Hepatitis C and HIV

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Overview

In 2016 HIV requires more frequent testing among people at risk and earlier ART initiation, and the need for an HIV vaccine or other interventions to reduce set-point viral load and the viral reservoir. These requirements also place emphasis on the important need for early HIV testing and engagement with care given the implications for treatment and prevention.
Case Study

• Alyssa is a 17 year old female runaway referred by the STD Clinic
• She’s been on the streets for 6 months living with her new boyfriend, Derek
• This was the first time she has ever had an STI
• She only has sex with Derek
  – oral, vaginal and anal sex
• She is not using birth control and her last menstrual period was about 6-8 weeks ago
• She only engaged in injection drug use once and shared her boyfriend’s needle
Objectives

• Summarize epidemiology for HIV and Hepatitis C.
• Discuss ongoing changes in HIV and Hepatitis C guidelines
• Discuss new drug development for Hepatitis C and HIV
• Review DAA for the treatment of Hepatitis C
• Highlight research from recent CROI Conference
Case Study

Test Results

• Her urine pregnancy test is positive
• The wet prep of her vaginal secretions shows trichomonads and her vaginal pH is 6.0
• Cervical NAATS = + GC, - CT
• Pharyngeal NAATS = +GC, -CT
• Rectal NAATS = +GC, +CT
• Serologic Tests for Syphilis = RPR+ 1:2/FTA positive
• HIV ELISA +/WB +; CD4 count 250; VL > 1 million
• Hepatitis screen = HEP A, B and C negative
Case Study

• What other questions do you ask?
• Would you order additional tests?
• What about Derek?
• Would you refer?
• To whom?
Topics

HIV
• Epidemiology
• New Drug Development
• Guidelines
• Vaccines
• Treatment as Prevention

Hepatitis C
• Epidemiology
• Screening
• Pathophysiology
• Cost
• Guidelines
• Coinfection
• Treatment
• Referral
## HIV Diagnoses during 2012 Ranked by Estimated Rates

<table>
<thead>
<tr>
<th>STATE/TERRITORY</th>
<th>Reported Cases</th>
<th>Estimated Cases</th>
<th>Estimated Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. District of Columbia</td>
<td>665</td>
<td>887</td>
<td>140.2</td>
</tr>
<tr>
<td>2. Georgia</td>
<td>2,089</td>
<td>4,047</td>
<td>40.8</td>
</tr>
<tr>
<td><strong>3. Maryland</strong></td>
<td><strong>1,347</strong></td>
<td><strong>1,810</strong></td>
<td><strong>30.8</strong></td>
</tr>
<tr>
<td>4. Louisiana</td>
<td>1,177</td>
<td>1,247</td>
<td>27.1</td>
</tr>
<tr>
<td>5. Florida</td>
<td>4,937</td>
<td>5,100</td>
<td>26.4</td>
</tr>
<tr>
<td>6. Puerto Rico</td>
<td>663</td>
<td>886</td>
<td>24.2</td>
</tr>
<tr>
<td>8. New Jersey</td>
<td>1,355</td>
<td>1,824</td>
<td>20.6</td>
</tr>
<tr>
<td>9. Texas</td>
<td>4,234</td>
<td>4,690</td>
<td>18.0</td>
</tr>
<tr>
<td>10. Illinois</td>
<td>1,741</td>
<td>2,186</td>
<td>17.0</td>
</tr>
</tbody>
</table>

