the "HIV reservoir." The vast majority are long-lived "resting memory" CD4 T-cells that contain HIV DNA that has integrated into the genome of the cell but not completed the remainder of the viral life cycle. HIV in this form is described as latent, because virus production can begin at a later time—even many, many years later—if the latently infected CD4 T-cell receives signals that cause it to become activated.

The job of memory CD4 T-cells is to coordinate the immune response to a particular pathogen that your body has encountered sometime in the past (for example, if you were vaccinated against measles as a child, you will still have some memory CD4 T-cells specific for the measles virus antigens contained in the vaccine), so they are designed to be able to survive in a resting state and only become active if they see the antigen that triggered their development.

Importantly, most latently infected CD4 T-cells do not show any outward signs of containing HIV because no viral proteins are being made, and this prevents the immune system from recognizing and targeting them for elimination. Estimates suggest that the average number of latently infected memory CD4 T-cells in an individual on ART is around a million, although recently it has been reported that this could be an underestimate and that the true number could be as much as 60-fold higher.

NOT SO FAST

A large amount of evidence points to the potential benefits of limiting or reducing the size of the HIV reservoir. The most widely publicized involves three individuals who, for a brief and tantalizing period, were thought to have possibly joined Timothy Brown as examples of HIV cures. One is the "Mississippi baby," who acquired HIV infection from her mother and was started on aggressive ART extremely early after being born. An interruption in ART occurred at around 18 months of age and very unusually, viral load did not rebound; furthermore no HIV reservoir was detectable.

The infant remained off ART for 27 months and there were hopes that she was cured, but then in mid-2014 HIV viral load became detectable again and ART was restarted.

The two other cases are known as the "Boston patients": these are two HIV-positive men who underwent stem cell transplants to treat cancers. Unlike Timothy Brown, they received stem cells from normal donors lacking the CCR5-Delta32 mutation. But they remained on ART throughout the procedure and it was thought this might prevent HIV from infecting the newly transplanted immune system cells.

After the procedures, an HIV reservoir was not detectable and both ultimately underwent an ART interruption. The virus remained undetectable for three and eight months, respectively, but then viral load returned and ART was restarted.

Although the lack of a cure in these individuals was disappointing, their experience is in line with mathematical modeling indicating that significant reductions in the HIV reservoir can equate to extended periods of "remission" from viral replication. These models predict that diminishing the reservoir even further could lead to a lifelong absence of viral load rebound in a majority of HIV-positive people.

But the magnitude of the task is daunting: it's estimated the amount of latent HIV declined around 3 logs (1,000-fold) in the Boston patients, but that reductions of 5–6 logs (100,000–1 million-fold) would be needed for lifelong remission.

Nevertheless, the correlation between smaller reservoir size and longer time off ART provides a starting point for one route toward a cure.

EARLY ART

The Mississippi baby case highlights the potential for starting ART soon after infection to greatly limit the size of the reservoir, and a trial testing whether similar—or longer—periods of remission can be obtained in other perinatally infected newborns began recently. The closest adult equivalent is individuals identified very soon after HIV acquisition, and rapid initiation of ART in this setting is also associated with very small or even undetectable HIV reservoirs. A number of studies are investigating whether early ART, with or without additional interventions, can lead to remission in adults. Some

encouragement comes from an unusual group of 20 early-treated individuals in France—known as the VISCONTI cohort—in whom a degree of remission may have occurred; they have maintained extremely low or undetectable viral loads for an average of over nine years after an ART interruption, in the presence of very modest but detectable HIV reservoirs.

LATENCY REVERSAL

Efforts to deplete the HIV reservoir currently center on compounds referred to as latency-reversing agents (LRAs). As the name implies, they aim to awaken latent HIV, thus either flagging the infected CD4 T-cell for elimination by the immune system or provoking its destruction by HIV's cell-killing effects. A class of anticancer agents called HDAC inhibitors have emerged as lead LRA candidates, and three—vorinostat, panobinostat, and romidepsin—have demonstrated the capacity to cause HIV production by latently infected CD4 T-cells in clinical trials.

At least six different LRAs are now in human testing, from multiple different classes (HDAC inhibitors, PKC agonists, and toll-like receptor agonists); this represents significant progress given that it was only a few years ago that the first trial of an LRA got underway.

The not so good news is that no decline in the HIV reservoir has yet been observed with any of these agents, meaning additional interventions are likely needed to prompt the killing of infected CD4 T-cells after viral latency is reversed. But the first tentative steps in this direction are occurring: a trial combining romidepsin with a therapeutic HIV vaccine in people on ART is ongoing.

Several other therapeutic HIV vaccine candidates are also being evaluated with a view to being paired with LRAs; the hope is that vaccination will boost or create immune responses capable of delivering the *coup de grace* to latently-infected cells after the LRA has done its work.

Infusions of neutralizing antibodies are being eyed as another means to achieving this end, as the antibodies can potentially bind to infected cells and mark them for destruction via a mechanism called antibody-mediated cellular cytotoxicity (ADCC). An antibody/LRA combination is being tested in macaques infected with SIV (simian immunodeficiency virus, a virus similar to HIV that is found in certain monkeys).

PROGRESS IS CERTAINLY BEING MADE, but most scientists suspect it will likely be decades before a widely applicable curative intervention might come to light.

COPING STRATEGIES

Uncertainty about the degree to which the HIV reservoir can be drained is not so much of an issue for approaches that aim to prepare the body to be able to deal with whatever virus is present when ART is interrupted. Gene therapies that modify vulnerable cells are at the forefront of this aspect of cure research, and several are in clinical trials.

It is early days however, and only hints of progress have been seen.

The most extensively studied is Sangamo's SB728-T, which involves extracting CD4 T-cells from HIV-positive individuals, genetically modifying them so they no longer express the CCR5 receptor, and then reinfusing them in large numbers. In clinical trials, a few isolated examples of prolonged control of viral load after an ART interruption have been reported, suggesting modified CD4 T-cells may be able to coordinate a more effective immune response against HIV.

The challenge is to attain more robust viral load control in greater numbers of people, and ways of modifying greater numbers of CD4 T-cells are being tested. A new trial that will use the technique on stem cells—which could potentially give rise to HIV-resistant CD4 T-cells in the body—has recently been given the green light by the FDA.

A company called Calimmune is also testing a gene therapy that seeks to generate HIV-resistant CD4 T-cells by altering and infusing stem cells (results from this trial are pending).

Over the past two decades, an array of different therapeutic HIV vaccines have been tested with the goal of promoting control of viral load when ART is stopped. But perhaps because CD4 T-cells—HIV's primary target—play such a crucial role in sustaining vaccine-induced immune responses, significant success has proven elusive.

Hence the recent shift in focus to combining therapeutic vaccines with LRAs to reduce the viral reservoir in people on ART, which may be a more modest task than controlling viral replication after ART withdrawal. There is a seemingly uniquely potent therapeutic vaccine candidate derived from a cytomegalovirus (CMV) vector that has shown success in macaques, but it has yet to be tested in humans.

An innovative alternative to vaccination made headlines recently and is worthy of mention: it comprises a highly potent inhibitor of HIV named eCD4-Ig delivered using an adeno-associated virus (AAV) vector. The AAV takes up residence in muscle tissue and acts as a factory for churning out eCD4-Ig, which could theoretically equip a person with a means of lifelong HIV suppression. The idea has shown promise as a preventive in macaques exposed to SIV, and therapeutic studies in this animal model are now planned.

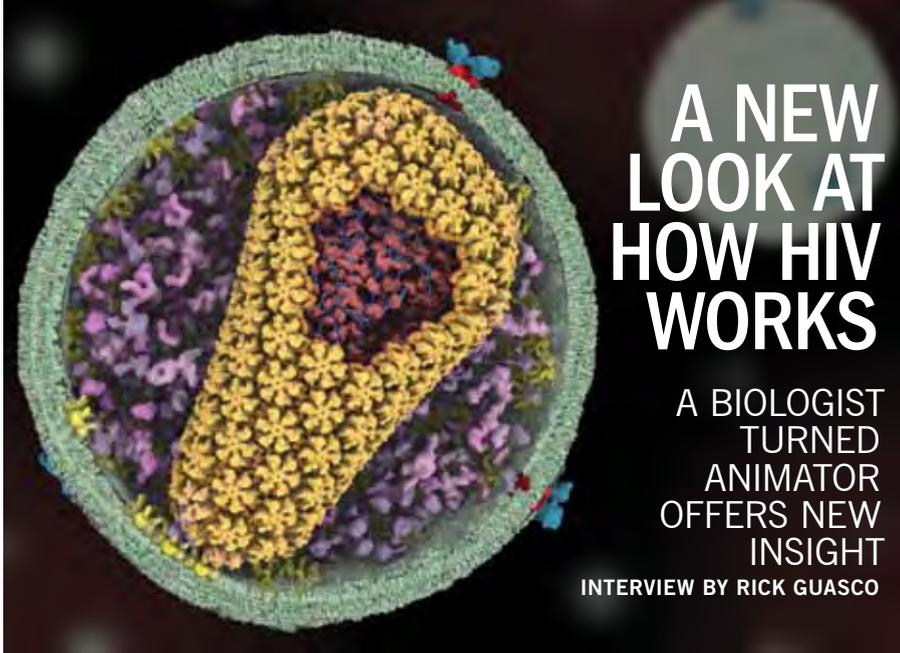
COLLABORATION

There is so much activity in the cure research realm that this brief review has only skimmed the surface, focusing on ideas that are in human trials or may soon get there. Progress is certainly being made, but most scientists suspect it will likely be decades before a widely applicable curative intervention might come to light.

Solving the many challenges on the horizon will require collaboration, and encouragingly many collaborative endeavors are underway or being formed. These include the International AIDS Society's Towards an HIV Cure initiative which is currently updating its global strategy recommendations; amfAR's Research Consortium for HIV Eradication (ARCHE); the National Institutes of Health's Martin Delaney Collaboratories (named after the activist and founder of Project Inform) which are soon to be expanded; the Forum for Collaborative HIV Research's cure project focused on the pathways toward regulatory approval; and a growing number of consortia globally such as CHERUB (Collaborative HIV Eradication of viral Reservoirs: UK BRC) in the United Kingdom.

Advocacy continues to be key in supporting and guiding this work, so that one day HIV can be conquered once and for all. 

Longtime activist **RICHARD JEFFERYS** is the Michael Palm Basic Science, Vaccines & Cure Project Director for the Treatment Action Group (TAG), in New York City. Go to treatmentactiongroup.org for additional cure research resources, including a listing of research studies.



A NEW LOOK AT HOW HIV WORKS

A BIOLOGIST TURNED ANIMATOR OFFERS NEW INSIGHT

INTERVIEW BY RICK GUASCO

Through decades of research, structural biologists have figured out the three-dimensional shapes of nearly all of the viral proteins, as well as many of the proteins in our cells that interact with HIV. Through biochemical and cell biological studies, we're gaining an increasingly clear picture of how the virus enters cells and co-opts the cellular machinery while evading detection by the immune system. I take this data and work with researchers to create a movie that depicts what they think is happening inside of cells. One of the things that makes it 'unprecedented' is that I'm creating animations of events that are too small to be seen by the naked eye. The animation is really a hypothesis—a video of what researchers think the virus is doing, based upon multiple sources of experimental evidence.

What goes into creating your animations?

The animations are created in close collaboration with HIV researchers, and are a direct reflection of their ideas. The length of time for different segments varies quite a bit, but generally, it can take weeks to months to finish even a short segment. A lot of this time is spent building a model, sharing it with the research collaborators, discussing it, and making changes to better reflect their ideas and experimental results. The Science of HIV project is funded by a grant from the National Institutes of Health.

Your animations are cutting edge biology, but the narration is so conversational. Who are your videos for?

ScienceofHIV.org is targeted at the public. One of the things that I think that animations are great at is being able to convey ideas without getting bogged down in jargon and terminology. This is especially important when trying to communicate molecular-level biology, which can be really intimidating to most people.

