The AMERICAN ACADEMY of HIV MEDICINE®

HIV SPECIALIST

PATIENT CARE, PRACTICE MANAGEMENT & PROFESSIONAL DEVELOPMENT INFORMATION for HIV CARE PROVIDERS

October 2012 Volume 4 No. 3 www.aahivm.org

The AFFORDABLE CARE ACT & HIV

New MATERIALS

Prevention IS Care

Incorporating Prevention into the Medical Care of Persons Living with HIV

Rx

Prevention IS Care

Latest Deskside Resource for HIV Providers

- New provider materials
- New patient education materials
- Leading evidence-based data

PREVENTION IS CARE
Screen for risky behavior. Prescribe healthy behavior.

To order your free materials, visit www.cdc.gov/PreventionIsCare or call 1-800-CDC-INFO (1-800-232-4636).

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

BY JAMES M. FRIEDMAN, MHA, EXECUTIVE DIRECTOR, AAHIVM

The Good (*and Sometimes Complicated*) Stuff

THE PAST FEW MONTHS have brought the Academy, our Members and the patients we serve some really good stuff. The Supreme Court delivered an affirmation of the Affordable Care Act (ACA). The Food and Drug Administration approved Truvada for PrEP and OraSure's over-the-counter HIV test. Both add to our ability to prevent the spread of HIV in this country.

The Academy just published the all-new, 2012 edition of the *Fundamentals of HIV Medicine*. This is the slimmed down version with just over 900 pages (it was over 1200 in 2007); and it includes a USB drive that permits you to download it on your computer. We are just completing this year's cycle of our Credentialing program. It continues to grow in size and acceptance.

I know that many of you were able to join us at our **Policy Forum for HIV Providers** held in Washington, DC just before the start of the International AIDS Conference (AIDS 2012). If you did not get the chance to attend, I hope you will take the time to view the video of the entire session that is available on our website. The presentations by government officials and thought leaders, and the dialogue between them and those in the audience, were extraordinary. This issue of *HIV Specialist* picks up where the Forum left off and provides many additional insights.

James M. Friedman

As you know, the Affordable Care Act provides new opportunities for affordable health coverage to millions of Americans who currently are not covered. This improved financial access to coverage will be helpful to HIV infected individuals who are currently in care, or should be. Yet seemingly with any new advancement comes complexity—and that complexity was highlighted in the Forum. Perhaps the most complicating factor in the implementation of the ACA is that it will differ substantially from state to state, and not just for HIV practitioners, but for all practitioners.

Another example of the complexity is the expansion of the Medicaid program. While the Federal government will pay for most of the cost of the expansion of Medicaid program, some states *may* choose not to expand. In those states that do expand Medicaid, many HIV patients who did not previously have insurance coverage will now be eligible.

However, many of the state Medicaid programs do or will soon run as managed care networks. In those cases, providers will need to understand how to qualify for and integrate their practices into the network. Some patient dislocations may occur in this transition.

This issue of *HIV Specialist* includes update articles by many of those presenting at the Forum. In addition to a summary of remarks by Dr. Aaron Lopata of the White House Office of National AIDS Policy, Dr. Deborah Parham Hopson, the Director of the HRSA HIV/AIDS Bureau focuses on her organization's involvement in the implementation of the ACA.

In addition we have asked HIV practitioners from five states (Georgia, Texas, Kentucky, Florida, and Massachusetts) to give an update of the major ACA issues in their respective states.

But a snapshot of ACA implementation is not enough. Implementation issues will continue to evolve at both the national and state levels. Decisions that have not yet been made will influence how HIV practitioners and their patients will be treated in the years ahead. I urge you to be vigilant, be proactive and keep me and your AAHIVM Chapter Chair informed of issues that are arising in your state.

I mark the start of my sixth year as the Executive Director of the Academy. To me, the greatest part of this experience has been the opportunity to work with an outstanding staff, Board and Membership. ***Together*** we have achieved a great deal:

- Solidified the Academy's financial footing by growing membership, expanding outside partnerships and engaging in nationwide provider outreach programs.
- Created and published this magazine, *HIV Specialist,* that highlights important issues for the HIV practitioner.
- Expanded the Credentialing Program to include Low Volume Providers and HIV Pharmacists.
- Completed an all-new edition of *The Fundamentals of HIV Medicine.*
- Worked with the CDC to develop *Referral Link* to facilitate quality referrals for newly identified HIV patients.
- Taken a leadership role on legislative/regulatory issues at the national and state level.
- Partnered with the American Geriatrics Society to develop treatment strategies for older HIV Patients.

Obviously there is much still to be done. I am confident that together we can continue to support the advance of HIV research and policy, while improving upon quality care for HIV patients in the years ahead. HIV

CONTENTS

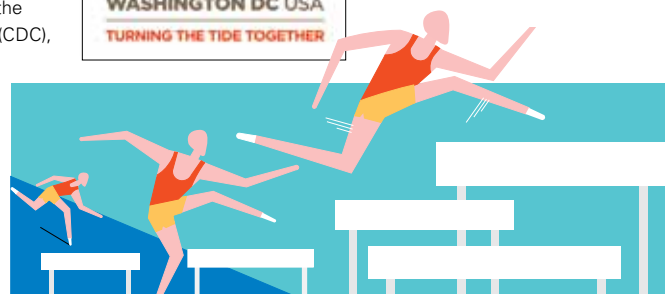
October 2012 Volume 4 No. 3
www.aahivm.org

FEATURES




ACA in the States

DEPARTMENTS



The AMERICAN ACADEMY of HIV MEDICINE®
HIV SPECIALIST
PATIENT CARE, PRACTICE MANAGEMENT & PROFESSIONAL DEVELOPMENT INFORMATION for HIV CARE PROVIDERS
VOLUME 4 / NUMBER 3 • OCTOBER 2012

PUBLISHER
THE AMERICAN ACADEMY OF HIV MEDICINE
1705 DeSales St., NW, Suite 700
Washington, D.C. 20036
p: 202-659-0699 • f: 202-659-0976
e: info@aahivm.org • w: www.aahivm.org

TOP NEWS from IAC

A wealth of new information from important studies and papers was reported at the International AIDS Conference in July in Washington, DC. An important message from the conference was that treating people with HIV early keeps them healthy, reduces chances of infecting others, and is a good financial investment.

In the US, most HIV patients have access to treatment, but just one in four has an undetectable viral load, according to the Centers for Disease Control and Prevention (CDC).

"We now need big thinking to improve that number," said Dr. Kevin Fenton, director of CDC's AIDS center. "We have the tools. Now we have to move them into real-world policy so they touch the lives of those who need them most."

Here is a summary of some of groundbreaking news emanating from the conference:

All Adult Patients Should Be Offered ART, Panel Says

The International Antiviral Society-USA panel recommends that all adult HIV patients, regardless of CD4 cell count, be offered antiretroviral therapy (ART).

The recommendations were contained in the July 25 issue of the *Journal of the American Medical Association* (JAMA) and reported by Melanie A. Thompson, MD, of the AIDS Research Consortium of Atlanta.

Dr. Thompson and colleagues with the International Antiviral Society-USA panel reviewed the medical literature to identify relevant evidence published since 2010, as well as data that had been published or presented in abstract form at scientific conferences over the past two years.

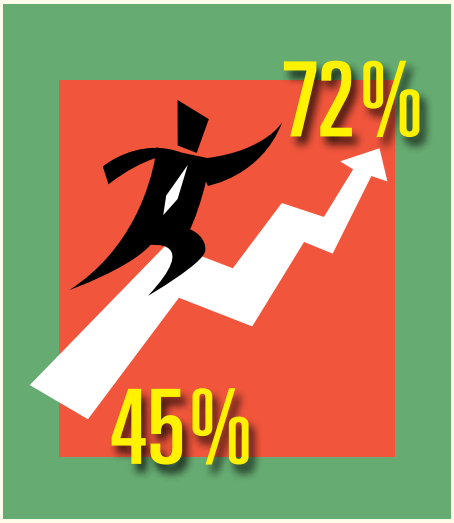
The revised guidelines reflect new data regarding recommendations of when to initiate ART, new options for initial and subsequent therapy, ART management in the setting of special conditions, new approaches to monitoring treatment success and quality, and managing antiretroviral failure.

The panel said treatment is recommended for all adults with HIV infection. The researchers found there is no CD4 cell count threshold at which starting therapy is contraindicated, but the strength of the recommendation and the quality of the evidence supporting initiation of therapy increase as the CD4 cell count decreases and when certain concurrent conditions are present. Patients should be monitored for their CD4 cell count, and also HIV-1 RNA levels, ART adherence, HIV drug resistance, and quality-of-care indicators.

Melanie A. Thompson, MD

THINKSTOCK

For more information on the new IAS-USA updated guidelines, see page 14.



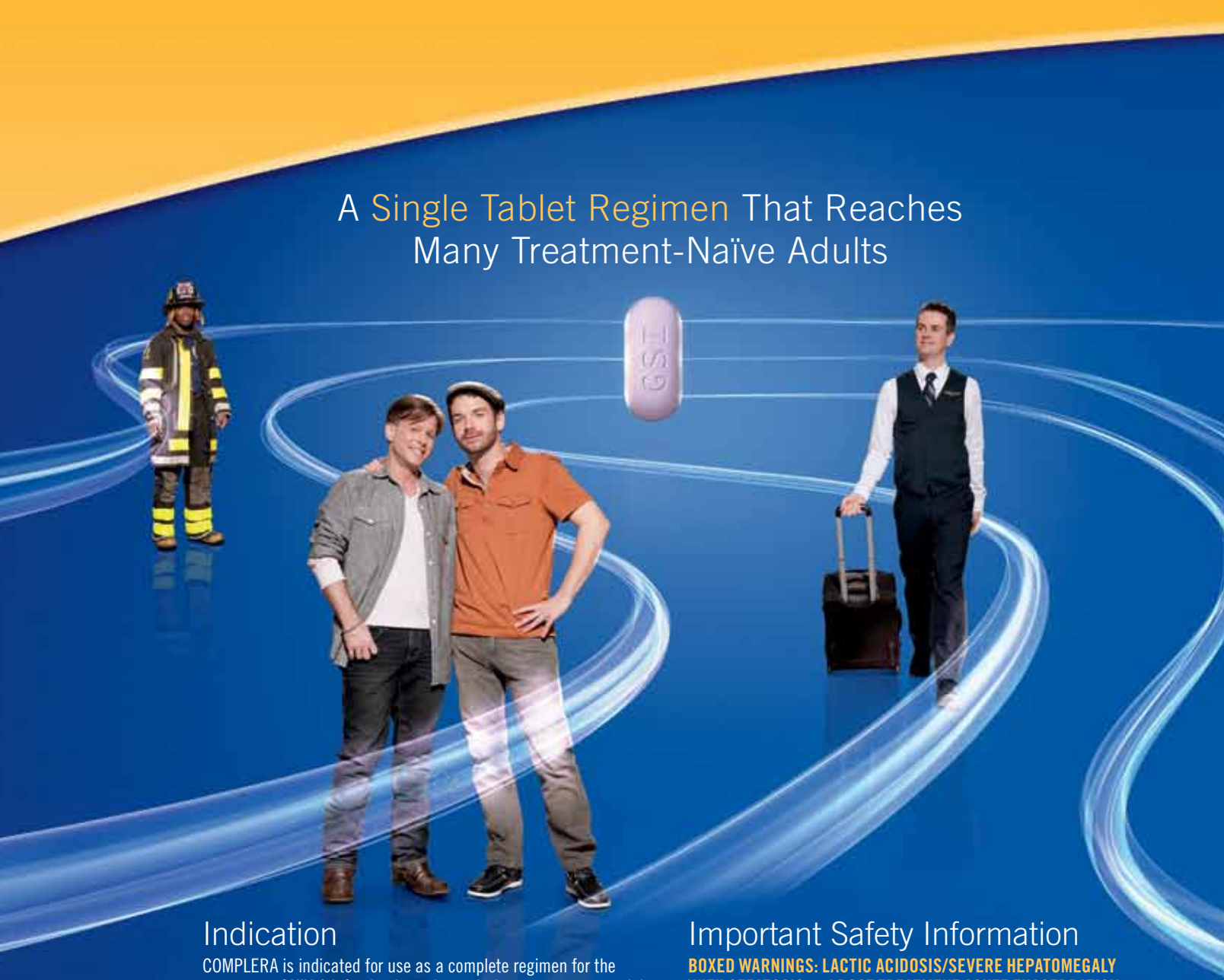
HIV Drug Benefits Increase, But Less than Expected

The percentage of HIV patients taking antiretroviral drugs who experienced the full benefit of the drugs jumped from 45 percent of 72 percent during the past decade, less than previous estimates.

The findings, considered important for HIV prevention efforts because patients whose virus is in tight control are less likely to transmit the infection to others, were published this week in the *Journal of the American Medical Association* (JAMA) by researchers from the Perelman School of Medicine at

continued on page 9

A Single Tablet Regimen That Reaches Many Treatment-Naïve Adults



Indication

COMPLERA is indicated for use as a complete regimen for the treatment of HIV-1 infection in antiretroviral treatment-naïve adults.

This indication is based on Week 48 safety and efficacy analyses from 2 randomized, double-blind, active controlled, Phase 3 trials in treatment-naïve subjects comparing rilpivirine to efavirenz.

The following points should be considered when initiating therapy with COMPLERA:

- More rilpivirine-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure compared to subjects with HIV-1 RNA less than 100,000 copies/mL at the start of therapy
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz
- More subjects treated with rilpivirine developed lamivudine/emtricitabine associated resistance compared to efavirenz

COMPLERA is not recommended for patients less than 18 years of age.

Please see additional Important Safety Information for COMPLERA on following pages.

Patient models. Pill shown is not actual size.

GILEAD

Important Safety Information

BOXED WARNINGS: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of COMPLERA, in combination with other antiretrovirals**
- **COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued EMTRIVA® (emtricitabine) or VIREAD® (tenofovir disoproxil fumarate), which are components of COMPLERA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted**

References: 1. Molina J-M, Cahn P, Grinsztejn B, et al; for ECHO Study Group. Rilpivirine versus efavirenz with tenofovir and emtricitabine in treatment-naive adults infected with HIV-1 (ECHO): a phase 3 randomised double-blind active-controlled trial. *Lancet.* 2011;378(9787):238-246. **2.** Cohen CJ, Andrade-Villanueva J, Clotet B, et al; for THRIVE Study Group. Rilpivirine versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (THRIVE): a phase 3, randomised, non-inferiority trial. *Lancet.* 2011;378(9787):229-237.

Put These Benefits Within Reach for Your Patients

Proven viral suppression through 48 weeks (HIV-1 RNA <50 copies/mL)[1,2]*

- Proven non-inferior viral suppression to efavirenz: 83% with rilpivirine + emtricitabine/tenofovir disoproxil fumarate (N=550) versus 81% with efavirenz + emtricitabine/tenofovir disoproxil fumarate (N=546)[1,2]
- Incidence of virologic failure: 13% with rilpivirine + emtricitabine/tenofovir disoproxil fumarate (N=550) versus 8% with efavirenz + emtricitabine/tenofovir disoproxil fumarate (N=546)
- More rilpivirine-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure compared to subjects with HIV-1 RNA less than 100,000 copies/mL at the start of therapy
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz
- More subjects treated with rilpivirine developed lamivudine/emtricitabine associated resistance compared to efavirenz

Demonstrated safety through 48 weeks

- The most common adverse drug reactions (Grades 2-4, ≥2%) were insomnia and headache
- Low rate of discontinuation due to adverse reactions (2% with rilpivirine + emtricitabine/tenofovir disoproxil fumarate versus 5% with efavirenz + emtricitabine/tenofovir disoproxil fumarate)
- Smaller mean changes in fasting lipid levels (rilpivirine + emtricitabine/tenofovir disoproxil fumarate versus efavirenz + emtricitabine/tenofovir disoproxil fumarate)
  - Total cholesterol (0 mg/dL versus 25 mg/dL), HDL cholesterol (3 mg/dL versus 9 mg/dL), LDL cholesterol (–2 mg/dL versus 13 mg/dL), triglycerides (–11 mg/dL versus 8 mg/dL)

Additional information: Pregnancy Category B

- There are no adequate and well-controlled studies in pregnant women
- COMPLERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus
- To monitor fetal outcomes of pregnant women exposed to COMPLERA, an Antiretroviral Pregnancy Registry has been established and healthcare providers are encouraged to register patients by calling 1-800-258-4263

A complete once-daily, single tablet regimen

- The recommended dose of COMPLERA is one tablet taken orally once daily with a meal
- Because COMPLERA is a fixed-dose combination, it should not be prescribed for patients requiring dose adjustment such as those with moderate or severe renal impairment (creatinine clearance below 50 mL/min)

Safety and efficacy have not been established in patients less than 18 years old.

Scan this QR code to go directly to

complera.com/hcp

*Study designs: The efficacy of COMPLERA is based on the analyses of 48-week data from 2 randomized, double-blind, controlled studies C209 (ECHO) and C215 (THRIVE) in treatment-naïve, HIV-1–infected subjects (N=1368). The studies were identical in design with the exception of the BR. Subjects were randomized in a 1:1 ratio to receive either rilpivirine 25 mg (N=686) once daily or efavirenz 600 mg (N=682) once daily in addition to a BR. In the ECHO study (N=690), the BR was emtricitabine/tenofovir disoproxil fumarate. In the THRIVE study (N=678), the BR consisted of 2 NRTIs: emtricitabine/tenofovir disoproxil fumarate (60%, n=406), lamivudine/zidovudine (30%, n=204), or abacavir + lamivudine (10%, n=68). The median baseline plasma HIV-1 RNA was 5 $\log_{10}$ copies/mL (range 2-7). The primary endpoint was non-inferior viral suppression to efavirenz through 48 weeks (HIV-1 RNA <50 copies/mL).[1,2]

BR=background regimen; NNRTI=non-nucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor.

COMPLERA®
emtricitabine 200mg/rilpivirine 25mg/
tenofovir disoproxil fumarate 300mg tablets
ONE COMPLETE SINGLE TABLET

Important Safety Information for COMPLERA *(cont)*

Please see previous page for **Boxed WARNINGS** about **lactic acidosis, severe hepatomegaly with steatosis,** and **exacerbations of hepatitis B upon discontinuation of therapy**.