**United States** 42,181 48,893 15.4

## Adult/Adolescent HIV Diagnoses during 2014
Ranked by Estimated Rates

<table>
<thead>
<tr>
<th>Rank</th>
<th>State/Territory</th>
<th>Reported Cases</th>
<th>Estimated Cases</th>
<th>Estimated Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>District of Columbia</td>
<td>327</td>
<td>381</td>
<td>66.9</td>
</tr>
<tr>
<td>2</td>
<td>Louisiana</td>
<td>1,332</td>
<td>1,408</td>
<td>36.6</td>
</tr>
<tr>
<td>3</td>
<td>Florida</td>
<td>5,037</td>
<td>5,332</td>
<td>31.3</td>
</tr>
<tr>
<td>4</td>
<td>Maryland</td>
<td>1,121</td>
<td>1,388</td>
<td><strong>27.7</strong></td>
</tr>
<tr>
<td>5</td>
<td>U.S. Virgin Islands</td>
<td>21</td>
<td>24</td>
<td>27.4</td>
</tr>
<tr>
<td>6</td>
<td>Georgia</td>
<td>1,686</td>
<td>2,247</td>
<td>27.0</td>
</tr>
<tr>
<td>7</td>
<td>New York</td>
<td>3,529</td>
<td>3,817</td>
<td>22.8</td>
</tr>
<tr>
<td>8</td>
<td>Puerto Rico</td>
<td>594</td>
<td>686</td>
<td>22.7</td>
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<tr>
<td>9</td>
<td>Texas</td>
<td>4,377</td>
<td>4,817</td>
<td>22.1</td>
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<tr>
<td>10</td>
<td>Mississippi</td>
<td>488</td>
<td>519</td>
<td>21.0</td>
</tr>
<tr>
<td></td>
<td>United States</td>
<td><strong>40,333</strong></td>
<td><strong>44,608</strong></td>
<td><strong>16.6</strong></td>
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</tbody>
</table>

## HIV Diagnoses during 2012
### Ranked by Estimated Rates

<table>
<thead>
<tr>
<th>METROPOLITAN AREA</th>
<th>Reported Cases</th>
<th>Estimated Cases</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Atlanta-Sandy Springs-Roswell, GA</td>
<td>1,361</td>
<td>2,580</td>
<td>47.3</td>
</tr>
<tr>
<td>2. Miami-Fort Lauderdale-West Palm Beach, FL</td>
<td>2,330</td>
<td>2,408</td>
<td>41.8</td>
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<tr>
<td>3. Augusta-Richland County, GA-SC</td>
<td>114</td>
<td>222</td>
<td>38.6</td>
</tr>
<tr>
<td>4. Baton Rouge, LA</td>
<td>295</td>
<td>311</td>
<td>38.1</td>
</tr>
<tr>
<td>5. New Orleans-Metairie, LA</td>
<td>432</td>
<td>457</td>
<td>37.3</td>
</tr>
<tr>
<td>6. Memphis, TN-MS-AR</td>
<td>456</td>
<td>472</td>
<td>35.2</td>
</tr>
<tr>
<td><strong>7. Baltimore-Columbia-Towson, MD</strong></td>
<td><strong>687</strong></td>
<td><strong>917</strong></td>
<td><strong>33.3</strong></td>
</tr>
<tr>
<td>8. Jackson, MS</td>
<td>185</td>
<td>192</td>
<td>33.3</td>
</tr>
<tr>
<td><strong>9. Washington-Arlington-Alexandria, DC-VA-MD-WV</strong></td>
<td><strong>1,504</strong></td>
<td><strong>1,947</strong></td>
<td><strong>33.2</strong></td>
</tr>
<tr>
<td>10. Jacksonville, FL</td>
<td>391</td>
<td>402</td>
<td>29.2</td>
</tr>
<tr>
<td><strong>17. Philadelphia-Camden-Wilmington, PA-NJ-DE-MD</strong></td>
<td><strong>1,173</strong></td>
<td><strong>1,262</strong></td>
<td><strong>21.0</strong></td>
</tr>
</tbody>
</table>

*United States*: 42,168 reported cases, 48,875 estimated cases, 15.4 rate per 100,000

* 50 states, DC, and Puerto Rico, only.

