HIV Treatment and Prevention: The Who, What and Will Be

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Johns Hopkins University School of Medicine
Outline

◊ State of the HIV Epidemic in the U.S.
  ◊ Surveillance trends
  ◊ Ending the HIV Epidemic: A Plan for America
  ◊ Role of Ryan White HIV Care & ADAP Programs - Leave No One Behind
  ◊ U = U

◊ HIV Treatment Guidelines

◊ Maximizing Health Outcomes in Special Populations
Outline

- Treatment Pipeline
  - Advent of Long-acting Injectable ART/What ATLAS & FLAIR Tell Us
  - Administration and other clinical considerations
- What’s Happening with PrEP for HIV
  - USPSTF Grade A Recommendation; Planning for 2021 Implementation
  - TDF vs TAF: DISCOVER Study, FDA Approval & Generic TDF/FTC
  - STD Diagnosis, Treatment and Prevention in the era of PrEP
Press Release

For Immediate Release: Wednesday, February 27, 2019

Contact: Media Relations
(404) 639-3286

CDC data confirm: Progress in HIV prevention has stalled

Need for immediate action —
‘Ending the Epidemic: A Plan for America’

The dramatic decline in annual HIV infections has stopped and new infections have stabilized in recent years, according to a CDC report published today.

The report provides the most recent data on HIV trends in America from 2010 to 2016. It shows
Estimated HIV Incidence among Persons Aged ≥13 Years 2010–2016—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the 95% confidence intervals for the point estimate.
ENDING THE HIV EPIDEMIC:
A PLAN FOR AMERICA

www.hiv.gov
HIV HAS COST AMERICA TOO MUCH FOR TOO LONG

700,000
American lives lost to HIV since 1981

$20 billion
Annual direct health expenditures by U.S. government for HIV prevention and care

Without intervention and despite substantial progress another

400,000
Americans will be newly diagnosed over 10 years despite the available tools to prevent infection
THE TIME IS NOW: RIGHT DATA, RIGHT TOOLS, RIGHT LEADERSHIP

- **Epidemiology**
  - Most new HIV infections are clustered in a limited number of counties and specific demographics

- **Antiretroviral Therapy**
  - Highly effective, saves lives, prevents sexual transmission; increasingly simple and safe

- **Pre-exposure Prophylaxis (PrEP)**
  - FDA-approved and highly effective drug to prevent HIV infections

- **Proven Models of Effective Care and Prevention**
  - 25 years’ experience engaging and retaining patients in effective care

- **Detect and Respond Strategy**
  - Extensive surveillance infrastructure in place, rapid detection and response capacity increasing

There is a real risk of HIV exploding again in the U.S. due to several factors including injection drug use and diagnostic complacency among healthcare providers.
HRSA: RYAN WHITE HIV / AIDS PROGRAM

• More than half of people living with diagnosed HIV in the United States (>500,000) receive services through the Ryan White HIV/AIDS Program

• In 2017, **85.9 percent** of Ryan White HIV/AIDS Program clients were virally suppressed, exceeding the national average of 59.8 percent

• **The Program is funded at $2.3 billion** in fiscal year 2019; administered by the Health Resources and Services Administration (HRSA), HIV/AIDS Bureau (HAB)
HRSA: COMMUNITY HEALTH CENTERS

• Serve more than 27 million patients through nearly 1,400 health centers operating approximately 12,000 service delivery sites nationwide

• Health centers provide a variety of HIV services:
  - Nearly 2 million HIV tests conducted annually
  - More than 165,000 patients with HIV receive medical care services at health centers, including many sites co-funded by the Ryan White HIV/AIDS Program
  - Assure linkage to care and provide HIV prevention services, including Pre-Exposure Prophylaxis (PrEP)
In 2017, HIVMA endorsed the *U=U Consensus Statement*, saying definitively that when a person living with HIV has an undetectable viral load, they will not transmit HIV.

**The science is clear.**

- HPTN 052
- Opposites Attract
- PARTNER
- PARTNER 2

Combined data from 2008-2018 show that there were ZERO linked HIV transmissions after more than a hundred thousand condom-less sex acts within both heterosexual and male-male serodiscordant couples where the partner living with HIV had a durably undetectable viral load.