CONTRAINDICATIONS

COMPLERA should not be coadministered with the following drugs, as significant decreases in rilpivirine plasma concentrations may occur due to CYP3A enzyme induction or gastric pH increase, which may result in loss of virologic response and possible resistance to COMPLERA or to the class of NNRTIs

- the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- the antimycobacterials rifabutin, rifampin, rifapentine
- proton pump inhibitors, such as esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole
- the glucocorticoid systemic dexamethasone (more than a single dose)
- St. John's wort (*Hypericum perforatum*)

WARNINGS AND PRECAUTIONS

New onset or worsening renal impairment

- Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of tenofovir disoproxil fumarate. Assess creatinine clearance (CrCl) before initiating treatment with COMPLERA. Monitor CrCl and serum phosphorus in patients at risk for renal impairment, including patients who have previously experienced renal events while receiving HEPSERA® (adefovir dipivoxil). Avoid administering COMPLERA with concurrent or recent use of nephrotoxic drugs. Patients with CrCl below 50 mL per minute should not receive COMPLERA

Drug interactions

- COMPLERA should be used with caution when given with drugs that may reduce the exposure of rilpivirine
- COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes

Depressive disorders

- The adverse reaction depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) has been reported with rilpivirine. During the Phase 3 trials (N=1368), the incidence of depressive disorders (regardless of causality, severity) reported among rilpivirine (N=686) or efavirenz (N=682) was 8% and 6%, respectively. Most events were mild or moderate in severity. The incidence of Grade 3 and 4 depressive disorders (regardless of causality) was 1% for both rilpivirine and efavirenz. The incidence of discontinuation due to depressive disorders among rilpivirine or efavirenz was 1% in each arm. Suicide attempt was reported in 2 subjects in the rilpivirine arm while suicide ideation was reported in 1 subject in the rilpivirine arm and in 3 subjects in the efavirenz arm. Patients with severe depressive symptoms should seek immediate medical evaluation to assess the possibility that the symptoms are related to COMPLERA, and if so, to determine whether the risks of continued therapy outweigh the benefits

Decreases in bone mineral density

- Bone mineral density (BMD) monitoring should be considered for patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures) have been reported in association with the use of VIREAD® (tenofovir disoproxil fumarate)

Coadministration with other products

- COMPLERA should not be administered concurrently with other medicinal products containing any of the same active components, emtricitabine, rilpivirine, or tenofovir disoproxil fumarate (EMTRIVA® [emtricitabine], EDURANT™ [rilpivirine], VIREAD, TRUVADA® [emtricitabine/tenofovir disoproxil fumarate], ATRIPLA® [efavirenz/emtricitabine/tenofovir disoproxil fumarate]), with medicinal products containing lamivudine (EPIVIR® or EPIVIR-HBV® [lamivudine], EPZICOM® [abacavir sulfate/lamivudine], COMBIVIR® [zidovudine/lamivudine], TRIZIVIR® [abacavir sulfate/lamivudine/zidovudine]), or with adefovir dipivoxil (HEPSERA)

Fat redistribution

- Redistribution/accumulation of body fat has been observed in patients receiving antiretroviral therapy

Immune reconstitution syndrome

- Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including the components of COMPLERA. Further evaluation and treatment may be necessary

ADVERSE REACTIONS

- The most common adverse drug reactions to rilpivirine (incidence greater than or equal to 2%, Grades 2-4) were insomnia and headache
- The most common adverse drug reactions to emtricitabine and tenofovir disoproxil fumarate (incidence ≥10%) were diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash

DRUG INTERACTIONS

- COMPLERA should not be used with drugs where significant decreases in rilpivirine plasma concentrations may occur **(See CONTRAINDICATIONS)**
- COMPLERA is a complete regimen for the treatment of HIV-1 infection; therefore, COMPLERA should not be administered with other antiretroviral medications
- **Drugs inducing or inhibiting CYP3A enzymes**: Rilpivirine is primarily metabolized by cytochrome P450 (CYP) 3A, and drugs that induce or inhibit CYP3A may thus affect the clearance of rilpivirine. Coadministration of rilpivirine and drugs that induce CYP3A may result in decreased plasma concentrations of rilpivirine and loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs. Coadministration of rilpivirine and drugs that inhibit CYP3A may result in increased plasma concentrations of rilpivirine
- **Drugs increasing gastric pH**: Coadministration of rilpivirine with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine and loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs
- **Drugs affecting renal function**: Because emtricitabine and tenofovir are primarily eliminated by the kidneys, coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of emtricitabine, tenofovir, and/or other renally eliminated drugs. Some examples include, but are not limited to, acyclovir, adefovir dipivoxil, cidofovir, ganciclovir, valacyclovir, and valganciclovir
- **QT prolonging drugs**: There is limited information available on the potential for a pharmacodynamic interaction between rilpivirine and drugs that prolong the QTc interval of the electrocardiogram. In a study of healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the electrocardiogram. COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes

DOSAGE AND ADMINISTRATION

Adults: The recommended dose of COMPLERA is one tablet taken orally once daily with a meal.

Renal Impairment: Because COMPLERA is a fixed-dose combination, it should not be prescribed for patients requiring dose adjustment such as those with moderate or severe renal impairment (creatinine clearance below 50 mL per minute).

Please see brief summary of Full Prescribing Information for COMPLERA on following pages, including **Boxed WARNINGS** about **lactic acidosis, severe hepatomegaly with steatosis,** and **exacerbations of hepatitis B upon discontinuation of therapy**.

GILEAD

COMPLERA®
emtricitabine 200mg/rilpivirine 25mg/
tenofovir disoproxil fumarate 300mg tablets

COMPLERA® (emtricitabine 200 mg/rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg) tablets Brief Summary of full prescribing information. See full prescribing information. Rx Only.

WARNINGS: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of COMPLERA, in combination with other antiretrovirals *[See Warnings and Precautions]*.

COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued EMTRIVA or VIREAD, which are components of COMPLERA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted *[See Warnings and Precautions]*.

INDICATIONS AND USAGE

COMPLERA (emtricitabine/rilpivirine/tenofovir disoproxil fumarate) is indicated for use as a complete regimen for the treatment of HIV-1 infection in antiretroviral treatment-naive adults.

This indication is based on Week 48 safety and efficacy analyses from 2 randomized, double-blind, active controlled, Phase 3 trials in treatment-naive subjects comparing rilpivirine to efavirenz *[See Clinical Studies in Full Prescribing Information]*.

The following points should be considered when initiating therapy with COMPLERA:

- More rilpivirine-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure compared to subjects with HIV-1 RNA less than 100,000 copies/mL at the start of therapy *[See Clinical Studies in Full Prescribing Information]*.
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz *[See Microbiology in Full Prescribing Information]*.
- More subjects treated with rilpivirine developed lamivudine/emtricitabine associated resistance compared to efavirenz *[See Microbiology in Full Prescribing Information]*.

COMPLERA is not recommended for patients less than 18 years of age *[See Use in Specific Populations]*.

DOSAGE AND ADMINISTRATION

Adults: The recommended dose of COMPLERA is one tablet taken orally once daily with a meal *[See Clinical Pharmacology in Full Prescribing Information]*.

Renal Impairment: Because COMPLERA is a fixed-dose combination, it should not be prescribed for patients requiring dose adjustment such as those with moderate or severe renal impairment (creatinine clearance below 50 mL per minute).

DOSAGE FORMS AND STRENGTHS

COMPLERA is available as tablets. Each tablet contains 200 mg of emtricitabine (FTC), 27.5 mg of rilpivirine hydrochloride (equivalent to 25 mg of rilpivirine) and 300 mg of tenofovir disoproxil fumarate (TDF, equivalent to 245 mg of tenofovir disoproxil).

The tablets are purplish-pink, capsule-shaped, film-coated, debossed with "GSI" on one side and plain-faced on the other side.

CONTRAINDICATIONS

COMPLERA should not be coadministered with the following drugs, as significant decreases in rilpivirine plasma concentrations may occur due to CYP3A enzyme induction or gastric pH increase, which may result in loss of virologic response and possible resistance to COMPLERA or to the class of NNRTIs *[See Drug Interactions and Clinical Pharmacology in Full Prescribing Information]*:

- the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- the antimycobacterials rifabutin, rifampin, rifapentine
- proton pump inhibitors, such as esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole
- the glucocorticoid systemic dexamethasone (more than a single dose)
- St. John's wort (*Hypericum perforatum*)

WARNINGS AND PRECAUTIONS

Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of COMPLERA, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with COMPLERA should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Patients Coinfected with HIV-1 and HBV: It is recommended that all patients with HIV-1 be tested for the presence of chronic hepatitis B virus before initiating antiretroviral therapy. COMPLERA is not approved for the treatment of chronic HBV infection and the safety and efficacy of COMPLERA have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued emtricitabine or tenofovir disoproxil fumarate, two of the components of COMPLERA. In some patients infected with HBV and treated with EMTRIVA, the exacerbations of hepatitis B were associated with liver decompensation and liver failure. Patients who are coinfected with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

New Onset or Worsening Renal Impairment: Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of tenofovir disoproxil fumarate *[See Adverse Reactions]*.

It is recommended that creatinine clearance be calculated in all patients prior to initiating therapy and as clinically appropriate during therapy with COMPLERA. Routine monitoring of calculated creatinine clearance and serum phosphorus should be performed in patients at risk for renal impairment, including patients who have previously experienced renal events while receiving HEPSERA.

COMPLERA should be avoided with concurrent or recent use of a nephrotoxic agent.

Emtricitabine and tenofovir are principally eliminated by the kidney; however, rilpivirine is not. Since COMPLERA is a combination product and the dose of the individual components cannot be altered, patients with creatinine clearance below 50 mL per minute should not receive COMPLERA.

Drug Interactions: Caution should be given to prescribing COMPLERA with drugs that may reduce the exposure of rilpivirine *[See Contraindications, Drug Interactions, and Clinical Pharmacology in Full Prescribing Information]*.

In healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the electrocardiogram *[See Drug Interactions and Clinical Pharmacology in Full Prescribing Information]*. COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes.

Depressive Disorders: The adverse reaction depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) has been reported with rilpivirine. During the Phase 3 trials (N = 1368), the incidence of depressive disorders (regardless of causality, severity) reported among rilpivirine (N = 686) or efavirenz (N = 682) was 8% and 6%, respectively. Most events were mild or moderate in severity. The incidence of Grade 3 and 4 depressive disorders (regardless of causality) was 1% for both rilpivirine and efavirenz. The incidence of discontinuation due to depressive disorders among rilpivirine or efavirenz was 1% in each arm. Suicide attempt was reported in 2 subjects in the rilpivirine arm while suicide ideation was reported in 1 subject in the rilpivirine arm and in 3 subjects in the efavirenz arm. Patients with severe depressive symptoms should seek immediate medical evaluation to assess the possibility that the symptoms are related to COMPLERA, and if so, to determine whether the risks of continued therapy outweigh the benefits.

Decreases in Bone Mineral Density: Bone mineral density (BMD) monitoring should be considered for HIV-1 infected patients who have a history of pathologic bone fracture or are at risk for osteopenia. Although the effect of supplementation with calcium and Vitamin D was not studied, such supplementation may be beneficial for all patients. If bone abnormalities are suspected then appropriate consultation should be obtained.

Tenofovir Disoproxil Fumarate: In a 144 week study of HIV-1 infected treatment-naive adult subjects treated with tenofovir disoproxil fumarate (Study 903), decreases in BMD were seen at the lumbar spine and hip in both arms of the study. At Week 144, there was a significantly greater mean percentage decrease from baseline in BMD at the lumbar spine in subjects receiving tenofovir disoproxil fumarate + lamivudine + efavirenz (-2.2% ± 3.9) compared with subjects receiving stavudine + lamivudine + efavirenz (-1.0% ± 4.6). Changes in BMD at the hip were similar between the two treatment groups (-2.8% ± 3.5 in the tenofovir disoproxil fumarate group vs. -2.4% ± 4.5 in the stavudine group). In both groups, the majority of the reduction in BMD occurred in the first 24–48 weeks of the study and this reduction was sustained through 144 weeks. Twenty-eight percent of tenofovir disoproxil fumarate treated subjects vs. 21% of the comparator subjects lost at least 5% of BMD at the spine or 7% of BMD at the hip. Clinically relevant fractures (excluding fingers and toes) were reported in 4 subjects in the tenofovir disoproxil fumarate group and 6 subjects in the comparator group. Tenofovir disoproxil fumarate was associated with significant increases in biochemical markers of bone metabolism (serum bone-specific alkaline phosphatase, serum osteocalcin, serum C telopeptide, and urinary N telopeptide), suggesting increased bone turnover. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving tenofovir disoproxil fumarate.

The effects of tenofovir disoproxil fumarate-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. For additional information, please consult the VIREAD prescribing information.

Cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures) have been reported in association with the use of VIREAD *[See Adverse Reactions]*.

Coadministration with Other Products: COMPLERA should not be administered concurrently with other medicinal products containing any of the same active components, emtricitabine, rilpivirine, or tenofovir disoproxil fumarate (EMTRIVA, EDURANT, VIREAD, TRUVADA, ATRIPLA), with medicinal products containing lamivudine (EPIVIR, EPIVIR-HBV, EPZICOM, COMBIVIR, TRIZIVIR), or with adefovir dipivoxil (HEPSERA).

Fat Redistribution: Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are unknown. A causal relationship has not been established.

Immune Reconstitution Syndrome: Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including the components of COMPLERA. During the initial phase of combination antiretroviral treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections [such as *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia (PCP), or tuberculosis], which may necessitate further evaluation and treatment.

ADVERSE REACTIONS

The following adverse drug reactions are discussed in other sections of the labeling:

- Lactic Acidosis/Severe Hepatomegaly with Steatosis *[See Boxed Warning, Warnings and Precautions]*.
- Severe Acute Exacerbations of Hepatitis B *[See Boxed Warning, Warnings and Precautions]*.
- New Onset or Worsening Renal Impairment *[See Warnings and Precautions]*.
- Depressive Disorders *[See Warnings and Precautions]*.
- Decreases in Bone Mineral Density *[See Warnings and Precautions]*.
- Immune Reconstitution Syndrome *[See Warnings and Precautions]*.

Adverse Reactions from Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Studies C209 and C215 – Treatment-Emergent Adverse Drug Reactions: The safety assessment of rilpivirine, used in combination with other antiretroviral drugs, is based on pooled data from 1368 patients in the Phase 3 trials TMC278-C209 (ECHO) and TMC278-C215 (THRIVE) in antiretroviral treatment-naive HIV-1 infected adult patients. A total of 686 patients received rilpivirine in combination with other antiretroviral drugs as background regimen; most (N= 550) received emtricitabine + tenofovir disoproxil fumarate as background regimen. The number of subjects randomized to the control arm efavirenz was 682, of which 546 received emtricitabine + tenofovir disoproxil fumarate as background regimen *[See Clinical Studies in Full Prescribing Information]*. The median duration of exposure for subjects in either treatment arm was 56 weeks.

Adverse drug reactions (ADR) observed in patients who received rilpivirine or efavirenz plus emtricitabine + tenofovir disoproxil fumarate as background regimen are shown in Table 1. The adverse drug reactions observed in this subset of patients were generally consistent with those seen for the overall patient population participating in these studies (refer to the prescribing information for EDURANT).

The proportion of subjects who discontinued treatment with rilpivirine or efavirenz + emtricitabine/tenofovir disoproxil fumarate due to ADR, regardless of severity, was 2% and 5%, respectively. The most common ADRs leading to discontinuation were psychiatric disorders: 8 (1.5%) subjects in the rilpivirine + emtricitabine/tenofovir disoproxil fumarate arm and 12 (2.2%) subjects in the efavirenz + emtricitabine/tenofovir disoproxil fumarate arm. Rash led to discontinuation in 1 (0.2%) subjects in the rilpivirine + emtricitabine/tenofovir disoproxil fumarate arm and 10 (1.8%) subjects in the efavirenz + emtricitabine/tenofovir disoproxil fumarate arm.

Common Adverse Drug Reactions

Clinical ADRs to rilpivirine or efavirenz of at least moderate intensity (≥ Grade 2) reported in at least 2% of adult subjects are shown in Table 1.

Table 1 Selected Treatment-Emergent Adverse Reactions[a] (Grades 2–4) Reported in ≥2% of Subjects Receiving Rilpivirine or Efavirenz in Combination with Emtricitabine/Tenofovir Disoproxil Fumarate in Studies C209 and C215 (Week 48 analysis)

	Rilpivirine + FTC/TDF N=550	Efavirenz + FTC/TDF N=546
Gastrointestinal Disorder		
Nausea	1%	2%
Nervous System Disorders		
Headache	2%	2%
Dizziness	1%	7%
Psychiatric Disorders		
Depressive disorders[b]	1%	2%
Insomnia	2%	2%
Abnormal dreams	1%	3%
Skin and Subcutaneous Tissue Disorders		
Rash	1%	5%

a. Frequencies of adverse reactions are based on all treatment-emergent adverse events, assessed to be related to study drug.

b. Includes adverse drug reactions reported as depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicide ideation.

Rilpivirine: Treatment-emergent adverse drug reactions of at least moderate intensity (≥ Grade 2) that occurred in less than 2% of subjects treated with rilpivirine plus any of the allowed background regimen (N=686) in clinical studies C209 and C215 include (grouped by Body System): vomiting, diarrhea, abdominal discomfort, abdominal pain, fatigue, cholecystitis, cholelithiasis, decreased appetite, somnolence, sleep disorders, anxiety, glomerulonephritis membranous and glomerulonephritis mesangioproliferative.

Emtricitabine and Tenofovir Disoproxil Fumarate: The following adverse reactions were observed in clinical trials of emtricitabine or tenofovir disoproxil fumarate in combination with other antiretroviral agents:

The most common adverse drug reactions occurred in at least 10% of treatment-naive subjects in a phase 3 clinical trial of emtricitabine and tenofovir disoproxil fumarate in combination with another antiretroviral agent are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. In addition, adverse drug reactions that occurred in at least 5% of treatment-experienced or treatment-naive subjects receiving emtricitabine or tenofovir disoproxil fumarate with other antiretroviral agents in clinical trials include abdominal pain, dyspepsia, vomiting, fever, pain, nasopharyngitis, pneumonia, sinusitis, upper respiratory tract infection, arthralgia, back pain, myalgia, paresthesia, peripheral neuropathy (including peripheral neuritis and neuropathy), anxiety, increased cough, and rhinitis.

Skin discoloration has been reported with higher frequency among emtricitabine-treated subjects; it was manifested by hyperpigmentation on the palms and/or soles and was generally mild and asymptomatic. The mechanism and clinical significance are unknown.

Laboratory Abnormalities: The percentage of subjects treated with rilpivirine + emtricitabine/tenofovir disoproxil fumarate or efavirenz + emtricitabine/tenofovir disoproxil fumarate in studies C209 and C215 with selected treatment-emergent laboratory abnormalities (Grade 1 to 4), representing worst grade toxicity are presented in Table 2.