The process of creating an animation can help researchers, too. Most molecular biologists, including HIV researchers, are trying to understand processes that involve numerous molecules moving over time and space, but lack the ability to visualize these processes. Animation software allows us to do that, and that can help researchers wrap their heads around problems, and give them ideas of where to go next. **PA**

TO WATCH JANET IWASA'S TED TALK AND HER HIV ANIMATIONS, GO TO POSITIVELYAWARE.COM.



JANET IWASA, PHD, is a cellular biologist who has become a computer animator. She believes animation can not only help people visualize how HIV works, but allow researchers to try out their theories and come up with new ideas about how to treat the virus.

"Animations aren't just useful for communicating an idea, they're also really useful for exploring a hypothesis," said Iwasa in her March 2014 presentation at a TED Talk lecture series. "Biologists, for the most part, are still using paper and pencil to visualize the processes they study."

Iwasa attended the University of California-San Francisco, where her mentor encouraged her to pursue her interest in animation. She created videos on the chemical origins of life for her postdoctoral work at Massachusetts General Hospital and the Museum of Science in Boston.

While she's passionate about how animation can change our understanding, Iwasa is especially focused on the fight against HIV. She recently took a moment from a trip to Toronto to discuss her work.

RICK GUASCO: You're a cellular biologist; how did you get into animation?

JANET IWASA: I was trained as a cell biologist, and got into animation during graduate school. I was studying the process by which cells (such as some immune cells) can move, and was interested in trying to create visualizations of what we thought was happening on a molecular scale. These are events that are too small to be seen even using the best light microscopes, so we can't directly see what's happening. But from different sources of data, we know quite a bit about what they might look like. These molecular processes are dynamic and three-dimensional, so I

decided to learn 3D animation so that I could learn to create these visualizations. The software I use is from the entertainment industry; it's the same software used in making animated movies and Hollywood-style visual effects.

Although my path has diverged a bit from the typical research scientist, I still consider myself to be a biologist first, with a very deep interest in scientific communication, education, and visualization.

Is HIV your main area of scientific interest? What made you focus on HIV?

I currently spend about half of my time working on visualizations with HIV researchers. One of the reasons I focused on this topic was that I felt that there is decades of research about how HIV works, but much of it would be difficult for non-scientists to understand. From these studies, however, we know in great detail how HIV is able to infect our bodies at a molecular scale. Using animation, I hope to make this body of research more accessible to the general public. I want people to see how the virus works, and how drugs are able to stop the virus at various stages of its life cycle. And I hope that these 3D animations will give researchers a better visual model of the virus to help push their research forward.

What advances have come about that have allowed you to create what one NIH blog called 'unprecedented views of HIV'?

What is STRIBILD?

STRIBILD is a prescription medicine used to treat HIV-1 in adults who have never taken HIV-1 medicines before. STRIBILD combines 4 medicines into 1 pill to be taken once a day with food. STRIBILD is a complete single-tablet regimen and should not be used with other HIV-1 medicines.

STRIBILD does not cure HIV-1 infection or AIDS. To control HIV-1 infection and decrease HIV-related illnesses you must keep taking STRIBILD. Ask your healthcare provider if you have questions about how to reduce the risk of passing HIV-1 to others. Always practice safer sex and use condoms to lower the chance of sexual contact with body fluids. Never reuse or share needles or other items that have body fluids on them.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about STRIBILD?

STRIBILD can cause serious side effects:

- **Build-up of an acid in your blood (lactic acidosis),** which is a serious medical emergency. Symptoms of lactic acidosis include feeling very weak or tired, unusual (not normal) muscle pain, trouble breathing, stomach pain with nausea or vomiting, feeling cold especially in your arms and legs, feeling dizzy or lightheaded, and/or a fast or irregular heartbeat.
- **Serious liver problems.** The liver may become large (hepatomegaly) and fatty (steatosis). Symptoms of liver problems include your skin or the white part of your eyes turns yellow (jaundice), dark “tea-colored” urine, light-colored bowel movements (stools), loss of appetite for several days or longer, nausea, and/or stomach pain.
- **You may be more likely to get lactic acidosis or serious liver problems** if you are female, very overweight (obese), or have been taking STRIBILD for a long time. In some cases, these serious conditions have led to death. Call your healthcare provider right away if you have any symptoms of these conditions.

- **Worsening of hepatitis B (HBV) infection.** If you also have HBV and stop taking STRIBILD, your hepatitis may suddenly get worse. Do not stop taking STRIBILD without first talking to your healthcare provider, as they will need to monitor your health. STRIBILD is not approved for the treatment of HBV.

Who should not take STRIBILD?

Do not take STRIBILD if you:

- **Take a medicine that contains:** alfuzosin, dihydroergotamine, ergotamine, methylergonovine, cisapride, lovastatin, simvastatin, pimozide, sildenafil when used for lung problems (Revatio®), triazolam, oral midazolam, rifampin or the herb St. John’s wort.
- **For a list of brand names for these medicines,** please see the Brief Summary on the following pages.
- **Take any other medicines to treat HIV-1 infection,** or the medicine adefovir (Hepsera®).

What are the other possible side effects of STRIBILD?

Serious side effects of STRIBILD may also include:

- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do regular blood and urine tests to check your kidneys before and during treatment with STRIBILD. If you develop kidney problems, your healthcare provider may tell you to stop taking STRIBILD.
- **Bone problems,** including bone pain or bones getting soft or thin, which may lead to fractures. Your healthcare provider may do tests to check your bones.
- **Changes in body fat** can happen in people taking HIV-1 medicines.
- **Changes in your immune system.** Your immune system may get stronger and begin to fight infections. Tell your healthcare provider if you have any new symptoms after you start taking STRIBILD.

The most common side effects of STRIBILD include nausea and diarrhea. Tell your healthcare provider if you have any side effects that bother you or don’t go away.

What should I tell my healthcare provider before taking STRIBILD?

- **All your health problems.** Be sure to tell your healthcare provider if you have or had any kidney, bone, or liver problems, including hepatitis virus infection.
- **All the medicines you take,** including prescription and nonprescription medicines, vitamins, and herbal supplements. STRIBILD may affect the way other medicines work, and other medicines may affect how STRIBILD works. Keep a list of all your medicines and show it to your healthcare provider and pharmacist. Do not start any new medicines while taking STRIBILD without first talking with your healthcare provider.
- **If you take hormone-based birth control** (pills, patches, rings, shots, etc).
- **If you take antacids.** Take antacids at least 2 hours before or after you take STRIBILD.
- **If you are pregnant** or plan to become pregnant. It is not known if STRIBILD can harm your unborn baby. Tell your healthcare provider if you become pregnant while taking STRIBILD.
- **If you are breastfeeding** (nursing) or plan to breast-feed. Do not breastfeed. HIV-1 can be passed to the baby in breast milk. Also, some medicines in STRIBILD can pass into breast milk, and it is not known if this can harm the baby.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see Brief Summary of full Prescribing Information with **important warnings** on the following pages.



STRIBILD is a prescription medicine used as a complete single-tablet regimen to treat HIV-1 in adults who have never taken HIV-1 medicines before. STRIBILD does not cure HIV-1 or AIDS.

I started my personal revolution

Talk to your healthcare provider about starting treatment.

STRIBILD is a complete HIV-1 treatment in **1 pill**, once a day.

Ask if it's right for you.

STRIBILD[®] 

elvitegravir 150mg/ cobicistat 150mg/ emtricitabine 200mg/ tenofovir disoproxil fumarate 300mg tablets

 GILEAD

Patient Information

STRIBILD® (STRY-bild) (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg) tablets

Brief summary of full Prescribing Information. For more information, please see the full Prescribing Information, including Patient Information.

What is STRIBILD?

- **STRIBILD is a prescription medicine** used to treat HIV-1 in adults who have never taken HIV-1 medicines before. STRIBILD can also be used to replace current HIV-1 medicines for some adults who have an undetectable viral load (less than 50 copies/mL of virus in their blood), and have been on the same HIV-1 medicines for at least 6 months and have never failed past HIV-1 treatment, and whose healthcare provider determines that they meet certain other requirements.
- **STRIBILD is a complete HIV-1 medicine** and should not be used with any other HIV-1 medicines.
- **STRIBILD does not cure HIV-1 or AIDS.** You must stay on continuous HIV-1 therapy to control HIV-1 infection and decrease HIV-related illnesses.
- **Ask your healthcare provider about how to prevent passing HIV-1 to others.** Do not share or reuse needles, injection equipment, or personal items that can have blood or body fluids on them. Do not have sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

What is the most important information I should know about STRIBILD?

STRIBILD can cause serious side effects, including:

1. Build-up of lactic acid in your blood (lactic acidosis). Lactic acidosis can happen in some people who take STRIBILD or similar (nucleoside analogs) medicines. Lactic acidosis is a serious medical emergency that can lead to death. Lactic acidosis can be hard to identify early, because the symptoms could seem like symptoms of other health problems. **Call your healthcare provider right away if you get any of the following symptoms which could be signs of lactic acidosis:**

- feel very weak or tired
- have unusual (not normal) muscle pain
- have trouble breathing
- have stomach pain with nausea or vomiting
- feel cold, especially in your arms and legs
- feel dizzy or lightheaded
- have a fast or irregular heartbeat

2. Severe liver problems. Severe liver problems can happen in people who take STRIBILD. In some cases, these liver problems can lead to death. Your liver may become large (hepatomegaly) and you may develop fat in your liver (steatosis). **Call your healthcare provider right away if you get any of the following symptoms of liver problems:**

- your skin or the white part of your eyes turns yellow (jaundice)
- dark “tea-colored” urine
- light-colored bowel movements (stools)
- loss of appetite for several days or longer
- nausea
- stomach pain

You may be more likely to get lactic acidosis or severe liver problems if you are female, very overweight (obese), or have been taking STRIBILD for a long time.

3. Worsening of Hepatitis B infection. If you have hepatitis B virus (HBV) infection and take STRIBILD, your HBV may get worse (flare-up) if you stop taking STRIBILD. A “flare-up” is when your HBV infection suddenly returns in a worse way than before.

- Do not run out of STRIBILD. Refill your prescription or talk to your healthcare provider before your STRIBILD is all gone
- Do not stop taking STRIBILD without first talking to your healthcare provider
- If you stop taking STRIBILD, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking STRIBILD

Who should not take STRIBILD?

Do not take STRIBILD if you also take a medicine that contains:

- adefovir (Hepsera®)
- alfuzosin hydrochloride (Uroxatral®)
- cisapride (Propulsid®, Propulsid Quicksolv®)
- ergot-containing medicines, including: dihydroergotamine mesylate (D.H.E. 45®, Migranal®), ergotamine tartrate (Cafergot®, Migergot®, Ergostat®, Medihaler Ergotamine®, Wigraine®, Wigrettes®), and methylergonovine maleate (Ergotrate®, Methergine®)
- lovastatin (Advicor®, Altoprev®, Mevacor®)
- midazolam, when taken by mouth
- pimozide (Orap®)
- rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®)
- sildenafil (Revatio®), when used for treating lung problems
- simvastatin (Simcor®, Vytorin®, Zocor®)
- triazolam (Halcion®)
- the herb St. John’s wort

Do not take STRIBILD if you also take any other HIV-1 medicines, including:

- Other medicines that contain elvitegravir, cobicistat, emtricitabine, or tenofovir (Atripla®, Complera®, Emtriva®, Truvada®, Tybost®, Viread®, Vitekta®)
- Other medicines that contain lamivudine or ritonavir (Combivir®, EpiVir® or EpiVir-HBV®, Epzicom®, Kaletra®, Norvir®, Triumeq®, Trizivir®)

STRIBILD is not for use in people who are less than 18 years old.

What are the possible side effects of STRIBILD?

