Updates on the Management of HIV in Older Adults

To enter the Q&A and polling questions for this activity, go to ascp.com/qa and click on the title of this activity, as seen below.
Disclosures

- Elias B. Chahine
  - Speakers’ bureaus of Merck & Co, Inc. and Paratek Pharmaceuticals, Inc.
- Edward Grace
  - Nothing to disclose

Goal

- Upon completion of this presentation, the learner should develop an understanding of the treatment of HIV-1 in older adults.
Learning Objectives

• At the conclusion of this presentation, pharmacists should be able to:
  • Review the pathophysiology of the HIV virus and its pathogenicity in humans.
  • Identify recently approved antiretroviral agents for HIV Infection and prevention during the past 3-years.
  • Apply knowledge of newer antiretroviral agents in order to create effective combinations for the suppression and prevention of HIV infections.
  • Evaluate appropriate antiretroviral combinations suitable for older adults given specific adverse effects, monitoring parameters, and drug interactions.
  • Formulate a treatment plan for the management of antiretroviral related adverse effects and drug/food interactions in the older adult.

Abbreviations

• ADR: Adverse-drug reactions
• AIDS: acquired immunodeficiency syndrome
• AML: acute myeloid leukemia
• ART: Antiretroviral therapy
• ARV: antiretroviral
• cART: Combination antiretroviral therapy
• HIV: human immunodeficiency virus
• INSTI: integrase strand transfer inhibitor
• IVDU: intravenous drug use
• NICM: Non-infectious comorbidities
• NNRTI: non-nucleoside reverse transcriptase inhibitor
• nPEP: non-occupational post-exposure prophylaxis
• NRTI: nucleoside/nucleotide reverse transcriptase inhibitor
• OALWH: Older adults living with HIV
• OI: opportunistic infections
• oPEP: occupational post-exposure prophylaxis
• PEP: post-exposure prophylaxis
• PI: protease inhibitor
• PLWH: People Living with HIV
• PP: Polypharmacy
• PrEP: pre-exposure prophylaxis
• SCT: stem cell transplantation
Outline

• The Berlin patient/ London patient
• Epidemiology
• Transmission
• Pathophysiology
• Treatment
• Prevention
• Prophylaxis

The Berlin Patient/London Patient

• Timothy Ray Brown
• Diagnosed with HIV in 1995 while living in Berlin, Germany
• Virally suppressed for years with antiretroviral therapy (ART)
• Later diagnosed with AML in 2007 for which he underwent a SCT
• His doctor chose a donor who was positive for the homozygous CCR5Δ32 mutation
  • Patients with this mutation are resistant to M-tropic strains of HIV-1, which prevents HIV-1 from entering into CD4 cells
• Brown stopped taking ART the day he received the first SCT
• He was HIV negative 3 months after his first SCT
• He has remained HIV negative for more than 12 years

Epidemiology

• There were 36.7 million people living with HIV worldwide in 2017

• Approximately 1.1 million of those people live in the U.S.

• There were 15,807 deaths among people with HIV in 2016

• 1 in 7 people living with HIV are unaware of their infection

https://www.who.int/features/qa/71/en/
https://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html
New HIV Diagnoses by Race/Ethnicity, 2016

- Multiple races: 2% (872)
- American Indians/Native Alaskans: 1% (212)
- Native Hawaiians/Other Pacific Islanders: <1% (59)
- Hispanics/Latinos*: 26% (9,908)
- Black/African Americans: 43% (16,694)
- Whites: 26% (10,049)
- Asians: 2% (945)

New HIV Diagnoses by Age, 2017

- 13-24: 8,164
- 25-34: 13,433
- 35-44: 7,397
- 45-54: 5,735
- 55-64: 3,026
- 65+: 885

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https://www.cdc.gov/hiv/basics/statistics.html

https://www.cdc.gov/hiv/statistics/overview/ataglance.html
Transmission

- Contact with:
  - Blood
  - Breast milk
  - Broken skin
  - Mucus membranes
  - Semen/pre-semen
  - Vaginal fluid
  - Wounds

- Methods:
  - IVDU
    - highest risk
  - Sexual behaviors
    - Receptive anal sex – highest risk
    - Oral sex – lowest risk
  - Needle sticks
  - Breastfeeding

NOT transmitted via air, saliva/secretions, or skin-to-skin contact

New HIV Diagnoses by Transmission Category, 2017

- Male-to-Male Sexual Contact
  - 66% (25,748)
- Heterosexual Contact
  - 24% (9,170)
- Injection Drug Use
  - 6% (2,389)
- Male-to-Male Sexual Contact + Injection Drug Use
  - 3% (1,252)

https://www.cdc.gov/hiv/basics/index.html
https://www.cdc.gov/hiv/basics/statistics.html
Pathophysiology

**Binding**
HIV binds to CD4 cell

**Fusion**
HIV envelope and cell membrane fuse together, and HIV enters the cell

**Reverse Transcriptase**
HIV RNA is converted into HIV DNA via reverse transcriptase

**Integration**
HIV DNA is inserted into cell DNA via integrase enzyme

**Replication**
HIV DNA replicates to produce chains of HIV protein

**Assembly**
New HIV proteins and RNA move to surface of the cell to form immature HIV

**Budding**
Immature (non-infectious) HIV pushes itself out of the CD4 cell

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To access the polling questions, go to this link: ascp.com/qa and select the “Updates on the Management of HIV in Older Adults” activity, as seen below.
Question

- You are precepting two students during an advanced pharmacy practice experience in HIV. You are teaching them about the HIV life cycle. What is the order of the seven stages of HIV replication?