## Total HIV Diagnoses during 2014

**Ranked by Estimated Cases**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Metropolitan Area</th>
<th>Reported Cases</th>
<th>Estimated Cases</th>
<th>Estimated Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>New York-Newark-Jersey City, NY-NJ-PA</td>
<td>4,077</td>
<td>4,496</td>
<td>22.4</td>
</tr>
<tr>
<td>2</td>
<td>Los Angeles-Long Beach-Anaheim, CA</td>
<td>2,235</td>
<td>2,578</td>
<td>19.4</td>
</tr>
<tr>
<td>3</td>
<td>Miami-Fort Lauderdale-West Palm Beach, FL</td>
<td>2,399</td>
<td>2,535</td>
<td>42.8</td>
</tr>
<tr>
<td>4</td>
<td>Houston-The Woodlands-Sugar Land, TX</td>
<td>1,474</td>
<td>1,567</td>
<td>24.1</td>
</tr>
<tr>
<td>5</td>
<td>Chicago-Naperville-Elgin, IL-IN-WI</td>
<td>1,347</td>
<td>1,544</td>
<td>16.2</td>
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<tr>
<td>6</td>
<td>Dallas-Fort Worth-Arlington, TX</td>
<td>1,311</td>
<td>1,498</td>
<td>21.5</td>
</tr>
<tr>
<td>7</td>
<td>Atlanta-Sandy Springs-Roswell, GA</td>
<td>1,095</td>
<td>1,454</td>
<td>25.9</td>
</tr>
<tr>
<td>8</td>
<td>Washington-Arlington-Alexandria, DC-VA-MD-WV</td>
<td>1,108</td>
<td>1,304</td>
<td>21.6</td>
</tr>
<tr>
<td>9</td>
<td>Philadelphia-Camden-Wilmington, PA-NJ-DE-MD</td>
<td>942</td>
<td>1,019</td>
<td>16.8</td>
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<tr>
<td>10</td>
<td>San Francisco-Oakland-Hayward, CA</td>
<td>725</td>
<td>798</td>
<td>17.4</td>
</tr>
<tr>
<td>11</td>
<td>Baltimore-Columbia-Towson, MD</td>
<td>549</td>
<td>678</td>
<td>24.3</td>
</tr>
<tr>
<td></td>
<td>United States (50 states, DC, PR only)</td>
<td>40,472</td>
<td>44,760</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Narrowing the gap in life expectancy for HIV+ compared with HIV- individuals

• Kaiser Permanente Healthcare systems of California Study
• Gap narrowed from 44 in 96-97 to 12 years in 2011
• Even closer on those who started CART therapy at or above 500
Background

- Antiretroviral therapy (ART) has extended the lifespan of HIV+ individuals, with over half now aged 50 or older\(^1\)

- However, studies have suggested HIV+ individuals have not yet reached a normal life expectancy\(^2-8\)

- Most of these studies compared to the general population, with limited ability to account for differences by HIV status
  - Sociodemographic factors and access to care
  - Lifestyle risk factors that affect survival

1. Effros et al., CID, 2008
2. Samji et al., PLOS ONE, 2013
5. Patterson et al., BMC Infect Dis, 2015
6. Harrison et al., JAIDS, 2010
7. May et al., BMJ, 2011
8. Wada et al., Am J Epidemiol, 2013
Summary

- HIV+ had a 13-year gap in life expectancy relative to HIV- in 2008-2011, and an 8-year gap with ART initiation at CD4 ≥500
- Lowest life expectancies for HIV+ Blacks and IDUs, and highest for Hispanics
- Life expectancy gap was narrowed in subgroups without a history of hepatitis B or C, drug/alcohol abuse, or smoking
- Comparing HIV+ at KP to the general U.S. population underestimated the survival gap
Decreasing mortality rates and increasing life expectancy for HIV+, while stable for HIV-.
Life expectancies at age 20 for HIV+ and HIV-
By race/ethnicity

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>37</td>
<td>50</td>
</tr>
<tr>
<td>Black</td>
<td>63</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>46</td>
</tr>
<tr>
<td>Hispanic</td>
<td>65</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>52</td>
</tr>
</tbody>
</table>

- Significant increases for HIV+ Whites, Blacks, and Hispanics ($P<0.001$ for all)
- HIV+ Whites and Hispanics reached higher life expectancies than Blacks ($P=0.007$ and $P=0.001$)
- Significant gaps remained compared with HIV- Whites, Blacks, and Hispanics ($P<0.001$ for all)
Strengths and limitations

Strengths

- First study, to our knowledge, to directly compare life expectancy by HIV status, accounting for individual-level factors and access to care
- Complete ascertainment of deaths
- Generalizable to the broader insured population

