THE ART OF HIV MANAGEMENT: AN ANTIRETROVIRAL THERAPY REVIEW

Sarah Pérez, PharmD, PhC, BCACP, AAHIVP

Disclosure

☐ The speaker has no actual or potential conflicts of interest in relation to this presentation.

Objectives

☒ Pharmacist
☐ Identify recommended initial antiretroviral therapy (ART) regimens for most treatment-naïve people with HIV
☐ Evaluate common drug-drug interactions between ART and other medications
☐ Describe the role pharmacist in various setting can play in HIV patient care

☒ Pharmacy Technicians
☐ Identify commonly prescribed antiretroviral therapy (ART) regimens
☐ Identify medications that contain tenofovir disoproxil fumarate vs tenofovir alafenamide
☐ Describe the role pharmacy technicians can play in HIV patient care

HIV in United States

☐ At the end of 2016, an estimated 1.1 million people aged 13 and older had HIV infection
☐ Approximately 38,700 Americans became newly infected in 2016
☐ 52% of these new infections were in the South
☐ 1 in 7 individuals living with HIV are unaware of their status

HIV in New Mexico—2016

- 3,442 people were living with HIV infection
- 134 new HIV diagnosis is adults and adolescents
- 54 people were newly classified as having stage-3 HIV infection (AIDS)
- 34 people had HIV infection progress to stage-3

HIV Care Continuum, 2015

- Diagnosed
- Received Care
- Retained in Care
- Viral Suppression

HIV Transmission Risk

<table>
<thead>
<tr>
<th>Potentially infectious</th>
<th>NOT infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Urine</td>
</tr>
<tr>
<td>Breast milk</td>
<td>Saliva</td>
</tr>
<tr>
<td>Tissue</td>
<td>Sweat</td>
</tr>
<tr>
<td>Semen</td>
<td>Tears</td>
</tr>
<tr>
<td>Vaginal secretions</td>
<td>Nasal secretions</td>
</tr>
<tr>
<td>Visibly bloody fluids</td>
<td>Sputum</td>
</tr>
<tr>
<td>Other bodily fluids</td>
<td>Vomitus</td>
</tr>
<tr>
<td></td>
<td>Stool</td>
</tr>
</tbody>
</table>

Estimated Per-Act Probability of Acquiring HIV from an Infected Source

<table>
<thead>
<tr>
<th>Type of Exposure</th>
<th>Risk per 10,000 Exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td></td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>9,250</td>
</tr>
<tr>
<td>Needle Sharing/Intramuscular Drug Use</td>
<td>63</td>
</tr>
<tr>
<td>Percutaneous (Needle Stick)</td>
<td>23</td>
</tr>
<tr>
<td>Sexual</td>
<td></td>
</tr>
<tr>
<td>Rectal Anal Intercourse</td>
<td>16</td>
</tr>
<tr>
<td>Intrauterine Anal Intercourse</td>
<td>15</td>
</tr>
<tr>
<td>Intrauterine Vaginal Intercourse</td>
<td>8</td>
</tr>
<tr>
<td>Intrauterine Vaginal Intercourse</td>
<td>6</td>
</tr>
<tr>
<td>Rectal Rectal Intercourse</td>
<td>Low</td>
</tr>
<tr>
<td>Intrauterine Rectal Intercourse</td>
<td>Low</td>
</tr>
</tbody>
</table>

Treatment as Prevention

- People with HIV who maintain an undetectable viral load for at least 6 months do not transmit HIV through condomless sex.

Facilitators and Barriers to Treatment

- Social issues
- Fatigue
- Nausea
- Access to food
- Transportation
- Social support
- Comorbidities
- Psychosocial issues
- Stigma
- Insurance
- Access to services
- Formulation
- Prior authorization
- Reimbursement to specialty pharmacies
- Stigma/discrimination
- Cultural competency
Facilitators and Barriers to Treatment

**ART Regimen**

- Healthcare System
- Patient

Antiretroviral Drug Targets

- NRTIs: Nucleoside Reverse Transcriptase Inhibitors
- NNRTIs: Non-nucleoside Reverse Transcriptase Inhibitors
- Integrase Inhibitors
- Protease Inhibitors
- Co-receptor antagonist

