The Role of the Pharmacist in Managing HIV Treatment

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This activity is funded by an educational grant from ViiV Healthcare.

Learning Objectives
At the completion of this activity, participants will be able to:
• Examine the clinical and economic impact of an HIV infection to a patient
• Analyze the existing and emerging treatment options for HIV
• Explore the correlation between antiretroviral therapy (ART) adherence and viral load suppression
• Identify the pharmacy quality measures in place to improve adherence to ART therapy
• Demonstrate best practices in pharmacy for patient counseling in HIV management

Session Roadmap
• Epidemiology/economic burden of HIV infection
• Pathophysiology
• Treatment initiation
• Correlation between antiretroviral therapy (ART) adherence and virologic suppression
• Quality measures to improve adherence to ART
• Best practices for ART counseling and the role of the pharmacist
• Conclusion
Epidemiology

- 1.1 million people in the United States are living with HIV infection
- 39,513 people diagnosed in 2015
- New diagnoses decreased by 9% between 2010 and 2014
- Highest rate of diagnosis in ages 25-29 years
- More predominant in males
- Highest rates in blacks/African Americans
- Economic impact
  - Average lifetime costs range $253,000-$402,000
  - Early diagnosis and treatment increases duration and quality of life and reduces transmission rates, yet increases overall lifetime costs
  - Adverse effects of ART significantly impact adherence and cost
  - Diabetes resulted in an average of 3.4 more health care services than those without diabetes as an adverse effect
- $26.4 billion in federal funding directed to domestic funding of HIV/AIDS care, housing, prevention, research in fiscal year 2016

Overview of Antiretrovirals

- Terminology
  - Generic name
  - Brand name
  - Acronyms
- Classes
  - Nucleoside reverse transcriptase inhibitors (NRTIs)
  - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
  - Protease inhibitors (PIs)
  - Fusion inhibitors
  - CCR5 antagonist
  - Integrase strand transfer inhibitors (INSTIs)

Evolution of Antiretroviral Therapy

- 1987-1991
  - Zidovudine (AZT) monotherapy
- 1991-1995
  - Dual nucleoside therapy
- 1996-present
  - NNRTI-, PI-, or INSTI-based therapy
  - “Cocktails”
  - Dual NRTI backbone
  - HAART/ART

2006
- First single tablet regimen (STR) FDA approved
- Tenofovir disoproxil fumarate/emtricitabine/efavirenz
- Zidovudine removed from market

Numerous options
- 6 STRs
- 8 NRTIs
- 5 NNRTIs
- 8 PIs
- 3 INSTIs

Pathophysiology/Sites of Action of ART

Case Overview

ST is a 25-year-old woman who presents to the HIV clinic for initiation of ART. She was diagnosed 4 weeks ago by her new primary care provider (PCP), who performed an HIV test as part of her labwork for entry into care.

PMH: depression, migraine headaches

SH: heterosexual
- Sexually active with boyfriend
- Social alcohol use
- Works night shift 5x/week as a toll collector

NKDA

Current medications
- Ibuprofen 600 mg PO Q8h prn headache
- Citalopram 10 mg PO daily

Labs
- HIV RNA: 26,000 copies/mL
- CD4+: 640 cells/mm³
- SCR: 0.8 mg/dL
- CrCl: 85 mL/min
- AST: 20 units/L
- ALT: 11 units/L
- HIV genotyping: wild-type virus, no resistance mutations present
- HLA-B*5701 status: negative
- HCV: negative
- Total cholesterol: 150 mg/dL
ART Initiation: Factors to Consider When Choosing an Initial Regimen

- Overall goal
  - Choose a durable, tolerable, safe, convenient regimen that will permit patient to achieve and maintain virologic suppression

- Initial characteristics of the patient
  - Baseline viral load and CD4 count
  - Genotypic resistance test results
  - HLA-B*5701 status
  - Individual patient preferences
  - Anticipated adherence to treatment