Limitations

- Imperfect measurement of risk factors
- Some missing data on race/ethnicity for HIV- subjects
- HIV+ life expectancy may have increased further since 2011
Biopharmaceutical Company Researchers Are Developing More Than 40 Medicines and Vaccines For HIV Infection Treatment and Prevention
HIV- AIDS in the United States

THEN AND NOW

Since HIV/AIDS was first recognized in 1981, advances in medicines have helped lower the death rate by 83%. Prior to 1995, when the first antiretroviral treatment was approved by the FDA, an HIV diagnosis was a death sentence. Now, thanks to medicines developed by biopharmaceutical scientists and their research partners, it is a chronic condition with manageable costs and patients are able to reach nearly a full life expectancy.

ARTHUR ASHE
Due to the lack of effective medicines, Arthur Ashe succumbed to AIDS-related pneumonia at 50 years old in 1993, just 10 years after he contracted the disease and 5 years after diagnosis.

MAGIC JOHNSON
Despite being diagnosed with HIV/AIDS in 1991, Magic is expected to meet his full life expectancy due to the treatments available at the outset of his diagnosis.

PROGRESS IN THE FIGHT

1995: the first protease inhibitors were approved by the FDA, and the HIV/AIDS death rate decreased 67% over a few years.

2%: transmission rates between mother and infant dropped below 2%

2012: U.S. death rate dropped 83%

Source: Magic Johnson Foundation, Arthur Ashe Learning Center (AALC).
44 Medicines and vaccines in development

HIV/AIDS in the United States

44 Medicines & Vaccines in Development for HIV Infection

25 Antivirals

3 Cell/Gene Therapy

16 Vaccines

Source: 2014 PhRMA Medicines in Development for HIV/AIDS, PhRMA.
HIV Resistant CD4 cells

Figure 1. HIV lifecycle and strategies to engineer HIV-resistant cells.

- 1) Entry
- 2) Uncoating
- 3) Reverse transcription
- 4) Integration
- 5) Transcription
- 6) RNA export
- 7) Translation
- 8) Assembly
- 9) Budding, maturation

Markers:
- C46
- Rh-hu Trim5a
- siRNA/ribozyme
- CCR5
- ZFNs

Restriction factors/inhibitor
Summary and Conclusions

• **SB-728 CD4 T-cells after Cytoxan Conditioning**
  - Cytoxan conditioning at doses up to 1 gm/m² improves adoptive transfer of total CD4 T-cells and CCR5-modified CD4 T-cells with minimal toxicity
  - Eighteen subjects have been treated with Cytoxan and SB-728-T modified CD4 T-cells and four remain on long-term treatment interruption (40-71 weeks with VL ranging from 1,230-14,300 copies/mL)

• **SB-728 CD4/CD8 T-cells after Cytoxan Conditioning**
  - Three subjects have been treated with a CCR5 modified T-cell product that contains both CD4 and CD8 T-cells
    • CD8 repletion did not affect the safety profile
    • Three subjects have shown a doubling of their CD8 T-cells (2000-4000 cells/ul)
    • CCR5 modified CD4 and CD8 T-cells were high—reflecting expansion of CD8 T-cells
    • One subject has controlled VL during TI, another subject had delayed onset of viremia

• **The large increase in CCR5 modified CD8 T-cells may mimic elite controllers and may improve HIV control through CD8 HIV cytolytic T-cells**
Development of a New Medicine

The Drug Development and Approval Process

- **Drug Discovery**: Pre-discovery, basic research and screening (Tens of thousands of compounds).
- **Clinical Trials**: Phase I (20-100 volunteers), Phase II (100-500 volunteers), Phase III (1,000-5,000 volunteers).
- **FDA Review**, Scale-Up to Manufacturing, Phase IV/Ongoing Research and Monitoring.

Duration:
- 3-6 years: Pre-discovery and screening.
- 6-7 years: Clinical trials.
- 0.5-2 years: FDA review and manufacturing.
- Indefinite: Phase IV and ongoing research.