  - A) Budding → Assembly → Replication → Integration → Reverse transcription → Fusion → Binding
  - B) Budding → Assembly → Reverse transcription → Integration → Replication → Fusion → Binding
  - C) Binding → Fusion → Replication → Integration → Reverse transcription → Assembly → Budding
  - D) Binding → Fusion → Reverse transcription → Integration → Replication → Assembly → Budding

Treatment

- Baseline laboratory tests
- Goals of therapy
- Contemporary ARVs
- ARV sites of action
- First-line ART
- INSTIs
- Dual NRTIs
- NNRTIs
- PIs
- Treatment response
- U=U campaign
  - Undetectable viral load = Untransmittable
- Causes of treatment failure
- Second-line ART
- Switching regimens
- Switching to a two-drug regimen
Baseline Laboratory Tests

- CD4 count
- HIV viral load
- Resistance testing (genotypic preferred over phenotypic)
- HLA-B*5701 (if considering ABC)
- Hepatitis B (HBV) and C (HCV) testing
- Routine labs (CBC, BMP, liver and renal function tests)
- Urinalysis
- Pregnancy test

Goals of Therapy

- Maximally and durably suppress plasma HIV RNA
- Restore and preserve immunologic function
- Reduce HIV-associated morbidity
- Prolong the duration and quality of survival
- Prevent HIV transmission
## Contemporary ARVs

<table>
<thead>
<tr>
<th>INSTIs</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir (BIC)</td>
<td>Abacavir (ABC)</td>
<td>Efavirenz (EFV)</td>
<td>Atazanavir (ATV)</td>
</tr>
<tr>
<td>Dolutegravir (DVG)</td>
<td>Dolutegravir (FTC)</td>
<td>Doravirine (DOR)</td>
<td>Darunavir (DRV)</td>
</tr>
<tr>
<td>Elvitegravir (EVG)</td>
<td>Lamivudine (3TC)</td>
<td>Rilpivirine (RPV)</td>
<td></td>
</tr>
<tr>
<td>Raltegravir (RAL)</td>
<td>Tenofovir alafenamide fumarate (TAF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tenofovir disoproxil fumarate (TDF)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Bictegravir (BIC)
- Dolutegravir (DVG)
- Elvitegravir (EVG)
- Raltegravir (RAL)
- Abacavir (ABC)
- Dolutegravir (FTC)
- Lamivudine (3TC)
- Tenofovir alafenamide fumarate (TAF)
- Tenofovir disoproxil fumarate (TDF)
- Efavirenz (EFV)
- Doravirine (DOR)
- Rilpivirine (RPV)
- Atazanavir (ATV)
- Darunavir (DRV)

### ARV Sites of Action

**Entry Inhibitors** (not discussed)

1. **Binding (also called Attachment):** HIV bonds (attaches RNA) to receptors on the surface of a CD4 cell.
   - CCR5 antagonists
   - Post-attachment inhibitors

2. **Fusion:** The HIV envelope and the CD4 cell membrane fuse (join together), which allows HIV to enter the CD4 cell.
   - Fusion inhibitors

3. **Reverse Transcription:** Inside the CD4 cell, HIV releases and uses reverse transcriptase (an HIV enzyme) to convert its genetic material—HIV RNA—into HIV DNA. The conversion of HIV RNA to HIV DNA allows HIV to enter the CD4 cell nucleus and combine with the cell's genetic material—cell DNA.
   - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
   - Nucleoside reverse transcriptase inhibitors (NRTIs)

[https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle](https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle)
ARV Sites of Action

https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle

First-Line ART

For most people with HIV

INSTI + 2 NRTIs

- BIC/TAF/FTC
- DTG/ABC/3TC
- DTG + [TAF or TDF]/FTC
- RAL + [TAF or TDF]/FTC

For certain clinical situations

<table>
<thead>
<tr>
<th>INSTI + 2 NRTIs</th>
<th>Boosted PI + 2 NRTIs</th>
<th>NNRTI + 2 NRTIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVG/[TAF or TDF]/FTC</td>
<td>DRV/c or DRV/r + [TAF or TDF]/FTC</td>
<td>DOR/TDF/3TC</td>
</tr>
<tr>
<td>RAL + ABC/3TC</td>
<td>[ATV/c or ATV/r] + [TAF or TDF]/FTC</td>
<td>DOR + TAF/FTC</td>
</tr>
<tr>
<td></td>
<td>[DRV/c or DRV/r] + ABC/3TC</td>
<td>EFV + [TDF/FTC] or [TDF/3TC] or [TAF/FTC]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RPV/[TAF or TDF]/FTC</td>
</tr>
</tbody>
</table>