Table 2 Selected Laboratory Abnormalities (Grades 1-4) Reported in Subjects Who Received Rilpivirine or Efavirenz in Combination with Emtricitabine/Tenofovir Disoproxil Fumarate in Studies C209 and C215 (Week 48 Analysis)

Laboratory Parameter Abnormality, (%)	DAIDS Toxicity Range	Rilpivirine + FTC/TDF N=550	Efavirenz + FTC/TDF N=546
BIOCHEMISTRY			
Increased Creatinine			
Grade 1	≥1.1-≤1.3 x ULN[a]	5%	<1%
Grade 2	>1.3-≤1.8 x ULN	<1%	1%
Increased AST			
Grade 1	≥1.25-≤2.5 x ULN	13%	16%
Grade 2	> 2.5-≤5.0 x ULN	3%	7%
Grade 3	>5.0-≤10.0 x ULN	2%	2%
Grade 4	>10.0 x ULN	<1%	1%
Increased ALT			
Grade 1	≥1.25-≤2.5 x ULN	16%	19%
Grade 2	>2.5-≤5.0 x ULN	4%	6%
Grade 3	>5.0-≤10.0 x ULN	1%	2%
Grade 4	>10.0 x ULN	1%	1%
Increased Total Bilirubin			
Grade 1	≥1.1-≤1.5 x ULN	5%	<1%
Grade 2	>1.5-≤2.5 x ULN	2%	<1%
Grade 3	>2.5-≤5.0 x ULN	<1%	<1%
Increased Total Cholesterol (fasted)			
Grade 1	5.18-6.19 mmol/L 200-239 mg/dL	13%	29%
Grade 2	6.20-7.77 mmol/L 240-300 mg/dL	4%	15%
Grade 3	>7.77 mmol/L >300 mg/dL	<1%	2%
Increased LDL Cholesterol (fasted)			
Grade 1	3.37-4.12 mmol/L 130-159 mg/dL	11%	25%
Grade 2	4.13-4.90 mmol/L 160-190 mg/dL	5%	11%
Grade 3	>4.91 mmol/L >191 mg/dL	1%	2%
Increased Triglycerides (fasted)			
Grade 2	5.65-8.48 mmol/L 500-750 mg/dL	1%	1%
Grade 3	8.49-13.56 mmol/L 751-1,200 mg/dL	<1%	1%

N = number of subjects per treatment group

a. ULN = Upper limit of normal value.

Note: Percentages were calculated versus the number of subjects in ITT population with emtricitabine + tenofovir disoproxil fumarate as background regimen.

Emtricitabine or Tenofovir Disoproxil Fumarate: The following laboratory abnormalities have been previously reported in subjects treated with emtricitabine or tenofovir disoproxil fumarate with other antiretroviral agents in other clinical trials: Grade 3 or 4 laboratory abnormalities of increased pancreatic amylase (>2.0 x ULN), increased serum amylase (>175 U/L), increased lipase (>3.0 x ULN), increased alkaline phosphatase (>550 U/L), increased or decreased serum glucose (<40 or >250 mg/dL), increased glycosuria (≥3+), increased creatine kinase (M: >990 U/L; F: >845 U/L), decreased neutrophils (<750/mm³) and increased hematuria (>75 RBC/HPF) occurred.

Adrenal Function: In the pooled Phase 3 trials of C209 and C215, in subjects treated with rilpivirine plus any of the allowed background regimen (N=686), at Week 48, the overall mean change from baseline in basal cortisol showed a decrease of -13.1 nmol/L in the rilpivirine group, and an increase of +9.0 nmol/L in the efavirenz group. At Week 48, the mean change from baseline in ACTH-stimulated cortisol levels was lower in the rilpivirine group (+16.5 ± 6.14 nmol/L) than in the efavirenz group (+58.1 ± 6.66 nmol/L). Mean values for both basal and ACTH-stimulated cortisol values at Week 48 were within the normal range. Overall, there were no serious adverse events, deaths, or treatment discontinuations that could clearly be attributed to adrenal insufficiency. Effects on adrenal function were comparable by background N(t)RTIs.

Serum Creatinine: In the pooled Phase 3 trials of C209 and C215 trials in subjects treated with rilpivirine plus any of the allowed background regimen (N=686), increases in serum creatinine occurred within the first four weeks of treatment and remained stable through 48 weeks. A mean change of 0.09 mg/dL (range: -0.20 mg/dL to 0.62 mg/dL) was observed after 48 weeks of treatment. In subjects who entered the trial with mild or moderate renal impairment, the serum creatinine increase observed was similar to that seen in subjects with normal renal function. These changes are not considered to be clinically relevant and no subject discontinued treatment due to increases in serum creatinine. Creatinine increases were comparable by background N(t)RTIs.

Serum Lipids: Changes from baseline in total cholesterol, LDL-cholesterol and triglycerides are presented in Table 3.

Table 3 Lipid Values Reported in Subjects Receiving Rilpivirine or Efavirenz in Combination with Emtricitabine/ Tenofovir Disoproxil Fumarate in Studies C209 and C215[a]

	Pooled Data from the C209 and C215 Trials							
	Rilpivirine + FTC/TDF N=550				Efavirenz + FTC/TDF N=546			
Mean	N	Baseline Mean (mg/dL)	Week 48 Mean (mg/dL)	Week 48 Mean Change[b] (mg/dL)	N	Baseline Mean (mg/dL)	Week 48 Mean (mg/dL)	Week 48 Mean Change[b] (mg/dL)
Total Cholesterol (fasted)	460	162	162	0	438	160	185	25
HDL-cholesterol (fasted)	459	42	45	3	437	40	49	9
LDL-cholesterol (fasted)	457	97	95	-2	436	95	109	13
Triglycerides (fasted)	460	122	111	-11	438	129	138	8

N = number of subjects per treatment group

a. Excludes subjects who received lipid lowering agents during the treatment period.

b. The change from baseline is the mean of within-patient changes from baseline for patients with both baseline and Week 48 values.

Subjects Coinfected with Hepatitis B and/or Hepatitis C Virus: In patients coinfected with hepatitis B or C virus receiving rilpivirine in studies C209 and C215, the incidence of hepatic enzyme elevation was higher than in subjects receiving rilpivirine who were not coinfected. The same increase was also observed in the efavirenz arm. The pharmacokinetic exposure of rilpivirine in coinfected subjects was comparable to that in subjects without coinfection.

Postmarketing Experience

The following adverse reactions have been identified during postapproval use of emtricitabine or tenofovir disoproxil fumarate. Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Emtricitabine: No postmarketing adverse reactions have been identified for inclusion in this section.

Tenofovir Disoproxil Fumarate:

Immune System Disorders: allergic reaction, including angioedema

Metabolism and Nutrition Disorders: lactic acidosis, hypokalemia, hypophosphatemia

Respiratory, Thoracic, and Mediastinal Disorders: dyspnea

Gastrointestinal Disorders: pancreatitis, increased amylase, abdominal pain

Hepatobiliary Disorders: hepatic steatosis, hepatitis, increased liver enzymes (most commonly AST, ALT gamma GT)

Skin and Subcutaneous Tissue Disorders: rash

Musculoskeletal and Connective Tissue Disorders: rhabdomyolysis, osteomalacia (manifested as bone pain and which may contribute to fractures), muscular weakness, myopathy

Renal and Urinary Disorders: acute renal failure, renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis (including acute cases), nephrogenic diabetes insipidus, renal insufficiency, increased creatinine, proteinuria, polyuria

General Disorders and Administration Site Conditions: asthenia

The following adverse reactions, listed under the body system headings above, may occur as a consequence of proximal renal tubulopathy: rhabdomyolysis, osteomalacia, hypokalemia, muscular weakness, myopathy, hypophosphatemia.

DRUG INTERACTIONS

COMPLERA is a complete regimen for the treatment of HIV-1 infection; therefore, COMPLERA should not be administered with other antiretroviral medications. Information regarding potential drug-drug interactions with other antiretroviral medications is not provided. Please refer to the EDURANT, VIREAD and EMTRIVA prescribing information as needed.

There were no drug-drug interaction trials conducted with the fixed-dose combination tablet. Drug interaction studies were conducted with emtricitabine, rilpivirine, or tenofovir disoproxil fumarate, the components of COMPLERA. This section describes clinically relevant drug interactions with COMPLERA *[See Contraindications and Clinical Pharmacology in Full Prescribing Information]*.

Drugs Inducing or Inhibiting CYP3A Enzymes

Rilpivirine is primarily metabolized by cytochrome P450 (CYP) 3A, and drugs that induce or inhibit CYP3A may thus affect the clearance of rilpivirine *[See Clinical Pharmacology in Full Prescribing Information, Contraindications]*. Coadministration of rilpivirine and drugs that induce CYP3A may result in decreased plasma concentrations of rilpivirine and loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs. Coadministration of rilpivirine and drugs that inhibit CYP3A may result in increased plasma concentrations of rilpivirine.

Rilpivirine at a dose of 25 mg once daily is not likely to have a clinically relevant effect on the exposure of drugs metabolized by CYP enzymes.

Drugs Increasing Gastric pH

Coadministration of rilpivirine with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine and loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs *[see Table 4]*.

Drugs Affecting Renal Function

Because emtricitabine and tenofovir are primarily eliminated by the kidneys through a combination of glomerular filtration and active tubular secretion, coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of emtricitabine, tenofovir, and/or other renally eliminated drugs. Some examples of drugs that are eliminated by active tubular secretion include, but are not limited to, acyclovir, adefovir dipivoxil, cidofovir, ganciclovir, valacyclovir, and valganciclovir.

QT Prolonging Drugs

There is limited information available on the potential for a pharmacodynamic interaction between rilpivirine and drugs that prolong the QTc interval of the electrocardiogram. In a study of healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the electrocardiogram *[See Clinical Pharmacology in Full Prescribing Information]*. COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes.

Established and Other Potentially Significant Drug Interactions

Important drug interaction information for COMPLERA is summarized in Table 4. The drug interactions described are based on studies conducted with emtricitabine, rilpivirine, or tenofovir disoproxil fumarate as individual medications that may occur with COMPLERA or are potential drug interactions; no drug interaction studies have been conducted using COMPLERA (for pharmacokinetic data see *Clinical Pharmacology*, Tables 6-7 *in Full Prescribing Information]*. The tables include potentially significant interactions, but are not all inclusive.

Table 4 Established and Other Potentially Significant[a] Drug Interactions: Alteration in Dose or Regimen May Be Recommended Based on Drug Interaction Studies or Predicted Interaction

Concomitant Drug Class: Drug Name	Effect on Concentration[b]	Clinical Comment
Antacids: antacids (e.g., aluminium, magnesium hydroxide, or calcium carbonate)	↔ rilpivirine (antacids taken at least 2 hours before or at least 4 hours after rilpivirine) ↓ rilpivirine (concomitant intake)	The combination of COMPLERA and antacids should be used with caution as coadministration may cause significant decreases in rilpivirine plasma concentrations (increase in gastric pH). Antacids should only be administered either at least 2 hours before or at least 4 hours after COMPLERA.
Azole Antifungal Agents: fluconazole itraconazole ketoconazole posaconazole voriconazole	↑ rilpivirine[c,d] ↓ ketoconazole[c,d]	Concomitant use of COMPLERA with azole antifungal agents may cause an increase in the plasma concentrations of rilpivirine (inhibition of CYP3A enzymes). No dose adjustment is required when COMPLERA is coadministered with azole antifungal agents. Clinically monitor for breakthrough fungal infections when azole antifungals are coadministered with COMPLERA.
H_2-Receptor Antagonists: cimetidine famotidine nizatidine ranitidine	↔ rilpivirine[c,d] (famotidine taken 12 hours before rilpivirine or 4 hours after rilpivirine) ↓ rilpivirine[c,d] (famotidine taken 2 hours before rilpivirine)	The combination of COMPLERA and H_2-receptor antagonists should be used with caution as coadministration may cause significant decreases in rilpivirine plasma concentrations (increase in gastric pH). H_2-receptor antagonists should only be administered at least 12 hours before or at least 4 hours after COMPLERA.
Macrolide antibiotics: clarithromycin erythromycin troleandomycin	↑rilpivirine ↔ clarithromycin ↔ erythromycin ↔ troleandomycin	Concomitant use of COMPLERA with clarithromycin, erythromycin and troleandomycin may cause an increase in the plasma concentrations of rilpivirine (inhibition of CYP3A enzymes). Where possible, alternatives such as azithromycin should be considered.
Narcotic Analgesics: methadone	↓ R(−) methadone[c] ↓ S(+) methadone[c] ↔ rilpivirine[c] ↔ methadone[c] (when used with tenofovir)	No dose adjustments are required when initiating coadministration of methadone with COMPLERA. However, clinical monitoring is recommended as methadone maintenance therapy may need to be adjusted in some patients.

a. This table is not all inclusive.

b. Increase = ↑; Decrease = ↓; No Effect = ↔

c. The interaction was evaluated in a clinical study. All other drug-drug interactions shown are predicted.

d. This interaction study has been performed with a dose higher than the recommended dose for rilpivirine. The dosing recommendation is applicable to the recommended dose of rilpivirine 25 mg once daily.

Drugs with No Observed or Predicted Interactions with COMPLERA

No clinically significant drug interactions have been observed between emtricitabine and famciclovir or tenofovir disoproxil fumarate. Similarly, no clinically significant drug interactions have been observed between tenofovir disoproxil fumarate and entecavir, methadone, oral contraceptives, ribavirin, or tacrolimus in studies conducted in healthy subjects.

No clinically significant drug interactions have been observed between rilpivirine and acetaminophen, atorvastatin, chlorzoxazone, ethinylestradiol, norethindrone, sildenafil, and tenofovir disoproxil fumarate. No clinically relevant drug-drug interaction is expected when rilpivirine is coadministered with ribavirin.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B

Emtricitabine: The incidence of fetal variations and malformations was not increased in embryofetal toxicity studies performed with emtricitabine in mice at exposures (AUC) approximately 60 times higher and in rabbits at approximately 120 times higher than human exposures at the recommended daily dose.

Rilpivirine: Studies in animals have shown no evidence of embryonic or fetal toxicity or an effect on reproductive function. In offspring from rat and rabbit dams treated with rilpivirine during pregnancy and lactation, there were no toxicologically significant effects on developmental endpoints. The exposures at the embryo-fetal No Observed Adverse Effects Levels in rats and rabbits were respectively 15 and 70 times higher than the exposure in humans at the recommended dose of 25 mg once daily.

Tenofovir Disoproxil Fumarate: Reproduction studies have been performed in rats and rabbits at doses up to 14 and 19 times the human dose based on body surface area comparisons and revealed no evidence of impaired fertility or harm to the fetus due to tenofovir.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, COMPLERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Antiretroviral Pregnancy Registry: To monitor fetal outcomes of pregnant women exposed to COMPLERA, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263.

Nursing Mothers

The Centers for Disease Control and Prevention recommend that HIV infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Studies in rats have demonstrated that tenofovir is secreted in milk. Studies in lactating rats and their offspring indicate that rilpivirine was present in rat milk. It is not known whether emtricitabine, rilpivirine, or tenofovir is excreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions in nursing infants, **mothers should be instructed not to breastfeed if they are receiving COMPLERA.**

Pediatric Use

COMPLERA is not recommended for patients less than 18 years of age because not all the individual components of the COMPLERA have safety, efficacy and dosing recommendations available for all pediatric age groups *[See Clinical Pharmacology in Full Prescribing Information]*.

Geriatric Use

Clinical studies of emtricitabine, rilpivirine, or tenofovir disoproxil fumarate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patients should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy *[See Clinical Pharmacology in Full Prescribing Information]*.

Renal Impairment

Because COMPLERA is a fixed-dose combination, it should not be prescribed for patients requiring dosage adjustment such as those with moderate, severe or end stage renal impairment (creatinine clearance below 50 mL per minute) or that require dialysis *[See Warnings and Precautions, Clinical Pharmacology in Full Prescribing Information]*.

Hepatic Impairment

No dose adjustment of COMPLERA is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. COMPLERA has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) *[See Clinical Pharmacology in Full Prescribing Information]*.

OVERDOSAGE

If overdose occurs the patient must be monitored for evidence of toxicity. Treatment of overdose with COMPLERA consists of general supportive measures including monitoring of vital signs and ECG (QT interval) as well as observation of the clinical status of the patient.

Emtricitabine: Limited clinical experience is available at doses higher than the therapeutic dose of EMTRIVA. In one clinical pharmacology study, single doses of emtricitabine 1200 mg were administered to 11 subjects. No severe adverse reactions were reported. The effects of higher doses are not known.

Hemodialysis treatment removes approximately 30% of the emtricitabine dose over a 3-hour dialysis period starting within 1.5 hours of emtricitabine dosing (blood flow rate of 400 mL per minute and a dialysate flow rate of 600 mL per minute). It is not known whether emtricitabine can be removed by peritoneal dialysis.

Rilpivirine: There is no specific antidote for overdose with rilpivirine. Human experience of overdose with rilpivirine is limited. Since rilpivirine is highly bound to plasma protein, dialysis is unlikely to result in significant removal of rilpivirine.

If indicated, elimination of unabsorbed active substance may be achieved by gastric lavage. Administration of activated charcoal may also be used to aid in removal of unabsorbed active substance.

Tenofovir Disoproxil Fumarate: Limited clinical experience at doses higher than the therapeutic dose of VIREAD 300 mg is available. In one study, 600 mg tenofovir disoproxil fumarate was administered to 8 subjects orally for 28 days, and no severe adverse reactions were reported. The effects of higher doses are not known.

Tenofovir is efficiently removed by hemodialysis with an extraction coefficient of approximately 54%. Following a single 300 mg dose of VIREAD, a four-hour hemodialysis session removed approximately 10% of the administered tenofovir dose.

PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (Patient Information)

A statement to patients and healthcare providers is included on the product's bottle label: **ALERT: Find out about medicines that should NOT be taken with COMPLERA from your healthcare provider.** A Patient Package Insert for COMPLERA is available for patient information.