STRIBILD may cause the following serious side effects:

- **See “What is the most important information I should know about STRIBILD?”**
- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood and urine tests to check your kidneys before you start and while you are taking STRIBILD. Your healthcare provider may tell you to stop taking STRIBILD if you develop new or worse kidney problems.
- **Bone problems** can happen in some people who take STRIBILD. Bone problems include bone pain, softening or thinning (which may lead to fractures). Your healthcare provider may need to do tests to check your bones.
- **Changes in body fat** can happen in people who take HIV-1 medicine. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms and face may also happen. The exact cause and long-term health effects of these conditions are not known.

- **Changes in your immune system** (Immune Reconstitution Syndrome) can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having any new symptoms after starting your HIV-1 medicine.

The most common side effects of STRIBILD include:

- Nausea
- Diarrhea

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

- These are not all the possible side effects of STRIBILD. For more information, ask your healthcare provider.
- Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What should I tell my healthcare provider before taking STRIBILD?

Tell your healthcare provider about all your medical conditions, including:

- If you have or had any kidney, bone, or liver problems, including hepatitis B infection
- If you are pregnant or plan to become pregnant. It is not known if STRIBILD can harm your unborn baby. Tell your healthcare provider if you become pregnant while taking STRIBILD.
 - There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry.
- If you are breastfeeding (nursing) or plan to breastfeed. Do not breastfeed if you take STRIBILD.
 - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
 - Two of the medicines in STRIBILD can pass to your baby in your breast milk. It is not known if the other medicines in STRIBILD can pass into your breast milk.
 - Talk with your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements:

- STRIBILD may affect the way other medicines work, and other medicines may affect how STRIBILD works.
- Be sure to tell your healthcare provider if you take any of the following medicines:
 - Hormone-based birth control (pills, patches, rings, shots, etc)
 - Antacid medicines that contain aluminum, magnesium hydroxide, or calcium carbonate. Take antacids at least 2 hours before or after you take STRIBILD
 - Medicines to treat depression, organ transplant rejection, or high blood pressure
 - amiodarone (Cordarone®, Pacerone®)
 - atorvastatin (Lipitor®, Caduet®)
 - bepridil hydrochloride (Vasacor®, Bepadin®)
 - bosentan (Tracleer®)
 - buspirone
 - carbamazepine (Carbatrol®, Eptol®, Equetro®, Tegretol®)
 - clarithromycin (Biaxin®, Prevpac®)
 - clonazepam (Klonopin®)
 - clorazepate (Gen-xene®, Tranxene®)

- colchicine (Colcris®)
- medicines that contain dexamethasone
- diazepam (Valium®)
- digoxin (Lanoxin®)
- disopyramide (Norpace®)
- estazolam
- ethosuximide (Zarontin®)
- flecainide (Tambocor®)
- flurazepam
- fluticasone (Flovent®, Flonase®, Flovent Diskus®, Flovent HFA®, Veramyst®)
- itraconazole (Sporanox®)
- ketoconazole (Nizoral®)
- lidocaine (Xylocaine®)
- mexiletine
- oxcarbazepine (Trileptal®)
- perphenazine
- phenobarbital (Luminal®)
- phenytoin (Dilantin®, Phenytek®)
- propafenone (Rythmol®)
- quinidine (Neudexta®)
- rifabutin (Mycobutin®)
- rifapentine (Priftin®)
- risperidone (Risperdal®, Risperdal Consta®)
- salmeterol (Serevent®) or salmeterol when taken in combination with fluticasone (Advair Diskus®, Advair HFA®)
- sildenafil (Viagra®), tadalafil (Cialis®) or vardenafil (Levitra®, Staxyn®), for the treatment of erectile dysfunction (ED). If you get dizzy or faint (low blood pressure), have vision changes or have an erection that last longer than 4 hours, call your healthcare provider or get medical help right away.
- tadalafil (Addcirca®), for the treatment of pulmonary arterial hypertension
- thioridazine
- voriconazole (Vfend®)
- warfarin (Coumadin®, Jantoven®)
- zolpidem (Ambien®, Edlular®, Intermezzo®, Zolpimist®)

Know the medicines you take. Keep a list of all your medicines and show it to your healthcare provider and pharmacist when you get a new medicine. Do not start any new medicines while you are taking STRIBILD without first talking with your healthcare provider.

Keep STRIBILD and all medicines out of reach of children.

This Brief Summary summarizes the most important information about STRIBILD. If you would like more information, talk with your healthcare provider. You can also ask your healthcare provider or pharmacist for information about STRIBILD that is written for health professionals, or call 1-800-445-3235 or go to www.STRIBILD.com.

Issued: December 2014



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PANORAMA FROM THE SPACE NEEDLE: A NEARLY 360-DEGREE VIEW THAT INCLUDES (FROM LEFT) PUGET SOUND, MAGNOLIA, QUEEN ANNE HILL, LAKE UNION, CAPITOL HILL, DOWNTOWN SEATTLE, ELLIOTT BAY, AND WEST SEATTLE.

GREAT EXPECTATIONS GIVE WAY TO

THE CONFERENCE on Retroviruses and Opportunistic Infections, or CROI, has long been an important gathering for clinical scientists, doctors, and epidemiologists to discuss the latest research and study results for the prevention and treatment of HIV/AIDS and opportunistic infections. Here are some of the most important news items from CROI 2015, held from February 23–26 in Seattle, Washington.

BY ENID VÁZQUEZ

HIV CAN BE prevented with the use of four pills taken around the time of sex. CROI 2015 brought this and a lot of other good news on using the HIV medication Truvada to prevent infection with the virus in HIV-negative people (an intervention called PrEP, for pre-exposure prophylaxis).

Meanwhile, researchers reported zero linked infections in nearly 6,000 acts of condomless anal sex in 152 male serodiscordant couples when the HIV-positive partner had undetectable viral load on therapy, a strategy called Treatment as Prevention, or TasP (Grulich, 1019LB).

On demand PrEP

Doctors from Montreal and Paris teamed up to study Truvada PrEP around the time of sexual risk, and found an 86% decrease in risk of HIV with the strategy.

The IPERGAY study design was based on one in macaque monkeys showing “you almost fully protect” them with Truvada before and after exposure to virus, said presenter Jean-Michel Molina, MD, of the HIV research collaborative ANRS in Paris.

Participants used three doses totalling four tablets for prevention (see infographic). Anyone having sexual intercourse more than once in a week was advised to continue taking one pill a day, followed by the two doses after the last encounter. Altogether, most people used sixteen tablets a month, for an average of one sex act a week.

Then again, participants did not always use PrEP. “Overall, 28% of these participants did not use PrEP during the last intercourse, so patients were able to select the type of sexual [act] including the type of partner with whom they would want to use PrEP,” Molina said.

Wait for confirmation of

the results before trying this at home.

Among its conclusions, the research group reported that on demand PrEP is an “attractive alternative to daily PrEP [as FDA approved] in high-risk MSM [men who have sex with men] who do not use condoms consistently.”

The group expected to show at least a 50% decrease in HIV incidence and the 86% reduction they saw surprised them. Due to the success of the Truvada group in staying HIV free, the placebo arm was discontinued early and everyone in that group offered the opportunity to take the drug.

Real-world PrEP

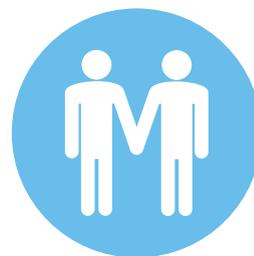
British researchers decided to check on the PrEP potential in the real world following a 44% reduction in HIV seen in the landmark iPrEx study.

Presenter Sheena McCormack, MD, noted that effectiveness might be less in the real world because iPrEx participants were seen monthly and had strong resources for adherence support, and because they received behavioral interventions and were constantly reminded that PrEP may not work.

Would people take greater risks knowing that Truvada PrEP does work to prevent HIV?

As with IPERGAY, taking Truvada succeeded in achieving an 86% reduction in new HIV

PrEP ON DEMAND



IPERGAY PARTICIPANTS TOOK THREE DOSES FOR PREVENTION:



TWO TABLETS

TAKEN TOGETHER, 2–24 HOURS BEFORE SEX, FOLLOWED BY



ONE TABLET

24 HOURS AFTER SEX, AND



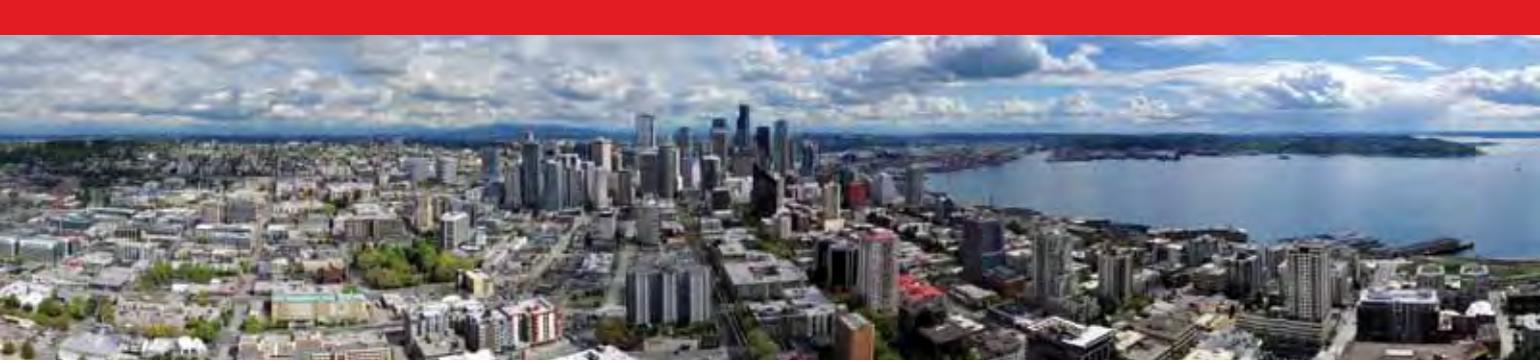
ONE TABLET

48 HOURS AFTER SEX.

infections. Participants were recruited from sexual health clinics in London.

These men also needed to be at high risk of infection. They reported condomless anal sex in the past 90 days and were likely to have condomless sex again.

Also as with IPERGAY, the Truvada PrEP group did so well at preventing HIV that the data monitoring board recommended



GREATER PROMISE IN SEATTLE

giving the drug to all participants in the study. And again as in IPERGAY, the research team was surprised at how many infections they saw in the group not given Truvada. It was three times the number of HIV infections they expected to see.

The group concluded, among other things, that, “Our concerns about PrEP being less effective in the real world were unfounded.”

“What is absolutely fantastic,” said McCormack, “is that given [the successful] results for PrEP, people who need it really came forward.”

¡Adios, HIV!

Not mincing their words, the Partners Demonstration Project researchers called the results of their study with Truvada “the near elimination of HIV.”

While high levels of adherence to either PrEP or ART (HIV therapy) can reduce the risk of infection by more than 90%, said presenter Jared M. Baeten, MD, PhD, of the University of Washington, there are issues to consider. Delays in starting HIV therapy are common, and transmission risk may continue for months after starting treatment until a person’s virus is undetectable. Some studies have reported that not everyone offered HIV therapy wishes to take it. As for PrEP, not all at-risk individuals use it when it is offered.

This study looked at PrEP

as a prevention bridge in the HIV-negative partners of serodiscordant couples in four African countries, hoping to keep them uninfected until the positive partners get their virus down to undetectable through therapy. It found that PrEP reduced infections by 96% (from the expected rate of more than 5% a year down to a half-percent).

“Our results also speak to the potential for HIV protection from integrated PrEP and ART in other high-risk populations, we would argue, including MSM and women at risk,” said Baeten.

San Francisco

Using a mathematical model, leading medical providers from San Francisco showed that the city can reduce its number of new HIV infections by 70%.

Presenter Robert M. Grant, MD, of iPrEx study fame, said that although PrEP use was “negligible” when it became available in 2011, it increased over time. In turn, increasing PrEP use correlates with decreasing numbers of new HIV infections, he said.

New infections went down from 420 in 2012 to 359 in 2013, and so far for 2014, have gone down to 320 (some of the cases need to be confirmed, so the number may be even lower).

