ACTHIV 2018: A State-of-the-Science Conference for Frontline Health Professionals
Meet the Professor: ART
Initial Therapy for Patients with HIV

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Disclosures

Scientific Advisory Board
Gilead Sciences

There will be no off-label/investigational uses discussed in this presentation.
Learning Objectives

• Discuss the HIV Care Continuum and Interventions to Improve Adherence

• Review Principles of treatment and Mechanisms of Action of ART

• Review Recommendations for Initial ART via Case Scenarios
Interventions to Improve Retention and Adherence are Needed

• 9 out of 10 HIV infections are transmitted by people who are unaware of their infection or not in care.

• Reducing the number of undiagnosed HIV infections and getting more people into care represents the greatest opportunity to improve viral suppression.

• Viral suppression allows people with HIV to live longer, healthier lives and dramatically reduces their risk for spreading HIV to others.
HIV Care Continuum, US, 2014

- Overall Viral Suppression is approximately 49%, up from 28% in 2010

- Disparities continue to exist
  - While African Americans make up 13% of the US population, they represent 43% of everyone living with HIV in the US
  - 43 percent of African Americans and 48 percent of Latinos with HIV had the virus under control, compared with 57 percent of whites.

HIV Care Continuum, US, 2014

Only 56% of 13- to 24-year-olds with HIV had their infection diagnosed.
Just 27% of young people with HIV had the virus under control.
Role of the Multidisciplinary Care Team

- Interventions to improve linkage, retention, and adherence to care are essential.
- Barriers to adherence to ART and appointments should be assessed prior to initiating therapy and thereafter, as needed.
- Multidisciplinary approaches to address adherence issues are often necessary.
  - Collaboration with social work and case management to help mitigate competing priorities (e.g. housing, food insecurity, transportation, employment status, out-of-pocket costs) is recommended.
  - Linking patients to counseling to overcome stigma, substance use, or depression improves outcomes.
  - A care team approach to continued education and linkage to resources to overcome barriers is encouraged.

Multidisciplinary Team Members

- Social Work
- Case Management
- Mental Health
- Harm Reduction
- Nursing
- Entitlement Specialist
- Peer Educators
- Pharmacist
- Clinical Providers
Factors Influencing HIV behavior and Readiness to Initiate Treatment

**Interpersonal / Network**
- Social support and trust
- Communication level
- Relationship intimacy / interpersonal violence
- Social networks/coalitions

**Individual**
- Knowledge/information
- Risk perception
- Motivation
- Substance use
- Denial of status
- Readiness to change
- Reactions to stress
- Personal income
- Distrust of health care
- Fear of stigma
- Mental health
- Personal beliefs about treatment

**Structural**
- Poverty
- Access to services: transportation
- Public policy: criminalization of at-risk groups, IVDU, sex workers
- Education curriculum
- Cost of services, care
- Gender equity

**Institutional / health system**
- Provision and sufficient resourcing of services (e.g. harm reduction)
- Competent / supportive providers
- Peer navigators / advisors
- Confidentiality / privacy
- Support tools: texts, appt reminders

**Community**
- Stigma
- Peer pressure / social norms
- “-isms” racism, sexism, heterosexism
- Position of religious, cultural leaders
- Cultural norms (e.g. masculinities)

Kaufman MR, JAIDS, 2014
Assessments and Interventions to Improve Adherence

Social Work
- Insurance
- Living Situation
- Transportation
- Language Barriers
  - Literacy Assessment
- Entitlements
  - Food Insecurity
  - Housing
- Assistance with Competing Priorities
  - Child Care
  - Legal Issues

Case management / Peer Educators
- Expectations of care
- HIV basics
- Principles of care
- Partner notification
- Pre-Exposure Prophylaxis for Partners

Mental Health
- Assessment of known diagnoses
- Screening for depression / adjustment disorder
- Referral for MH services

Harm Reduction Counseling
- Alcohol Use Assessment (including binge drinking)
- Illicit drug use
  - Screening for prescription pain pills, anxiety medication
- Referrals for Harm Reduction Services
### Assessments and Interventions to Improve Adherence

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<th>Nursing</th>
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<td>• Expectations of care</td>
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<td>• HIV basics</td>
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<td>• Medication Education</td>
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<th>Practice Operations</th>
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<td>• Review of clinic policies</td>
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<td>• Appointment reminders, ease of rescheduling</td>
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Principles for HIV Treatment

• Immediate treatment is recommend for all patients living with HIV infection regardless of CD4 count or viral load, once individualized readiness has been assessed.
  