When ABC and TAF/TDF cannot be used

- DTG + 3TC
- DRV/r + RAL (BID) or 3TC

Treatment duration is INDEFINITE
Poll: KP is a 68 y/o AAM who is in your infectious diseases clinic with a new diagnosis of HIV-1 infection. His HIV-1 RNA viral load is 55,000 copies/mL. His HIV genotypic test reveals no resistance. He is positive for HLA-B*5701. All other laboratory parameters are WNL. He is ready to begin treatment. What is the best option for KP?

To access the polling questions, go to this link: ascp.com/qa and select the “Updates on the Management of HIV in Older Adults” activity, as seen below.

Question

- KP is a 68 y/o AAM who is in your infectious diseases clinic with a new diagnosis of HIV-1 infection. His HIV-1 RNA viral load is 55,000 copies/mL. His HIV genotypic test reveals no resistance. He is positive for HLA-B*5701. All other laboratory parameters are WNL. He is ready to begin treatment. What is the best option for KP?

  - A) BIC/TAF/FTC (Biktarvy®)
  - B) DTG/ABC/3TC (Triumeq®)
  - C) EFV/TDF/FTC (Atripla®)
  - D) TDF/FTC (Truvada®)
# INSTIs

<table>
<thead>
<tr>
<th>Dosing frequency</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Once daily</td>
<td>• Once daily</td>
<td>• Once daily</td>
<td>• Once or twice daily</td>
<td></td>
</tr>
</tbody>
</table>

## Available coformulations

<table>
<thead>
<tr>
<th>BIC/TAF/FTC (Biktarvy®)</th>
<th>DTG/ABC/3TC (Triumeq®)</th>
<th>EVG/c/TAF/FTC (Genvoya®)</th>
<th>EVG/c/TDF/FTC (Stribild®)</th>
<th>No coformulations</th>
</tr>
</thead>
</table>

## ADRs

- Nausea, diarrhea, headache, insomnia
- Rare: depression, suicidality (more common in pre-existing psychiatric conditions)
  - ↑ CPK
  - Hypersensitivity, hepatotoxicity, myositis, ↑ CPK
  - Fetal neural tube defects (CI in pregnancy)
  - ↑ TG; ↑ LDL
  - Hypersensitivity, SJS/TEN, myopathy, ↑ CPK

## DDIs

- CYP3A4 substrate
- UGT1A1 substrate
- OAT1 and MATE2 inhibitor
  - Antacids 2 hrs BEFORE
  - 2 hrs BEFORE or 6 hrs AFTER antacids
  - Separate antacids by 2 hrs (BEFORE or AFTER)
  - Do not coadminister antacids; use alternative acid-reducing agent

## Dual NRTIs

<table>
<thead>
<tr>
<th>ABC/3TC</th>
<th>TAF/FTC</th>
<th>TDF/FTC</th>
<th>TDF/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing frequency</td>
<td>• Once daily</td>
<td>• Once daily</td>
<td>• Once daily</td>
</tr>
</tbody>
</table>

## Available coformulations

<table>
<thead>
<tr>
<th>ABC/3TC (Epzicom®)</th>
<th>DTG/ABC/3TC (Triumeq®)</th>
<th>TAF/FTC (Descovy®)</th>
<th>BIC/TAF/FTC (Biktarvy®)</th>
<th>DRV/c/TAF/FTC (Symtuza®)</th>
<th>EVG/c/TAF/FTC (Genvoya®)</th>
<th>RPV/TAF/FTC (Odefsey®)</th>
<th>TDF/3TC (Cimduo®)</th>
<th>DOR/TDF/3TC (Delstrigo®)</th>
<th>EFV 600 mg/TDF/3TC (Symfi®)</th>
<th>EFV 400 mg/TDF/3TC (Symfi Lo®)</th>
</tr>
</thead>
</table>

## ADRs

- ABC
  - Hypersensitivity in the presence of HLA-B*5701 allele
  - Increase in CV events
- TAF
  - Renal insufficiency (TDF > TAF)
  - Decreased BMD (TDF > TAF)
  - ↑ LDL
- TDF
  - Renal insufficiency (TDF > TAF)
  - Decreased BMD (TDF > TAF)

## Considerations

- Required HLA-B*5701 testing prior to initiation
- If positive, allergy to ABC must be documented
- If HIV RNA > 100,000 copies/mL, use only with DTG