Strategies for Reaching Treatment Goals

- Select optimal antiretroviral regimen
  - Appropriate combinations
    - Efficacy
    - Toxicity issues
    - Tailor regimen to optimize adherence
    - Single-tablet regimen (STR) options

- Improve adherence
  - Poor adherence => reduced response to treatment (next slide)
  - Recognize factors that hinder adherence to a regimen
    - Regimen complexity
    - Patient factors
    - Health-system barriers

Correlation Between ART Adherence and Virologic Suppression

- Paterson and colleagues
  - Landmark observational trial
  - Demonstrated that at least 90% adherence required to achieve optimal virologic outcomes
  - Illustrated that patients are poor at predicting adherence
  - Small trial with only 99 individuals
  - Increased HIV therapy
  - Kobin and Sheth
    - Systematic review
    - Suggest that ≥80% adherence to boosted PI sufficient
    - Considered that lower adherence rates to NNRTIs may be possible, but resistance is a concern


Correlation Between ART Adherence and Virologic Suppression

- Thoughts
  - Goal should be 100% adherence!
  - Even if we commonly use INSTIs with higher genetic barriers to resistance
  - Discuss data as a counseling point before and during ART
  - Consider that ≥80% adherence means missing less than 1 dose per month
  - We have difficulty predicting who will not be adherent to therapy
  - Need to provide counseling that is tailored to the individual patient while never making assumptions
  - Provide quality adherence counseling

**Initial ART Regimens: DHHS Categories**

- **Recommended**
  - Randomized controlled trials show optimal efficacy and durability
  - Favorable tolerability and toxicity profiles
- **Alternative**
  - Effective but have potential disadvantages or limitations to use less data to support use
  - May be the optimal regimen for an individual patient
- **Other**
  - Less virologic efficacy, lack of efficacy data, larger pill burden, drug interaction potential, or greater toxicities

**Recommended Initial ART Regimens**

<table>
<thead>
<tr>
<th>Category</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI-based</td>
<td>Darunavir/ritonavir + tenofovir (DF or AF)/emtricitabine</td>
</tr>
<tr>
<td>INSTI-based</td>
<td>Dolutegravir/lamivudine/abacavir</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>+ tenofovir (DF or AF)/emtricitabine</td>
</tr>
</tbody>
</table>

**Coformulated Combination Products as STRs: Recommended Regimens per DHHS Guidelines**

<table>
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<tr>
<th>Components</th>
<th>Strength</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutegravir/lamivudine/abacavir</td>
<td>50/300/300 mg tablet</td>
<td>Triumeq</td>
</tr>
<tr>
<td>Dolutegravir/lamivudine/abacavir</td>
<td>150/150/10/200 mg tablet</td>
<td>Genvoya</td>
</tr>
<tr>
<td>Dolutegravir/lamivudine/abacavir</td>
<td>150/150/300/200 mg tablet</td>
<td>Stribild</td>
</tr>
<tr>
<td>Efavirenz/tenofovir disoproxil fumarate/emtricitabine</td>
<td>600/300/200 mg tablet</td>
<td>Atripla</td>
</tr>
<tr>
<td>Rilpivirine/tenofovir disoproxil fumarate/emtricitabine</td>
<td>25/300/200 mg tablet</td>
<td>Complera</td>
</tr>
<tr>
<td>Rilpivirine/tenofovir alafenamide/emtricitabine</td>
<td>25/25/200 mg tablet</td>
<td>Odefsey</td>
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</tbody>
</table>

**Coformulated Combination Products as STRs: Alternative Regimens per DHHS Guidelines**

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</table>

**Practical Aspects: STR Options**

- **Advantages**
  - Simple, 1 tablet daily dosing
  - Convenient for patient
  - Single co-pay
  - Prevents nonadherence to an individual regimen component
- **Disadvantages**
  - Unable to dose-adjust individual components
  - Tenofovir disoproxil fumarate
  - Cobicistat
  - Potential for medication errors (next slide)
- **Emerging options**
  - Bictegravir/tenofovir alafenamide/emtricitabine
  - Darunavir/cobicistat/tenofovir alafenamide/emtricitabine