Antiretroviral Regimen Selection

- 2 to 3 drug regimen from at least 2 different drug classes
- Factors to consider for ART selection:
  - Pretreatment HIV VL and CD4 count
  - HIV genotype drug resistance testing
  - ART history
  - HLA-B*5701 status
  - Patient preference
  - Anticipated adherence to regimen

Treatment Goals

- Maximally and durably suppress plasma HIV RNA
  - Undetectable HIV viral load
- Restore and preserve immunologic function
  - Improve and maintain high stable CD4 count
- Reduce HIV-associated morbidity and prolong duration & quality of survival
- Prevent HIV transmission

Recommended Initial Regimen for Most People with HIV

- **1 INSTI + 2 NRTIs**
  - Bictegravir/emtricitabine/TAF
  - Dolutegravir/lamivudine/abacavir
  - Dolutegravir + emtricitabine/TDF OR emtricitabine/TAF
  - Raltegravir + emtricitabine/TDF OR emtricitabine/TAF

Predictors of Virologic Success

- Low baseline viremia
- High potency of the ART regimen
- Tolerability of the regimen
- Convenience of the regimen
- Excellent adherence to the regimen


*INSTI = Integrase Strand Transfer Inhibitor
*NRTI = Nucleoside Reverse Transcriptase Inhibitor
*TDF = Tenofovir disoproxil fumarate
*TAF = Tenofovir alafenamide
*Only for patients HLA-B*5701 negative
Tenofovir Disoproxil Fumarate VS Tenofovir Alafenamide


darunavir + ritonavir + emtricitabine/tenofovir alafenamide
bictegravir/emericitabine/tenofovir alafenamide
bictegravir/emtricitabine/tenofovir alafenamide
rilonavir/dolutegravir

Other Common ART (NNRTI-Based)
- Rilpivirine (Edurant®)
  - Must be taken with a full meal
  - Do not initiate in individuals with CD4 count <200 or HIV VL > 100,000
- Rilpivirine/emtricitabine/TDF (Complera®)
- Rilpivirine/emtricitabine/TAF (Odefsey®)

Other Common ART (PI-Based)
- Darunavir (Prezista®)
  - Should be taken with food
  - 600mg BID dosing in pregnancy or treatment experienced with darunavir resistance
- Darunavir/ritonavir (Norvir®) + Truvada® OR Descovy®
- Darunavir/cobicistat (Prezista®) + Truvada® OR Descovy®
- Darunavir/cobicistat/emtricitabine/TAF (Symtuza®)
Other Common ART (INSTI-Based)
- Elvitegravir
  - Should be taken with food
  - Always administered with cobicistat
- Elvitegravir/cobicistat/emtricitabine/TDF (Stribild®)
- Elvitegravir/cobicistat/emtricitabine/TAF (Genvoya®)

Other Common ART (2 drug NNRTI/INSTI)
- Rilpivirine/dolutegravir (Juluca®)
  - Indication: individual with HIV virologically suppressed on a stable ART regimen for ≥ 6 months with no history of treatment failure and no known resistance to the individual components
  - Must be taken with a full meal

Management of Treatment-Experienced Patients
- Based on ART history and resistance patterns
- Generally at least 2 to 3 active drugs if possible
- Often 2 NRTIs + another class
- May be NRTI sparing
- May require dose adjustment of ART agents

Facilitators and Barriers to Treatment
- ART Regimen
- Drug Interactions
- Healthcare System
- Patient

Complexity of ART
- Increased number of antiretroviral agents and combination products
- Patients may be unable to recall complex regimens
- Lack of medication knowledge by prescribers
- Non-HIV/ID providers are not well familiar with appropriate ART
- High adherence rates required for virologic suppression
- Drug resistance can drastically limit future ART options

Medication Errors in HIV-Infected Hospitalized Patients
- Occur in ~30% to 40% of patients
- Common Errors:
  - Improper antiretroviral regimens
  - Inappropriate dosing
  - Missing agents
  - Drug interactions
  - Omission of opportunistic infection prophylaxis
Drug-Drug Interactions

- Pharmacokinetic (PK) drug interactions between ART and concomitant medications can cause increased or decreased drug exposures to either drug.
- PK interactions can occur during absorption, metabolism, or elimination of ART.
- Effects on ART drug levels can cause increased toxicities or decreased therapeutic response.
- ART treatment failure is a possible result of drug interactions.