<table>
<thead>
<tr>
<th>ABC/3TC</th>
<th>TAF/FTC</th>
<th>TDF/FTC</th>
<th>TDF/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAF</td>
<td>All formulations: CrCl ≥ 30 mL/min</td>
<td>TDF</td>
<td>Renal and bone toxicity are exacerbated by boosters</td>
</tr>
<tr>
<td>• Truvada®: CrCl ≥ 30 mL/min</td>
<td>• Stribild®: CrCl ≥ 70 mL/min</td>
<td>• All others: CrCl ≥ 50 mL/min</td>
<td></td>
</tr>
</tbody>
</table>
### NNRTIs

<table>
<thead>
<tr>
<th></th>
<th>DOR</th>
<th>EFV</th>
<th>RPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing frequency</strong></td>
<td>Once daily</td>
<td>Once daily</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>Food requirement</strong></td>
<td>With or without food</td>
<td>On an empty stomach</td>
<td>With a meal</td>
</tr>
<tr>
<td><strong>Available coformulations</strong></td>
<td>DOR/TDF/3TC (Delstrigo®)</td>
<td>EFV 600 mg/TDF/FTC (Atripla®)</td>
<td>RPV/TAF/FTC (Odefsey®)</td>
</tr>
<tr>
<td></td>
<td>DOR (Pfeltro®)</td>
<td>EFV 600 mg/TDF/3TC (Symfi®)</td>
<td>RPV/TDF/FTC (Complera®)</td>
</tr>
<tr>
<td><strong>ADRs</strong></td>
<td>Well tolerated</td>
<td>CNS side effects (Symfi &gt; Symfi Lo)</td>
<td>Depression, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(dizziness, abnormal dreams, headache, depression, suicidality, somnolence, and insomnia)</td>
<td>Skin rash</td>
</tr>
<tr>
<td><strong>DDIs</strong></td>
<td>CYP3A4 substrate</td>
<td>CYP3A4 substrate</td>
<td>PPIs (contraindicated - absorption is reduced with increased gastric pH)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CYP2B6 &amp; CYP2C19 inducer</td>
<td></td>
</tr>
</tbody>
</table>

### PIs

<table>
<thead>
<tr>
<th></th>
<th>ATV</th>
<th>DRV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing frequency</strong></td>
<td>Once daily</td>
<td>Once or twice daily</td>
</tr>
<tr>
<td><strong>Available coformulations</strong></td>
<td>ATV (Reyataz®)</td>
<td>DRV/c (Prezobix®)</td>
</tr>
<tr>
<td></td>
<td>ATV/c (Evotaz®)</td>
<td>DRV/c/TAF/FTC (Symtuza®)</td>
</tr>
<tr>
<td><strong>ADRs</strong></td>
<td>Jaundice</td>
<td>Skin rash</td>
</tr>
<tr>
<td></td>
<td>Indirect hyperbilirubinemia</td>
<td>Increase in serum transaminases</td>
</tr>
<tr>
<td></td>
<td>Cholelithiasis</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td>Nephrolithiasis</td>
<td>Higher CV risk compared to ATV regimens</td>
</tr>
<tr>
<td><strong>DDIs</strong></td>
<td>CYP3A4 substrate and inhibitor</td>
<td>CYP3A4 substrate and inhibitor</td>
</tr>
<tr>
<td><strong>Considerations</strong></td>
<td>PK boosting is generally recommended, however unboosted ATV is approved to treatment naive patients</td>
<td>Should only be administered with a booster</td>
</tr>
</tbody>
</table>
Poll: HB is a 65 y/o Hispanic female who is in your community pharmacy complaining of frequent nightmares and difficulty concentrating. Her PMH is significant for HIV-1 infection and GERD. She is negative for HLA-B*5701. Her current medications include EFV/TDF/FTC (Atripla®) PO QHS and omeprazole PO twice daily. Which medication is most likely the cause of her symptoms?

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Question

- HB is a 65 y/o Hispanic female who is in your community pharmacy complaining of frequent nightmares and difficulty concentrating. Her PMH is significant for HIV-1 infection and GERD. She is negative for HLA-B*5701. Her current medications include EFV/TDF/FTC (Atripla®) PO QHS and omeprazole PO twice daily. Which medication is most likely the cause of her symptoms?