  – Data from the START and TEMPRANO trials demonstrated 50% reduction in mortality even in patients who initiated treatment with CD4 > 500

• Initial ART regimen for a treatment-naive patient generally consists of two Nucleoside Reverse Transcriptase Inhibitors, plus a drug from one of three drug classes:
  
  an Integrase Inhibitor, an non-NRTI, or a boosted PI

Mechanism of Action for ART

HIV Life Cycle

1. Attachment
2. Co-Receptor Engagement
3. Fusion
4. Reverse Transcription
5. Integration
6. Translation
7. Protein Processing
8. Budding and Maturation

Rambaut, Nature Reviews Genetics, 2004
### Available Antiretroviral Agents

#### Nucleoside RTIs
- Zidovudine (ZDV)
- Didanosine (ddI)
- Zalcitabine (ddC)
- Stavudine (d4T)
- Lamivudine (3TC)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Tenofovir (TDF)

#### Nonnucleos(t)ide RTIs
- Nevirapine (NVP)
- Delavirdine (DLV)
- Etravirine (ETR)
- Efavirenz (EFV)
- Rilpivirine (RPV)

#### Protease Inhibitors
- Saquinavir (SQV)
- Ritonavir (RTV)
- Indinavir (IDV)
- Nelfinavir (NFV)
- Amprenavir (APV)
- Fosamprenavir (Fos-APV)
- Tipranavir (TPV)
- Lopinavir/r (LPV/r)
- Atazanavir (ATV)
- Darunavir (DRV)

#### Integrase Inhibitors
- Raltegravir (RAL)
- Dolutegravir (DTG)
- Elvitegravir (EVG)
- Bictegravir (BIC)

#### CCR5 Antagonist
- Maraviroc (MVC)

#### Boosters
- Ritonavir (RTV)
- Cobicistat (cobi)

#### Fusion Inhibitor
- Enfuvirtide (T-20)
An integrase inhibitor based regimen containing TAF/FTC or ABC/3TC is recommended for initial in treatment naïve individuals.

- Bictegravir/TAF/emtricitabine
- Dolutegravir/abacavir/lamivudine
- Elvitegravir/cobicistat/TAF/emtricitabine
- Dolutegravir plus TAF/emtricitabine
- Raltegravir plus TAF/emtricitabine

* Bictegravir/TAF/emtricitabine was added to the DHHS HIV guidelines as a first line recommended regimen on March 27, 2018. It has not yet been added to the IAS-USA guidelines.

Günthard HF, IAS-USA HIV treatment guidelines JAMA 2016
Case 1

53 AA M h/o hypertension, pre-diabetic (Hgb A1c = 6.3%), recently diagnosed with HIV CD4 248 cells/mm$^3$, VL pending, HLA B57 negative.

Fam hx significant for father with MI at 52

MEDS: Lisinopril, amlodipine
Case 1

- BP 146 / 98 mmHg
- 5’10”, 210 lbs (BMI 30)
- total Cholesterol 215 mg/dL, HDL 43 mg/dL, LDL 148 mg/dL
- Former smoker, quit 2 years ago
- ASCVD 10 year risk score = 14.8 %
Case 1

1. BIC/FTC/TAF
2. EVG/c/FTC/TAF
3. DTG/ABC/3TC
4. RPV/FTC/TAF
Principles

• Drug-drug interactions with boosting agent
  – Calcium channel blockers
  – Careful monitoring with metformin
  – Choice of statin

• Controversy over ABC and cardiovascular risk
  – Guidelines discourage use of ABC in someone with pre-existing CVD

• Potency of RPV based regimens with VL >100,000, CD4<200
Case 2

27 M MSM no significant PMH recently diagnosed HIV
CD4 482 cells/mm³, VL 45,000 copies/mL

Infected by his partner, 24 year old MSM, perinatally infected, h/o poor compliance, known to have failed an integrase based regimen
Case 2

- ATZ/r + FTC/TAF
- DRV/c + FTC/TDF
- BIC/FTC/TAF
- RPV/FTC/TAF
- EFV/FTC/TDF
Principles

- Potency of regimens with concern for inherited resistance
  - Low genetic barrier to resistance with EFV, RPV

- Choice of PI based initial regimen
  - In general, DRV based regimen is preferred over ATZ

- Need to screen for integrase resistance when obtaining the genotype
Pros and Cons

DARUNAVIR
- low rate of resistance even with poor adherence
- drug interactions with required boosting
- inferior to integrase inhibitor based regimens

RILPIVARINE
- small size
- not recommended for VL > 100,000 or CD4 < 200
- must be taken with meal
- staggered dosing with PPI

EFAVIRENZ
- longest track record
- CNS side effects
Case 3

45 Latino W h/o pill swallowing phobia secondary to esophageal strictures (due to ingestion of caustic liquid in childhood – requires occasional endoscopic balloon dilation)

CD4 592, VL 10,015 copies/mL, genotype with no resistance, HLA B57 negative
Case 3

1. BIC/FTC/TAF
2. EVG/c/FTC/TAF
3. DTG/ABC/3TC
4. RPV/FTC/TAF
5. DTG + TAF/FTC
Principles

• Patient preference and tolerability are importance factors to consider to improve adherence
  – Concerns over pill size and desire for single tablet regimens are becoming more common
Summary

The overriding principles for initial ART regimen are patient safety, efficacy, tolerability, and options that lead to improved compliance.

Integrase inhibitor based regimens are recommended by guidelines as first line therapy based on data from comparative clinical trials.

Attention should be given to choice and timing of initial ART regimen in special populations at increased risk of adverse events and drug-drug interactions.

Adherence, safety, cost, and access are among the factors to consider when choosing initial therapy. The interplay of cost effectiveness and the availability of lower priced generics is evolving.

“Guidelines are just that . . . Guidelines”
- Judith Aberg
Thank You