Information for Patients

Patients should be advised that:

- Patients should remain under the care of a healthcare provider when using COMPLERA.
- Patients should be informed that COMPLERA is not a cure for HIV infection. Patients should stay on continuous HIV therapy to control HIV infection and decrease HIV-related illnesses. Patients should be told that sustained decreases in plasma HIV RNA have been associated with a reduced risk of progression to AIDS and death.
- Patients should be advised to continue to practice safer sex and to use latex or polyurethane condoms to lower the chance of sexual contact with any body fluids such as semen, vaginal secretions or blood. Patients should be advised never to re-use or share needles.
- It is important to take COMPLERA on a regular dosing schedule with a meal and to avoid missing doses. A protein drink does not constitute a meal. If the patient misses a dose of COMPLERA within 12 hours of the time it is usually taken, the patient should take COMPLERA with a meal as soon as possible and then take the next dose of COMPLERA at the regularly scheduled time. If a patient misses a dose of COMPLERA by more than 12 hours, the patient should not take the missed dose, but resume the usual dosing schedule. Inform the patient that he or she should not take more or less than the prescribed dose of COMPLERA at any one time.
- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported. Treatment with COMPLERA should be suspended in any patients who develop clinical symptoms suggestive of lactic acidosis or pronounced hepatotoxicity (including nausea, vomiting, unusual or unexpected stomach discomfort, and weakness) *[See Warnings and Precautions]*.
- Patients with HIV-1 should be tested for hepatitis B virus (HBV) before initiating antiretroviral therapy. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued EMTRIVA or VIREAD *[See Warnings and Precautions]*. COMPLERA should not be discontinued without first informing their healthcare provider.
- Renal impairment, including cases of acute renal failure and Fanconi syndrome, has been reported in association with the use of VIREAD. COMPLERA should be avoided with concurrent or recent use of a nephrotoxic agent *[See Warnings and Precautions]*.
- COMPLERA may interact with many drugs; therefore, patients should be advised to report to their healthcare provider the use of any other prescription or nonprescription medication or herbal products, including St. John's wort *[See Warnings and Precautions]*.
- COMPLERA should not be coadministered with the following drugs, as significant decreases in rilpivirine plasma concentrations may occur due to CYP3A enzyme induction or gastric pH increase, which may result in loss of virologic response and possible resistance to COMPLERA or to the class of NNRTIs: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, phenytoin; the antimycobacterials rifabutin, rifampin, rifapentine; proton pump inhibitors, such as esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole; the glucocorticoid systemic dexamethasone (more than a single dose); or St. John's wort (*Hypericum perforatum*) *[See Contraindications]*.
- Patients should be informed that depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) have been reported with COMPLERA. If they experience depressive symptoms, they should seek immediate medical evaluation *[See Warnings and Precautions]*.
- Decreases in bone mineral density have been observed with the use of VIREAD. Bone monitoring should be considered in patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss *[See Warnings and Precautions]*.
- COMPLERA should not be coadministered with ATRIPLA, TRUVADA, EMTRIVA, VIREAD or EDURANT; or with drugs containing lamivudine, including COMBIVIR, EPIVIR or EPIVIR-HBV, EPZICOM, or TRIZIVIR; or with HEPSERA *[See Warnings and Precautions]*.
- Redistribution or accumulation of body fat may occur in patients receiving antiretroviral therapy and that the cause and long-term health effects of these conditions are not known *[See Warnings and Precautions]*.
- In some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. Patients should be advised to inform their healthcare provider immediately of any symptoms of infection *[See Warnings and Precautions]*.

GILEAD

continued from page 3

the University of Pennsylvania and Johns Hopkins University School of Medicine.

The researchers analyzed 32,483 HIV-infected patients cared for in 12 clinics across the United States between 2001 and 2010. During that time, the percentage of patients taking antiretroviral drugs who exhibited sustained viral suppression—having no detectable HIV virus in the blood every time the virus is measured—increased from 45 percent to 72 percent.

Despite this increase, the number of patients with tightly controlled HIV infection was significantly less than the 77 percent to 87 percent figures reported in prior studies, which were based on one-time only measures of HIV virus in the blood, rather than considering every time the virus was measured.

Merck Insentress Study Reveals Positive Results

Merck has announced final results from the STARTMRK study—the longest double-blind Phase III non-inferiority study evaluating an integrase inhibitor in treatment-naïve adults with HIV-1.

In this pre-specified exploratory analysis of Insentress® (raltegravir) 400 mg film-coated tablets in combination therapy in previously untreated adult HIV-1 patients, virologic efficacy was better than the efavirenz-based regimen at 240 weeks. At all pre-specified time points, the regimen containing Insentress had fewer drug-related adverse events versus the comparator. The 240-week analysis showed that the regimen containing Insentress demonstrated long-term viral suppression and a greater immunologic response, as well as a proven safety and tolerability profile.

Insentress is an integrase inhibitor indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adults. This indication is based on analyses of plasma HIV-1 RNA levels in three double-blind controlled studies of Insentress. Two of these studies were conducted in clinically advanced, three-class ARV [non-nucleoside reverse transcriptase inhibitor (NNRTI), nucleoside reverse transcriptase inhibitor (NRTI), protease inhibitor (PI)] treatment-experienced adult patients through 96 weeks and one was conducted in treatment-naïve adults through 156 weeks.

The use of other active agents with Insentress is associated with a greater likelihood of treatment response. Severe, potentially life-threatening and fatal skin reactions have been reported with Insentress (raltegravir). Additionally, during the initial phase of treatment, immune reconstitution syndrome may occur.

Despite Treatment, HIV Boosts HCV Liver Risks

People with both HIV and hepatitis C (HCV) are at increased risk for hepatic decompensation, despite effective antiretroviral therapy, compared with people who have only the liver disease, according to Vincent Lo Re, MD, of the University of Pennsylvania in Philadelphia.

In a large retrospective cohort, those with both viruses had a 6.3 percent rate of decompensation compared with 5 percent for those with just HCV (HR 1.83, 95 percent CI 1.54 to 2.18, P=0.004).

Their risk of liver cancer and death was also markedly higher, according to the study. Fibrosis, anemia, and race all were factors that affected the risk of decompensation among those with both viruses.

The findings come from an analysis of outcomes for more than 10,000 patients in the Veterans Aging Cohort Study, including 4,280 with both viruses and 6,079 with just HCV, Lo Re said.

All patients in the cohort had HCV viremia but had not been treated for the virus. Those with both viruses were newly on HIV therapy but had been on combination treatment for at least a year.

The National Institute of Allergy and Infectious Diseases supported the study.

Low-Dose Aspirin Helps Cut ART Cardiovascular Risk

Low-dose aspirin shows efficacy in attenuating platelet activation among adults with HIV, according to a study from the New York University Medical School, New York, NY.

While the specific causes of the increased cardiovascular risk with HIV are unclear, one theory is that heightened inflammation helps to promote a prothrombotic state, said Meagan O'Brien, MD, and colleagues.

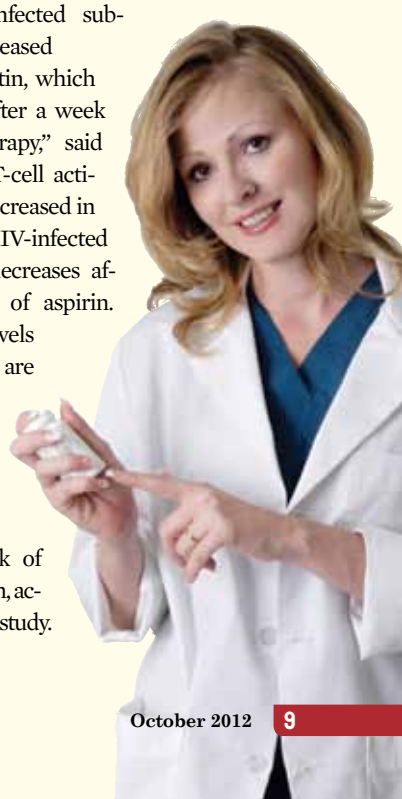
"Activated platelets have been implicated in thrombotic cardiovascular events in HIV-infected patients because of their proinflammatory and thrombogenic effects," the authors said. "HIV-infected patients have increased circulating platelet-monocyte complexes and their platelets express high levels of P-selectin."

With aspirin known as a low-risk and low-cost platelet inhibitor boasting immunomodulatory properties, Dr. O'Brien and colleagues evaluated platelet aggregation in 25 patients with HIV and compared them with 29 healthy HIV-negative controls.

HIV-positive patients showed increased platelet aggregation in response to submaximal adenosine diphosphate (ADP, 0.4µM), compared with controls: (10.8 percent vs. 7.6 percent; P=.02); AA (54.9 percent vs. 11 percent; P<.05), and without agonist (SPA) 7.5 percent vs. 5 percent; P<.05). After one week of aspirin 81 mg daily, however, the percentage of aggregation in response to ADP and AA decreased significantly (P<.01 for each comparison). In comparison with controls, patients with HIV who are on ART showed increased HLA-DR + CD38 + CD4 + T cells (8.3 percent vs. 3.9 percent; P=.01) and percent HLA-DR + CD38 + CD8 + T cells (0.46 percent vs. 0.21 percent; P=.01).

The patients with HIV also showed a significant decrease in HLA-DR + CD38 + CD4 + T cells following aspirin therapy (P<.01), and a trend in decreased HLA-DR + CD38 + CD8 + T cells (P=.08), in HIV patients, while no significant change was noted in controls.

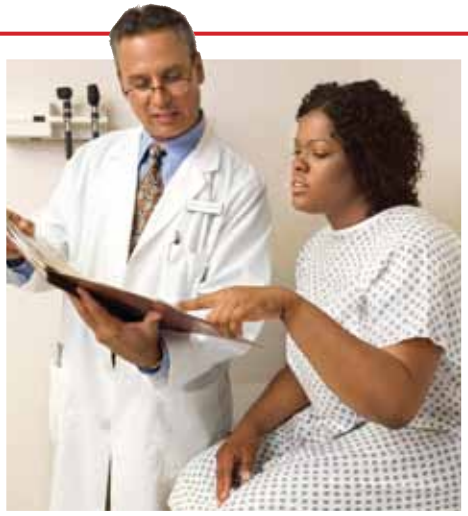
The study showed that "ART-treated HIV-infected subjects have increased soluble P-selectin, which is decreased after a week of aspirin therapy," said Dr. O'Brien. T-cell activation also is increased in ART-treated HIV-infected patients and decreases after one week of aspirin. Meanwhile, levels of CD4, which are elevated in ART-treated, HIV-infected subjects, are decreased after one week of low-dose aspirin, according to the study.



THINKSTOCK, ISTOCK

IN THE NEWS

Study Suggests Combining Pap Smears with HPV Testing



A NEW STUDY PUBLISHED in the July 25 issue of the *Journal of the American Medical Association* (JAMA) suggests that combining standard Pap smears with testing for human papillomavirus (HPV) may allow women living with HIV to reduce the frequency of cervical cancer screening and unnecessary biopsies.

Marla Keller, MD

"This study found similar risk of cervical precancer and cancer in HIV-infected women and HIV-uninfected women with normal [Pap smears] and a negative test [for cancer-causing HPV strains] at enrollment," concluded Marla Keller, MD, of Albert Einstein College of Medicine in the Bronx, New York, and her colleagues. "Specifically, through five years of follow-up, we observed no meaningful differences in the cumulative incidence of [precancerous lesions] between HIV-uninfected women and HIV-infected women, regardless of CD4 cell count in this cohort."

Keller and her colleagues reasoned that for women with normal cervical cells and no evidence of cervical HPV infection, the risk of cervical precancer or cancer is likely to be very low for several years regardless of HIV status, thereby reducing the burden of frequent Pap smears and, by extension, unnecessary biopsies.

The results of this study suggest that HIV-infected women undergoing long-term clinical follow-up who have normal Pap smears and are negative for HPV have a risk of cervical precancer similar to that in HIV-uninfected women through five years of follow-up, the authors said.

Green Tea, Chocolate, Red Wine May Ease HIV Neuro Problems

New research from Johns Hopkins University has discovered that a group of plant polyphenols known as catechins, which naturally occur in green tea and the seed of the cacao tree, may help in the prevention of neurological complications. The study is published online in Springer's *Journal of NeuroVirology*.

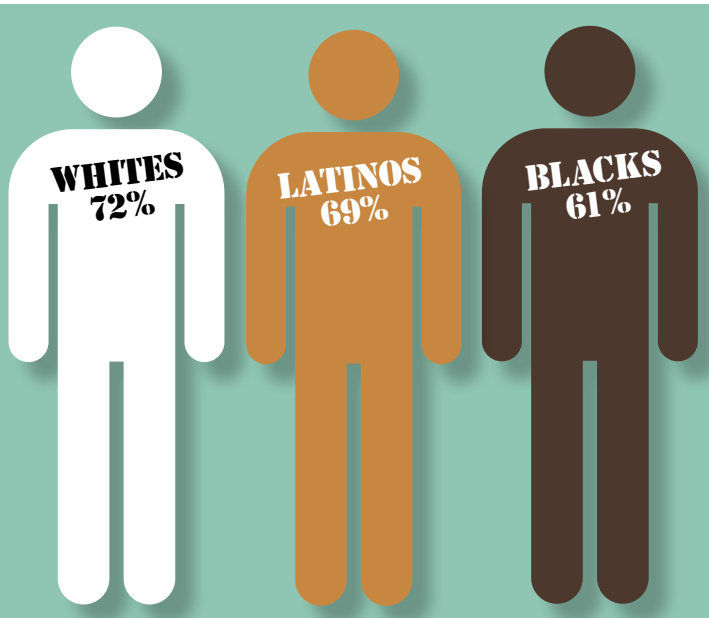
Previous research has established the critical role of a protein called brain-derived neurotrophic factor (BDNF) in supporting the survival and growth of neurons in the brain. This protein is active in areas of the brain vital to learning, memory and higher thinking. Patients with HIV have been found to have lower levels of BDNF in their brains than healthy individuals suggesting that this could be directly responsible for the cognitive impairment suffered.

In their research, Joseph Steiner and colleagues analyzed the effects of 2000 compounds, identified a series of compounds, which had the potential to help protect neurons in the brain. Nine of these were related to epicatechin, which is found in cocoa and green tea leaves. Further screening and comparison with resveratrol, the antioxidant found in red wine, specifically identified epicatechin and epigallocatechin gallate (EGCG) as being the most effective at helping protect neurons by inducing production of BDNF.

The authors conclude: "Due to its simpler structure and more efficient blood-brain barrier penetration properties, epicatechin might be the best therapeutic candidate for neurodegenerative diseases. These include HIV-associated cognitive disorders where oxidative stress is an important pathophysiological mechanism." Further research in patients with HIV is required to elucidate just how effective these naturally occurring compounds could be, the authors said.

THINKSTOCK, BONOTOM STUDIO

Racial Disparities in ART Adherence Remains Major Issue in U.S.



Blacks living with HIV in the United States are 40 percent less likely to maintain 100 percent adherence to their antiretroviral regimens compared with white HIV-positive people and have an average adherence rate that is 11 percent lower than whites, according to an analysis of 13 studies involving more than 1,800 participants.

According to the paper published in the August 15 issue of the *Journal of Acquired Immune Deficiency Syndromes* (JAIDS), average adherence rates were 72 percent among whites, 61 percent among blacks and 69 percent among Latinos. Most patients studied were using twice-daily regimens

Lead author Jane Simoni, PhD, of the University of Washington in Seattle and her colleagues could not explain the disparities, but suggested that experiences of racial discrimination, conspiracy beliefs and poor health literacy among many blacks with HIV may contribute to poor adherence.

CDC Issues New Guidelines for Gonorrhea Prevention

THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) no longer recommends the oral antibiotic cefixime as a first-line treatment option for gonorrhea because of the possibility that the bacteria which causes gonorrhea is becoming resistant to the drug. The change was prompted by trends in laboratory data showing that cefixime, marketed under the brand name Suprax, is becoming less effective in treating the sexually transmitted disease.

According to the revised guidelines, published Aug. 9 in CDC's *Morbidity and Mortality Weekly Report*, the most effective treatment for gonorrhea is a combination therapy: the injectable antibiotic ceftriaxone along with one of two other oral antibiotics, either azithromycin or doxycycline.

In the past, gonorrhea has developed resistance to every antibiotic recommended for treatment, leaving the cephalosporins, which include cefixime and ceftriaxone, as the final recommended class of drugs. In light of this history and the recent lab data, CDC researchers are concerned that continued use of cefixime may prompt gonorrhea to develop resistance to all cephalosporins. Limiting the use of cefixime now may help preserve ceftriaxone as a treatment option for a little longer.

"As cefixime is losing its effectiveness as a treatment for gonorrhea infections, this change is a critical pre-emptive strike to preserve ceftriaxone, our last proven treatment option," said Kevin Fenton, MD, director of the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention. "Changing how we treat infections now may buy the time needed to develop new treatment options."

To guard against the threat of drug resistance, the guidelines outline additional follow-up steps providers should take to closely monitor for ceftriaxone treatment failure. According to the new recommendations, patients who have persistent symptoms should be retested with a culture-based gonorrhea test, which can identify antibiotic-resistant infections. The patient should return one week after re-treatment for another culture test – called a test-of-cure – to ensure the infection is fully cured.

In some instances, cefixime may be needed as an alternative treatment option, CDC said in its revised guidelines, noting that if ceftriaxone is not readily available, providers may prescribe a dual therapy of cefixime plus either azithromycin or doxycycline. Azithromycin may be given alone if a patient has a severe allergy to cephalosporins. However, to closely monitor for resistance, if either of these alternative regimens is prescribed, providers should perform a test-of-cure one week after treatment.

These revised guidelines are one aspect of CDC's response to the threat of untreatable gonorrhea. CDC also published a public health response plan, offering guidance on steps state and local health departments can take to keep a watchful eye on the emergence of drug resistance. In addition to closely monitoring for resistance nationally, CDC is working with the World Health Organization to monitor for emerging resistance on the global level, and the agency is also collaborating with the National Institutes of Health to test new combinations of existing drugs.

Gail Bolan, MD, director of CDC's Division of STD Prevention, says that additional measures will be needed to stay ahead of untreatable gonorrhea.

"It is imperative that researchers and pharmaceutical companies prioritize research to identify or develop new, effective drugs or drug combinations," Bolan said. "Health departments and labs can help CDC monitor for emerging resistance by enhancing or re-building their ability to do culture testing."

Gonorrhea is one of the most common STDs in the United States with more than 700,000 infections estimated to occur each year.

FDA Approves Home HIV Test Kit

Pharmacists need to provide guidance to patients

ON JULY 3 2012, the Food & Drug Administration (FDA) approved the first over-the-counter HIV-1 and HIV-2 home test kit, OraQuick. This is a self-administered test and pharmacists need to be completely familiar so they can provide sound advice to patients who come to them with their questions.

OraQuick reports the results within minutes, unlike the previously available home HIV test by Home Access Health® where people mailed in the samples on a swab and received their results over the phone.

Individuals will collect a sample of the oral fluid simply by swabbing the upper and lower gums, followed by placing it in the developer vial and reading their results within 20 to 40 minutes. This test will detect HIV antibodies to HIV-1 and HIV-2; however, to rule-out false positive, the positive results will need further confirmation by a healthcare provider.

On the other hand, patients with negative results will have to take the "Window Period" into consideration in a case of a recent exposure within 3 months.