Quality Pearl

- Avoidance of dispensing errors
  - Look-alike, sound-alike names
  - Tenofovir DF (TDF) vs tenofovir AF (TAF)
  - Lengthy generic names with duplicative components

- Case in point
  - Dispensing errors with elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya) and elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild)
  - Tablet appearance is similar
  - Upon review in drug database

- Personal observations
  - Additional errors

- Strategies for prevention

Brief Review of Key Counseling Points With Recommended Regimens

- Recommended regimen components
  - Always consult current references for additional information

Tenofor disoproxil fumarate (TDF) or tenofovir alafenamide (TAF)/emtricitabine

- Dual NRTI backbone
- Take without regard to food
- Adverse effects
  - Headaches
  - Low incidence of headache, nausea, vomiting, diarrhea, flatulence
- Differences between TDF and TAF
  - Renal insufficiency
  - Reductions in bone mineral density
- Drug interactions
  - TDF: indinavir
  - TAF: raltegravir
- Special considerations
  - Renal dosing
  - Contraindications

Abacavir/lamivudine

- Dual NRTI backbone
- Take without regard to food
- Adverse effects
  - Fatigue, rash, headache, GI upset
  - Hypersensitivity reaction
    - 8% of cases occur in first 6 weeks of therapy
    - Flu-like symptoms, fever, rash, nausea, vomiting, shortness of breath, fatigue
  - Must discontinue immediately and never rechallenge
- Combination products issue
  - HLA-B*5701 screening
  - Possible increased risk of cardiovascular disease
- Special considerations
  - Contraindicated in drug interacions

Darunavir

- Protease inhibitor
- Take with food
- Adverse effects
  - Rash
  - PI class adverse effects
  - Increased lipids, fat maldistribution, hyperglycemia, elevated liver function tests
- Special considerations
  - Drug interactions
  - Must take darunavir and ritonavir at the same time
  - Caution in sulfasulfisalicylic acid

Raltegravir

- INSTI
- Take without regard to food
- Adverse effects
  - Headache
  - Nausea
  - Diarrhea
  - Increased creatine kinase
- Special considerations
  - Dosed twice daily
Elvitegravir

- INSTI
- Take with food
- Adverse effects
  - Headache
  - Diarrhea
- Special considerations
  - Must be administered with a pharmacokinetic booster (cobicistat)
  - Coformulated within 2 STRs
    - 1 with TAF, 1 with TDF
  - Potential for errors
  - Drug interactions
    - Decreased concentrations when coadministered with multivalent cations
      - Does not interact with proton pump inhibitors


Dolutegravir

- Take with food
- Adverse effects
  - Insomnia
  - Headache
- Special considerations
  - Once-daily dosing for most patients
  - Coformulated with abacavir/lamivudine as STR
  - Twice-daily dosing required for treatment-experienced patients and/or interacting ART
  - Note that STR cannot be used in these situations
- Drug interactions
  - Decreased concentrations when coadministered with multivalent cations


Quality Measures to Improve Adherence to ART

- Why are these necessary?
  - Clinical ramifications of nonadherence
    - Disease progression
    - Resistance development
  - Economic consequences
    - Disease progression = higher costs
  - Correlation of virologic suppression with prescription refills
  - Guidance
    - For prescribers, pharmacists, and the entire health care team

Quality Measures to Improve Adherence to ART

- Pharmacy Quality Alliance (PQA) performance measures pertinent to ART
  1. Proportion of days covered (PDC)
     - Percentage of patients ≥18 years of age who met the PDC threshold during the measurement period
     - ART: threshold of 90% for at least 2 medications
  2. Drug-drug interactions
     - Percentage of patients who received a prescription for a target medication during the measurement period
     - Who were dispensed a concurrent prescription for a precipitant medication
  3. Completion rate for comprehensive medication review (CMR)
     - The percentage of prescription drug plan members who met eligibility criteria for medication therapy management (MTM) services and who received a CMR during the eligibility period