**But the need remains great.**

- Only 15% of Americans believe that ART is “very effective” in preventing HIV.
- Only 50% of people living with HIV are engaged in care and virally suppressed.

“The body of scientific evidence to-date has established that there is effectively no risk of sexual transmission of HIV when the partner living with HIV has a durably undetectable viral load, validating the U=U message of HIV treatment as prevention.”

*Anthony S. Fauci, MD*
*July 2018*
Why Is U=U Important?

- Knowing U=U can be transformative for people living with HIV (PLWH) and their interpersonal relationships. This affirms that they are not disease vectors and can be touched and loved.

- Many PLWH still face both institutional & personal stigma and discrimination. As a result, many avoid relationships, sexual or otherwise, because of their perceived potential to transmit HIV.

Talk to Your Patients about U=U

1. Counsel them on the necessity of staying undetectable for U=U to work.

2. Educate them on the importance of taking HIV medications every day to stay healthy and also prevent transmission to their sexual partners.

3. Explain and reinforce that when the virus is suppressed, they will not transmit HIV to partners.

4. Encourage patients to know their viral load by keeping their medical appointments so they and their partners are sure of their undetectable status.

5. Counsel patients about STD risk and preventive measures such as condoms and screening.

Resources & Information for Providers

Prevention Access Campaign:
“Consensus Statement” & FAQs [bit.ly/2w6xYKN]

New York City Department of Health:
“HIV U=U Information for Providers” [on.nyc.gov/2NH50X]

The Well Project:
“U=U: Contextualizing a Campaign in the Lives of Women Living with HIV” [bit.ly/2Qnylsa]

National Institutes of Health (NIH):
“10 Things to Know about HIV Suppression” [bit.ly/2hAeBoB]

“HIV Treatment, Viral Reservoir & HIV DNA” [bit.ly/2NbWuEi]

Centers for Disease Control and Prevention (CDC):

“HIV Transmission Prevention: Information for Health Care Providers” [bit.ly/2DOFsUG]

“Evidence of HIV Treatment and Viral Suppression in Preventing the Sexual Transmission of HIV” [bit.ly/2HNHQeZ]

Clinical Consultation Center:
“HIV Warm Line” (800) 933-3413, M-F 9am-8pm ET

Contact HIVMA if you’re interested in learning more or have suggestions for new resources: info@hivma.org
Antiretroviral Treatment Guidelines (ART)
DHHS
IAS-USA
What to Start in Most People with HIV: Integrase Inhibitor + 2 NRTI

<table>
<thead>
<tr>
<th>Recommended for Most People with HIV</th>
<th>Recommended Initial Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bictegravir/TAF/FTC</td>
<td>• Bictegravir/TAF/FTC</td>
</tr>
<tr>
<td>• Dolutegravir/abacavir/3TC</td>
<td>• Dolutegravir/abacavir/3TC</td>
</tr>
<tr>
<td>• Dolutegravir + TAF/FTC or TDF/FTC</td>
<td>• Dolutegravir + TAF/FTC</td>
</tr>
<tr>
<td>• Raltegravir + TAF/FTC or TDF/FTC</td>
<td></td>
</tr>
</tbody>
</table>

- Fewer long-term safety and efficacy data with BIC than with DTG
- If substantial cost difference, TDF (with FTC or 3TC) is effective and generally well-tolerated, esp. if pt not at high risk for bone, renal disease
- Differences between TAF and TDF accentuated when TDF is used with ritonavir or cobicistat

References:

Considerations for Antiretroviral Use in Special Populations of Persons Living with HIV (PLWH)

- Older Persons Living with HIV (OPLWH)
- Persons Living with HIV and Substance Use Disorders (PLWHUSD)
- Transgender Persons Living with HIV (TPLWH)
HIV Medication Pipeline