As with the Partners Demonstration Project, the San Francisco group expects HIV treatment and PrEP to bolster

each other’s effectiveness for prevention, and as with the London group, it noted that people at highest risk for HIV had the greatest uptake of PrEP.

“Remarkably, the uptake of PrEP is strongly and positively correlated with reported HIV risk, such that 63% of men reporting condomless anal sex in the last six months reported having used PrEP,” said Grant, who is now Chief Medical Officer for the San Francisco AIDS Foundation. “People with lower levels of risk have much less uptake.”

WATCH WEBCASTS OF THESE PREP FINDINGS AT THE CONFERENCE WEBSITE, CROICONFERENCE.ORG, AND READ A LONGER VERSION OF THIS REPORT AT POSITIVELYAWARE.COM.

Body composition

The early days of highly active medication for HIV were known for resulting in undesirable body composition changes. Although the causes of these changes are not completely understood to this day, the AIDS Clinical Trials Group (ACTG) presented data showing that the virus itself may not only contribute to increased fat, but do so more than the medications.

Presenter Grace A. McComsey, MD, of Case Western Reserve University, said that lipoatrophy (fat loss in the face and limbs) wasn’t

seen with newer medications, but fat gain was.

“A 30% gain in fat after two years? That’s really bad,” she said in response to a question from the audience. “It’s a relatively short duration of treatment.”

The effects were similar no matter what regimen people took. It was the strong correlation with the virus that came as an even greater surprise.

“I think it’s amazing that regardless of the regimen you looked at, the fat gains were so much more if you start with high viral load [over 100,000],” McComsey continued. “Then, if you adjust for inflammation markers, viral load remains by itself associated with higher gains. The research, especially on central fat, needs to continue and needs to be geared towards inflammation and other markers, rather than just the drugs.”

The metabolic sub-study of A5257 looked at fat loss and increases along with measurements of inflammation in 328 individuals who were using regimens containing Isentress (raltegravir, an integrase inhibitor) or Prezista (darunavir) or Reyataz (atazanavir), both protease inhibitors (PIs).

Although the protease inhibitor class of drugs was thought to be responsible for fat gain back in the day, this study found no difference in fat gain between Isentress and the two PIs.

Lipitor

In a small study with 40 individuals living with HIV, half were put on the statin medication Lipitor (atorvastatin).

“As compared to placebo, statin therapy reduces noncalcified plaque volume and high risk plaque features in HIV-infected patients with subclinical coronary atherosclerosis,” researchers reported.

Plaque consists of fatty deposits and other types of cells that build up in arteries. This can cause the progressive disease atherosclerosis.

The group from Harvard Medical School wrote that, “Further studies should assess whether reduction in high risk coronary artery disease may translate into effective prevention of cardiovascular events in this at-risk population of HIV patients.”

The team noted that while drugs known as statins can reduce the risk of cardiovascular disease events and deter the progression of atherosclerosis, “no studies have yet assessed the ability of statin treatment to achieve regression of coronary atherosclerosis in HIV-infected patients, a population demonstrated to have elevated risk of myocardial infarction [heart attack].”

Kaletra vs. Viramune for children

The IMPAACT P1060 study had earlier reported short-term superiority of Kaletra over Viramune (nevirapine or NVP) for infants through 24 weeks of life, regardless of any exposure to

Viramune for HIV prevention around the time of birth. “In contrast,” the research group wrote, “those on NVP had marginally superior improvements in CD4% and growth (weight and height z-scores).”

Now the group reports that in longer term follow-up, “Early modest gains in CD4% and growth associated with NVP were no longer statistically significant beyond one year after ART initiation.”

“These findings further support the current WHO recommendation for LVP/r [Kaletra]-based ART as first-line therapy for HIV-infected children aged three or younger,” they wrote.

Short-cycle therapy

Teenagers put on five days of therapy followed by weekends off continued to have the same treatment success as those continuing with daily HIV medication. At one year, the results were similar for viral load, safety, virus drug resistance, and signs of inflammation.

The BREATHER Study included 199 young people from 11 countries in Europe, Thailand, Uganda, Argentina, and the U.S. Before entering the study, all of them had undetectable viral loads under 50 for at least one year with efavirenz (Sustiva, called Stocrin in the UK, Europe, and elsewhere) and two nucleoside drugs (such as Viread and Emtriva).

Karina Butler, of Our Lady's Children's Hospital in Dublin, said the teenagers preferred taking a couple of days away from treatment on the weekends. They were happy not to have to take their HIV medications during a sleepover, for example.

There is also a cost savings with the fewer pills. For now, the abbreviated regimen is not approved for use.

TAF non-inferior to TDF with improved safety profile

BY JEFF BERRY

TENOFOVIR disoproxil fumarate (TDF), a component of Truvada and included in most HIV regimens used to treat HIV, is associated with clinically significant renal and bone toxicity. TDF is a prodrug of the active drug tenofovir diphosphate (DP). TDF is converted to the active tenofovir in the blood plasma, then makes its way into the cells.

A new “version” of TDF, tenofovir alafenamide fumarate (TAF), is also a prodrug of tenofovir DP but is metabolized largely within the cell, making levels in the blood plasma much lower (90% lower in studies), resulting in reduced side effects and increased concentrations of the drug within cells. So there has been a lot of interest in seeing this drug move forward.

David Wohl, MD, presented Phase 3 48-week data in a planned analysis from two identically designed, international, randomized, double-blind active-controlled studies (104 and 111) in 1,733 individuals. The two studies compared a once-daily single-tablet regimen (STR) of elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/TAF 10 mg (E/C/F/TAF) to the currently available Stribild, an STR which contains TDF (E/C/F/TDF). Both studies were in treatment-naïve individuals who had a viral load equal to or greater than 1,000 copies/mL and an eGFR (glomerular filtration rate, a marker of kidney function) of at least 50 (lower than the current Stribild threshold of 70).

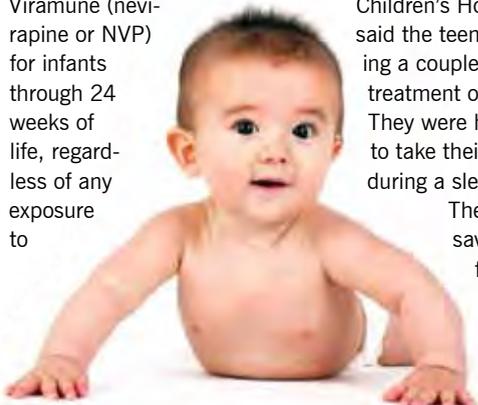
The median age was 34; 50% of the participants were

female, 25% black or African descent, and 19% Latino. The average viral load of study participants at baseline (when they started) was 4.58 log¹⁰, with 23% having a baseline viral load over 100,000, and 5% over 400,000 c/mL. The median CD4 count was 400.

TAF and TDF achieved comparable levels of viral suppression in patients with viral load above and below 100,000. Similarly for CD4 count, those with CD4 count less than 200 saw no difference in rates of viral suppression. Results were similar across all groups when broken down by age, race, and sex. There was a “robust” CD4 count increase during the trial, and at week 48 there was a greater increase of 30 CD4+ T-cells in the TAF group versus the TDF group (211 vs. 181), which was statistically significant. The rate of virologic failure was 4% in both groups, while emergent resistance was less than one percent.

Safety was “well-balanced” between both arms in the two studies. Any serious adverse event (AE) was less than 10% in both arms, with less than 1% in the TAF group and 1.5% in the TDF group experiencing a treatment-related discontinuation. There were varying reasons given for treatment discontinuation, but as Wohl stated, “importantly in the TAF arm there was no new signal or anything to differentiate between the two arms, and no discontinuation due to renal or bone toxicity in the TAF arm.”

Overall 92% treated with E/C/F/TAF achieved virologic suppression through week 48 in this combined analysis of two



If you're on HIV meds,
Fulyzaq may help you...

LEAVE DIARRHEA BEHIND

Is diarrhea holding you back? If you are on HIV medications, Fulyzaq is a plant-based, FDA-approved prescription medication that may help manage your diarrhea.

Fulyzaq may help manage your diarrhea over time by making your bowel movements less frequent and loose. Fulyzaq works by normalizing the flow of water in your gut. Fulyzaq did not interfere with commonly used HIV medications, and did not affect CD4 count or viral load in a 4-week study.

 **It's time to stop dealing with diarrhea and 'Start the Conversation' about Fulyzaq today.**

Indication

FULYZAQ® (crofelemer) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy.

Important Safety Information about FULYZAQ

FULYZAQ® (crofelemer) delayed-release tablets should not be used for the treatment of infectious diarrhea. It is important that your healthcare provider considers infectious causes of diarrhea before you start taking FULYZAQ. If infectious causes are not considered, and you begin taking FULYZAQ based on a probable diagnosis of noninfectious diarrhea, there is a risk that you will not receive the appropriate treatments, and your disease may worsen.

- FULYZAQ tablets should be swallowed whole. FULYZAQ tablets should not be crushed or chewed. You may take FULYZAQ with or without food. You should follow the instructions of your healthcare provider.
- If you are pregnant, or planning to become pregnant, talk to your healthcare provider before taking FULYZAQ. The safety and effectiveness of FULYZAQ have not been established in people younger than 18 years of age.
- In clinical studies, the most common adverse reactions associated with FULYZAQ – occurring in at least 3% of patients taking FULYZAQ – were upper respiratory tract infection, bronchitis (inflammation of the lining of the tubes which carry air to and from your lungs), cough, flatulence (intestinal gas passed through your rectum), and increased bilirubin (a waste product of the breakdown of red blood cells).
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch/ or call 1-800-FDA-1088.

Please see following page for brief summary of Prescribing Information for FULYZAQ.


Fulyzaq®
(crofelemer) 125 MG
DELAYED-RELEASE TABLETS



Snap a picture of our logo and show your doctor to 'Start the Conversation'



Fulyzaq[®]

(crofelemer) 125 MG
DELAYED-RELEASE TABLETS

IMPORTANT PATIENT INFORMATION

The following is a brief summary only. See complete Prescribing Information at Fulyzaq.com or request complete Prescribing Information by calling 1-800-508-0024. This information does not take the place of talking with your doctor about your medical condition or your treatment.

WHAT IS FULYZAQ?

FULYZAQ is a prescription medication used to improve symptoms of noninfectious diarrhea (diarrhea not caused by a bacterial, viral, or parasitic infection) in adult patients with HIV/AIDS who take HIV medication.

WHO SHOULD NOT TAKE FULYZAQ?

- FULYZAQ should not be taken if you have diarrhea caused by an infection
- Your doctor and you should make sure your diarrhea is not caused by an infection (such as bacteria, virus, or parasite) before you start taking FULYZAQ

WHAT ARE THE POSSIBLE SIDE EFFECTS OF FULYZAQ?

- Upper respiratory tract infection (nasal or sinus infection)
- Bronchitis (inflammation of the lining of the tubes which carry air to and from your lungs)
- Cough
- Flatulence (intestinal gas passed through your rectum)
- Increased bilirubin (a waste product of the breakdown of red blood cells)

For a full list of side effects, please talk to your doctor.

Tell your doctor if you have any side effect that bothers you or does not go away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

SHOULD I TAKE FULYZAQ IF I AM:

Pregnant or Planning to Become Pregnant?

- Studies in animals show that FULYZAQ could cause harm to an unborn baby or affect the ability to become pregnant
- There are no studies in pregnant women taking FULYZAQ
- This drug should only be used during pregnancy if clearly needed

A Nursing Mother?

- It is not known whether FULYZAQ is passed through human breast milk
- If you are nursing, you should tell your doctor before starting FULYZAQ
- Your doctor will help you to make a decision whether to stop nursing or to stop taking FULYZAQ

Under 18 or Over 65 Years of Age?

- FULYZAQ has not been studied in children under 18 years of age
- FULYZAQ studies did not contain a large number of patients over the age of 65; therefore, it is unclear if this age group will respond differently

Talk to your doctor to find out if FULYZAQ is right for you.

HOW SHOULD I TAKE FULYZAQ?