MidAtlantic AETC
HIV in the Headlines

Robert C. Gallo, MD

Most widely known for the discovery of human retroviruses, the co-discovery of HIV and development of the HIV blood test

HIV/AIDS Presents an Unprecedented Challenge to Developing a Vaccine

Posted: 10/29/2014 12:07 pm EDT  |  Updated: 12/29/2014 5:59 am EST
Shot for Prevention

• new drug cabotegravir has been shown to protect monkeys from infection by an HIV-like virus
• Long acting cabotegravir has the potential to create an option that could improve adherence by making it possible to receive the drug by injection once every three months.
Shot for Prevention

While we are still a long way off from showing that this drug works for HIV prevention in humans, our hope is that it may one day offer high risk women, as well as men, an additional option for HIV prevention.
Cabotegravir + Rilpivirine as Long-Acting Maintenance Therapy: LATTE-2 Week 32 Results

David A. Margolis,¹ Juan Gonzalez-Garcia,² Hans-Jürgen Stellbrink,³ Joe Eron,⁴ Yazdan Yazdanpanah,⁵ Sandy K. Griffith,¹ David Dorey,⁶ Kimberly Y. Smith,¹ Peter E. Williams,⁷ William R. Spreen¹

¹ViiV Healthcare, Research Triangle Park, NC; ²Hospital La Paz, Madrid, Spain; ³ICH Hamburg, Germany; ⁴University of North Carolina, Chapel Hill, NC; ⁵Hôpital Bichat Claude Bernard, Paris, France; ⁶GlaxoSmithKline, Mississauga, Ontario, Canada; ⁷Janssen Research and Development, Beerse, Belgium

23rd Conference on Retroviruses and Opportunistic Infections; February 22-25, 2016; Boston, MA
Background

- CAB is an HIV-1 integrase inhibitor
  - Oral 30 mg tablet (t½, ~40 hours)
  - LA nanosuspension 200 mg/mL (t½, ~20-40 days)
- RPV is an HIV-1 NNRTI
  - Oral 25 mg tablet (t½, ~50 hours)
  - LA nanosuspension 300 mg/mL (t½, ~30-90 days)
- Oral 2-drug CAB + RPV proof of efficacy through Week 96 in LATTE-1

BL, baseline; CAB, cabotegravir; CI, confidence interval; EFV, efavirenz; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine; t½, half-life.
Conclusions

- LATTE-2 results successfully demonstrate the potential to maintain HIV-1 viral load <50 c/mL with LA IM CAB + RPV, dosed once Q4W or Q8W

- Two subjects met PDVF criteria
  - Q8W (n=1), oral CAB (n=1); both without evidence of resistance at failure

- Injection tolerability
  - Majority of ISRs were Grade 1 to 2 pain, with a median duration of 3 days
  - Few subjects had an ISR that led to discontinuation, with high overall reported satisfaction

- Regimen selection criteria
  - Neither Q4W IM or Q8W IM dosing was ruled out on the basis of pre-specified criteria
  - Upcoming Week 48 analysis will contribute to final dose selection for phase III studies
FDA Approved Antiretroviral Drugs 2016/Combination ART

**NNRTI**
- Sustiva (Efavirenz/EFV)
- Viramune (nevirapine)
- Rescriptor (delavirdine)
- Intelence (etravirine)
- Edurant (rilpivirine)

**NRTI**
- Hivid (ddC)
- Zerit (d4T)
- Videx (ddl)
- Retrovir (AZT)
- Epivir (3TC)
- Abacavir (Ziagen/ABC)
- Viread (tenofovir)
- Emtriva (FTC)

**PI**
- Viracept (nelfinavir)
- Norvir (Ritonavir)
- Crixivan (indinavir)
- Fortovase (saquinavir)
- Invirase (saquinavir mesylate)
- Kaletra (lopinavir/ritonavir)
- Agenerase (amprenavir)
- Reyataz (atazanavir)
- Evotaz (atazanavir/cobicistat)
- Lexiva (Fosamprenavir)
- Prezista (Darunavir)
- Prezobix (Darunavir/cobicistat)