  - A) Efavirenz (EFV)
  - B) Emtricitabine (FTC)
  - C) Omeprazole
  - D) Tenofovir disoproxil fumarate (TDF)
U=U Campaign

1-6 months + 6 months = EFFECTIVELY NO RISK
to ACHIEVE undetectable viral load
to MAINTAIN undetectable viral load after first undetectable test result

Take every pill every day as prescribed

Causes of Treatment Failure

• Non-adherence to ART

• Transmitted or acquired drug resistance

• Higher pretreatment HIV RNA levels

• Suboptimal pharmacokinetics (i.e. absorption, metabolism)

• Drug-drug interactions
Switching Regimens

• Reasons to consider switching regimens in virally suppressed patients:
  • To simplify a regimen by reducing pill burden and/or dosing frequency
  • To enhance tolerability and/or decrease toxicity
  • To prevent or mitigate drug-drug interactions (DDIs)
  • To eliminate food or fluid requirements
  • To allow for optimal use of ART during pregnancy or in cases where pregnancy may occur
  • To reduce costs

Question

• HB is a 65 y/o Hispanic female who is in your community pharmacy complaining of frequent nightmares and difficulty concentrating. Her PMH is significant for HIV-1 infection and GERD. She is negative for HLA-B*5701. Her current medications include EFV/TDF/FTC (Atripla®) PO QHS and omeprazole PO twice daily. Which ART is the best for HB at this time?
  • A) DTG /ABC/3TC (Triumeq®)
  • B) EFV/TDF/3TC (Symfi®)
  • C) RPV/TAF/FTC (Odefsey®)
  • D) RPV/TDF/FTC (Complera®)
Prevention

- Abstain from sexual intercourse
- Be in a monogamous relationship with an uninfected partner
- Limit the number of sexual partners
- Do not share needles
- Use condoms
- Use PrEP

Prophylaxis

<table>
<thead>
<tr>
<th>PrEP</th>
<th>PEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Used for those who are at high risk of becoming infected with HIV</td>
<td>• Used only in emergency situations when there is a potential exposure to HIV</td>
</tr>
<tr>
<td>• Requires a 2-drug ARV regimen</td>
<td>• oPEP: needle sticks</td>
</tr>
<tr>
<td>• Duration: indefinite or until no longer high risk</td>
<td>• nPEP: sex, rape, shared needles</td>
</tr>
<tr>
<td></td>
<td>• Requires a 3-drug ARV regimen</td>
</tr>
<tr>
<td></td>
<td>• Duration: 28 days</td>
</tr>
</tbody>
</table>
PrEP

- Who should get PrEP?
  - Patients who have had sex with partners other than their main partner in the past 6 months
  - Patients in a monogamous relationship with an HIV+ partner
  - Patients with IVDU in the past 6 months
  - Patients with history of any sexually transmitted infections (STIs)
  - Patients with a high number of sexual partners

- Before initiating PrEP:
  - Perform plasma HIV testing
  - Assess renal function (CrCl > 30 mL/min)
  - Perform HBV and HCV testing
  - Determine pregnancy status
  - Obtain baseline bone mineral density test

- FDA-approved PrEP regimens:
  - TDF 300mg/FTC 200mg (Truvada®) once daily
  - TAF 25mg /FTC 200mg (Descovy®) once daily

- Monitoring on PrEP:
  - Test for HIV infection every 3 months
  - Monitor renal function every 6 months

PEP

- When to initiate PEP?
  - When there has been exposure to a bodily fluid that has the potential to transmit HIV
  - Within 72 hours of potential exposure

- Monitoring on PEP:
  - HIV infection status at baseline, 4-6 weeks, 3 months, and 6 months after potential exposure
  - Renal function at baseline and 4-6 weeks after potential exposure

- Preferred PEP Regimen:
  - TDF 300mg/FTC 200 mg (Truvada®) once daily
    PLUS
    - RAL (Isentress®) 400 mg BID
    OR
    - DTG (Tivicay®) 50 mg once daily

- Alternative PEP Regimen:
  - TDF 300 mg/FTC 200 mg (Truvada®) once daily
    PLUS
    - DRV 800 mg (Prezista®) once daily
    AND
    - RTV 100 mg (Norvir®) once daily
Poll: GS, a 61 y/o HIV-1 negative WM, is engaged to BT, a 64 y/o HIV-1 positive WM. BT has been virally suppressed for 3 months with the use of Biktarvy®; however, he does not take his medication regularly. GS is requesting information on the use of PrEP since they are ready to become sexually active. What is the best option for GS?

To access the polling questions, go to this link: ascp.com/qa and select the “Updates on the Management of HIV in Older Adults” activity, as seen below.

**Question**

- GS, a 61 y/o HIV-1 negative WM, is engaged to BT, a 64 y/o HIV-1 positive WM. BT has been virally suppressed for 3 months with the use of Biktarvy®; however, he does not take his medication regularly. GS is requesting information on the use of PrEP since they are ready to become sexually active. What is the best option for GS?

  - A) Educate GS that PrEP is not indicated since BT is virally suppressed
  - B) Truvada® (TDF/FTC) PO daily
  - C) Biktarvy® (BIC/TAF/FTC) PO daily
  - D) Atripla® (EFV/TDF/FTC) PO QHS
Poll: JL, a 60 y/o WF consultant pharmacist. She accidentally stuck herself with a needle after administering a vaccine to a patient. The patient’s HIV status is unknown. What is the most appropriate treatment option for this student?