- FULYZAQ should be taken orally, by mouth 2 times per day
- FULYZAQ tablets may be taken with or without food
- FULYZAQ tablets should not be crushed or chewed
- FULYZAQ tablets should be swallowed whole

WHAT SHOULD I KNOW ABOUT TAKING FULYZAQ WITH OTHER MEDICATIONS?

- If you are taking any prescription or over-the-counter (OTC) medications, or herbal supplements or vitamins, tell your doctor before starting FULYZAQ

WHAT IF I HAVE MORE QUESTIONS ABOUT FULYZAQ?

- For more information, please see the full Prescribing Information at Fulyzaq.com or speak to your doctor or pharmacist

To report side effects, a product complaint, or for additional information, call: 1-800-508-0024.

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FUL50-0614



The botanical drug substance of FULYZAQ is extracted from *Croton lechleri* (the botanical raw material) that is harvested from the wild in South America.

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ADVANCING TREATMENT IN GASTROENTEROLOGY™

“very well-powered” clinical trials, demonstrating non-inferiority to E/C/F/TDF.

In a separate presentation (143LB) at the conference Paul Sax, MD, presented a subset of data on renal and bone safety from the two studies. The decrease in spine and hip bone mineral density (BMD) was significantly less in the TAF arm compared to the TDF arm, and there was less of a GFR decline in TAF vs. TDF. Increases in lipids were greater in the TAF arm, including HDL (the “good” cholesterol).

A related poster at the conference showed that patients with mild to moderate renal impairment (eGFR 30-69 mL/min) who switch to E/C/F/TAF saw bone mineral density and markers of kidney function improve through 48 weeks (Pozniak, Poster #795).

Maturation inhibitor BMS-955176

Novel antiretrovirals that target different steps of the virus life cycle, have unique resistance profiles, and display long-term tolerability with manageable drug-drug interactions are important, especially for treatment-experienced patients who may have limited options due to treatment emergent or

transmitted resistance, and/or regimen complexity.

Maturation in the viral life-cycle process is especially important, because it’s the point at which the virus changes structure and becomes infectious. Maturation inhibitors (MIs) bind to the Gag polyprotein of the budding virus and block a key protease cleavage event (past the point where protease inhibitors, or PIs, work), thereby blocking maturation.

176 is a second-generation MI in development by Bristol-Myers Squibb (BMS) with no significant safety issues identified to date. This was a Phase 2a dose-ranging study in 60 individuals who were either treatment naïve (92%) or experienced (PI and MI naïve), with a viral load equal to or greater than 5,000 copies, and CD4 count greater than 200 who received doses of 5, 10, 20, 40, 80, or 120 mg or placebo once daily (QD) for 10 days. The study was conducted in Germany in mostly white males, median (half above, half below) age 37, median viral load 4 logs, and median CD4 512. Median change drop in HIV-1 RNA from baseline to day 11 was 1.4 log¹⁰.

The greatest response was with the 40 mg dose. In its conclusion, the study team reported

that, “Unlike 1st-generation MIs, in this proof-of-concept study BMS-955176 showed similar antiviral activity in subjects with wild-type HIV-1 or HIV-1 with Gag polymorphisms. BMS-955176 was generally well tolerated at all doses.”

TLR7 GS-9620

As discussed in the cure article in this issue (page 20), research is looking for ways to eliminate the HIV reservoir, where the virus lays sleeping in the body (called “latency”). One method seeks to “kick” the virus out of its hiding spot so it can be targeted and destroyed by HIV treatment. There was exciting data about a new drug in development from a class called TLR7 agonist.

Increased HIV levels in the test tube were seen when GS-9620, being developed by Gilead Sciences, was added to blood cells donated by four HIV-positive individuals. Another small study showed that the drug worked well in monkeys and is going on into human research.

A third research team noted that, “Pharmacologic activation of latent HIV reservoirs is considered to be a key part of the strategy towards eradicating HIV-1 infection,” and reported that GS-9620 was successful in activating the virus in the blood cells of HIV-positive patients (specifically, peripheral blood mononuclear cells, or PBMCs). The team said that together with the monkey data, the results support further research with HIV-positive people on therapy with undetectable virus “for possible activation and reduction of the viral reservoir.” This study has been initiated.

According to a report from Project Inform, “Toll-like receptors [TLRs] are receptors on immune system cells that, among other things, can result in the production of proteins that

regulate the immune response to viruses, bacteria, and other pathogens. ... TLR7 has been implicated in autoimmune responses (where the body attacks itself), so it is something of a surprise that the TLR7 agonist being studied by Gilead appears to be safe to use. [GS-9620] is already in Phase 2 studies as a treatment for hepatitis B, and experience with the drug led scientists at Gilead to believe that it might be effective in a kick-and-kill model aimed at reversing HIV latency.”

Abacavir and heart attacks

New data was presented on the possible link between heart attacks and the HIV medication abacavir (brand name Ziagen, also found in Epzicom and Triumeq). Once again, research found greater risk from traditional factors for myocardial infarction (MI, or heart attack).

Looking at 301 heart attacks among 16,733 individuals with HIV here in the U.S., the NA-ACCORD study reported that, “We found an increased risk for MI with recent [within the past six months] ABC [abacavir] use that diminished in magnitude and statistical significance after adjusting for traditional and HIV-associated MI risk factors, many of which were significantly more prevalent in ABC users. Further analyses are underway to account for potential time-dependent confounding of risks for MI.”

The results showed a 34% higher risk of MI (after adjustments), but this was not a statistically significant difference.

People who went on abacavir had greater risks, in part, because their medical condition did not allow them to go on the drug’s main competitor, tenofovir DF (for example, the presence of kidney disease).



WITH AN ESTIMATED POPULATION OF 652,405 (AS OF 2013), SEATTLE IS THE LARGEST CITY IN THE STATE OF WASHINGTON. THE CITY’S SKYLINE IS DOMINATED BY THE 605-FOOT TALL SPACE NEEDLE, BUILT FOR THE 1962 WORLD’S FAIR. LOOMING IN THE DISTANCE IS MOUNT RAINIER, 54 MILES SOUTHEAST OF SEATTLE, AT A HEIGHT OF 14,411 FEET.



Reversing the trend for those with HIV/HCV co-infection

BY ANDREW REYNOLDS
PROJECT INFORM

IN RECENT YEARS, other infectious diseases besides HIV have been featured prominently at CROI, most especially hepatitis C (HCV). CROI 2015 was no exception and with more than 100 abstracts, HCV research was well represented. This brief review provides information on the latest data from a selection of posters and presentations, with particular emphasis on HIV/HCV co-infected persons.

Curing HCV: ION-4 and ALLY-2

Today, co-infected patients are more likely to experience the same cure rates as those infected only with HCV.

Prior to the direct acting antiviral (DAA) era, treating HCV in HIV/HCV co-infected persons was very challenging: Pegylated interferon and ribavirin were the standard of care and the combination of length of treatment, severe side effects, and low success rates stood as significant barriers for patients and their medical providers.

In the DAA era, we are not only seeing high sustained virologic response (SVR, or virologic cure) rates in HCV mono-infected

people, but we are also seeing nearly the same rates in co-infected people. Indeed, the AASLD/IDSA/IAS HCV treatment guidelines recommend that HIV/HCV co-infected persons should be treated and re-treated the same as those without HIV (once drug-drug interactions have been addressed). Several presentations at CROI provide further support for both the FDA-approved and off-label use (when there is no FDA approval but evidence of potential benefit exists) of DAAs in co-infected patients.

The fixed-dose combination of ledipasvir/sofosbuvir, brand name Harvoni, was approved by the FDA in October 2014 for the treatment of HCV in genotype 1 in mono-infected persons, but not for HIV/HCV co-infection. Although we have seen some very compelling evidence that this treatment is effective in co-infected persons—an NIH study comprising 50 non-cirrhotic HIV/HCV co-infected patients had an SVR rate of 98% (49 of 50)—the numbers were too small to draw any conclusions regarding its efficacy in larger groups.

Results from the ION-4 demonstrated an SVR12 (sustained virologic response at 12 weeks)

of 96%, offering compelling evidence that co-infected persons can be treated for HCV with a once-daily regimen.

ION-4 is a Phase 3 study of co-infected patients with HCV genotype (GT) 1 and 4. The study was open to both HCV treatment-naïve and -experienced patients, and 20% of participants had compensated cirrhosis (early liver disease). Patients were on a variety of HIV regimens, and all had HIV RNA of less than 50 copies and CD4 cell count greater than 100.

Of the 335 patients, 276 (82%) were male, 115 (34%) were African American, 56 (17%) were Latino/a, and the average age was 52. The vast majority, 327 (98%), were GT1, and 185 (55%) were HCV treatment-experienced.

The study results showed high SVR rates, with no impact on HIV disease severity or treatment and minimal side effects. Overall, 321 of 335 patients, or 96%, achieved an SVR12. A breakdown of the SVR rates by treatment experience and sustained virologic responses in ION-4 are as follows:

**ION-4
SUSTAINED
VIROLOGIC RESPONSES**
OVERALL SVR: **96%**
TREATMENT-NAÏVE **95%**
TREATMENT-EXPERIENCED: **97%**
NO CIRRHOSIS: **96%**
CIRRHOSIS: **94%**

There were 10 HCV viral relapses and two treatment failures (both had poor adherence to the regimen), while one person was lost to follow-up and another died of non-treatment related causes (injection drug-related fatality). The 10 patients who relapsed were all African American. There were no clear explanations as to why their virus came back. Previous

research has shown high response rates with this regimen in African Americans who were HCV mono-infected. This effect will be monitored going forward to see if this regimen does not perform as well in HIV/HCV co-infected African Americans as it does in other groups.

All patients maintained stable CD4 counts both during treatment and afterwards, and no patient experienced an HIV virologic rebound. The regimen was very well tolerated, with 257 (77%) reporting some side effects, but all were on the mild to tolerable level. Reported side effects included headaches, fatigue, diarrhea, nausea, arthralgia (joint pain), and upper respiratory tract infections. No one discontinued HCV treatment due to these side effects.

The results of the ION-4 study are very promising for patients with HIV/HCV co-infection and show that a once-daily regimen of LDV/SOF can cure people at very high rates with minimal side effects, and no impact on their HIV care. Although LDV/SOF has not been FDA approved for HIV/HCV co-infection, these results will further support patients and providers who wish to treat HCV off-label.

The ALLY-2 study, a Phase 3 clinical trial evaluating the effectiveness of daclatasvir (DCV) and sofosbuvir (SOF, brand name Sovaldi) for 8 or 12 weeks for patients living with HIV/HCV co-infection, shows very promising results for people with genotypes 1–4 with 12 weeks of therapy.

Daclatasvir is a pangenotypic (it works against GT 1–4) NS5A inhibitor taken once per day that is under review in the United States. Sofosbuvir, also pangenotypic, is an NS5B inhibitor that is taken once daily that has been FDA approved since late 2013. Both drugs are safe and well tolerated, and both

ALLY-2 DACLATASVIR PLUS SOFOSBUVIR SVR12 RESPONSE RATES, BY GENOTYPE AND PATIENT TYPE

PATIENT TYPE	GENOTYPE 1a	GENOTYPE 1b	GENOTYPE 2	GENOTYPE 3	GENOTYPE 4
Treatment-naïve	96% (68 OUT OF 71)	100% (12 OUT OF 12)	100% (11 OUT OF 11)	100% (6 OUT OF 6)	100% (1 OUT OF 1)
Treatment-experienced	97% (32 OUT OF 33)	100% (11 OUT OF 11)	100% (2 OUT OF 2)	100% (4 OUT OF 4)	100% (1 OUT OF 1)

have few drug-drug interactions, making them ideally suited for use in people living with HIV.

ALLY-2 comprised 203 patients with HIV/HCV co-infection, with genotypes 1–6. Study participants were given DCV plus SOF for 8 or 12 weeks. There were 151 treatment-naïve patients who were randomized into the 8-week arm (50 participants) or 12-week arm (101 participants). There were 52 treatment-experienced patients (all of whom took an interferon-based regimen in the past) who were all given 12 weeks of treatment. Most (98%) were on HIV ARTs, with HIV under control and high CD4 cell counts.