Pipeline products in HIV and generics

2014: GPEP (5/16), R/TAF (5/16)
2015: GTV (12/16), EFV (12/17), EFV (12/17)
2016: GATV (7/17)
2017: GATV (7/17), GFDC (12/18)
2018: GFDC (12/18), SFV (12/19), GATV (12/20)
2019: GATV (12/20), GFDC (12/21)
2020+: GFDC (12/21)

Generics

Novel Pipeline

Triumeq (2/16)
Pruzex (DRV/Cobi) (1/16)
Evotaz (ATV/Cobi) (1/16)
Darvile (RAI/STC) (2/15)
DTG/RTV (3/16)
RAL/GDF (4/16)

Approved, not commercially available in the US

Disclaimer: Patent expiration dates referenced herein are based on public information currently available. These dates are subject to change based on circumstances that may affect patent terms not known at this time.
Long-Acting Therapies on the Horizon

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Administration</th>
<th>Potential Dosing Frequency</th>
<th>Ongoing Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAB + RPV</td>
<td>INSTI + NNRTI</td>
<td>IM injection</td>
<td>Once a month or once every 2 months</td>
<td>Phase 3</td>
</tr>
<tr>
<td>MK-8591 (+ DOR and 3TC)</td>
<td>NRTTI</td>
<td>Oral</td>
<td>Once a week</td>
<td>Phase 2b</td>
</tr>
<tr>
<td>GS-6207</td>
<td>Capsid inhibitor</td>
<td>SC injection</td>
<td>Once every 3 months</td>
<td>Phase 1</td>
</tr>
<tr>
<td>PRO-140 (leronlimab)</td>
<td>CCR5 antagonist</td>
<td>SC injection</td>
<td>Once a week</td>
<td>Phase 2/3</td>
</tr>
<tr>
<td>Albuvirtide</td>
<td>Fusion inhibitor</td>
<td>IV; potential for SC</td>
<td>Once a week</td>
<td>Phase 2/3 (China)</td>
</tr>
<tr>
<td>TAF</td>
<td>NRTI</td>
<td>Subdermal implant</td>
<td>Once every 6 or 12 months</td>
<td>Pre-clinical</td>
</tr>
</tbody>
</table>

How do you see the impact of emerging long-acting formulations on patient stigma and adherence?

MOA = Mechanism of Action; DOR = Doravirine; NRTTI = Nucleoside Reverse Transcriptase Translocation Inhibitor; SC = Subcutaneous; IV = Intravenous; IM = Intramuscular.

Long-Acting (LA) CAB/RPV

- Cabotegravir: Integrase inhibitor (InSTI) being developed for HIV Tx and PrEP; similar to dolutegravir
- Rilpivirine: NNRTI; first approved May 2011
- Both formulated as long-acting, injectable nanoparticle suspensions for intramuscular (IM) administration
- Also formulated/available as immediate-release oral tablets for daily administration
- Possible FDA approval: Dec 2019; Available January 2020
What Can we Learn from the ATLAS and FLAIR Studies?
FLAIR: Randomized, Open-Label, Noninferiority Study in ART-Naïve Adults

**Screening Phase**
- N=809
- ART-naïve
- HIV-1 RNA ≥1000
- Any CD4 count
- HBsAg-negative
- NNRTI RAMs excluded*

**Induction Phase**
- N=629
- DTG/ABC/3TC single-tablet regimen for 20 weeks†

**Maintenance Phase**
- DTG/ABC/3TC
- Oral daily n=283
- Oral CAB + RPV n=283
- CAB LA (400 mg) + RPV LA (600 mg)‡
- IM monthly n=278

**Extension Phase**

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ATLAS: Randomized, Open-Label, Noninferiority Study in Adults with Viral Suppression