CDC estimates that approximately 21 percent of the 1.2 million people living with HIV/AIDS in the United States are not aware of their diagnosis and consequently are responsible for transmission of over 50 percent of the 50,000 new infections annually. This test provides another tool that will identify those individuals and serve as a positive step towards preventing further transmission. Obviously, knowing one's status is imperative in the prevention efforts.

Since this test will be sold over-the -counter in retail pharmacies, it is crucial for the pharmacists to feel comfortable in providing education to the individual who will be utilizing the test. Pharmacists should familiarize themselves with the sensitivity and specificity of this test. OraQuick In-Home HIV Test offers a 92 percent sensitivity, defined

Quad Approval: What Does it Mean for HIV?

BY PAUL SAX, MD

AS OF LATE AUGUST 2012, THE FOOD AND DRUG ADMINISTRATION (FDA) approved Gilead's Stribild, a single-pill regimen available for HIV treatment, co-formulated tenofovir/emtricitabine/elvitegravir/cobicistat. The approval process began in late 2011 and has since been an eagerly awaited decision by the HIV community.

For HIV practitioners, the approval has provided yet another option for treatment. As an HIV care provider, let me share my thoughts about this approval, with the disclosure that I was an investigator on one of the phase III studies that led to its approval:

- The combination, which I'll continue to call "Quad" (at least for now), is just as active virologically as two preferred initial regimens: TDF/FTC/EFV (the first of the single pill treatments), and TDF/FTC + atazanavir/r (the most commonly used boosted PI regimen).
- The side effect profile was different from TDF/FTC/EFV, with less CNS disturbance and rash, and more nausea. The side effects were quite similar to the boosted ATV/r regimen, except for hyperbilirubinemia from atazanavir, of course, possibly because cobicistat and ritonavir are related.
- The renal issues with cobicistat are potentially tricky, as it causes a 0.1-0.2 mg/dL increase in creatinine that is re lated to inhibition of tubular secretion of creatinine, and hence does not actually decrease GFR. As a result, the regimen should not be used in patients with impaired renal function, and they were not studied in the Quad trials.
- One potentially helpful number to remember is 0.4, as the small number of patients with tenofovir tubular toxicity in the Quad studies also had an increase in serum creatinine of at least this much -- hence distinguishing them from the more benign smaller increase from cobicistat.
- Separate studies of Quad in patients with renal insufficiency and in women are planned. (Only a small proportion of study patients were women).

The bottom line is that Quad is an effective, very convenient option for initial HIV treatment. I suspect how much traction it gets from providers will depend on their experience in clinical practice related to safety and tolerability, and in the future to pharmacoeconomic factors, as generic antiretroviral strategies will become increasingly available that might challenge use of coformulated regimens. (This article originally appeared as blog entry on *www.thebodypro.com*).

ROLLINGOUT.COM, THINKSTOCK, BONOTOM STUDIO

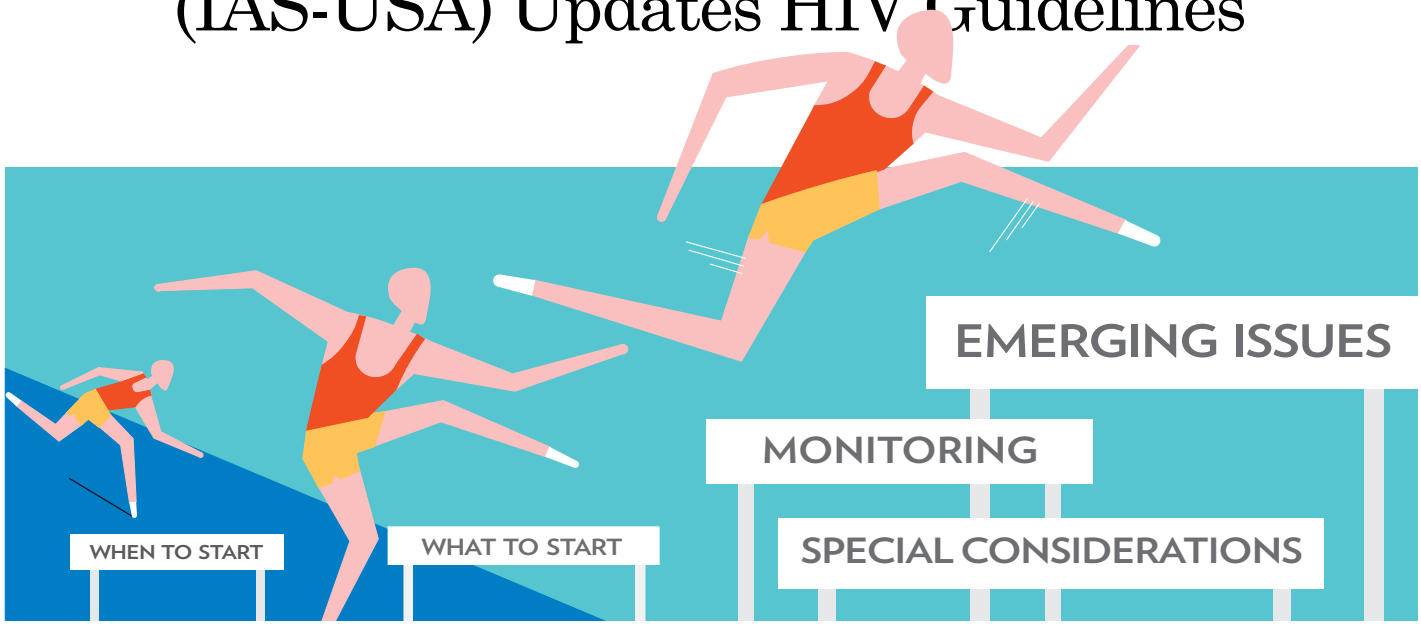
as the percentage of results that will be positive when HIV antibodies are present. This will result in one false-negative result out of every 12 tests performed in HIV-infected individuals. Thus, we need to remind the individual regarding the "window period" and encourage a re-test within 3 months.

The OraQuick In-Home HIV Test offers a 99.98 percent test specificity, which means the test is negative when HIV antibodies are not present. This will lead to one false-positive result out of every 5,000 tests in HIV uninfected individuals. The manufacturer of the OraQuick is offering a consumer support center, available 24/7 via phone to provide general information on HIV/AIDS, assist with the proper administration of the test and interpretation of the results.

Retail pharmacists will be approached by their customers seeking guidance with this test. Pharmacists' role, as a member of the healthcare team, can become central in providing education on re-testing, incubation period (window period), post-exposure prophylaxis, pre-exposure prophylaxis, safe sex practices, and linkage to care. HIV

ABOUT THE AUTHOR:
Sami Shafiq PharmD, CPH, AAHIVE, is Lead HIV/AIDS Clinical Pharmacist, Miami Dade County, Walgreens Pharmacy. She is also a mentor and preceptor for the PharmD candidates from Nova Southeastern University, Palm Beach Atlantic University and Howard University. She has been a member of the AAHIVM Steering Committee for the Florida Chapter since 2009.

International Antiviral Society-USA Panel (IAS-USA) Updates HIV Guidelines



AS THEY HAVE DONE SINCE 1996, the International Antiviral (formerly AIDS) Society-USA (IAS-USA) Panel recently updated its adult HIV treatment guidelines. Key aspects of the newest guidelines were formally presented in July at the XIX International AIDS Conference in Washington, DC by Dr. Melanie Thompson, chair of the 15-member IAS panel.[1]

A systematic literature review using PubMed and EMBASE was done to identify relevant evidence published since the last report. In addition, new data presented at scientific conferences, released as safety reports by the FDA, or by data and safety monitoring boards of clinical trials, were also considered. The updated guidelines were published concurrently in the special edition of JAMA that is released biannually during the conference.[2]

The IAS-USA document addresses several important aspects of HIV care. These include when to initiate antiretroviral therapy (ART), specific options for first-line therapy, ART management in the setting of special clinical situations, approaches to monitoring patients on ART, and a brief discussion of the emerging area of antiretroviral prophylaxis for high-risk HIV-seronegative persons.

Regarding the "When to Start" question, the guidelines state that all adults with HIV infection should be offered ART regardless of their CD4 cell count. Several caveats to consider include: patient readiness to start and adhere to therapy; that benefits of ART are unknown in patients who are elite controllers or long-term non-progressors (CD4 count > 500/µL and HIV-1 RNA < 1000 copies/ml while not taking ART); and the fact that the benefit of ART in asymptomatic acutely infected patients has not been as well-studied as in those with symptomatic acute infection. The strength of the recommendations and quality of evidence supporting initiation of ART increases as the CD4 count decreases and when certain concurrent conditions are present (See table 1).

In terms of "What to Start" the guidelines recommend that an initial ART regimen for a treatment-naïve patient should include one of the following: the NNRTI efavirenz, a boosted protease inhibitor, or an integrase inhibitor. These agents should be given with either tenofovir/emtricitabine or abacavir/lamivudine. The abacavir/lamivudine combination can be used for patients who are HLA-B*5701 negative and have HIV-RNA levels < 100,000 copies/mL. For pregnant women, the preferred first-line regimen remains lopinavir/ritonavir plus zidovudine/lamivudine. (See table 2)

A section of the IAS guidelines addresses "Special considerations" when ART should be used. Clinical scenarios including pregnancy, cardiovascular, renal, hepatic, and bone disease are discussed. Opportunistic infections often present issues of drug interactions and tolerability. However, the IAS recommendations are that ART should be started as soon as possible after an OI diagnosis, preferably within the first two weeks. Delay of ART may be considered for some patients with Cryptococcal meningitis or tuberculosis if the CD4 count is greater than 50/µL.

An update in the "Monitoring" section of the guidelines notes that suppression of plasma HIV-1 RNA to less than 50 copies/mL should occur by 24 weeks in all patients, re-

SHUTTERSTOCK, BONOTOM STUDIO

gardless of whether they are treatment-naïve or experienced. For patients with low-level viremia (50-200 copies/mL) the panel notes a lack of data and thus lack of consensus on optimal management. The AIDS Clinical Trials Group defines virologic failure as detectable HIV-1 RNA >200 copies/mL after suppression. However, the IAS-USA panel states that for patients with HIV-1 RNA of 50-200 copies/mL, there should be an evaluation of factors leading to failure and consideration of switching ART regimens for these patients.

A new section "Emerging issues: Pre-exposure prophylaxis (PrEP)" has been included in the guidelines. The effectiveness of PrEP, specifically combination tenofovir/emtricitabine in several clinical trials is discussed. Now that these two agents have been approved for PrEP by the FDA, forthcoming recommendations will be included as an update to the current IAS-USA guidelines.

In a press briefing at the International AIDS conference, Dr. Thompson noted "we realized these guidelines are aspirational, and should guide treatment." She added, "This is going to be a problem for insurance companies...but I reject the idea that there is not enough money. This is the right thing to do."

Readers are encouraged to review the full document which can be downloaded from the JAMA website.[2] Please see the article on Pg. 30 , "The ART of ART" by Dr. David Hardy for additional details. HIV

References:

1. Thompson, MA. AIDS 2012: XIX International AIDS Conference. Presented at press briefing—July 22, 2012.

2. Thompson, MA, Aberg JA, Hoy JF et al. Antiretroviral Treatment of Adult HIV Infection—2012 Recommendations of the International Antiviral Society—USA Panel. JAMA, July 25, 2012; 308(4):387-402. http://jama.jamanetwork.com/article.aspx?articleid=1221704

ABOUT THE AUTHOR: **Jeffrey T. Kirchner, DO, FAAFP, AAHIVS** is Medical Director at Comprehensive Care Medicine for HIV, Lancaster General Hospital, Lancaster, PA. He chairs the *HIV Specialist* Editorial Advisory Group.

TABLE 1

When to Start ART: IAS-USA Recommendations 2012

- Patient readiness should be considered when deciding to initiate antiretroviral therapy (ART)
- Art should be offered regardless of CD4 cell counts (increasing strength of the recommendation as CD4 decreases)
  - —CD4 ≤ 500 cells/μL (AIa)
  - —CD4 > 500 cells/μL (BIII)
  - —Pregnancy (AIa)
  - —Chronic HBV (AIIa)
  - —HCV (may delay until after HCV treatment if CD4 > 500) (CIII)
  - —Age older than 60 (BIIa)
  - —HIV-associated nephropahy (AIIa)
  - —Acute phase of primary HIV infection, regardless of symptoms (BIII)

TABLE 2

Recommended Initial Antiretroviral Regimens*

Component	Recommended Regimens
NNRTI plus nRTIs	• Efavirenz/tenofovir/emtricitabine (AIa) • Efavirenz plus abacavir/lamivudine (AIa) in HLA-B*5701-negative patients with baseline plasma HIV-1 RNA < 100,000 copies/mL
PI/r plus nRTIs	• Darunavir/r plus tenofovir/emtricitabine (AIa) • Atazanavir/r plus tenofovir/emtricitabine (AIa) • Atazanavir/r plus abacavir/lamivudine (AIa) in patients with plasma HIV-1 RNA < 100,000 copies/m
InSTI plus nRTIs	• Raltegravir plus tenofovir/emtricitabine (AIa) • Raltegravir plus tenofovir/emtricitabine (AIa

*See comments

Thompson et al, JAMA, 2012

TABLE 3

Alternative Initial Antiretroviral Regimens*

Component	Alternative Regimens
NNRTI plus nRTIs	• Nevirapine plus tenofovir/emtricitabine or abacavir/lamivudine (BIa) • Rilpivirine/tenofovir/emtricitabine (or rilpivirine plus abacavir/lamivudine) with baseline plasma HIV-1 RNA < 100,000 copies/mL (BIa)
PI/r plus nRTIs	• Darunavir/r plus abacavir/lamivbudine BIII) • Lopinavir/r plus tenofovir (BIa) (or abacavir/lamivudine) (BIa)
InSTI plus nRTIs	• Raltegravir plus abacavir/lamivudine (BIIa) • Elvitegravir/cobicistat/tenofovir/emtricitabine**(BIb)

*See comments

Thompson et al, JAMA, 2012

The AFFORDABLE CARE ACT & HIV

HIV Specialist examines the impact of the **PATIENT PROTECTION and AFFORDABLE CARE ACT** on HIV care providers as they manage the health of their patients in the years ahead.

THE PATIENT PROTECTION AND AFFORDABLE CARE ACT, upheld by the Supreme Court earlier this year, will allow for more people living with HIV to obtain lifesaving treatment and medications. The expansion of Medicaid and creation of insurance exchanges will enable more people to afford care. The law's impact will differ from state to state, primarily depending upon each state's decision on whether or not to implement the changes.

This issue of *HIV Specialist* examines these factors with a report from the AAHIVM's Policy Forum held in conjunction with the International AIDS Conference in July, and with articles discussing developments in selected states.

In addition, we are pleased to bring you an article authored by Deborah Parham Hopson, PhD, RN, FAAN, associate administrator of the HIV/AIDS Bureau in the Health Resources and Services Administration (HRSA) outlining many of the major provisions of the law as they apply to HIV and offer advice to providers. We also have an article summarizing the remarks at our Forum by Aaron Lopata, MD, from the White House Office of National AIDS Policy.

— Bob Gatty, Editor

BONO MITCHELL

It's in *your* hands

The **Affordable Care Act** promises important benefits for HIV care—but providers must help make sure the right decisions are made in their own states.

BY HOLLY A. KILNESS, MA

With the recent affirmation of the Patient Protection and Affordable Care Act by the Supreme Court, one thing is now certain...change is coming. The ACA will bring changes to almost every aspect of the U.S. health care system, and to every corner of HIV care. While many of the changes will be positive in net effect, details are still being worked out on both the federal and state levels and many HIV providers understandably are confused as to what those policy changes will mean for their practice, their patients, and the future of HIV care.

To help better define what the challenges and opportunities will be for HIV care providers nationwide, AAHIVM hosted a policy forum in conjunction with the International AIDS Conference (AIDS 2012) in Washington, DC The forum, entitled ***"What's Ahead for HIV Providers with the Affordable Care Act, Ryan White and Medicaid,"*** was designed to help HIV providers understand what lies ahead. This included looking at the coming changes to the major health care programs under the Affordable Care Act, and how HIV providers can prepare.

The event received a considerable amount of interest from both providers and advocates in the weeks before it was held. Much of the interest in the event stemmed from a general sense that providers need information right now about what is going to transpire in the days ahead.

AAHIVM invited key government officials to the Forum to address these topics, including Dr. Deborah Parham Hopson, associate administrator for the HIV/AIDS Bureau (HAB) at the Health Resources and Services Administration (HRSA), and Dr. Steve Cha, medical director for the Center for Medicaid, at the Centers for Medicare & Medicaid Services (CMS), and also Dr.


Dr.Steve Cha


Jeffrey Crowley


Dr. Jennifer Kates

Aaron Lopata from the White House Office of National AIDS Policy (ONAP). In addition, a special panel of HIV/AIDS policy experts participated in a roundtable discussion during the Forum, including Jeffrey Crowley, the former director of the White House Office of National AIDS Policy, Dr. Jennifer Kates, the vice president and director of HIV policy at The Kaiser Family Foundation, Dr. Donna Sweet from the University of Kansas School of Medicine and the chair of the AAHIVM Board of Directors, Amy Killelea, the senior manager for health care access at the National Alliance of State & Territorial AIDS Directors (NASTAD), and Courtney Mulhern-Pearson, director of state and local affairs for the San Francisco AIDS Foundation.

There were many important areas covered during the Forum, such as the positive improvements the Affordable Care Act will bring to HIV care and treatment in the United States, the impact of the Supreme Court's recent decisions, and the lessons learned in the state of California's experience. However, if there was an overarching message to HIV providers that came out of the Forum, it might be summed up in a statement echoed by several of the speakers: HIV providers need to carefully watch what is happening in their state, learn about the decisions that are being made, and then weigh in with decision makers on crucial matters.

Many major decisions that will significantly affect providers' practices and patients are being made right now in every state by the governor, the health administration, or the legislature. Some states are reaching out to stakeholders for input in these decisions, and others are not. But either way, if HIV advocates do not become involved, then HIV interests are likely to be overlooked.

California was the first state to fully implement the Affordable Care Act. The summary report on California's lessons learned was published in last month's issue, and is available on the AAHIVM website to review. If California's experience has taught us anything, it is that HIV providers can't wait to be invited to the table. They must start demanding a seat at the table—every table—to weigh in on what is needed, to guide the decisions that are being made, and to make sure their practice and their patients are considered.

However, the Forum speakers did not address the Affordable Care Act as a reason for distress. Each speaker asserted that the law is an extremely positive change for people with HIV.