**Fusion Inhibitors**
- Fuzeon (Enfuvirtide)
- Maraviroc (Selzentry)

**Integrase Inhibitors**
- Raltegravir (Isentress)
- Dolutegravir (Tivicay)

**Combivir** = AZT + 3TC
**Trizivir** = ABC + AZT + 3TC
**Truvada** = FTC + Tenofovir
**Epzicom** = ABC + 3TC

**Atripla** = Truvada + Sustiva
**Complera** = Truvada + Edurant
**Triumeq** = Abacavir + Dolutegravir
Attachment Inhibitor

BACKGROUND

- BMS-663068 is a prodrug metabolized to the active moiety BMS-626529, a first-in-class attachment inhibitor that binds to HIV-1 gp120, preventing initial viral attachment and entry into the host CD4+ T cell (Figures 1a & 1b).\(^1\)\(^2\)

- Unlike CCR5 antagonists, BMS-626529 binds directly to the virus rather than the host cell\(^2\)\(^3\) and therefore:
  - acts prior to co-receptor binding and fusion\(^2\)
  - is active against CCR5-, CXCR4- and dual-tropic (R5X4) strains of HIV-1.\(^2\)\(^4\)\(^-\)\(^7\)

- BMS-626529 has:
  - *in vitro* activity against HIV-1 viruses (except subtype AE and Group O)\(^4\)
  - a unique resistance profile and no *in vitro* cross-resistance has been observed with other classes of antiretrovirals (ARVs).\(^4\)\(^5\)
Attachment Inhibitor

Figure 1a: Conversion of BMS-663068 to BMS-626529

Gastrointestinal lumen

BMS-663068 (prodrug)

↓

Alkaline phosphatase

BMS-626529 (active moiety)

↓

BMS-626529

Blood plasma

Figure 1b: BMS-626529 attachment inhibitor: proposed mechanism of action

No drug

With drug

- BMS-626529

gp120

Conformational changes

gp41

CD4 binding site

CD4 binding

CD4 receptor

Cell surface

Conformational changes inhibited

CD4 binding blocked
Attachment Inhibitor

RESULTS

Baseline characteristics

- Baseline demographic and disease characteristics were broadly similar across all treatment groups (Table 1).
  - Median age 39 years; 60% male.
  - 66% HIV-1 subtype B.
  - Median baseline HIV-1 RNA: $4.85 \log_{10} \text{ c/mL}$.
  - Median baseline CD4+ T-cell count: 229.5 cells/μL.
  - ~50% of subjects had ≥1 major protease inhibitor (PI), nucleoside reverse transcriptase inhibitor (NRTI) or non-NRTI resistance-associated mutation at baseline (M184V/I, 31%; K103N, 29%; thymidine analogue mutations, 13%; major PI mutations, 2%).
When to Start Therapy: Balance Now Favors Early ART

- Drug toxicity
- Preservation of limited Rx options
- Risk of resistance (and transmission of resistant virus)

- ↑ potency, durability, simplicity, safety of current regimens
- ↓ emergence of resistance
- ↓ toxicity with earlier therapy
- ↑ subsequent treatment options
- Risk of uncontrolled viremia at all CD4 levels
- ↓ transmission
START: 57% Reduced Risk of Serious Events or Death With Immediate ART

- 4.1% vs 1.8% in deferred vs immediate arms experienced serious AIDS or non-AIDS–related event or death (HR: 0.43; 95% CI: 0.30-0.62; P < .001)
DHHS, IAS-USA, EACS Guidelines: Recommended Regimens for First-line ART

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</thead>
<tbody>
<tr>
<td>INSTI</td>
<td>DTG/ABC/3TC</td>
<td>DTG + ABC/3TC</td>
<td>DTG/ABC/3TC</td>
</tr>
<tr>
<td></td>
<td>DTG + TDF/FTC</td>
<td>DTG + TDF/FTC</td>
<td>DTG + TDF/FTC</td>
</tr>
<tr>
<td></td>
<td>EVG/COBI/TDF/FTC</td>
<td>EVG/COBI/TDF/FTC</td>
<td>EVG/COBI/TDF/FTC</td>
</tr>
<tr>
<td></td>
<td>EVG/COBI/TAF/FTC</td>
<td>RAL + TDF/FTC</td>
<td>RAL + TDF/FTC</td>
</tr>
<tr>
<td></td>
<td>RAL + TDF/FTC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boosted PI</td>
<td>DRV + RTV + TDF/FTC</td>
<td>DRV + RTV + TDF/FTC</td>
<td>DRV + RTV + TDF/FTC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ATV + RTV + TDF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ATV + RTV + ABC/3TC</td>
<td></td>
</tr>
<tr>
<td>NNRTI</td>
<td>EFV/TDF/FTC</td>
<td>EFV + ABC/3TC</td>
<td>RPV/TDF/FTC</td>
</tr>
<tr>
<td></td>
<td>RPV/TDF/FTC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Recommendations may differ based on baseline viral load, CD4+ count, CrCl, eGFR, HLA-B*5701 status, HBsAg status, and osteoporosis status
- Publication of these guidelines preceded the availability of DTG/ABC/3TC as a single-tablet regimen