**Randomization**
- N=705
- PI-, NNRTI-, or INSTI-based regimen with 2 NRTI backbone*

**Baseline**
- Day 1

**Week 4**
- Oral CAB + RPV n=308
- CAB LA (400 mg) + RPV LA (600 mg)§
- IM monthly n=303

**Extension Phase or transition to the ATLAS-2M study**

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# FLAIR & ATLAS Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FLAIR Total N=566</th>
<th>ATLAS Total N=616</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range) – year</td>
<td>34 (18–68)</td>
<td>42 (18–82)</td>
</tr>
<tr>
<td>Age ≥50 years – n (%)</td>
<td>62 (11)</td>
<td>162 (26)</td>
</tr>
<tr>
<td>Female – n (%)</td>
<td>127 (22)</td>
<td>203 (33)</td>
</tr>
<tr>
<td>Race – n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>417 (74)</td>
<td>421 (68)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>103 (18)</td>
<td>139 (23)</td>
</tr>
<tr>
<td>Other or missing</td>
<td>46 (8)</td>
<td>56 (9)</td>
</tr>
<tr>
<td>HIV-1 RNA, copies/mL – n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100,000</td>
<td>454 (80)</td>
<td></td>
</tr>
<tr>
<td>≥100,000</td>
<td>112 (20)</td>
<td></td>
</tr>
<tr>
<td>Median baseline CD4+ cell count (IQR) cells/mm³</td>
<td>444 (320, 604)</td>
<td>653 (150–2543)</td>
</tr>
<tr>
<td>HIV-1–HCV co-infection – n (%)</td>
<td></td>
<td>28 (5)</td>
</tr>
<tr>
<td>Median duration of prior ART (range) – year</td>
<td></td>
<td>4 (1–21)</td>
</tr>
<tr>
<td>Baseline third ART agent class – n (%)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI</td>
<td>310 (50)</td>
<td></td>
</tr>
<tr>
<td>INSTI</td>
<td>201 (33)</td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>105 (17)</td>
<td></td>
</tr>
</tbody>
</table>
FLAIR: Achieved Noninferiority for Primary and Secondary Endpoints

**Virologic Outcomes**

<table>
<thead>
<tr>
<th>Proportion of Participants (%)</th>
<th>CAB LA + RPV LA (n=283)</th>
<th>DTG/ABC/3TC (n=283)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virologic nonresponse (≥50 c/mL)</td>
<td>93.6</td>
<td>93.3</td>
</tr>
<tr>
<td>2.1</td>
<td>2.5</td>
<td>4.2</td>
</tr>
</tbody>
</table>

- 3TC, lamivudine; ABC, abacavir; CAB, cabotegravir; CI, confidence interval; DTG, dolutegravir; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.
- *Adjusted for sex and baseline HIV-1 RNA (< vs ≥100,000 c/mL).

**Adjusted Treatment Difference (95% CI)*

**Primary endpoint:**
LA noninferior to DTG/ABC/3TC (≥50 c/mL) at Week 48

<table>
<thead>
<tr>
<th>Difference (%)</th>
<th>CAB LA + RPV LA</th>
<th>DTG/ABC/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.4</td>
<td>-2.8</td>
<td>2.1</td>
</tr>
<tr>
<td>6% NI margin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key secondary endpoint:**
LA noninferior to DTG/ABC/3TC (<50 c/mL) at Week 48

<table>
<thead>
<tr>
<th>Difference (%)</th>
<th>DTG/ABC/3TC</th>
<th>CAB LA + RPV LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3.7</td>
<td></td>
<td>4.5</td>
</tr>
<tr>
<td>-10% NI margin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ATLAS: Achieved Noninferiority for Primary and Secondary Endpoints

Virologic Outcomes

- CAB, cabotegravir; CAR, current antiretroviral; CI, confidence interval; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.
- *Adjusted for sex and baseline third agent class.