The 8-week results were not promising: 76% of patients achieved an SVR. The patients who took 12 weeks of DCV and SOF, however, achieved an overall SVR12 of 97%. A breakdown by genotype is in the chart above.

The regimen was safe and well tolerated, and did not impact HIV care and treatment. No one discontinued HCV therapy due to side effects or serious adverse events.

With liver disease the leading cause of non-AIDS death and significant morbidity in people co-infected with HIV/HCV, safe and effective treatments with little drug-drug interaction and impact on HIV disease is extremely important. The combination of DCV with SOF for 12 weeks looks to fit those criteria, and will potentially provide patients and providers with an option to cure HCV without compromising their HIV care.

The benefits of treating and curing HCV

Hepatitis C infection is a major cause of suffering in people living with HIV: HCV-related liver disease is the leading non-AIDS cause of death, and people with HIV/HCV co-infection suffer from higher rates of extra-hepatic complications such as heart disease and bone fractures. Additionally, sexually active HIV-positive gay men are at greater risk of sexual transmission of HCV, or re-infection with HCV. That said, although there are both compelling individual and public health reasons to treat and cure HIV-positive people for HCV, access to insurance coverage for said treatments can be limited to only those with more advanced liver disease due to cost barriers and the perception that patients can wait, as HCV disease progression is relatively slow.

In an effort to come to a better understanding of the benefits of SVR, Janet Tate and colleagues, in a poster entitled “The Impact of SVR on Liver Decompensation and Hepatic Fibrosis Markers in HIV/HCV,” presented data from the Veterans Aging Cohort Study (VACS) and the VA Hepatitis C case registry to evaluate the rates of liver decompensation and death, and to compare changes in fibrosis markers over time in these two groups.

The study authors looked at 12,067 HCV mono-infected and 372 HIV/HCV co-infected patients who were treated and achieved SVR with pegylated interferon and ribavirin-based regimens. The main outcomes

for the study were hepatic decompensation, death, platelet count, and AST to Platelet Ratio Index (APRI) scores.

The authors found that SVR is associated with reducing the risks of decompensation and death in mono-infected patients, and found no decompensation in the HIV/HCV co-infected group. Additionally, all patients who achieved an SVR had improvements in their platelet counts and APRI scores, indicating an improvement in their liver fibrosis.

In a study that further highlights the importance of early treatment and achievement of SVR in HIV/HCV co-infected people for both the purposes of improving individual health and preventing transmission to others, Cindy Zahnd and colleagues with the Swiss HIV and Hepatitis C Cohort Studies presented the “Impact of Deferring HCV Treatment on Liver-Related Events in HIV-Positive Patients” and showed that the longer HCV treatment is deferred, the greater the risk of developing hepatocellular carcinoma (HCC), end-stage liver failure, and death. Additionally, the longer one waits to be treated, the longer the time of infectiousness that patient has and the greater the risk of HCV transmission.

Using a mathematical model to predict the progression of liver disease, the researchers found that if treatment was initiated within one year of diagnosis the risks of developing decompensated liver disease, HCC, or liver-related deaths were dramatically reduced. As treatment was delayed to higher Fibrosis

Index (FI) levels (F2, F3, and F4), the results progressively worsened. For example, if one is treated at F3 rather F2, the risk of liver-related death is twice as high. Wait until F4, and the risk is four times greater.

Additionally, the longer one waits for treatment, particularly in F3 and F4, the patient’s risk for developing these complications remains even after achieving SVR.

Similarly, if one is treated and achieves SVR earlier, their risk of transmitting to others is limited. By contrast, if you wait until a patient achieves F4, their period of HCV infectiousness is as long as 20 years. This model provides compelling evidence for the early detection and treatment of HCV in HIV-positive persons regardless of the amount of fibrosis they may have.

Conclusions

These select treatment results from both ION-4 and ALLY-2 offer hope for the treatment and cure of HCV in people living with HIV/HCV co-infection. We also see the compelling evidence for the benefits of cure for both individual and public health.

EDITOR’S NOTE: Congratulations to Andrew Reynolds on his appointment to the guidelines panel of the AASLD/ISDA/IAS “Recommendations for the Testing, Management, and Treatment of Hepatitis C.”

VISIT THE CONFERENCE WEBSITE, CROICONFERENCE.ORG, FOR MORE INFORMATION (INCLUDING WEBCASTS) ON ALL OF THESE REPORTS.

WHAT IS PREZCOBIX™?

- PREZCOBIX™ is a prescription HIV-1 (Human Immunodeficiency Virus 1) medicine used with other antiretroviral medicines to treat HIV-1 infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). PREZCOBIX™ contains the prescription medicines PREZISTA® (darunavir) and TYBOST® (cobicistat).
- It is not known if PREZCOBIX™ is safe and effective in children under 18 years of age.
- **When used with other antiretroviral medicines to treat HIV-1 infection, PREZCOBIX™ may help:**
 - reduce the amount of HIV-1 in your blood. This is called “viral load.”
 - increase the number of CD4+ (T) cells in your blood that help fight off other infections.
- PREZCOBIX™ is always taken in combination with other HIV medications for the treatment of HIV-1 infection in adults. PREZCOBIX™ should be taken once daily with food.
- PREZCOBIX™ does not cure HIV-1 infection or AIDS, and you may still experience illnesses associated with HIV-1 infection. You must keep taking HIV-1 medicines to control HIV-1 infection and decrease HIV-related illnesses.
- Ask your healthcare provider if you have any questions on how to prevent passing HIV to other people.
- **Please read the Important Safety Information below and talk to your healthcare provider to learn if PREZCOBIX™ is right for you.**

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about PREZCOBIX™?

- **PREZCOBIX™ may cause liver problems.** Some people taking PREZCOBIX™ may develop liver problems which may be life-threatening. Your healthcare provider should do blood tests before and during your treatment with PREZCOBIX™.
 - Chronic hepatitis B or C infection may increase your chance of developing liver problems. Your healthcare provider should check your blood tests more often.
 - Signs and symptoms of liver problems include dark (tea-colored) urine, yellowing of your skin or whites of your eyes, pale-colored stools (bowel movements), nausea, vomiting, pain or tenderness on your right side below your ribs, or loss of appetite. Tell your healthcare provider if you develop any of these symptoms.
- **PREZCOBIX™ may cause severe or life-threatening skin reactions or rash.** Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. Call your healthcare provider right away if you develop a rash.
 - **Stop taking PREZCOBIX™** and call your healthcare provider right away if you develop any skin changes with symptoms such as fever, tiredness, muscle or joint pain, blisters or skin lesions, mouth sores or ulcers, red or inflamed eyes like “pink eye” (conjunctivitis).
- **PREZCOBIX™ when taken with certain other medicines, can cause new or worse kidney problems, including kidney failure.** Your healthcare provider should check your kidneys before you start and while you are taking PREZCOBIX™.

Who should not take PREZCOBIX™?

- **Do not take PREZCOBIX™** with any of the following medicines: alfuzosin (Uroxatral®), cisapride (Propulsid®, Propulsid® Quicksolv), colchicine (Colcrys®, Mitigare®) if you have liver or kidney problems), dronedarone (Multaq®), dihydroergotamine (D.H.E. 45®, Emborex®, Migranal®), ergotamine tartrate (Cafergot®, Ergomar®, Ergostat®,

Medihaler®, Migergot®, Wigraine®, Wigrettes®), methylergonovine (Methergine®), lovastatin or a product that contains lovastatin (Altoprev®, Advicor®, Mevacor®), lurasidone (Latuda®), oral midazolam (Versed®), pimozone (Orap®), ranolazine (Ranexa®), rifampin (Rifadin®, Rifater®, Rifamate®, Rimactane®), sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH), simvastatin or a product that contains simvastatin (Simcor®, Vytorin®, Zocor®), St. John's Wort (*Hypericum perforatum*) or a product that contains St. John's Wort, or triazolam (Halcion®).

- Serious problems can happen if you take any of these medicines with PREZCOBIX™.

What should I tell my healthcare provider before taking PREZCOBIX™?

- **About all health problems.** Tell your healthcare provider if you have liver problems, including hepatitis B or hepatitis C, have kidney problems, are allergic to sulfa (sulfonamide), have diabetes, have hemophilia, or have any other medical condition, are pregnant, breastfeeding, or plan to become pregnant or breastfeed. Tell your healthcare provider if you become pregnant while taking PREZCOBIX™.
- **About all medicines you take.** Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with PREZCOBIX™. **Keep a list of your medicines to show your healthcare provider and pharmacist. Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take PREZCOBIX™ with other medicines.

What are the possible side effects of PREZCOBIX™?

- **The most common side effects of darunavir, one of the medicines in PREZCOBIX™, include** diarrhea, nausea, rash, headache, stomach area (abdominal) pain, and vomiting.
- **Other possible side effects include:**
 - **High blood sugar, diabetes or worsening diabetes, and increased bleeding in people with hemophilia** have been reported in patients taking protease inhibitor medicines, including PREZCOBIX™.
 - **Changes in body fat can happen in people who take HIV-1 medicines.** The exact cause and long-term health effects of these changes are not known.
 - **Changes in your immune system** (Immune Reconstitution Syndrome) can happen when you start taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time.

These are not all of the possible side effects of PREZCOBIX™. For more information, ask your healthcare provider.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

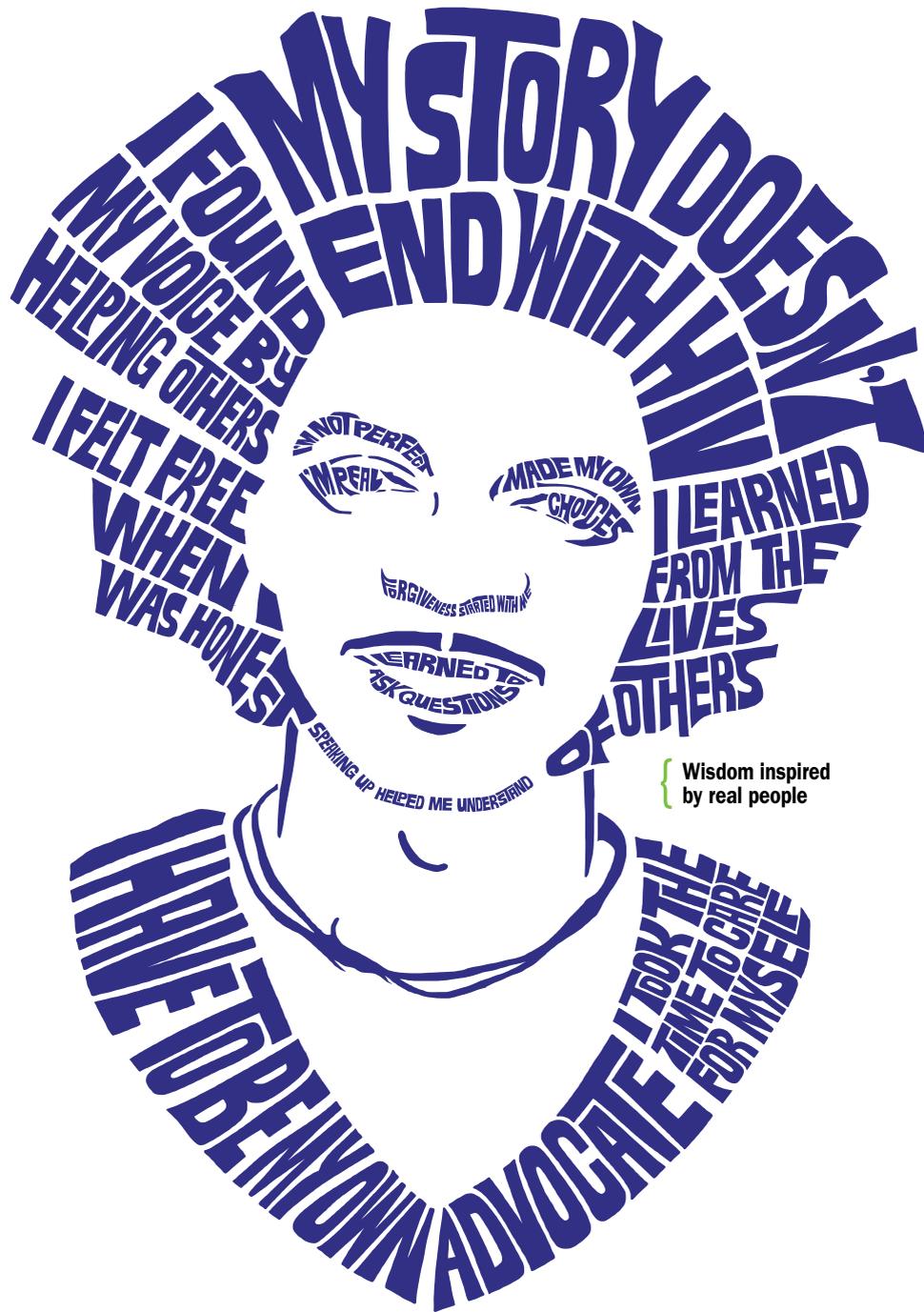
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Visit PREZCOBIX.com to hear wisdom inspired by experts and people like you living with HIV.
Ask your provider if Once-Daily* PREZCOBIX™ is right for you.