NRTI Drug Interactions

- Minimal number of clinically significant drug interactions.
- Do NOT coadminister emtricitabine and lamivudine.
- Do NOT coadminister TDF and TAF.
- Caution with other nephrotoxic drugs and TDF.
- Avoid major CYP3A4 inducers with TAF.
  - Carbamazepine
  - Oxcarbazepine
  - Phenytoin
  - Phenobarbital

NNRTI Drug Interactions

- Rilpivirine (RPV)
  - Requires acidic environment for absorption.
  - Major substrate of CYP3A4.
  - Antacids: give at least 2 hours before or 4 hours after RPV.
  - H2 blockers: give H2 blocker at least 12 hours before or 4 hours after RPV.
  - Proton pump inhibitors: CONTRAINDICATED. Do not coadminister.

INSTI Drug Interactions

- Polyvalent cations (Al, Mg, Ca, Fe) may chelate with INSTIs.
- Each INSTI has specific separation recommended (most separate by >2hrs).
- Avoid coadministration of raltegravir and aluminum or magnesium.
- Max dose of metformin coadministered with dolutegravir is 1000mg Qday.
- Elvitegravir/cobicistat has many drug interactions as both are major substrates of CYP 3A4 and cobicistat is a strong CYP3A4 inhibitor.

PI Drug Interactions

- Most PIs and boosters are major substrates of CYP 3A4 and strong CYP3A4 inhibitor = MANY DRUG INTERACTIONS.
- Corticosteroids: coadministration can result in adrenal insufficiency and Cushing's syndrome.
  - Inhaled or intranasal corticosteroids: beclomethasone & flunisolide safe.
- Statins: lovastatin & simvastatin CONTRAINDICATED.
- Atorvastatin and rosuvastatin may be titrated and based on PI have a max dose recommended.
- Contraindicated with some hepatitis C direct-acting antiviral agents.

Resources for ART Drug Interactions

- Make sure references are updated on a regular basis and using most updated version.
- Panel on Antiretroviral Guidelines for Adults and Adolescents (DHHS Guidelines):
- University of Liverpool HIV Drug Interaction Checker:
  - https://www.hiv-druginteractions.org
- Other drug reference databases (Lexicomp, Clinical Pharmacology, Micromedex, etc.).

Medication Adherence
- Whether patients take their medications as prescribed and continue to take their medication correctly
- Reasons why medication adherence can be difficult
  - Medication side effects
  - Busy schedule
  - Dose schedule
  - Medication cost
  - Illness or depression
  - Alcohol or drug use
  - Homelessness
  - Fear of others finding out patient has HIV

Facilitators and Barriers to Treatment

Medication Adherence Tools

Pharmacist Role in HIV Care
- Adherence counseling (refill reminders, refill syncing, pill boxes, blister packs, alarms)
- Patient education (regarding dosing, adverse effects, drug interactions, missed doses)
- Maintain ART inventory
- Dispense complete regimens
- ART regimen selection
- Medication reconciliation at hospital admission and discharge
- ART safety monitoring (renal/hepatic dose adjustment, adverse effects, drug interactions)
- Opportunist infection prophylaxis and treatment monitoring
- Provider/pharmacy education
- Smoking cessation & other comorbidity management
- Referrals

Pharmacy Technician Role in HIV Care

- Benefits investigation
- Help with prior authorization
- Help maintain inventory
- Copay assistance enrollment
- Refill reminders
- Avoid HIV disclosure


Conclusion

- Only about 50% of individuals living with HIV in the US are retained in care and have viral suppression
- There are numerous safe and effective ART agents available
- ART is complex in terms of increased numbers of agents and combinations, drug interactions, and high adherence rates required for virologic suppression
- Pharmacy teams in various settings can impact and improve HIV care

Which of the following is a possible role a pharmacist can take in HIV patient care?

- Counsel a patient on OTC medications to avoid drug interactions
- Perform medication reconciliation upon admission to ensure ART appropriately restarted
- Sync a patient’s refills to ensure they pick up a complete ART regimen
- All of the above

THE ART OF HIV MANAGEMENT: AN ANTIRETROVIRAL THERAPY REVIEW
Sarah Pérez, PharmD, PhC, BCACP, AAHIVP