Primary endpoint: LA noninferior to CAR (HIV-1 RNA ≥50 c/mL) at Week 48

Key secondary endpoint: LA noninferior to CAR (HIV-1 RNA <50 c/mL) at Week 48

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 139.
### FLAIR & ATLAS

**Adverse Events**

<table>
<thead>
<tr>
<th></th>
<th>FLAIR CAB+RPV (LA) N=283</th>
<th>FLAIR DTG/ABC/3TC N=283</th>
<th>ATLAS CAB+RPV (LA) N=308</th>
<th>ATLAS Combo ART N=308</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any AE (≥10%), n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any event (per participant)</td>
<td>246 (87)</td>
<td>225 (80)</td>
<td>264 (86)</td>
<td>220 (71)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>56 (20)</td>
<td>48 (17)</td>
<td>52 (17)</td>
<td>42 (14)</td>
</tr>
<tr>
<td>Headache</td>
<td>39 (14)</td>
<td>21 (7)</td>
<td>34 (11)</td>
<td>17 (6)</td>
</tr>
<tr>
<td>Upper resp tract infection</td>
<td>38 (13)</td>
<td>28 (10)</td>
<td>32 (10)</td>
<td>25 (8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>32 (11)</td>
<td>25 (9)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Drug-related AEs (≥3%), n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any event (per participant)</td>
<td>79 (28)</td>
<td>28 (10)</td>
<td>88 (29)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>NR</td>
<td>NR</td>
<td>11 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (5)</td>
<td>4 (1)</td>
<td>11 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>13 (5)</td>
<td>0</td>
<td>11 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>NR</td>
<td>NR</td>
<td>11 (4)</td>
<td>0</td>
</tr>
<tr>
<td><strong>AEs leading to withdrawal</strong></td>
<td>9 (3)</td>
<td>4 (1)</td>
<td>10 (3)</td>
<td>5 (2)</td>
</tr>
</tbody>
</table>
## Confirmed Virologic Failure

<table>
<thead>
<tr>
<th>FLAIR</th>
<th>ATLAS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Virologic failure (VF) rate, CAB + RPV arm (week of suspected VF)</strong></td>
<td>1.4% (Wk 20, 28, 48)</td>
</tr>
<tr>
<td>HIV RNA at confirmed VF</td>
<td>287 - 488 c/mL</td>
</tr>
<tr>
<td><strong>Mutations at baseline</strong></td>
<td><strong>RT</strong></td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mutations at VF</strong></td>
<td><strong>RT</strong></td>
</tr>
<tr>
<td><strong>(Treatment Emergent)</strong></td>
<td>E138A/K/T K101E E138K</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HIV-1 subtype</strong></td>
<td>All A1; Russia</td>
</tr>
</tbody>
</table>

* 1 pt with prior nevirapine use had NNRTI but no INSTI mutations at VF
## FLAIR & ATLAS: Injection Site Reactions

<table>
<thead>
<tr>
<th></th>
<th>FLAIR CAB+RPV (LA) N=283</th>
<th>ATLAS CAB+RPV (LA) N=308</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants receiving injections</td>
<td>278</td>
<td>303</td>
</tr>
<tr>
<td>Injections given</td>
<td>7,708</td>
<td>6,978</td>
</tr>
<tr>
<td>ISR events</td>
<td>2,203 (28.6)</td>
<td>1,460 (20.9)</td>
</tr>
<tr>
<td>Pain</td>
<td>1,879 (85.3)</td>
<td>1,208 (82.7)</td>
</tr>
<tr>
<td>Nodule</td>
<td>86 (3.9)</td>
<td>54 (3.7)</td>
</tr>
<tr>
<td>Induration</td>
<td>82 (3.7)</td>
<td>54 (3.7)</td>
</tr>
<tr>
<td>Swelling</td>
<td>38 (1.7)</td>
<td>48 (3.3)</td>
</tr>
<tr>
<td>Warmth</td>
<td>38 (1.7)</td>
<td>NR</td>
</tr>
<tr>
<td>Grade 3 ISR pain</td>
<td>12 (&lt;1)</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td>Median duration of ISRs, days</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Participant with ISR leading to withdrawal</td>
<td>2 (&lt;1)</td>
<td>4 (1.3)</td>
</tr>
</tbody>
</table>
FLAIR and ATLAS: Participant Satisfaction

"They like not having to worry about taking their pills every day...they get their injection and they're good to go. They don't have to think about having HIV every day, they don't have to worry about co-workers or housemates seeing their pill bottles – there's maybe some relief of the stigma of HIV if they don't have to think about it every day."