The law will bring significantly more health care coverage to HIV patients. Nearly one quarter of all people living with HIV in this country are without any insurance coverage. The ACA will change that. The Medicaid expansion will create a base of coverage for an even more significant portion of HIV patients, and will also cover preventive services. New insurance options will become available to HIV patients, many of whom will attain private insurance coverage. There will no longer be lifetime spending caps for people with HIV and insurance companies will not be able to refuse coverage to people with pre-existing conditions. Additionally, insurers will not be able to rescind coverage based on a change in health status. These are extremely positive changes for HIV in this country.

These fundamental changes are, however, dependent on the states implementing them. Several governors and legislatures have vowed not to accept the Medicaid expansion, and not to create a state insurance exchange.

HIV providers can't wait to be invited to the table. They must start demanding a seat at the table…to … make sure their practice and patients are considered.

As the panel discussed, the Supreme Court decision did not invalidate the Medicaid expansion—far from it. It upheld the expansion as a valid law passed by Congress. That decision means that the implementation of the Medicaid expansion is law, although, the decision removed the enforcement mechanism for the federal government to make states comply, prompting some governors to refuse to implement the law.

The federal government is still trying to

figure out the details of where things will go from here. Will states have to make a firm decision to implement the expansion or not? When must they declare their intention to implement or not to the federal government? Does the decision lie with the governor or the legislature? All of these questions will have to be addressed.

States that walk away from the Medicaid expansion leave millions of dollars from the federal government on the table. The law provides 100 percent funding to states that implement the expansion initially, and then 90 percent funding later. That alone is a huge incentive for states to accept the expansion.

State lawmakers need to understand what the Medicaid expansion would mean for HIV patients.

There is still time for HIV providers to weigh in, and they should. State lawmakers need to understand what the Medicaid expansion would mean for HIV patients. There are other issues that should be raised as well, such as provider referrals and billing. Even if a state has decided to participate in the Medicaid expansion, HIV providers (including Ryan White providers) must get connected to the state's Medicaid system. Otherwise, patients may find their providers out of network, and have to face the choice of changing providers.

As several of the speakers at the Forum said, HIV advocates should not wait to be invited to make these points to decision-makers. In California, HIV advocates were not included in decision-making panels, and the result was a hugely inadequate system that did not take the needs of HIV patients into account, and did not provide for an adequate network of providers. Many of the Forum speakers referred to the lessons learned in the California transition as a good guide for states on what *not* to do for people with HIV and HIV care providers.

In addition to the Medicaid questions, many decisions regarding the health insurance exchanges confront every state. By November, states must let the federal government know if they are going to establish a state-run exchange, or defer to the federal government to establish a federally funded exchange in the state. There is also an option to set up a hybrid of these two options—a partnership between the state and the federal government.

The Affordable Care Act provides funding to low-income individuals to purchase the insurance plans available in the exchanges. However, as it was written into the law, the subsidies are only available to those above the limit of what would be covered in the Medicaid expansion. States who do not expand will leave the poorest of the poor without any financial assistance, but with a mandate to obtain insurance nonetheless. In this regard, some state lawmakers may not realize the full ramifications of turning down the Medicaid expansion.

Each state also faces a significant decision of selecting a benchmark plan for all of the insurance plans in the state. This benchmark will set the starting point for benefits, networks, formularies, etc. for all the plans in the exchanges. HIV advocates in each state must push for selection of a benchmark that is adequate for the needs of HIV patients.

For example, the details of the formulary in the benchmarks are especially important to HIV patients, given their complex medication needs.

As Jeff Crowley stated, the HIV advocacy community went through a similar fight in terms of the transition to managed care. HIV advocates must advocate for provider networks in the state exchanges plans to include HIV care providers, otherwise HIV patients may arrive at the provider's office and be told they are no longer in network. The fight for the ability to be included in the plans, networks, and referral systems of the state will be key to the welfare of HIV providers' practices in the coming years. If we do not advocate for adequate plans, and inclusive networks now, in 2014 we may face many patients in every state losing access to their coverage, their medications, and their providers.


Dr. Donna Sweet


Amy Killelea


Richard Sorian

Courtney Mulhern-Pearson

Dr. Aaron Lopata

Ryan White providers may face the most difficult prospects in terms of access to their patients. The Ryan White program is a payer of last resort. If a patient is eligible for any other program (whether Medicaid or private insurance) he must access it first. According to the key speakers at the Forum, CMS and HRSA are working together closely to try and take some of the lessons and successes of the Ryan White program and apply them to Medicaid. The Affordable Care Act already took one of the greatest innovations of the Ryan White program—the medical home model—and made it available to states.

However, some audience members at the Forum expressed doubt as to whether the Medicaid expansion was able to provide a better care system to HIV patients than the Ryan White program. The policy experts on the panel responded that although Ryan White has been an amazing pillar of HIV care for decades, Medicaid has always been the largest provider of HIV coverage in this country.

The Ryan White program also regularly falls victim to budget cuts and reauthorization battles at both the state and federal levels. One only needs to look at the AIDS Drug Assistance Program (ADAP) waiting list "crisis" that occurred in the last three years to understand how fragile the program's safety net can become.

Don't expect anything to be handed to you on a silver platter… Don't wait to be invited. Get involved.

Dr. Hopson reminded the Forum audience that Ryan White was always a "wrap-around program," in that the program's services wrapped around the system that was available in each state. The Ryan White program looks different in each state and communities and this will likely continue as Affordable Care Act is implemented. The program will continue to serve in that same wrap-around function, regardless of what the new system looks like. How strong the state's health system is to begin with, requires the attention of advocacy efforts from the HIV community.

Panelist Dr. Donna Sweet pointed out that there is already a dearth of providers who take Medicaid patients. Although the Affordable Care Act provided a small increase in reimbursement levels for Medicaid for two years, she saw this as unlikely to create widespread change. Ryan White clinics also receive funding from the program for building and development that are not available with Medicaid. So although more patients will be covered, she wondered whether there would be enough HIV providers for them.

Dr. Hopson recommended to the Forum that within their own practice, HIV care providers should begin to screen clients who are newly eligible for Medicaid or other coverage. Providers should also ensure their HIV care team is informed about the ACA changes that may affect patients.

If there was an overarching message to HIV care providers at the Forum, it might be summed up in a statement echoed by several of the speakers: Don't expect anything over the next few years to be handed to you on a silver platter. They urged HIV providers to get involved in their state's process; learn which wrap-around services are most likely to be needed, given the specific plans and option - being offered in your area. Also, don't wait to be invited; find out when meetings are, and how you as a stakeholder can get involved in as decisions are made about essential health benefits, the benchmark plans, and Medicaid expansion.

The complexity of these types of decisions being made in each of the 50 states makes it imperative for those in each state to speak up and get involved. HIV providers absolutely must be involved in their state's planning processes. HIV care providers must push to be included on the right managed care contracts. They must push the state to accept the accountable care and health home funding available under the ACA. They must explain to decision-makers what an adequate network, formulary, and benchmark must include to be effective.

The coming years hold the potential for vast improvement to the systems of coverage, care and treatment of HIV in each state and across the country. However, that improvement will require a significant amount of involvement from those who have understanding of HIV disease, patients, and care if the promise is to be achieved. HIV

ABOUT THE AUTHOR: **Holly A. Kilness, MA** is Director of Public Policy at the American Academy of HIV Medicine.

Cascade to Care

Office of National AIDS Policy prepares for implementation of health care reform

BY BOB GATTY

DR. AARON LOPATA was asked to accept a temporary assignment at the White House Office of National AIDS Policy (ONAP), after serving eight years at the Office of Management and Budget as a budget and policy analyst. His assignment: find ways to help providers, community-based organizations and health departments prepare for, and transition to, the full implementation of the Affordable Care Act in 2014.

In the process, Dr. Lopata says he has spoken with providers and representatives of these organizations and health departments and attended -- and addressed -- the AAHIVM conference in Washington in July so he could learn firsthand "what is happening on the ground and what the challenges are."

At OMB, Dr. Lopata was working on the Ryan White Program, and was invited to ONAP to work on these issues in the context of ACA transition. The first step, he explained, was to get a better sense of how the ACA will impact the Ryan White Program and budget so OMB officials could be prepared 2014 budget preparation this fall.

"We also needed a better understanding of the challenges faced by the Ryan White grantees and all federal grantees that work with HIV/AIDs population, whether they are health departments, community-based organizations or providers," he said. "What are the challenges they are facing now, and will face when they prepare for 2014 when ACA takes effect? What assistance do they need?"

One of the key steps, he said, is to provide technical assistance, which requires a clear understanding of the challenges that exist.

"The ACA provides great opportunities, but there are also some challenges, so I am trying to learn from providers what kind of technical assistance is needed so we can be ready for 2014," he explained.

All of this is taking place while the Obama administration is implementing the National HIV/AIDS Strategy, which Dr. Lopata said "provides its own set of challenges and requires a new way of thinking."

According to Dr. Lopata, the Strategy "has done a great job of focusing on what we have to do." The question now, he said, is determining how to refocus funding to the areas of greatest burden. "How do we coordinate federal resources better, both at the federal level and on the ground? How do we work with communities to implement more coordinated systems to implement effective cascades – outreach, linkage to testing, linkage to care, retention in care?"

This effort has gained attention with the emphasis on treatment and prevention, the recent research showing the effectiveness of antiretrovirals when people are virally maximally depressed, thus preventing transmission of the virus, he added.

Implementing 'Effective Cascades'

"There is even more focus now on helping communities implementing these types of effective cascades, and it is not just one provider, one community-based organization, one health department. It takes health departments, community based-organizations and providers all working together as a team to achieve this," Dr. Lopata said.

"So what we really want to do is to help providers, whether they are a federal grantee or not, to deal with the transition to the ACA so that when 2014 comes they are not so overburdened that they are unable to do what is necessary to achieve an effective cascade."

Dr. Lopata empathized with the recipients of federal grants who must comply with a myriad of paperwork requirements while still trying to meet their responsibilities of patient care. He said the government hopes to provide some relief.

"One thing that is not new to grantees is the current reporting burden that they face from all agencies and how that is making implementation of the national strategy more difficult," he said. "You have all of these challenges and then you have this reporting burden that is a very significant problem. This is something we are going to focus on to a great extent over the next year."

Recently, the Secretary of Health & Human Services released a memorandum calling for the development of core indicators and a reduction in the reporting burden on grantees by 20 or 25 percent.

"As part of that process, we at ONAP and OMB will work with HHS to determine what can be done, while still meeting statutory requirements, to help free-up federal grantees so they can focus more resources on providing services rather than pulling together data and filing reports every month," he said. "This is an issue that must be addressed in preparation for 2014 if we want to see effective implementation of this Strategy continue."

One of the other issues Dr. Lopata said needs attention is the increased burden of additional patients on providers that will, no doubt, result from ACA implementation.

"We saw this in Massachusetts after they passed health reform, so it is not something new," he said. "Are there enough primary care providers and enough HIV/AIDs providers? These are the challenges that we want to deal with in cooperation with other federal agencies, including the Health Resources & Services Administration (HRSA)."

Dr. Lopata said the two agencies, ONAP and OMB, "are constantly engaged" in listening and learning from providers on the ground as well as the health departments and community-based organizations to gain a better understanding of the challenges they face and how we can help to address them.

"The goal is to put us in a strong position to help with the transition to 2014 so that this is effort is successful and we are able to achieve our goals and objectives of helping providers and patients alike," he said. HIV

ABOUT THE AUTHOR: *Editor of HIV Specialist*, **Bob Gatty** is a Washington, DC-area health policy writer and publications professional. He is founder of G-Net Strategic Communications and can be reached at bob@gattyedits.com.

PEPFAR.GOV

How will the **Affordable Care**

BY DEBORAH PARHAM HOPSON PHD, RN, FAAN

MANY OF THE CHANGES brought about by the Affordable Care Act (ACA) will help us reach the three primary goals outlined in the President's National HIV/AIDS Strategy: reducing the number of people who become infected with HIV; increasing access to care and optimizing health outcomes for people living with HIV/AIDS (PLWHA); and reducing HIV-related health disparities.

As recently as last November, only 13 percent of people living with HIV/AIDS (PLWHA) in the U.S. had private insurance coverage and nearly a quarter of them had no coverage at all. The remaining population of PLWHA relies on federal and state programs, including Medicaid, the Ryan White Program and Medicare, for their HIV care.

With the Supreme Court's recent decision upholding the ACA, it is imperative for providers, patients, and the HIV/AIDS community to be aware of how these programs and the private insurance market have been or will be affected by this sweeping new law.

Here are some of the most important changes in the law that will affect public programs that treat PLWHA, as well as new protections within the private insurance market that are vital to HIV patients:

Private Market protections

- No more lifetime spending caps from insurance companies; no annual caps beginning in 2014.
- Insurance companies are no longer be able to deny coverage based on pre-existing conditions, such as HIV status for children and beginning in 2014 coverage cannot be denied for adults based on pre-existing conditions.
- Insurers cannot rescind coverage for adults or children because of changes in health status.

Federal-State Program changes

- AIDS Drug Assistance Program (ADAP) benefits are now considered contributions toward a Medicare beneficiary's true Out-of-Pocket Spending Limit for drug coverage, a huge relief for low-income beneficiaries living with HIV and AIDS because it helps them move through the donut hole more quickly.
- New insurance coverage options will become available for people living with HIV/AIDS and Ryan White clients, such as increased access to Medicaid in many states for childless adults up to 133 percent of the Federal Poverty Level.

There are other exciting provisions that are also helpful to PLWHA, including:

- Medicare and many private insurance plans are now required to cover recommended preventive services, including HIV screening.
- The law recognizes the value of patient-centered medical homes as a way to strengthen the quality of care, especially for people with complex chronic conditions, such as HIV. Medical homes help to coordinate care by bringing providers and patients together to address medical needs comprehensively through preventive, chronic and acute care services—this is vitally important for PLWHA.
- Many plans beginning this year are required to provide HIV counseling at no cost or low-cost for sexually active women.
- The law calls for increased diversity and cultural competency for all health care providers, to reduce health care disparities.
- The law will also increase the number of community clinical providers that are able to provide services for PLWHA. This will help to increase access to care in underserved communities.

With so many changes in our health care system resulting from the ACA, what does this mean for the Ryan White Program?

SHUTTERSTOCK, DREAMSTIME

Reduce the number of people who become infected with HIV

Act affect HIV Care?

As the ACA will have a major impact on care for PLWHA, including Ryan White Program clients, the Health Resources and Services Administration (HRSA) has begun to closely examine the interaction between the ACA and the Ryan White Program. HRSA is working to better understand how Ryan White client needs may change, if at all, after 2014.

In October 2009, the Ryan White HIV/AIDS Program, administered by HRSA, was reauthorized through September 2013. The Obama administration supports reauthorization of the Ryan White program beyond 2013.

The Ryan White Program has proven its success, as a payer of last resort, to help PLWHA who are low-income, uninsured or underinsured gain access to quality, effective HIV/AIDS care.

The program has helped thousands of individuals to find care and be retained into care. Through the ADAP program, Ryan White clients are provided lifesaving medications that may otherwise not be available because of economic, social, or other barriers to care. The Ryan White Program funds training and education services for health care professionals treating HIV/AIDS patients.

Ryan White also serves as wrap-around coverage for many services or medications that private insurers or Medicaid may not cover.

While service needs may change for some Ryan White clients, it is expected that a substantial need for Ryan White Program services will continue after full implementation of ACA.

In order to prepare for ACA implementation, there are several things that HIV/AIDS providers and their care teams can do to get ahead. Here are a few recommendations:

- If you are a Ryan White provider, begin planning to screen clients who may be newly eligible for Medicaid or other coverage available in your state.
- In addition, learn which wrap-around services may be needed most in your state based on coverage offered in health exchange plans and Medicaid.
- Compare services covered under the Ryan White Program and your State Medicaid Program.
- Learn the required essential health benefits for private insurance plans in your state as they are developed.
- Ensure that your provider team is informed about ACA changes that may affect your patients.
- Visit www.HealthCare.gov to familiarize yourself with the ACA.
- Refer your patients and clients to www.HealthCare.gov to learn how ACA impacts PLWHA.

In short, become as familiar with the new law as possible so you fully understand how it will affect your HIV-infected patients. There are many provisions that will be life-changing for PLWHA, and we look forward to many positive outcomes in both coverage and care for PLWHA in the United States.

As you know, HIV is often difficult for people to manage when access to care is limited. The ACA will reduce difficulties and barriers to care that have existed for PLWHA for decades. HIV

ABOUT THE AUTHOR: **Deborah Parham Hopson, PhD, RN, FAAN** is associate administrator, Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau.

Massachusetts: Where Health Reform Began

BY STEVEN L. KEENHOLTZ, MD

AS A PRIMARY CARE INTERNIST and infectious disease specialist since 1981, I was at ground zero of the HIV epidemic. During my 32 years in private practice, I continually treated HIV and AIDS patients. Today, my work is at North Shore Primary Care, PC, part of Beverly Hospital, Beverly, MA, affiliated with a suburban community hospital on the north shore of Boston.

We are very fortunate in Massachusetts. We have not had a wait list here, and we have a very liberal formulary as far as medications are concerned. That is largely due to long term support for access to HIV care from the Commonwealth and support through federal funds such as Ryan White funding.

Now, under the new federal health reform law, I do not expect much to change in Massachusetts, except perhaps for patients on Medicare with Part D prescription coverage, an area where we've had some formulary restrictions to contend with, causing some treatment challenges.

Similarly for patients co-infected with hepatitis C who have Medicare, there are more obstacles and we have found it a lot more difficult to deal with from a formulary perspective than with other patients. This is largely due to the limited experience with co-infection and the lack of FDA support for treating co-infection.

Other than that, from my perspective we are not going to see very much of a change. After all, Obamacare was modeled after Romneycare. Irrespective of HIV, we are 2 percent below the national average in terms of unemployment, so Romneycare was not a jobs killer. Most people who have good paying jobs also have good paying insurance, so it is the lower income individuals who have not had insurance, and now we are seeing all of those people getting coverage. As a result there is improved access to primary preventive services.

Regarding HIV, we have had excellent coverage largely due to Ryan White and the AIDS Drug Assistance Program (ADAP), even before Romneycare was enacted. There has not been a barrier to access for patients here unlike some other more conservative states with less available funding.

We have our share of HIV and AIDS patients here. It is not very dissimilar to other major urban centers in the Northeast corridor. I practice both primary care and infectious diseases in a suburban setting. We have a number of communities that have higher incidents of HIV (Lynn, Lawrence and Lowell). We see a mix of risk behaviors including injection drug use, MSM, female heterosexuals, and, rarely, congenitally infected young adults.

The provisions preventing insurance companies from limiting coverage due to pre-existing conditions and from placing a cap on coverage are going to be very important in other states for people with HIV, but those are not things we have had to worry about here. We have 98 percent of our population covered because of Romneycare.