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Question

• JL, a 60 y/o WF consultant pharmacist. She accidentally stuck herself with a needle after administering a vaccine to a patient. The patient’s HIV status is unknown. What is the most appropriate treatment option for this student?

  • A) Truvada® (TDF/FTC) daily + Isentress® (RAL) BID PO for 28 days
  • B) Truvada® (TDF/FTC) PO daily for 28 days
  • C) Atripla® (EFV/TDF/FTC) PO QHS for 28 days
  • D) No PEP is required because the patient’s HIV status is unknown
NICM in PLWH: Cardiovascular Disease

- Certain ARVs are linked to increased cardiovascular disease (CVD) events in PLWH
- ARVs associated with CVD events are due to:
  - Increases in serum cholesterol level leading to increase incidence of coronary artery disease
    - Protease inhibitors (especially when boosted with ritonavir/cobicistat)
      - Atazanavir and darunavir
    - NRTIs
      - Switch from TDF to TAF
  - Other mechanisms (increased platelet activation)
    - NRTIs
      - Abacavir

Obel N. HIV Med 2010; 11(2):130-136
Lundgren JD. AIDS 2008; 22(14):F17-F24
Sabin CA. Lancet 2008; 371(9622):1417-1426
**NICM in PLWH: Cardiovascular Disease**

**Abacavir**

- Three studies showed that ABC is associated with a 2-4.25 fold increase risk of CVD events compared to other NRTIs
  - Risk factors for CVD events while on ABC:
    - >45 years of age, male, smoking, total/high-density lipoprotein cholesterol greater than 4, blood-pressure lowering treatment, lipid-lowering treatment, prior CVD, diabetes, and ischemic changes on the ECG
    - 47% increase risk of CVD event within 5 years
  - Two meta-analysis of 28- and 54-studies showed that ABC was not associated with an increased risk of CVD events/MI compared to other NRTIs

References:
- Obel N. HIV Med 2010; 11(2):130-136
- Lundgren JD. AIDS 2008; 22(14):F17-F24
- Sabin CA. Lancet 2008; 371(9622):1417-1426
- Cutrell A. Lancet 2008; 371(9622):1413

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**NICM in PLWH: Osteoporosis and fracture**

**Tenofovir**

- BMD decrease/Osteomalacia
  - by ≥5% in lumbar spine: 11% with TAF and 25% with TDF*
  - Change from baseline to 96 weeks:*
    - Lumbar spine: -0.7% with TAF and -2.6% with TDF
    - Total hip: -0.3% with TAF and -2.5% with TDF
  - However, one study in 56,660 veterans found that TDF was not associated with osteoporotic fractures after controlling for age, diabetes, chronic kidney disease, and hepatitis C infection
  - 2 studies have found greater risk of TDF-associated bone damage in younger when compared to OALWH
- Increase in LDL
  - Seen following the switch from TDF to TAF

References:
- Sabin CA. Lancet 2008; 371(9622):1417-1426
- Cutrell A. Lancet 2008; 371(9622):1413
NICM in PLWH: Osteoporosis and fracture
Tenofovir

• Decrease in GFR and Fanconi Syndrome
  • Possible risk factors:
    • Worse baseline renal function
    • Concomitant nephrotoxic medications
    • Low body weight
    • Older age
    • Lower CD4+ count

• Severe hepatomegaly with steatosis
  • Risk factors:
    • Female gender
    • Obesity
    • Prolonged exposure

<table>
<thead>
<tr>
<th>Median % Change from baseline from week 48</th>
<th>E/C/F/TAF (N=959)</th>
<th>TDF-Based Regimen (N=477)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Protein: Creatinine ratio</td>
<td>-20.9%</td>
<td>+9.6%</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Urine Albumin: creatinine ratio</td>
<td>-17.9%</td>
<td>+8.5%</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Urine retinol binding protein: creatinine ratio</td>
<td>-33.4%</td>
<td>+18.1%</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Urine Beta-2 macroglobulin: creatinine ratio</td>
<td>-52.3%</td>
<td>+18.7%</td>
<td>P=0.001</td>
</tr>
</tbody>
</table>

• Drug-Drug interactions:
  • Resulting in increased TDF/TAF exposure:
    • Verapamil, clarithromycin, itraconazole, NSAIDS, acyclovir, and minerals/multi-vitamins

  • Resulting in decreased TDF/TAF exposure:
    • Rifabutin, rifampicin, St. John’s Wort
### First-Line ART in OALWH