— Dr. Susan Swindells, University of Nebraska, ATLAS Investigator

FLAIR: 99% preferred the injected LA regimen over the oral induction phase treatment

• ATLAS: 97% preferred LA regimen over previous oral therapy
Dosing and Administration

- **Dosing**
  - Oral regimen to achieve virologic suppression – minimum of 20 weeks (FLAIR)?
  - Four-week oral lead-in dosing with cabotegravir and rilpivirine?
  - Loading CAB/RPV doses: 2 injections of 3 mL
  - Maintenance CAB/RPV doses every four weeks: 2 injections of 2 mL

- Cold-chain storage required (for rilpivirine)

- Scheduling, privacy/exam room space, provider availability, follow up, benefits determination/coordination
Intramuscular Administration

Gluteus Medius

- May require staff training
- Not evaluated in people with buttock implants
- Need private space for administration

Z-Tracking

90°
Mind the PK “Tail” (CAB Example)

Drug persists in 17% of volunteers 52 weeks after last injection

RWHAP Provider Administration

- Viiv Healthcare primarily focused on clinic and office administration
- RWHAP medical providers
  - Clients living with HIV usually seen every three to six months
  - Capacity and staffing to support monthly injections – scheduling, exam rooms, wait times, MD/PA/NP/RN availability, drug product storage and inventory management
  - Capacity and staffing to support monthly retention; client reminders and diligent missed-appointment follow up
  - Provider network sufficiency to meet monthly administration needs of clients where they are
Pre-exposure Prophylaxis (PrEP) for HIV
### ACA mandates that private insurance plans and Medicaid expansion programs cover preventive services with a USPSTF A or B rating at no cost

### Plans must adopt in the plan year that begins at least one year following the final USPSTF recommendation (for PrEP that means January 2021 for most plans and Medicaid)

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons at high risk of HIV acquisition</td>
<td>The USPSTF recommends that clinicians offer pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition</td>
<td>A</td>
</tr>
</tbody>
</table>
## Implementation Considerations

<table>
<thead>
<tr>
<th>Access to the medication</th>
<th>Access to PrEP services beyond medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Competition in the PrEP medication space; individuals need access to clinically recommended regimen, but may not be appropriate to push for open formulary</td>
<td></td>
</tr>
<tr>
<td>• Potential for UM to be used in discriminatory ways (e.g. prior authorization to determine risk should be prohibited)</td>
<td></td>
</tr>
<tr>
<td>• Lab tests and clinical visit costs at initiation and every three months should be covered without cost sharing, but are not explicitly included in USPSTF recommendation</td>
<td></td>
</tr>
</tbody>
</table>
DISCOVER Study: FTC/TAF (Descovy) Noninferior (Similar) to FTC/TDF (Truvada) for PrEP Efficacy

- Primary analysis conducted when 100% completed Wk 48, 50% completed Wk 96
- Noninferiority of FTC/TAF maintained in sensitivity analysis excluding suspected BL infections
  - IRR: 0.55 (95% CI: 0.20-1.48)

### Outcome, n

<table>
<thead>
<tr>
<th>Possible causes of HIV infection</th>
<th>FTC/TAF</th>
<th>FTC/TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected BL infection</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Low TFV-DP in DBS</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Medium/high TFV-DP in DBS</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resistance genotype performed</th>
<th>FTC/TAF</th>
<th>FTC/TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTC</td>
<td>0</td>
<td>4*</td>
</tr>
<tr>
<td>TFV</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*All with suspected BL infection.
DISCOVER Study: Safety, Tolerability and Incidence of STIs

- Similar AE rates with FTC/TAF vs FTC/TDF
  - Study drug-related AEs: 20% vs 23%
  - AEs leading to d/c: 1% vs 2%
- Similar on-study incidence of gonorrhea, chlamydia, or syphilis per AE reporting
  - Incidence per 100 PY: 145.1 vs 138.8
  - Lab-assessed GC/CT rate steady through Wk 96 in each arm (~10% to 15%)
- Deaths: 1 vs 2
  - Included traffic accident, metastatic squamous cell carcinoma, unknown