## Potential Advantages and Disadvantages of Single-Tablet Regimens

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Simplicity</td>
<td>▪ Inability to adjust dosages of components if needed due to drug–drug interactions or tolerability issues, eg, renal insufficiency</td>
</tr>
<tr>
<td>▪ Convenience</td>
<td>▪ Not available for all ART regimens</td>
</tr>
<tr>
<td>▪ Fewer copays</td>
<td>▪ Not available for all NRTI pairings</td>
</tr>
<tr>
<td>▪ Reduces selective nonadherence to components of regimen</td>
<td></td>
</tr>
</tbody>
</table>

Slide credit: [clinicaloptions.com](http://clinicaloptions.com)
### Available Single-Tablet Regimens

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type</th>
<th>Year of FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz/tenofovir DF/emtricitabine (EFV/TDF/FTC)</td>
<td>NNRTI + dual NRTI</td>
<td>2006</td>
</tr>
<tr>
<td>Rilpivirine/tenofovir DF/emtricitabine (RPV/TDF/FTC)</td>
<td>NNRTI + dual NRTI</td>
<td>2011</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat/tenofovir DF/emtricitabine (EVG/COBI/TDF/FTC)*</td>
<td>INSTI + booster + dual NRTI</td>
<td>2012</td>
</tr>
<tr>
<td>Dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)*</td>
<td>INSTI + dual NRTI</td>
<td>2014</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (EVG/COBI/TAF/FTC)*</td>
<td>INSTI + booster + dual NRTI</td>
<td>2015</td>
</tr>
</tbody>
</table>

*DHHS recommended regimen for initial ART.
Take-Home Points

• Randomized trial data support ART initiation in pts with CD4+ cell count > 500 cells/mm$^3$
• ART guidelines recommend ART for all pts regardless of CD4+ cell count
• Recommended regimens for ART initiation have been revised
  – NNRTIs removed from DHHS first-line options
  – EVG/COBI/TAF/FTC added to DHHS first-line options, safe in pts with CrCl ≥ 30 mL/min
Switch from F/TDF to F/TAF

- Randomized, double-blind, double-dummy, active-controlled study

Virologically Suppressed (< 50 c/mL)
- F/TDF + Third Agent
- eGFR ≥50 mL/min

n=333

F/TAF (200/10 or 200/25 mg)* QD
- F/TDF Placebo QD
- Continue Third Agent

n=330

F/TDF (200/300 mg) QD
- F/TAF* Placebo QD
- Continue Third Agent

Primary Endpoint
HIV-1 RNA <50 c/mL

Secondary Endpoint

F/TAF Dose:
- 200/10 mg with boosted PIs
- 200/25 mg with unboosted third agents
Virologic Success in Select Subgroups

- Overall
- Age: <50 yr, ≥50 yr
- Sex: Male, Female
- Race: Non-black, Black

<table>
<thead>
<tr>
<th>HIV-1 RNA &lt;50 c/mL, %</th>
<th>F/TAF (n=333)</th>
<th>F/TDF (n=330)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>94</td>
<td>93</td>
</tr>
<tr>
<td>Age</td>
<td>93 92</td>
<td>96 94</td>
</tr>
<tr>
<td>Sex</td>
<td>94 95</td>
<td>94 94</td>
</tr>
<tr>
<td>Race</td>
<td>94 94</td>
<td>94 90</td>
</tr>
</tbody>
</table>