#### For most people with HIV

<table>
<thead>
<tr>
<th>INSTI + 2 NRTIs</th>
<th>Boosted PI + 2 NRTIs</th>
<th>NNRTI + 2 NRTIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIC/TAF/FTC</td>
<td>DRV/c or DRV/r + [TAF or TDF]/FTC</td>
<td>DOR/TDF/3TC</td>
</tr>
<tr>
<td>DTG/ABC/3TC</td>
<td>[ATV/c or ATV/r] + [TAF or TDF]/FTC</td>
<td>DOR + TAF/FTC</td>
</tr>
<tr>
<td>DTG + [TAF or TDF]/FTC</td>
<td>[DRV/c or DRV/r] + ABC/3TC</td>
<td>EFV + [TDF/FTC] or [TDF/3TC] or [TAF/FTC]</td>
</tr>
<tr>
<td>RAL+ [TAF or TDF]/FTC</td>
<td></td>
<td>RPV/[TAF or TDF]/FTC</td>
</tr>
</tbody>
</table>

#### For certain clinical situations

<table>
<thead>
<tr>
<th>INSTI + 2 NRTIs</th>
<th>Boosted PI + 2 NRTIs</th>
<th>NNRTI + 2 NRTIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVG/[TAF or TDF]/FTC</td>
<td>DRV/c or DRV/r + [TAF or TDF]/FTC</td>
<td>DOR/TDF/3TC</td>
</tr>
<tr>
<td>RAL + ABC/3TC</td>
<td>[ATV/c or ATV/r] + [TAF or TDF]/FTC</td>
<td>DOR + TAF/FTC</td>
</tr>
<tr>
<td></td>
<td>[DRV/c or DRV/r] + ABC/3TC</td>
<td>EFV + [TDF/FTC] or [TDF/3TC] or [TAF/FTC]</td>
</tr>
</tbody>
</table>

#### When ABC and TAF/TDF cannot be used

- DTG + 3TC
- DRV/r + RAL (BID) or 3TC

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### HIV Management in OALWH: NRTIs

<table>
<thead>
<tr>
<th>Comparison</th>
<th>TDF</th>
<th>TAF</th>
<th>FTC</th>
<th>ABC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>Rare</td>
<td>Rare</td>
<td>Rare</td>
<td>5-8% of population Test for HLA-B* 5701</td>
</tr>
<tr>
<td>Reactions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Drug</td>
<td>Fanconi syndrome</td>
<td>Same as TDF with lower incidence</td>
<td>Hyperpigmentation of palms and soles</td>
<td>Myocardial infarction (lower in OALWH)</td>
</tr>
<tr>
<td>Reactions</td>
<td>Decreased BMD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clearance</td>
<td>Renal</td>
<td>Renal (active tubular secretion via OAT1B1/3)</td>
<td>Renal</td>
<td>Non-renal</td>
</tr>
<tr>
<td>CrCl cutoff (mL/min)</td>
<td>&lt;50</td>
<td>&lt;15</td>
<td>&lt;30 in combo</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;30 not in combo</td>
<td></td>
</tr>
<tr>
<td>DDI</td>
<td>P-gp &amp; BCRP substrate</td>
<td>P-gp &amp; BCRP substrate</td>
<td>Limited</td>
<td>Limited</td>
</tr>
<tr>
<td>HBV coverage</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

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HIV Management in OALWH: INSTIs

Raltegravir

• Low barrier to resistance

• Higher pill burden (twice daily dosing)

• Elevations in creatine kinase (CK) levels possibly leading to myopathy or rhabdomyolysis

• Sleep disturbances and headaches (minor)

• Systemic hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms – DRESS)

Drug-Drug Interactions:

• Decrease in Raltegravir exposure:
  • Phenytoin, carbamazepine, rifampicin, antacids, St. John’s Wort

• Increase in Raltegravir exposure
  • Proton-pump inhibitors and histamine-2 blockers
    • Interaction does not lead to significant increases in ADRs
HIV Management in OALWH: INSTIs
Elvitegravir

- Low barrier to resistance
- Requires boosting
- GI adverse effects most common including nausea
  - Most significant out of INSTIs
- Inhibition of renal tubular creatinine secretion leading to increases in serum creatinine levels without affecting renal function
- Sleep disturbances and headaches (minor)

HIV Management in OALWH: INSTIs
Elvitegravir

- Drug-Drug Interactions
  - Statins:
    - Multiple-fold increases in statin exposure except for rosvastatin (increase of 38%)
  - Calcium channel blockers
    - Increases in diltiazem and verapamil exposure
  - Anticoagulants
    - Decreases in warfarin exposure (increases in INR)
  - CNS drugs
    - Increases in benzodiazepine exposure, tricyclic antidepressants, and serotonin reuptake inhibitors (except for sertraline), and
    - Decreases EVG exposure with anticonvulsants (except lamotrigine)
HIV Management in OALWH: INSTI
Bictegravir

• High barrier to resistance
• Low pill burden
• Sleep disturbances and headaches
• Nausea
• Increases in serum creatinine without affecting renal function
• Hyperglycemia (increases in HbA1c and Blood glucose)
• Increases in ALT