- Significantly better bone and renal outcomes with FTC/TAF vs FTC/TDF

<table>
<thead>
<tr>
<th>Safety Outcome Through Wk 48</th>
<th>FTC/TAF</th>
<th>FTC/TDF</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change from BL, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spine BMD</td>
<td>0.50</td>
<td>-1.12</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Hip BMD</td>
<td>0.18</td>
<td>-0.99</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Median change from BL in eGFR\textsubscript{CG}, mL/min</td>
<td>1.8</td>
<td>-2.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Renal d/c, n</td>
<td>2</td>
<td>6</td>
<td>--</td>
</tr>
<tr>
<td>Fanconi syndrome, n</td>
<td>0</td>
<td>1</td>
<td>--</td>
</tr>
</tbody>
</table>

Hare. CROI 2019. Abstr 104LB.
FDA Panel: Split Decision for Descovy in PrEP

— Solid yes for men and transgender women, but consensus missing for cisgender women

by Molly Walker, Associate Editor, MedPage Today
August 07, 2019
Do All PLWH and Persons Receiving PrEP Need TAF?
Renal function trajectories after switching from TDF to TAF
A nationwide cohort study

Bernard Surial, Bruno Ledergerber, Alexandra Calmy, Matthias Cavassini, Huldrych Günthard- Helen Kovari, Marcel Stöckle, Enos Bernasconi, Pietro Vernazza, Christoph Fux, Hansjakob Furrer, Andri Rauch, Gilles Wandeler, and the Swiss HIV Cohort Study (SHCS)

@b_surial

Share your thoughts on this presentation with #IAS2019
Change in Kidney Function over Time

Adjusted for age, sex, ethnicity, diabetes, arterial hypertension, cardiovascular disease, HCV and HBV infection, use of ritonavir, cobicistat, dolutegravir and cotrimoxazole
Change in Kidney Function over Time

Adjusted for age, sex, ethnicity, diabetes, arterial hypertension, cardiovascular disease, HCV and HBV infection, use of ritonavir, cobicistat, dolutegravir and cotrimoxazole

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Change in Kidney Function over Time

Adjusted for age, sex, ethnicity, diabetes, arterial hypertension, cardiovascular disease, HCV and HBV infection, use of ritonavir, cobicistat, dolutegravir and cotrimoxazole.
Tenofovir alafenamide versus tenofovir disoproxil fumarate: is there a true difference in efficacy and safety?

Andrew Hill\textsuperscript{1*}, Sophie L Hughes\textsuperscript{2}, Dzintars Gotham\textsuperscript{2} and Anton L Pozniak\textsuperscript{3}

\textsuperscript{1} Department of Pharmacology and Therapeutics, University of Liverpool, UK
\textsuperscript{2} Faculty of Medicine, Imperial College London, UK
\textsuperscript{3} Chelsea and Westminster Hospital NHS Foundation Trust, London, UK

Abstract

\textbf{Background:} Higher plasma tenofovir concentrations are associated with higher risks of renal and bone adverse events. The pharmacokinetic boosters ritonavir (RTV) and cobicistat (COBI) significantly increase plasma area under the curve (AUC) concentrations of tenofovir disoproxil fumarate (TDF), by 25–37%. When combined with RTV or COBI, the dose of tenofovir alafenamide (TAF) is lowered from 25 mg to 10 mg daily, but the TDF dose is maintained at 300 mg daily.

\textbf{Objective:} To assess the differences in safety and efficacy between tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) in regimens with and without the pharmacokinetic boosters RTV and COBI.

\textbf{Methods:} A PubMed/Embase search inclusive of dates up to 17 July 2017 identified 11 randomised head-to-head trials (8111 patients) of TDF versus TAF. The Mantel–Haenszel method was used to calculate pooled risk differences and 95% confidence intervals using random-effects models. A pre-defined sub-group analysis compared TAF with TDF, either when boosted with RTV or COBI, or when unboosted.