 **PREZCOBIX™**
(darunavir 800 mg/
cobicistat 150 mg) tablets
PREZCOBIX.com

*PREZCOBIX™ is taken in combination with other HIV medications for the treatment of HIV-1 infection in adults.

IMPORTANT PATIENT INFORMATION

PATIENT INFORMATION PREZCOBIX (prez-koe-bix) (darunavir and cobicistat) tablets

Please read this information before you start taking PREZCOBIX and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment. **What is the most important information I should know about PREZCOBIX?**

- **PREZCOBIX may cause liver problems.** Some people taking PREZCOBIX may develop liver problems which may be life-threatening. Your healthcare provider should do blood tests before and during your treatment with PREZCOBIX. If you have chronic hepatitis B or C infection, your healthcare provider should check your blood tests more often because you have an increased chance of developing liver problems. Tell your healthcare provider if you have any of the below signs and symptoms of liver problems.
 - dark (tea colored) urine
 - yellowing of your skin or whites of your eyes
 - pale colored stools (bowel movements)
 - nausea
 - vomiting
 - pain or tenderness on your right side below your ribs
 - loss of appetite
- **PREZCOBIX may cause severe or life-threatening skin reactions or rash.** Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. Call your healthcare provider right away if you develop a rash. **Stop taking PREZCOBIX** and call your healthcare provider right away if you develop any skin changes with symptoms below:
 - fever
 - tiredness
 - muscle or joint pain
 - blisters or skin lesions
 - mouth sores or ulcers
 - red or inflamed eyes, like “pink eye” (conjunctivitis)
- **PREZCOBIX when taken with certain other medicines can cause new or worse kidney problems, including kidney failure.** Your healthcare provider should check your kidneys before you start and while you are taking PREZCOBIX.

See “**What are the possible side effects of PREZCOBIX?**” for more information about side effects.

What is PREZCOBIX?

PREZCOBIX is a prescription HIV-1 (Human Immunodeficiency Virus 1) medicine used with other antiretroviral medicines to treat HIV-1 infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

PREZCOBIX contains the prescription medicines PREZISTA (darunavir) and TYBOST (cobicistat).

It is not known if PREZCOBIX is safe and effective in children under 18 years of age.

When used with other antiretroviral medicines to treat HIV-1 infection, PREZCOBIX may help:

- reduce the amount of HIV-1 in your blood. This is called “viral load”.

- increase the number of CD4+ (T) cells in your blood that help fight off other infections.

Reducing the amount of HIV-1 and increasing the CD4+ (T) cells in your blood may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak (opportunistic infections).

PREZCOBIX does not cure HIV-1 infection or AIDS. You must keep taking HIV-1 medicines to control HIV-1 infection and decrease HIV-related illnesses.

Avoid doing things that can spread HIV-1 infection to others.

- Do not share or re-use needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

Ask your healthcare provider if you have any questions on how to prevent passing HIV to other people.

Who should not take PREZCOBIX?

Do not take PREZCOBIX with any of the following medicines:

- alfuzosin (Uroxatral®)
- cisapride (Propulsid®, Propulsid® Quicksolv)
- colchicine (Colcrys®, Mitigare®), if you have liver or kidney problems
- dronedarone (Multaq®)
- ergot-containing medicines:
 - dihydroergotamine (D.H.E. 45®, Embolex®, Migranal®)
 - ergotamine tartrate (Cafergot®, Ergomar®, Ergostat®, Medihaler®, Migergot®, Wigraine®, Wigrettes®)
 - methylergonovine (Methergine®)
- lovastatin or a product that contains lovastatin (Altoprev®, Advicor®, Mevacor®)
- lurasidone (Latuda®)
- midazolam (Versed®), when taken by mouth
- pimozide (Orap®)
- ranolazine (Ranexa®)
- rifampin (Rifadin®, Rifater®, Rifamate®, Rimactane®)
- sildenafil (Revatio®), when used for the treatment of pulmonary arterial hypertension (PAH)
- simvastatin or a product that contains simvastatin (Simcor®, Vytorin®, Zocor®)
- St. John’s Wort (*Hypericum perforatum*), or a product that contains St. John’s Wort
- triazolam (Halcion®)

Serious problems can happen if you take any of these medicines with PREZCOBIX.

What should I tell my healthcare provider before taking PREZCOBIX?

Before taking PREZCOBIX, tell your healthcare provider if you:

- have liver problems, including hepatitis B or hepatitis C
- have kidney problems
- are allergic to sulfa (sulfonamide)
- have diabetes
- have hemophilia
- have any other medical condition

IMPORTANT PATIENT INFORMATION

- are pregnant or plan to become pregnant. It is not known if PREZCOBIX will harm your unborn baby. Tell your healthcare provider if you become pregnant while taking PREZCOBIX.
- **Pregnancy Registry:** There is a pregnancy registry for women who take antiretroviral medicines during pregnancy. The purpose of the registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you take PREZCOBIX.
- You should not breastfeed if you have HIV-1 because of the risk of passing HIV to your baby.
- It is not known if PREZCOBIX can pass into your breast milk.
- Talk to your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with PREZCOBIX. **Keep a list of your medicines to show your healthcare provider and pharmacist.**

- You can ask your healthcare provider or pharmacist for a list of medicines that interact with PREZCOBIX.
- **Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take PREZCOBIX with other medicines.

How should I take PREZCOBIX?

- Take PREZCOBIX exactly as your healthcare provider tells you.
- Do not change your dose or stop taking PREZCOBIX without talking to your healthcare provider.
- Take PREZCOBIX 1 time a day with food.
- If you miss a dose of PREZCOBIX by less than 12 hours, take your missed dose of PREZCOBIX right away. Then take your next dose of PREZCOBIX at your regularly scheduled time.
- If you miss a dose of PREZCOBIX by more than 12 hours, wait and then take the next dose of PREZCOBIX at your regularly scheduled time.
- If a dose of PREZCOBIX is skipped, do not double the next dose. Do not take more or less than your prescribed dose of PREZCOBIX at any one time.
- If you take too much PREZCOBIX, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of PREZCOBIX?

PREZCOBIX may cause serious side effects including:

- See **“What is the most important information I should know about PREZCOBIX?”**
- **Diabetes and high blood sugar (hyperglycemia).** Some people who take protease inhibitors including PREZCOBIX can get high blood sugar, develop diabetes, or your diabetes can get worse. Tell your healthcare provider if you notice an increase in thirst or urinate often while taking PREZCOBIX.
- **Changes in body fat can happen in people who take HIV-1 medications.** The changes may include an increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms, and face may also happen.

The exact cause and long-term health effects of these conditions are not known.

- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.
- **Increased bleeding for hemophiliacs.** Some people with hemophilia have increased bleeding with protease inhibitors including PREZCOBIX.

The most common side effects of darunavir, one of the medicines in PREZCOBIX, include:

- diarrhea
- nausea
- rash
- headache
- stomach area (abdominal) pain
- vomiting

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of PREZCOBIX. For more information, ask your health care provider.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store PREZCOBIX?

- Store PREZCOBIX tablets at room temperature between 68°F to 77°F (20°C to 25°C).

Keep PREZCOBIX and all medicines out of reach of children.

General information about PREZCOBIX

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use PREZCOBIX for a condition for which it was not prescribed. Do not give PREZCOBIX to other people, even if they have the same symptoms that you have. It may harm them.

If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about PREZCOBIX that is written for health professionals.

For more information call 1-800-526-7736.

What are the ingredients in PREZCOBIX?

Active ingredients: darunavir and cobicistat

Inactive ingredients: colloidal silicon dioxide, crospovidone, hypromellose, magnesium stearate, and silicified microcrystalline cellulose. The tablets are film-coated with a coating material containing iron oxide black, iron oxide red, polyethylene glycol, polyvinyl alcohol (partially hydrolyzed), talc, and titanium dioxide.

Manufactured by:
Janssen Ortho LLC, Gurabo, PR 00778

Manufactured for:
Janssen Therapeutics, Division of Janssen Products, LP,
Titusville NJ 08560

Issued: January 2015

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027415-150108

WHAT ABOUT CONDOMS?

A heartfelt message from the creator of PrEP Facts: Rethinking HIV Prevention and Sex

BY DAMON L. JACOBS

“Why can’t people just use condoms?”

As a PrEP educator and psychotherapist, this is the reaction I receive most consistently when I explain the benefits of using pre-exposure prophylaxis (PrEP) to prevent HIV. There is an implicit notion that gay and bisexual men “should” use condoms to prevent HIV, to decrease disease, to take responsibility for one’s health. However, the proponents of this argument constantly ignore one tiny flaw in their logic: Skin-to-skin sex feels better for most people.

Believe me, I understand the essential role condoms have played in preventing HIV. My first experience of living and working in the gay community was in 1990 at The Patio Café on Castro Street. That was during the time when knowing people with AIDS, living with people with AIDS, working with people with AIDS, serving people with AIDS, loving

people with AIDS, fucking people with AIDS, meant losing people with AIDS. I did all of the above, and lost a lot during that era.

During this time I was also getting my undergraduate degree in psychology. However, nothing in academia encouraged or rewarded using education and activism to improve mental health. It seemed incongruent, if not unethical, for me to be living in one of the areas hit hardest by the AIDS epidemic and not be actively involved in the solution. How could I truly serve my community's emotional needs if I wasn't doing something to resolve the source of so much trauma and anguish? It was time to get active.

By 1992, we had a very clear understanding of how HIV was spread, and how condoms could prevent transmissions. The exact stats were always sketchy, but my early training taught they were "about 98%" effective if used consistently and correctly. With that in mind, I began volunteering for an organization that was running a "100%" campaign, handing out condoms, lube, pins, and pamphlets, on street corners and in bars, that said "100%". The intention of this marketing tool was to let people know that if everyone used condoms 100% of the time—everyone who is HIV-positive, everyone who is HIV-negative, everyone who is having sex at all—then we would eradicate this epidemic by the year 2000. We had people wear the shirts and pins as a sign of their commitment to 100% condom use. It made perfect sense.

But what happened? People didn't use condoms consistently. Even back during the darkest day of this epidemic, when the consequences of not using condoms were potentially an excruciatingly painful death, people didn't use condoms consistently. Moreover, one by one, many of my colleagues, co-workers, lovers, roommates, and friends became newly HIV-positive. So much for ending HIV by the new millennium.

I had an opportunity to ask a good friend about this many years later. I wondered to him, "Was getting HIV the result of a condom breaking? Was there an accident? We always talked about condom use, so how did this happen?" My friend, who is still very healthy today, told me, "Actually, Damon, I wasn't using condoms consistently. I understood what the risks were, and I was embarrassed to tell you because I knew you were right about that. But regardless of the facts, I wasn't using condoms 100% and was too ashamed to talk about how much better sex felt without them."