My main concern going forward is that people will die from lack of access to care in those states that choose to opt out of the expansion of Medicaid, which is allowed by the Supreme Court decision

It is clear that in treating HIV now, everyone except the elite controllers should be on HAART, so if restrictions are put between the physician and the patient in terms of the standard of care, that will have significant consequences in those states. We must continue to use resources judiciously as they are limited.

Fortunately, that is not something we are concerned about in Massachusetts, largely due to the health reform law enacted under Gov. Romney, the national version of which he now attacks as a candidate for President. HIV

DREAMSTIME, THINKSTOCK, BONOTOM STUDIO

ABOUT THE AUTHOR: **Steven L. Keenholtz, M.D.** is an infectious disease specialist at North Shore Primary Care in Danvers, MA. He is a member of the Northeast Physician Hospital Organization (NEPHO), a network of primary care and specialist physicians working with Beverly and Addison Gilbert hospitals.

Perceptions and Concerns

BY D. TREW DECKARD, PA-C, MHS, AAHIVS

SINCE I PROVIDE medical care to both internal medicine (non-HIV impacted) and HIV positive persons, I have seen some intere sting trends in the past three years.

Private insurance cost for premiums, deductibles, co-pays, co-insurance, and other out-of-pocket expenses have risen precipitously. I have had reliably adherent patients come to me out of ART medications for weeks or months. Usually it's been due to new stipulations in their policies—higher co-pays, new out-of-pocket expenses, prior approvals now needed, among a myriad of other reasons. These patients are adherent to clinical recommendations and their medications—they just can't get them.

I have seen younger patients derive a financial benefit by being able to obtain insurance under their parent's policies. This has allowed greater access, especially those with chronic illnesses, such as HIV/AIDS.

Texas is currently one of several states that has opted out of accepting the expanded Medicaid federal funds, which would begin distribution in January of 2014. Despite growing interest in implementing these important changes in Texas at both state and local levels, Governor Rick Perry and his administration have vowed to refuse the Federal funds necessary to put these changes into place.

I asked some of my colleagues here in Texas their perspectives on these issues.

Gene Voskuhl, MD, Medical Director of AIDS Arms in Dallas, said "I feel that it [the ACA] will expand access to people who need care that might not otherwise receive it. And I think a key will be what happens with Medicaid funding expansion in Texas. Ryan White is a payer of last resort, and so all of a sudden through the ACA, patients who haven't had coverage will now have coverage; however most of my patients would then probably fall under Medicaid." Currently about 70 percent of the clinic receives funds through Ryan White.

Dr. Voskuhl added, "If Medicaid expands and we don't get the federal funds, this would be disastrous for our clinic, assuming that most of the Ryan White funding would diminish and those patients become Medicaid eligible. We couldn't afford to take care all of those new patients. We currently receive between $33 and $44 for a visit per Medicaid patient and we couldn't afford to do that for very long."

I asked Robin Hardwicke, PhD, FNP-C, Associate Professor of Internal Medicine and Ob/GYN services at University of Texas Medical School at Houston, how the ACA would affect/impact her patient population.

"I expect more HIV patients are going to have some sort of insurance, Medicaid in particular," she said. "The patients I have now are usually below the 133 percent poverty line, so they should be able to get insurance. I would imagine a flood of more individuals would come in seeking care. Because of this [greater access], I would expect to see more patients, and perhaps the acuity would be higher because they've theoretically gone for a longer time without, and now they have insurance and can get care. I would anticipate that their immune system has had time to become more suppressed and so they may be sicker."

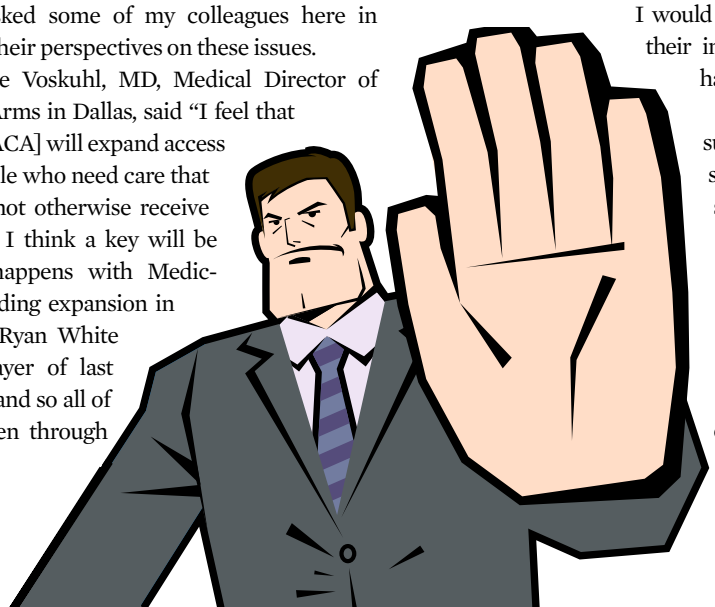
I also asked Dr. Hardwicke, how she thinks Gov. Perry's refusal to accept expanded Medicaid dollars will affect patients and our ability to care for them.

"He thinks it's an intrusion to the sovereignty of our state," Dr. Hardwicke said. "I don't. I want Gov. Perry to accept these funds because that would constitute expanding health care to everyone. So more individuals that would like to get primary care and couldn't afford it can now get it and avoid a severe disease or manifestation down the road. If he doesn't accept that money, they don't get that care. I'd rather have people have access to health care sooner than later, as opposed to them coming to me with some catastrophic or more difficult-to-manage illness."

I asked Marc Tribble, MD, AAHIVS, of Uptown Physicians Group in Dallas his thoughts on how ACA implementation will affect his patient population.

He replied, "I think that the pre-existing clause will positively affect my patients. Because many patients don't have insurance at the time of diagnosis [of HIV], the fact that they will be able to get insurance will be beneficial." Regarding Texas accepting additional Federal Medicaid funds, Dr. Tribble added, "I work in a private practice I don't think that it will impact my clinic, but I do think it will have a much greater impact on HIV positive individuals throughout the state."

It is clear that, depending upon one's practice setting, payor sources, level of acuity and patient load, perceptions of how the ACA, and more specifically how the Medicaid expansion will effect patient care, are variably interpreted. The constant theme, however, is that no matter what one's practice or affiliation, access to care is paramount. Gaining that access is clearly the challenge. HIV



ALASHA / ISTOCK

ABOUT THE AUTHOR: **D. Trew Deckard, PA-C, MHS, AAHIVS** is a physician assistant at Steven M. Pounders, MD, PA, Dallas-Fort Worth TX and Texas AAHIVM Committee Chair.

Despite Need, Medicaid Expansion is in Question

BY KAREN KRIGGER, MD, FAAFP, AAHIVS

THE NEED for improved health care in Kentucky, including care for people living with HIV, is great and becoming greater. As of June 30, 2011, there had been 8,121 cumulative HIV infections reported to the state health department since reporting began in 1982, and 5,400 infections had progressed to AIDS.

Of course, it is not only HIV that is a concern in our state, which is one of the top five in the nation for obesity and diabetes prevalence, according to the Centers for Disease Control and Prevention (CDC). These serious health concerns, which also face HIV patients, can only be expected to worsen as the population continues to age. As of January 25, 2011, the majority of HIV infected Kentuckians (51 percent) were aged 45-64 years old, with 41 percent age 25-44. This aging population will require even more chronic disease management skills.

The state of Kentucky has four Ryan White clinics serving Louisville and northern Kentucky, Lexington and central Kentucky, Paducah and western Kentucky and southern Illinois, and Henderson County serving western Kentucky and southern Indiana. The eastern part of the state, the Appalachian region, with the highest percentage of poverty and unemployment—and the highest percentage enrolled in Medicaid—is without a Ryan White clinic. Patients who live there, many of whom are essentially illiterate, must travel 200 miles or more to see an HIV provider.

The Affordable Care Act provides for the expansion of Medicaid, with the federal government paying 90 percent of the cost for the additional people who are covered, with the state paying 10 percent. Currently, the federal government pays 70 percent. However, it is uncertain whether our state will participate in that expansion—even though a report by the Kaiser Commission on Medicaid and the Uninsured says Kentucky would benefit more than any other state in the nation from the expansion.

Gov. Steve Beshear

Following the Supreme Court's decision on June 28 upholding the Affordable Care Act, Gov. Steve Beshear has been considering whether to opt out from the Medicaid expansion provision. As this is written in early September, no decision had been announced. In our state, more than 700,000 people receive insurance through Medicaid, our largest insurance provider.

On July 17, Gov. Beshear issued an executive order establishing the Kentucky Health Benefit Exchange, which will be an online marketplace that will provide one-stop shopping for individuals to enroll in qualified health coverage plans. The exchange also will help employers facilitate the enrollment of their employees in health plans, enable individuals to receive premium tax credits and premium subsidies and qualify small businesses for tax credits. The exchange will begin operation January 1, 2014.

But without expansion of Medicaid to cover the poor, many HIV patients will be caught in a very difficult position. The ACA requires nearly everyone to obtain health insurance or pay a penalty, but if the state does not provide support through Medicaid, many will be unable to afford even the most basic plan offered through the Exchange.

It is difficult to say how many Kentuckians would be eligible for Medicaid under the new rules. House Republicans cite Urban Institute numbers showing that 400,000 uninsured Kentuckians who earn less than 138 percent of the federal poverty level would be eligible for Medicaid under the expansion. Other estimates put the number at fewer than 350,000.

It is estimated that 20 percent of Kentucky's HIV patients will be eligible for the benefit exchange plan, while 80 percent would be eligible under expanded Medicaid program.

In Kentucky, there is a need for stable, quality outreach medical sites capable of providing medical, psychological, and social supports. Primary care providers are needed to accept patients for chronic disease management. Normalized testing and HIV medications in any pharmacy in the state is essential. Patient transportation resources are needed to connect patients with services and support groups.

Patients fear being stigmatized in inner city enclaves, as well as, rural towns and they need access to sites for unrecognizability. The stigma of HIV disease concerning cultural, gender, racial, linguistic, and religious bias complicates outreach efforts for testing, care, and retention in the state.

New influx of immigrants and populations of newly infected youth require special skill sets for outreach. Telemedicine, mobile medical units, and electronic transfer of records may provide expansion of needed services in the state's future. HIV

ABOUT THE AUTHOR: **Karen Krigger MD, MED, FAAFP, AAHIVS** is associate professor in the Department of Family and Geriatric Medicine at University of Louisville School of Medicine.

DREAMSTIME, GOVERNOR.KY.GOV, ISTOCK, BONOTOM STUDIO

Georgia (Challenges) on My Mind

BY RICHARD PROKESCH, MD, FACP, FIDSA, AAHIVS

"THE SOUTH SHALL RISE AGAIN" is used to refer to the belief by southerners with ancestors dating back to the Civil War that there was still hope for the Confederacy. That never came to fruition, but unfortunately with regard to to the HIV/AIDS epidemic, the South has risen again with roughly half of the new AIDS diagnoses occurring in Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, North Carolina, South Carolina and Tennessee, according to federal statistics.

According to 2010 data from Georgia HIV/AIDS surveillance, there were 2,037 newly diagnosed HIV cases and 743 AIDS cases. Anecdotally, in my private infectious diseases practice, we have been seeing five to seven new patients a week for approximately a year and one-half. About half are newly diagnosed with the remainder having been previously diagnosed but relocated to the region. There is a severe shortage of HIV care providers in the south, which obviously makes it difficult for all of the new patients to receive high quality care or even care at all.

The Affordable Care Act (ACA) potentially will exacerbate the difficulty in finding expert care for persons living with HIV/AIDS. Georgia Gov. Nathan Deal is among the state executives who have said they will not expand the Medicaid program, provided for in the law, but now not mandated by the recent Supreme Court ruling.

If he does not change this dictum, tremendous stress will be added to an already underfunded Ryan White program in Georgia. If ultimately the governor is convinced to expand the Medicaid program, different problems will result with up to 70 percent of current Ryan White patients becoming covered by Medicaid plus many of the newly diagnosed patients who do not have private insurance coverage.

In Georgia, many physicians will not see Medicaid patients because of low reimbursement for their services. There is a significant discrepancy in Medicaid reimbursement among the states and the South generally has the lowest rates. In 2010, according to data from the Health Resources and Service Administration (HRSA), there were 18,590 male, 9,074 female and 150 transgender Ryan White clients in Georgia. There will need to be significant changes in Georgia's program for patients to have access to care.

Even if Governor Deal expands the Georgia Medicaid program, there still will be a need for the Ryan White program. In addition to the 30 percent or so who will not qualify for Medicaid, there likely will be gaps in coverage for items such as some of the medications which could potentially be filled with the Ryan White and ADAP programs.

How all of this will ultimately play out remains unclear at this moment. There are so many moving parts including the November national election, Georgia's decision on expanding the Medicaid program, the reapproval of the Ryan White program and the growth of HIV expert providers in the state.

With the appropriate stress on "treatment is prevention," it is imperative that all Georgians living with HIV/AIDS have access to care and treatment. Somehow we must educate our legislators and governor about the importance of caring for this population. The larger the "undetectable" population residing in Georgia, the less the transmission of the virus and the less cost there will be for the system in treating new HIV and AIDS cases.

I would like to see Georgia expand the Medicaid population and also somehow increase the reimbursement for HIV care providers to reasonable levels to encourage participation by qualified physicians. There will need to be more HIV Specialists trained through the AAHIVM Credentialing Program and more training given to providers that see a smaller number of HIV patients. I have learned that AAHIVM is working to develop an on-line HIV training/certificate program developed explicitly for generalist practitioners who care for only a few HIV patients. This system will work especially well for academic centers. For example, I spoke to an Emory physician who is working in the Grady HIV clinic who is interested in starting a program to train and certify internal medicine residents in HIV care, in addition to the training of Infectious Diseases specialists.

I also hope there will be enhanced cooperation between the Ryan White clinics, county health departments and private practitioners in coordinating care for those living with HIV/AIDS. I can envision the transformation to medical homes where there is multidiscipline, high-level care rendered and all of the above-mentioned constituents are working together for the common goal of excellent care.

In my practice, we have always had excellent synergy between the Clayton County health department and our practice, and HIV patients can go back and forth to either setting based on their insurance coverage, and not drop out of care. The good communication and my practice's oversight of the Ryan White clinic ensure continuity of care. This sort of alliance for care will be even more necessary in the future.

The future is uncertain, but it is clear that no matter what transpires in the state there will be many challenges as well as opportunities to ultimately achieve excellent care for HIV/AIDS persons living in Georgia. There is a lot of work to be done, but the result of that labor holds the promise to be a positive game changer for both HIV/AIDS patients and their providers. HIV

ABOUT THE AUTHOR: **Richard Prokesch, MD, FACP, FIDSA, AAHIVS** is in private practice in Riverdale, GA. He is chair of AAHIVM's Georgia chapter and is on AAHIVM's Board of Directors.

A healthcare landscape at the crossroads

BY JOEY WYNN

FOR HEALTHCARE PROVIDERS and policy wonks throughout the state of Florida, trying to gauge where our public healthcare system for people living with HIV is going, and what the landscape will look like for these patients during and after healthcare reform is anyone's guess at this point. I will try to highlight a few key elements in an ever- changing melting pot of politics, funding streams, and provider infrastructure in the Sunshine state.

The Patient Protection and Affordable Care Act (PPACA) is a complex, multifaceted approach to providing much greater access to health care coverage for millions of Americans. These new regulations will both help and hurt the capacity of individual states to provide HIV care as it interacts with existing federal programs and Medicaid.

Given our current state budget crisis, Florida has had several substantial reductions in vital health care programs funded by Medicaid as well as some state funded Health Department programs. This has resulted in an outcry from patients and advocates for restored funding for the sickest and most frail in our communities.

In spite of this, our AIDS Drug Assistance Program (ADAP) waitlist was very recently reduced to near zero - for now. We can only wait to see how the wait list will be kept at bay, or if it will slowly creep back into the hundreds, if not thousands once again. The governor allowed a $1 million increase for ADAP, even though most other programs were experiencing major reductions; we also saw a modest increase for our AIDS Insurance Continuation Program (AICP) as well. These programs were able to eliminate their waiting lists, and accept new clients once again this year.

On the other hand, the governor continued strong resistance to the Affordable Care Act (ACA) moving forward in our state. Some say this is a benefit in a strange way to allow the federal program to create our state exchange, and thus utilize the expertise of the many advisory groups and national coalitions in crafting such complicated programs.

Other beneficial movements include the state legislature starting to identify costs and operational aspects if they do indeed move forward with the ACA efforts. This is a good sign, and perhaps the legislature can influence the governor to see this really is a great concept to allow Floridians to get access to health care, which would greatly reduce the burden and strain our statewide Public Hospital safety net currently experiences.

Once healthcare reform occurs, many HIV providers in most urban areas of the state should see minimal shifting, (although the movement will cause disruptions for eligibility workers, case managers and many others temporarily) as most of our Ryan White Medical Providers are also the Medicaid and Medicare providers in their areas. For those not currently accredited to provide these other programs, pressure will mount from the local community advocates for them to do so as quickly as possible.

The picture for the more rural areas of our state is more difficult. In areas where there are few or no Medicaid providers, this will cause a great challenge, especially for HIV patients searching for providers who have both HIV expertise and the ability to accept Medicaid.

For some, the refusal of healthcare reform means the Ryan White Care Act funding would remain almost the same, doing the same things. Some people don't like change, and would feel less nervous about this.

Others believe reform would allow much greater access to providers, and Ryan White funding could help serve in a wrap-around function, helping those that fall out of care (or are much less likely to ever access care in the first place) find meaningful engagement in the healthcare system.

Many of us are trying to stay informed, and follow the twists and turns the federal theater provides. Most providers are trying to diversify their funding payors and keep their clients informed. We recently joined our statewide HIV policy group (FHAAN) with other advocacy groups, like Florida Chain & FADAA and other advocacy groups. We are trying to learn to embrace new social media technology and are banding together to impart the needs of our patients, the return on investment of having everyone engaged in care, and what an overall healthier community would mean for Florida. HIV

Here is a snapshot of the current state of HIV care in Florida today:

Population: 18.8 million (4th in nation)

Cumulative AIDS cases: 124,069 (3rd in nation)

Cumulative pediatric AIDS cases: 1,543 (2nd in nation)

Cumulative HIV cases: 47,695 (2nd in nation of 46 states w/ HIV name reporting)

Persons living with HIV/AIDS: 95,335

Source: Florida Dept of Health, December 2011

ABOUT THE AUTHOR: **Joey Wynn** is Director of Public Policy for the Broward House AIDS Service organization in Broward, FL. Wynn has made a career in HIV advocacy, public policy and working in a variety of public health settings over 22 years in Florida.