\textbf{Results:} Nine clinical trials compared TAF and TDF for treatment of HIV-1 and two were for hepatitis B treatment. The eleven clinical trials documented 4574 patients with boosting RTV or COBI in both arms, covering 7198 patient-years of follow-up. Some 3537 patients received unboosted regimens, totalling 3595 patient-years of follow-up. Boosted TDF-treated patients showed borderline lower HIV RNA suppression <50 copies/mL ($P=0.05$), more bone fractures ($P=0.04$), larger decreases in bone mineral density ($P<0.001$), and more discontinuations for bone ($P=0.03$) or renal ($P=0.002$) adverse events. By contrast, there were no significant differences in HIV RNA suppression rates or clinical safety endpoints between unboosted TAF and unboosted TDF.

\textbf{Conclusions:} TDF boosted with RTV or COBI was associated with higher risks of bone and renal adverse events, and lower HIV RNA suppression rates, compared with TAF. By contrast, when ritonavir and cobicistat were not used, there were no efficacy differences between TAF and TDF, and marginal differences in safety. The health economic value of TAF versus low-cost generic TDF may be limited when these drugs are used without cobicistat or ritonavir.

\textbf{Keywords:} antiretroviral therapy; bone density; cobicistat; HIV; kidney; ritonavir; tenofovir
decreases in bone mineral density \( (P<0.001) \), and more discontinuations for bone \( (P=0.03) \) or renal \( (P=0.002) \) adverse events. By contrast, there were no significant differences in HIV RNA suppression rates or clinical safety endpoints between unboosted TAF and unboosted TDF.

**Conclusions:** TDF boosted with RTV or COBI was associated with higher risks of bone and renal adverse events, and lower HIV RNA suppression rates, compared with TAF. By contrast, when ritonavir and cobicistat were not used, there were no efficacy differences between TAF and TDF, and marginal differences in safety. The health economic value of TAF versus low-cost generic TDF may be limited when these drugs are used without cobicistat or ritonavir.

**Keywords:** antiretroviral therapy; bone density; cobicistat; HIV; kidney; ritonavir; tenofovir
Truvada and the truth: is HIV prevention propelling the STI epidemic?
New Diagnoses of STIs from 1996 to 2015 in MSM in England

Unemo M et al. Lancet Infect Dis 2017
Meta-Analysis of Effect of PrEP on STIs Diagnosis among MSM

- Significant increase in any **rectal STI** diagnosis (OR: 1.39, 95% CI: 1.03-1.87)
- Significant increase in **rectal chlamydia** (OR: 1.59, 95% CI: 1.19-2.13)
- Increase in STIs rates in more **recent studies** (OR: 1.47, 95% CI: 1.05-2.05)

Traeger MW et al. CID 2018
How to Contain the STIs Epidemic?

- A, B and C: promotion of condom use
  - Counseling and behavioral interventions
- Vaccines
  - Viral STIs (hepatitis A and B, HPV)
  - Bacterial STIs (gonorrhea, chlamydia, syphilis)
- Antibiotic Prophylaxis
- Test and Treat
  - Testing for STIs in high risk individuals
  - Treatment and the emergence of antibiotic resistance
- Partner notification and treatment
Everyone with symptoms

Asymptomatic: At least annually and every 3 months if multiple sex partners or recent bacterial STIs
  - HIV Ag/Ab serology if HIV-negative
  - Syphilis serology
  - Chlamydia, Gonorrhea
    - Urethral infection (NAAT)
    - Rectal infection (NAAT)
    - Pharyngeal infection gonorrhea (NAAT)
  - Hepatitis A, B, C serology

No recommendation to test asymptomatic MSM for *M. genitalium*

CDC 2017, BHIVA 2017, France 2018, MMWR STD Treatment Guidelines 2015
ART/PrEP implementation: high rates of condomless sex and STIs did not undermine high efficacy against HIV

New interventions to reinforce individual perception of STIs risk and promote condom use

Frequent testing, early diagnosis, appropriate treatment and better partner notification should help reduce STIs incidence

New behavioral and biomedical strategies to be tested

STIs should not be an excuse to deny PrEP access

Community and individual's empowerment is key

More research to meet 2030 WHO/UNAIDS targets: reduce incidence of HIV and STIs by 90%