Drug-Drug Interactions:
• Decrease in DTG exposure:
  • Phenytoin, carbamazepine, rifampicin, antacids, St. John’s Wort
• Increase in DTG exposure
  • Proton-pump inhibitors and histamine-2 blockers
    • Interaction does not lead to significant increases in ADRs
• BIC may increase metformin exposure
  • No dosage adjustment of metformin needed
HIV Management in OALWH: INSTIs
Dolutegravir

• High barrier to resistance
• Low pill burden
• Sleep disturbances and headaches
  • Most significant compared to other INSTIs
• Rash
• Nausea
• Increases in serum creatinine without affecting renal function
• Systemic hypersensitivity syndrome (rare)

Drug-Drug Interactions:
• Decrease in DTG exposure:
  • Phenytoin, carbamazepine, rifampicin, antacids, St. John’s Wort
• Increase in DTG exposure
  • Proton-pump inhibitors and histamine-2 blockers
    • Interaction does not lead to significant increases in ADRs
• DTG may increase metformin exposure
  • Limit starting dose of metformin to 1000mg daily
Question

• FR is a 74 y/o Asian male who is well known to your HIV clinic. He is maintained on RAL (Isentress®) PO BID and TDF/FTC (Truvada®) PO daily. His HIV-1 RNA viral load has been undetectable for the past 2 years but the patient has been experiencing significant BMD and decreased renal function likely due to his current regimen. He had previously tested negative for HLA-B*5701. Which of the following regimens would provide the patient with a regimen which does not affect BMD and/or renal function while also decreasing pill burden?

• A) Continue current regimen without change
• B) Switch to rilpivirine + FTC + TDF (Complera)
• C) Switch to DTG/RPV (Juluca®)
• D) Switch to DTG/3TC/ABC (Triumeq)

HIV Management in OALWH: Switching to a 2 Drug Regimen

• There is a growing evidence that some two-drug regimens are effective in maintaining virologic control in patients who achieved viral suppression for ≥ 1 year with a three-drug regimen

<table>
<thead>
<tr>
<th>2-Drug ART Regimens</th>
<th>Drug Classes Represented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutegravir/rilpivirine</td>
<td>INSTI, NNRTI</td>
</tr>
<tr>
<td>Dolutegravir + boosted darunavir</td>
<td>INSTI, PI, booster</td>
</tr>
<tr>
<td>Dolutegravir/lamivudine</td>
<td>INSTI, NRTI</td>
</tr>
<tr>
<td>Cabotegravir + rilpivirine</td>
<td>INSTI, NNRTI</td>
</tr>
</tbody>
</table>
HIV Management in OALWH: NNRTIs

Rilpivirine

- Rilpivirine (RPV) is a second-generation non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Metabolized by CYP3A4
- Requires acidic environment in the GI-tract for absorption
  - Contraindicated with proton-pump inhibitors
  - May be given concomitantly with histamine-2 blockers (H2B) or 12 hours after H2B
  - May be given 4-hours after an antacid or 2-hours prior to an antacid

HIV Management in OALWH: NNRTIs

Rilpivirine

- Adverse drug reactions
  - QT-prolongation of approximately 2 milliseconds
  - Increases in LFTs
  - Fat redistribution and accumulation
    - central obesity, dorsocervical fat enlargement, peripheral or facial wasting, breast enlargement, and “Cushingoid appearance”
  - Somnolence
  - Depression
HIV Management in OALWH: NNRTIs

Rilpivirine

• Drug-Drug Interactions:
  • Do NOT use with PPIs
    • Separate from H2B and antacids as previously discussed
  • Contraindicated with carbamazepine, oxcarbazepine, phenobarbital, or phenytoin
  • Contraindicated with >1 dose of dexamethasone
  • Contraindicated with fluoroquinolones, fluoxetine, escitalopram, aripiprazole, and ondansetron

Many Interactions

Question

• FR is a 74 y/o Asian male who is well known to your HIV clinic. He is maintained on RAL (Isentress®) PO BID and TDF/FTC (Truvada®) PO daily. His HIV-1 RNA viral load has been undetectable for the past 2 years. He would like to simplify his regimen and decrease his pill burden. What is the best regimen for FR at this time?

  • A) Discontinue ART because he is undetectable
  • B) Keep his current ART because it has proven to be effective
  • C) Switch to DTG/RPV (Juluca®)
  • D) Switch to TDF/FTC (Truvada®)
Take Home Message

- HIV is transmitted through infected bodily fluids
- All patients living with HIV should receive ART
- ART is highly effective at suppressing viral load
- New ARVs are highly effective and well tolerated
- Adjust the dose of certain ARV according to renal function
- Monitor older adults for adverse effects
- Screen older adults for drug interactions with ART
- Use PrEP and/or condoms to prevent HIV transmission

Key References and Readings


Social Q&A

To access Q&A, go to this link: ascp.cnf.io and select the “Updates on the Management of HIV in Older Adults” activity, as seen below.

Updates on the Management of HIV in Older Adults
2:45pm - 3:45pm

Eddie Grace
Elias Chahine