That was a difficult conversation to have. It forced me to understand how all my frantic efforts to get everyone in the community to use a condom 100% inadvertently shamed

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and alienated the individuals who weren't following suit. It made me realize that I wasn't someone my friends could trust with these pleasurable yet terrifying experiences. It revealed to me the limitations of a rigid HIV prevention strategy that reflected a medical ideal while ignoring complicated feelings of ambivalence, confusion, and hunger to share another man's body without barriers.

Over the next decade, new HIV rates in the U.S. remained consistent, at about 50,000 per year, with no significant rises or decreases. So in 2011, when I began learning about a daily pill called Truvada that can prevent HIV by up to 99% when used daily, I had to seriously take pause. Could this finally be the key to bringing down new infection rates after a decade of stagnation? I decided that for myself this would be the ideal strategy for remaining HIV-negative after 22 years of being sexually active and constantly worrying if and when and how I would someday become HIV-positive. For these reasons, I began using Truvada as PrEP on a daily basis on July 19, 2011.

However, despite the overwhelming evidence demonstrating PrEP's effectiveness in individuals who took it daily during the groundbreaking iPrEx study (not one single infection with daily use), people were not learning about this essential new strategy.

Initially, I attributed the dearth of media coverage and community dialogue to the fact that the Food and Drug Administration (FDA) had yet to approve its use. I figured that on the day the FDA approved PrEP people would swarm the streets of Manhattan in jubilation, much like they did when Marriage Equality passed in New York the year before.

Not so much. The FDA approved Truvada as PrEP as the first, and to date only, HIV prevention strategy (nope, condoms were never FDA approved) on July 16, 2012. I waited for the confetti, the glitter, the triumphant shouts of joy, or at least someone who was happy about this. Instead, nothing. There were no major announcements, community events, pride parties, organizational forums, subway ads, street rallies, bar crawls, nor mainstream communications that heralded this new era of hope. It wasn't until two years later, after the Centers for Disease Control (CDC) and the World Health Organization (WHO) both endorsed PrEP, that it seemed people started learning about it, talking about it, and making rational decisions about their own use.

Meanwhile, there are those who maintain that "condoms only" is still the best way to prevent HIV. They wish to ignore history, human nature, medical advances, pleasurable choices. They believe that if we continue to beat the drum of "condoms, condoms, condoms" that somehow people will wake up and use condoms more in 2015 than they did in 1992.

I learned from my failures in the '90s the most important lessons of my career: Listen to what people are telling you with their words and their actions. People want to experience the maximal pleasure, with the minimal consequences. They want to have more connection, with fewer barriers. They want to feel heightened physical sensations, with lowered medical risks. Why not support individuals of all HIV statuses in discovering the most proactive, responsible, empowered, and healthy means of experiencing pleasure as possible? **PA**

DAMON L. JACOBS has been working in HIV prevention education since 1991, and has been a Licensed Marriage and Family Therapist since 2003. His "PrEParing for P.L.E.A.S.U.R.E." presentation has now been seen throughout the state of New York, as well as the 2015 Conference on Retroviruses and Opportunistic Infections (CROI), and the 2015 European AIDS Treatment Group (EATG) conference. He has appeared on MSNBC, New York WPIX, Al Jazeera America, NPR, and The Huffington Post Live, as well as in *The New York Times*, *USA Today*, and *Out* magazine.

*EDITOR'S NOTE: The Truvada for PrEP drug label states that it should be used in addition to condoms, while at the same time stating that one of the populations indicated for PrEP use is people at high-risk who use condoms inconsistently or not at all. Moreover, data from the CDC indicate that the effectiveness of consistent use of condoms for HIV prevention is 70% among gay and other men who have sex with men. Also, although iPrEx estimated a 99% efficacy with Truvada PrEP for those who took the drug every day, the more widely accepted figure for the high end is 96% reduction in HIV infections with four tablets a week. See PA Associate Editor Enid Vázquez's blog, *Tell It To Enid*, for a one-on-one discussion with Damon L. Jacobs at positivelyaware.com.*



FOR THE LOVE OF DOG:
DR. ROB GAROFALO SHARES
A TENDER MOMENT WITH
HIS DOG FRED.

WHY I RIDE

THE RIDE FOR AIDS CHICAGO
ADDRESSES STIGMA WHILE
HELPING HIV-POSITIVE YOUTH

BY ROBERT GAROFALO, MD
PHOTOGRAPHS BY CHRIS BAUER



MY NAME IS ROBERT GAROFALO, captain of Team Fred for the 2015 Ride for AIDS Chicago. I am a pediatrician and Division Head of Adolescent Medicine at Ann & Robert H. Lurie Children's Hospital of Chicago. At Lurie Children's I am also the Director of the Adolescent HIV Program.

In addition to my work at Lurie Children's Hospital I am also the founder of a grass-roots charity established in 2012 called Fred Says (fredsays.org). Fred Says supports organizations that serve and support HIV-positive youth nationwide. Who is Fred? you may ask. Fred is an adorable Yorkie puppy that

saved my life when I adopted him following my own HIV-positive diagnosis. For 2014 and 2015, Team Fred has been a community partner in the Ride for AIDS Chicago—meaning that the proceeds our team raises are shared equally to support the missions of both Fred Says and Test Positive Aware

Network (TPAN), the publisher of POSITIVELY AWARE. It is an honor and privilege to be a community partner of the Ride. It is also a tremendous opportunity for our new non-profit, and I will forever be grateful to TPAN for continuing to work with us.

My commitment to the Ride predates my work with Fred Says. On those cold early Saturday mornings in early April, lying in a warm bed cozy with my dog Fred snuggled up beside me, I do often seriously wonder, "Why do I ride?" I mean, a two-day, 200-mile bike ride in the heat (or rain or wind) of the Chicago summer seems less appealing when

brunch, a BBQ, or a casual walk by the lake-front represent far less strenuous options.

However, once I drag myself out of bed, deftly avoid Fred's stink eye and obvious displeasure at my early arousal, and power through a shower while getting ready for an outdoor training ride, it all comes back to me.

Now in my fourth year, I do the Ride for AIDS Chicago for many reasons, but there are three that I think are the most important. First I ride because the Ride will forever be an integral part of the healing related to stigma that followed my own HIV diagnosis. Healing that, in part because of the Ride, has now turned into thriving.

Second, I ride because the people associated with the Ride have become my family and friends. They have shown me and others like me unwavering support, and demonstrate through action what it means to change the world.

And third, I ride because whether it means supporting the work TPAN does for our community or supporting the charitable work that Fred Says does for organizations serving HIV-positive youth, I am unwaveringly committed to making the world a better place for those affected by HIV/AIDS.

My own journey with the Ride began in 2012 (coincidentally the same year Fred Says became an official non-profit organization). I had had my share of challenges in the years leading up to my first Ride. I dealt with a cancer diagnosis in 2007; I spent the majority of 2008 and 2009 dealing with the loss of a man I loved deeply and the end of our 10-year relationship, one that I cherish to this day. And in 2010 I was utterly devastated by my own HIV diagnosis. I felt damaged, ashamed, and alone. Although I had always been in my mind a silly and fun-loving guy, each day was now a struggle. Self-pity had become my reality, and it was not pretty. I knew I needed to take back control of my life, I just didn't know how.

As a pediatrician at Lurie Children's Hospital I had devoted my career to helping adolescents and young people cope with and manage HIV. There was irony in the fact that I was unable to afford myself the same compassion I had spent my career giving to others. But in 2011, I took my first healing step. I drove to Gurnee, Illinois on a frigid winter day and adopted a 10-week old Yorkie puppy I aptly named Fred.

It was an impulsive decision, and one

that was not entirely rational. I had never had nor cared for a pet and at the time struggled to make sound decisions caring for myself. What made me think a dog would be the answer?

But Fred brought me back to life. With boundless positive energy and unconditional love, he was the antidote to my self-imposed isolation and he had no time or patience for my self-pity. In short order he taught me how to smile and laugh when I thought neither might be possible ever again. However, my healing was incomplete. Although Fred was without question my guardian angel, my life very quickly became about my dog. It was Fred and I (and me and Fred). I still struggled in efforts to make new friends and reconnect to the community around me.

So, one early afternoon in January 2012, sitting in my parked car on the side of the road with tears in my eyes following yet another intense session with my therapist, I got a Facebook notification on my cell phone, "Keith Stryker is at the Ride for AIDS Chicago Kick-Off Party." Keith was someone I had met briefly a few weeks earlier. He is one of those people who draws attention because he just exudes positive energy—you can feel kindness and warmth when around him. I had made a mental note to myself the day we met that this was someone I wanted in my life.

Without giving it much thought—like thinking that I did not even own a bike—I drove over and signed up for my first AIDS Ride. Keith was the captain of my team, Team CÜR. My first Ride was all about Team CÜR, and while it is not the kind of thing you say at the time, I'm not sure the group of guys that were Team CÜR ever quite knew how important they were (and are) to me.

That first year was also about meeting people from diverse segments of our community; people too many to name, who were it not for the Ride I would have never had the pleasure of getting to know. Working together with a singular fundraising focus, Team CÜR and the other teams and individuals that formed the Ride became a family of sorts, and I was honored to be part of it.

However, there was a defining moment in the Ride that first year during the closing ceremonies, when a group of HIV-positive riders called the Poz Pedalers walked out with a riderless bicycle symbolizing all those who have lost their lives to HIV/AIDS. In that moment I felt like a fraud, unable



or unwilling to step forward and be open and honest about my own status. I stood paralyzed with fear, afraid of being visible, especially as a physician, not wanting others to know about my struggles or about my HIV. I had talked freely and candidly over the years about overcoming cancer, but when it came to discussing my HIV, stigma ruled. I was always cleverly vague and used language such as "personal struggles" but could never utter the words "I am HIV-positive" in public. And in that moment during the closing ceremonies I stood silent, unable to just come out and say, "Hey! I am HIV positive, and I just killed it and rode 200 miles on my bike!" I was so disappointed in myself for giving HIV and stigma that much power and control. I vowed that the next year would be different, and it was.

I now participate in the Ride each year as an openly HIV-positive man. I take my



**'MY SECRET WEAPON
AGAINST THE STIGMA
THAT USED TO
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LOVE I RECEIVE FROM
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place alongside other Poz Pedalers next to that riderless bike, unapologetic about my past, proud of who I am, and feeling (pardon the pun) positive about my future. My secret weapon against the stigma that used to paralyze me remains the unconditional love I receive from my dog Fred, who walks by my side at the closing ceremonies, unaware of the power of his being. Honesty about my HIV has also allowed me to be open to receiving love and support from my family and friends, many of whom are fellow riders. Too many HIV-positive people still live as I once did, in the shadows, afraid to ask for help or afraid of being open with family or friends for fear that they may be judged or alienated. For me the Ride remains part of my own healing, and I hope that being more open about my diagnosis may in some small way help others to find the courage to do so as well.

In 2014, my third year doing the Ride, I became a team captain and formed Team Fred. As a community partner, it was an amazing opportunity to help establish the giving of our grassroots charity Fred Says while simultaneously supporting the work of TPAN. It was an opportunity we did not take lightly. In our first year Team Fred—almost 40 members strong—raised just under \$80,000, and had lots of fun doing it.

So, we are back for 2015! Each member of Team Fred may ride for different reasons, but we are committed to the Ride and to each other. For some, such as myself, the Ride may be part of their healing process. For some, the Ride may be about the camaraderie of teammates, friends, and family. But without question the one unifying reason for us all, is that the Ride is our way of helping those in our community affected by HIV/AIDS. **PA**

THE 2015 RIDE FOR AIDS CHICAGO takes place July 11–12; to register or for details go to rideforaids.org. For more information about TPAN or Fred Says go to tpan.com and fredsays.org.

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THE 2015 RIDE FOR AIDS CHICAGO

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