Quality Measures to Improve Adherence to ART

- Department of Health and Human Services
  - 7 core indicators identified
  - To track federally funded HIV programs
- Include
  - Late HIV diagnosis
  - Linkage to HIV medical care
  - Retention in care (medical visit frequency)
  - HIV viral load suppression
  - Adolescents and adults prescribed ART
  - HIV positivity
  - Housing status

Quality Measures to Improve Adherence to ART

- What is the role of the pharmacist? COUNSELING!!
  - Ensuring patients truly understand the importance of strict adherence to medication dosing and office visits
  - Discussion at every visit, refill, meeting
  - Linking this to virologic suppression
  - Emphasizing that we can help!
  - Identification/prevention of drug interactions
    - Encouraging consistent use of 1 pharmacy for all prescriptions
    - Performing a profile review at initiation and every refill
    - Emphasizing importance of disclosing medications from other practitioners to the HIV prescriber
    - Ensuring patient feels comfortable with disclosing use of nonprescription
  - Using software and Web resources to assess for interactions
  - Providing quality care
    - Provision of CMRs
    - Provision of comprehensive patient counseling

Quality Measures to Improve Adherence to ART

Best Practices for Counseling Patients About Their ART

• The pharmacist serves as a
  • Cheerleader
  • Motivator
  • Supporter
  • Listener
  • Communicator

• Counseling approaches
  • Treatment initiation in treatment-naive patients
  • Ongoing therapy
  • Changes in therapy

Initiation of Therapy: Patient Counseling

• Pathophysiology of HIV
• Goals of treatment and rationale
• Monitoring parameters (CD4, viral load)
• Medication counseling
  • Rationale for combination ART
  • Dosing (frequency, time of day, food requirements)
  • Crucial importance of adherence
  • Identification of potential barriers that would reduce adherence
  • Adverse effects
  • Special reminders
    • Any new prescriptions; call prescriber/pharmacist for drug interaction assessment
    • Mail order/specialty pharmacy considerations

Ongoing Therapy: Patient Counseling

• Brief, but still crucial
• Open-ended questions regarding
  • Adherence
  • Adverse effects
  • New medications
• Changes in therapy
  • Rationale for change
  • Specific discussion regarding new medications as done with initial treatment

Case Study (continued)

ST is grateful for all of the advice and guidance you have provided to her. She wonders how you will continue to play a role in her care as she continues along with her ART.

Role of the Pharmacist

• Continuing adherence assessments and proactive identification of potential barriers
  • Regular follow-up
  • Consistently assessing for drug interactions
  • Communication between all pharmacists involved in patient care (clinic, retail, specialty)
  • Increasing comfort level between patient and pharmacist to enhance disclosure of complementary and alternative regimens
• Monitoring the current literature for upcoming treatment options and opportunities to simplify ART
• Using the most up-to-date resources available for optimal patient care

Conclusion

• Importance of HIV pharmacotherapy knowledge for the practicing pharmacist in 2017
  • Helping patients achieve their goals
  • Providing high-quality care
  • Optimizing adherence counseling
  • Keeping current with the information explosion
  • Improving quality measures/performance
• Take-home points
  • Concepts in ART can be overwhelming for pharmacists, but we are in an ideal role to improve outcomes
  • Continue to maintain a current knowledge base in HIV pharmacotherapy through participation in educational sessions and online reading
  • Serve as a resource for patients and prescribers to improve care
  • Thorough and consistent patient counseling improves outcomes
Additional Resources

• AIDSinfo website
  • http://aidsinfo.nih.gov

• HIVInSite
  • http://hivinsite.org

• Toronto General Hospital Immunodeficiency Clinic
  • http://hivclinic.ca/

• University of Liverpool
  • http://www.hiv-druginteractions.org

• HIV and Hepatitis.com
  • http://www.hivandhepatitis.com/hiv_aids.html

• AIDS Education and Training Centers National Resource Center
  • http://www.aids-etc.org