THINKSTOCK, BONOTOM STUDIO

Good News from Alaska

Remote Pharmacy May be CDC Site for Rapid Screening Test

Rodney Gordon

WITH EVERYTHING that is happening this fall in the "lower 48" as we approach the 2012 Presidential election, I imagine few people are thinking much about the state of affairs in Alaska, or the remote region of northwest Alaska where I reside and work, in the small town of Nome.

Here, life for the majority of people continues relatively unchanged, with a focus on family and community activities which predate the modern era of life, with all the technological wizardry of the computer age. Things like berry picking, fishing, hunting, and other subsistence activities to prepare for winter, still consume much of the time of the local native population, as well as the 'gusacks' (new-comers, like myself) who find themselves working here for a variety of reasons. Some are here for short-term contracts involving commercial construction, or upgrading the local internet infrastructure to fiber optics, while others are temporary or permanent members of the local healthcare system.

It was healthcare that brought me to Nome. I am a pharmacist who has been fortunate to practice pharmacy for the last 32 years in a variety of settings, including Saudi Arabia, the U.S. Virgin Islands, North Carolina, Virginia, and most recently in Alaska, working in Anchorage, Barrow, and now in Nome.

After 32 years you might think I should be thinking of retirement, or at least cutting back to a more normal 40 hours per week, but nothing could be further from my mind. Now, more than ever, is the best time to be involved in healthcare, especially for a pharmacist like myself, a member of AAHIVM since 2007, who wants to make a difference in the practice of screening for, treating, and minimizing the spread of sexually transmitted infections and HIV.

I am fortunate to be the manager of the pharmacy department at the Norton Sound Regional Hospital, which is owned and operated by a local tribal organization called the Norton Sound Health Corporation. The corporation is comprised of a consortium of 20 native tribes located within a 44,000 square-mile Bering Strait region in northwest Alaska. (Yes, we *can* almost see Russia, unlike Sarah Palin in Wasilla.)

My excitement for healthcare in Nome now is twofold. We will soon move into a brand new $140 million dollar facility slated to be completed in December, 2012. Furthermore, our pharmacy was recently chosen to be one of 17 new sites for expanded rapid HIV screening supported by a Centers for Disease Control & Prevention (CDC)-funded program that is targeting community pharmacies and rural clinics across America.

The timing of this opportunity is perfect for our facility and our region of Alaska as we face a time when the need for added services matches the availability of support for those services.

Alaska is so remote from the rest of the U.S. that most people probably do not realize the demographics of healthcare data here, in particular relating to sexually transmitted infections. According to 2010 STD data from the CDC collected from all 50 states, Alaska ranked first in the nation in the incidence of Chlamydia per 100,000 people. For the same year, Alaska also ranked third in the incidence of Gonorrhea (Mississippi was first, Louisiana was second). It is common to hear sex described locally as "the Nome handshake". Clearly there is a lot of "handshaking" in Alaska, including our region of the state.

Historically our hospital has not routinely screened patients for HIV infection, except during pregnancy and/or at delivery, and HIV screening is not routinely bundled with STI tests. Consequently we have little evidence for the presence of HIV in our region of the state.

It is well known and reported by the CDC that an individual who has an STI is two to five times more likely to contract HIV than an uninfected person, if they are exposed to the HIV virus through sexual contact. Furthermore, there is significant biological evidence that having an STI increases the risk of transmitting HIV. Lastly, recent HIV prevention studies have vividly demonstrated the impact ART can have on decreasing the risk for transmitting the disease, and the DHHS guidelines now recommend offering treatment to anyone who tests positive for HIV, regardless of CD4 cell count.

The opportunity to participate in this CDC funded rapid HIV screening program is like a dream come true for our pharmacy, since it comes at a time when our passion to make a difference matches the availability of this support. Our determination to bring expanded HIV screening to the people of northwest Alaska will eventually happen because it compliments our hospital's commitment to promote wellness and improve the quality of life for "our people and community", including Nome and the 15 remote villages that we serve.

Yes, there is indeed good news from Alaska!!! HIV

ABOUT THE AUTHOR: **Rodney Gordon, RPh,** is director of pharmacy at Norton Sound Health Corporation, Nome, AK.

The Art of ART Adherence

A common-sense approach to helping patients adhere to life-saving drug therapy

TO DATE, volumes have been written and spoken regarding adherence to antiretroviral therapy (ART). Still, despite the unprecedented advances made in basic retrovirology, biochemistry and pharmacology that have made this life-saving treatment possible today, the cornerstone of its success remains high-level and consistent adherence.

With today's "finely tuned" (greater potency, less toxicity), simplified ART regimens, adherence is essential to achieve the primary goal of this treatment: maximal and durable suppression of viral load. Once this goal has been met and sustained, the other goals of ART: immunologic reconstitution, prevention of further viral transmission and reduction in HIV-related morbidity and mortality will follow. Secondary benefits such as minimization of viral resistance by avoidance of virologic breakthrough, persistent potency of current antiretroviral agents and achievement of long-term control of HIV infection are also realized.[1-3]

Despite these benefits, it is difficult to find a universally accepted or standardized definition of adherence to ART.[3-5] Studies using a number of assessment tools have demonstrated wide geographic and global variability, with higher adherence rates often reported from developing rather than developed countries.[3,6,7]

Both the March, 2012 DHHS and June 2012 IAS-USA Guidelines recommend initiation of ART for all treatment-naïve, HIV-infected individuals, with the strength of the recommendation increasing with an individual's declining number of CD4+ cells. Even more importantly, these Guidelines emphasize that clinicians should assess a patient's readiness to take antiretrovirals before writing the first prescription(s).[8]

With the exception of post-exposure prophylaxis (PEP), prevention of mother-to-child transmission (PMTCT) and treatment of acute retroviral infection, all of which have narrow time windows for commencing ART, the initiation of ART is rarely, if ever, an urgent medical decision. In almost all situations, clinicians need not be hasty to begin ART, but rather should thoughtfully assess a patient's readiness to begin and adhere to this life-long treatment.

Assessing Readiness

The determinants of consistent, successful adherence should be assessed prior to initiating ART. The March 2012 DHHS and June IAS-USA Guidelines will almost certainly increase the number of asymptomatic HIV-infected individuals who are candidates for initiating ART or who are urged by their healthcare provider to start ART.

Convincing these patients, most of whom have never personally experienced HIV-related symptoms or an opportunistic disease, to start therapy may be particularly challenging.

A "one-size-fits-all" approach to this critical discussion is not appropriate.

Providing these individuals with a clear, educationally and culturally appropriate explanation or translation of the, at times, admittedly inconsistent clinical rationale for when to initiate ART is truly what the "art of ART" is all about.

If an HIV-infected person is not ready to begin ART or, often just as important, if the healthcare provider is ambivalent about recommending it, ART adherence may be inconsistent or poor. A "one-size-fits-all" approach to this critical discussion is not appropriate. HIV providers must take time to build bidirectional, working relationships with their patients in order to not only educate, but also to get to know their patients.

Through this process of relationship building, a patient's readiness to begin ART can be determined accurately. Only when healthcare providers are confident of their patients' self-motivated commitment to start and adhere to ART should they write the first prescription. Often times, simply asking a patient about his or her goals, expectations and concerns about starting ART is a good way to bring this sense of self-commitment to light and identify previously unexpressed areas for further discussion. Accordingly, the ART Guidelines should direct but not necessarily dictate the ART initiation decision-making process.

How do we assess readiness?

For those patients who are immunologically at risk for developing an opportunistic infection (OI), clinicians should strongly consider initiating specific antibiotic prophylaxis. These medications can protect the patient from potentially life-threatening infections while navigating the process of accepting his or her new diagnosis of AIDS. Often, with the clear exception of an acute OI diagnosis, initiating ART at this time can be overwhelming and complicate adherence. Prophylactic antibiotics also provide patients with the experience of taking medication(s) on a regular basis with agents that do not have the viral resistance-inducing consequences of nonadherence to ART.

For those patients who do not require antibiotic prophylaxis, prescription of a simple regimen of vitamins or other nutritionals can serve as a "practice run" to explore the practical challenges of and solutions for daily pill taking prior to initiating ART. This is a good time to make patients aware of simple adherence re-enforcement techniques such as linking medications to daily activities (e.g., meals, getting ready for bed), weekly pill trays and even daily electronic reminders from cell or Smart phones. In all cases, the general concepts of consistent adherence can be addressed and instilled, paving the way for a better understanding of adherence to HIV medication for the future.

ISTOCK, THINKSTOCK

BY W. DAVID HARDY, MD, AAHIVS

Conditions to Address Prior to Starting ART

Concomitant medical conditions such as anxiety and depression are commonly diagnosed in HIV-infected persons. Clinicians should consider deferring the initiation of ART in a newly diagnosed HIV-infected patient until he or she is assessed for anxiety and depression.

One must remember that many patients are still struggling with their new diagnosis of HIV infection or AIDS. Even though many of us have delivered the news of a new HIV infection many times and feel secure in our ability to do this in a compassionate manner, the patient is hearing it for the first time. Starting ART in a setting of previously unrecognized or new anxiety or depression can seriously undermine adherence.

Drug use, including alcohol, can also negatively impact successful adherence. Alcohol intake in particular can increase during the early adjustment period as patients attempt to cope with the new diagnosis of HIV infection. Alcohol consumption as well as both illicit and prescription drug use should be discussed frankly to identify either remote or recent abuse, the extent of the problem, if any, and its potential impact on adherence. If any of the above concomitant medical conditions are identified, appropriate referrals to mental health and substance abuse treatment services are warranted.

HIV-infected patients with concomitant medical conditions such as hypertension or hyperlipidemia may already be taking medications daily. It is commonly assumed that these patients already know how to take medications and are consistently adherent to them. However, assuming this as a fact can be hazardous, particularly due to the high level of adherence required with ART compared to that with many other medications.

It should also not be assumed that the addition of antiretroviral medications will be easily assimilated into a patient's daily pill-taking routine. In fact, the opposite may be true. An additional one to four pills each day may prove to be overwhelming to some patients. Providers must be cognizant of the

total number of pills patients take each day as well as the complexity of their dosing regimens. Of note, some patients tend to equate their degree of illness with the number of medications or pills they take each day. Some patients can handle additional pills while others become concerned, thinking that their health is deteriorating.

Assessing Adherence

A patient's adherence to his or her antiretroviral regimen should be assessed at every visit following initiation of the regimen. This is especially important during the first several visits after ART initiation. Training a patient to be prepared to be queried about adherence is one of the most important foundations for long-term success that an HIV provider can instill. Although subsequent visits will necessarily include discussion of virologic and immunologic laboratory results as well as non HIV-related medical conditions, adherence discussions should never be dropped from an HIV patient visit.

Clinicians should not simply assume that patients will continue to adhere to ART indefinitely even if their viral load results suggest this. Here is where the "art of ART" surfaces once again. Asking simple, direct, open-ended questions such as "How many times did you miss your meds last month?" or "Which doses are the most difficult for you to remember to take?" offers patients the opportunity to respond honestly about their adherence challenges.

Follow-up inquiries such as "Let's talk about what happened that caused you to miss some doses" can elicit specific opportunities to identify and discuss new or recurrent adherence challenges. These conversations maintain an ongoing, open dialog about adherence with patients. Probing adherence with questions such as, "You haven't missed any meds, have you?" can be perceived as judgmental, accusatory, and chastising and should be avoided. Patients who sense their provider's disapproval of non-adherence are less likely to provide accurate, honest information.

Maintaining Access to ART

Practical and financial matters as well as medical issues influence adherence and must not be ignored. For example, not all HIV-infected patients, including those with all types of insurance, have consistent, stable access to their medications.

Almost all HIV medications used today are proprietary products (non-generic) and therefore are expensive, especially when used in combination as ART always is. HIV drugs typically carry high, out-of-pocket copays, commonly in the $25 to $50 range per drug, which is the patient's responsibility. Clinicians should consider providing copay cards to their privately insured patients. Every pharmaceutical company in the HIV product area offers copay cards, which cover up to $200 per month and are valid for one to two years.

HIV providers routinely should ask their patients—ncluding patients who report taking medications daily on a regular basis—whether there has been a period of time when their medications were not affordable and were missed. Specifically, patients should be asked questions such as "Has there been a lapse in your employment during which you had no health insurance?", or "Has your insurance supplied by a spouse, partner or family member been cut off due to their lack of employment?"

Clinicians should not simply assume that patients will continue to adhere to ART indefinitely even if their viral load results suggest this.

Because requirements for the AIDS Drug Assistance Programs (ADAP) vary from state to state, HIV care providers should be familiar with their state and local requirements. For instance, California ADAP requires patients to re-qualify for the program annually on their birth date. Consequently, clinicians should ask patients whether their ADAP registration is up-to-date as their birthday approaches. At these re-qualification time-points, patients will be required to present a physician's letter re-confirming their HIV diagnosis and medical necessity for taking medications for HIV infection—a programmatic regulatory requirement which, at times, seems ridiculous, but is entirely necessary to maintain ADAP access.

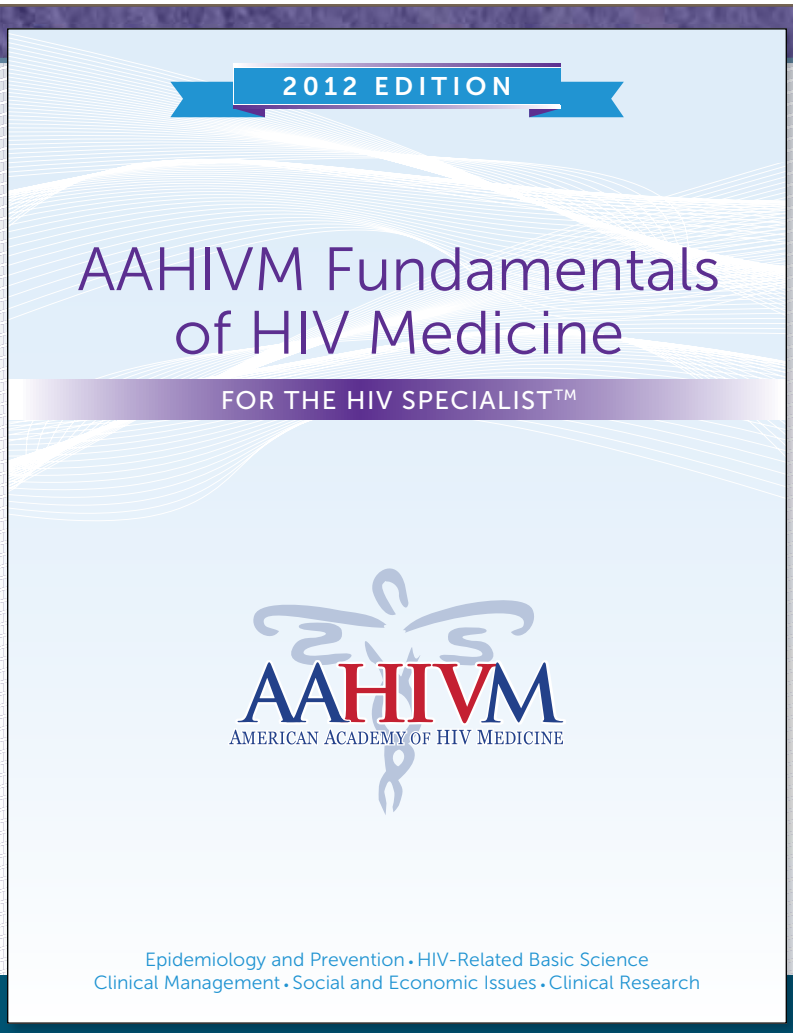
Conclusion

Sometimes it's the simplest things that can unwittingly determine the success or failure of a complex series of events. The scientific advances underlying the development of today's ART cannot be minimized; however, inconsistent or poor adherence can make it all for naught (or even deleterious). Respectful use of these powerful therapeutic tools will allow HIV providers to help their patients benefit from ART until a cure for HIV infection is a reality. Until then, high-level, consistent adherence remains our best ally in using these tools wisely.

References

1. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for Improving entry into and retention in care and antiretroviral adherence for persons with HIV: Evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med. 2012;156:817-833.
2. Sax PE, Meyers JL, Mugavero M, Davis KL. Adherence to antiretroviral treatment and correlation with risk of hospitalization among commercially insured HIV patients in the United States. PLos ONE. 2012;7:e31591.
3. Sahay S, Reddy KS, Dhayarkar S. Optimizing adherence to antiretroviral therapy. Indian J Med Res. 2011;134:835-839.
4. Sandelowski M, Voils CI, Chang Y, Lee E-J. A systematic review comparing antiretroviral adherence descriptive and intervention studies. AIDS Care. 2009;21:953-966.
5. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for Improving entry into and retention in care and antiretroviral adherence for persons with HIV: Evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med. 2012 March 5. [Epub ahead of print]
6. Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in Sub-Saharan Africa and North America. JAMA. 2006;296:679-690.
7. Wakibi SN, Ng'ang'a Z, Mbugua GG. Factors associated with non-adherence with highly active antiretroviral therapy in Nairobi, Kenya. AIDS Res Ther. 2011;8:43.
8. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. 1-239. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf

ABOUT THE AUTHOR: **Dr. Hardy , MD, AAHIVS,** is Director, Division of Infectious Diseases, Cedars-Sinai Medical Center and Professor of Medicine, UCLA David Geffen School of Medicine, Los Angeles, CA



The All-New

2012 AAHIVM Fundamentals of HIV Medicine

is Now Available

- **Comprehensive review across all facets of HIV management**
- **50 of the nation's leading HIV care providers, researchers and experts serving as authors**
- **Newly revised and updated chapters devoted to HIV and non-HIV related co-morbidities and complications**
- **Expanded chapter focused on transmission prevention strategies**
- **A cumulative maximum of 33.5 CME and ACPE credits available.**
- **Each publication comes with a digital copy of the textbook housed on a convenient flash drive at no additional cost**

TO ORDER, PLEASE GO TO WWW.AAHIVM.ORG

IS YOUR PRACTICE TECH SAVVY?

Apply for the 2013 AAHIVM/Institute for Technology in Health Care HIV Practice Award!

For the second year, the American Academy of HIV Medicine is proud to announce the opportunity for HIV practices using innovative models of technology to apply for two $10,000 unrestricted awards.

Last year's award recipients were Malcolm John, MD, MPH, from the 360: The Positive Care Center at UCSF for his use of urban telemedicine in San Francisco, and Raphael J. Landovitz, MD, MSc, from the UCLA Center for Clinical AIDS Research & Education for his use of social networking technology in enrolling young Gay men in HIV prevention research.

The award criteria, as well as an application form, will be available on the Academy website (www.aahivm.org) during the application enrollment period from October 15 to December 1.

The award is made available to the Academy each year with a generous gift from The Institute for Technology in Health Care

ITHC