- F/TAF (n=333): 314/333, 307/330
Changes in eGFR

*Median (Q1, Q3) change eGFR* (mL/min)

- F/TAF (n=333)
  - Week 48: 8.4 mL/min
  - p < 0.001

- F/TDF (n=330)
  - Week 48: 2.8 mL/min

*eGFR calculated with Cockcroft-Gault equation

Change in Renal Biomarkers at Week 48
Change in Bone Mineral Density through Week 48

**Spine**

- Mean % change (95% CI)
- BL: 0, 24: 1.5, 48: -0.2
- **p < 0.001**

**Hip**

- Mean % change (95% CI)
- BL: 0, 24: 1.1, 48: -0.2
- **p < 0.001**

**F/TAF, n**

- BL: 321, 24: 310, 48: 300
- BL: 320, 24: 310, 48: 306

**F/TDF, n**

- BL: 321, 24: 309, 48: 300
- BL: 317, 24: 305, 48: 303

≥ 3% BMD increase at Week 48

- **F/TAF**
  - 30%
  - **p < 0.001**

- **F/TDF**
  - 14%

- **F/TAF**
  - 17%
  - **p = 0.003**

- **F/TDF**
  - 9%
HIV Treatment as Prevention

- Pivotal Studies (HPTN 052)
- Community Viral Load
- High levels of access and treatment to ARV has the potential to reduce new infections
- Treating HIV infected persons will reduce transmissions
Routine HIV Testing

- **More people need to be tested for HIV!**
- Effective 2008 & 2015, Maryland amended HIV Testing Laws to make it *easier* to test for HIV.
- **Testing based on risk factors alone still fails to identify many people with HIV.**
- The CDC **recommends** HIV testing for all patients ages 13-64.
- The shift to universal HIV testing has been effective in identifying more people with HIV and at earlier stages of the disease.
Occupational Post Exposure Prophylaxis

- 600,000-800,000 needlestick or other percutaneous exposures annually in US
- Exposure by profession
  - Nurses 34%
  - Residents/Fellows 18%
  - Attending physicians 14%
  - Phlebotomists 5%
- Risk of HIV transmission ~0.3%
- 57 transmissions reported through 2010

Post Exposure Prophylaxis

Risk Factors for HIV Seroconversion in HCWs

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted Odds Ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep Injury</td>
<td>15.0</td>
</tr>
<tr>
<td>Visible Blood on Device</td>
<td>6.2</td>
</tr>
<tr>
<td>Terminal Illness in Source Patient</td>
<td>5.6</td>
</tr>
<tr>
<td>Needle in Source Vein/Artery</td>
<td>4.3</td>
</tr>
<tr>
<td>PEP with Zidovudine (AZT)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

HIV Treatment as Prevention

• HIV testing is the foundation for both prevention and care efforts.
• Early identification of infection empowers individuals to take action that benefits both their own health and the public health.
HIV Treatment as Prevention

• Early treatment of infected persons substantially reduces their risk of transmitting HIV to others.
• The prevention benefit of treatment can only be realized with effective treatment, which requires linkage to and retention in care, and adherence to antiretroviral therapy.
Interesting Facts

• John Hopkins approved to perform HIV positive to HIV positive organ transplants
• Under half in US analysis get genotype testing at linkage to care
• Three Maviroc PreP regimens protective
MTN-020/ASPIRE Summary

- A monthly vaginal ring containing dapivirine safely reduced incident HIV in African women.
  - Risk was reduced by \( \frac{1}{3} \) overall and by \( \frac{1}{2} \) among those aged \( \geq 22 \)

- These are the first results to demonstrate HIV-1 protection by a sustained-release approach for delivery of an antiretroviral for HIV-1 prevention.

- HIV-1 protection was greater in subgroups with evidence of better adherence to ring use.
Discussion - Age

• HIV-1 protection was not observed for women aged 18-21 and objective markers of adherence were lower in this subgroup compared to women older than 21.

• Both behavioral and biologic effects may have contributed to a lack of HIV-1 protection in women aged 18-21 in this study, and further research is needed to understand the unique prevention needs of this youngest group of women.