Adherence in the new era of HIV treatment – the role of the pharmacist

Blake Max, PharmD
University of Illinois at Chicago
Ruth Rothstein CORE Center
Cook County Bureau of Health Services

Disclosure

The speaker has a conflict of interest to disclose:

- GlaxoSmithKline, Pfizer: Stockholder
- ViiV Healthcare: Spouse is an employee

The conflict has been resolved through peer review of the presentation.

Points to Ponder

- "Adherence is the key mediator between medical practice and patient outcomes"
- "Drugs don't work in patients who don't take them"

  -C.Everett Koop MD

Scope of the Problem

- Four fundamental facts:
  1. Medication adherence is poor for most chronic diseases.
     - 40-80% of pts from clinical trials for of for a chronic condition
       Most dramatic ↓ after first 6 months of therapy (eg. statins)
  2. Many interventions have been tested to improve medication adherence, but a unifying recommendation for "best practice" is still missing.
  3. No consensus on what constitutes adequate adherence (70%, 80%,90%?)
  4. 33-69% of all medication-related hospitalizations are due to poor medication adherence.

Predictors of Virologic Success

- ↑ potency of ART regimen (the new HAART era)
- ***Excellent adherence***
- Low baseline viremia
- ↑ baseline CD4 count
- Rapid ↓ in VL (> 1 log drop in 4-12 weeks)

Adherence Factors

- All play an important role:

  1. The Patient
  2. The Regimen
  3. The Health-Care System

Patient Factors and Adherence

- Most important are psycho-social situations
  - Younger age
  - Substance use
  - Perceived stress
  - Depression
  - Lack if knowledge/literacy

All have shown to be important factors associated with ↓ adherence

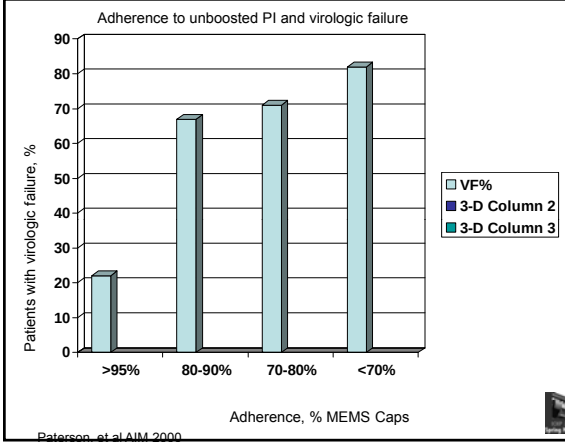
Adherence and ART
(The new era)

- Viral suppression, ↓ rates of resistance, improved survival are correlated with high rates of ART adherence.
- Treatment must be maintained for a lifetime.
- Adherence to HIV meds has been well studied, however interventions to improve ART adherence need further research.
- Less than 100% adherence may not apply in the new HAART era.
  - Improved potency
  - Simplified regimens
- Adherence is addressed in the DHHS treatment guidelines "as the cornerstone for effective HAART regimens"

What do we Know Now About Adherence to ART?

- How much adherence is enough?
  - Original estimation was > 95%, but it may be a bit less
  - Recent data by Bangsberg et al, show that adherence rates of around 70% may actually be sufficient for NNRTI- and boosted PI-based regimens.

Bangsberg DR et al, Clinical Infectious Diseases 2006; 43:939-41.
Bangsberg DR, et al. IAS 2007, Abstract WEPEB111



Paterson, et al AIM 2000

Ritonavir boosted PI and Adherence

n=53 (Kaletra)
Adherence measured using MEMS
Mean adherence = 73%

Adherence Rates	>95%	90-94.9%	80-89.9%	70-79.9%	50-69.9%	<50%
% pts with VL<400(n) at 24 weeks	70% (10)	88% (8)	100% (9)	100% (4)	55% (11)	73% (11)

Conclusions:
- Moderate levels of adherence can lead to virologic suppression in most pts on Kaletra.
- **These data challenge belief that near-perfect adherence is necessary to achieve virologic suppression in the current HAART era.**

-Shuter et al. JAIDS 45(1) 2007

Boosted PIs More Forgiving of Suboptimal Adherence

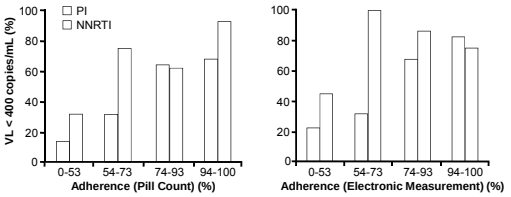
- Increased risk of virologic breakthrough with < 95% adherence to antiviral regimen (multivariate analysis)
  - Unboosted PI (n = 752): 66% increased risk
  - NNRTI (n = 631): 47% increased risk
  - RTV-boosted PI (n = 251): not significant

Variable Associated With Virologic Breakthrough	Adjusted Hazard Ratios (95% CI)		
	Single PI	NNRTI	Boosted PI
Adherence < 95%	**1.66 (1.38-2.01)**	**1.47 (1.01-2.14)**	**1.05 (0.46-2.42)**
IDU history	1.37 (1.15-1.63)	1.47 (1.08-2.02)	1.69 (0.86-3.34)
Viral load	1.06 (0.89-1.26)	1.12 (0.83-1.51)	0.63 (0.33-1.11)
CD4+ cell count	0.93 (0.89-0.96)	0.88 (0.81-1.51)	0.98 (0.6-1.27)

Gross R, et al. CROI 2006. Abstract 533.

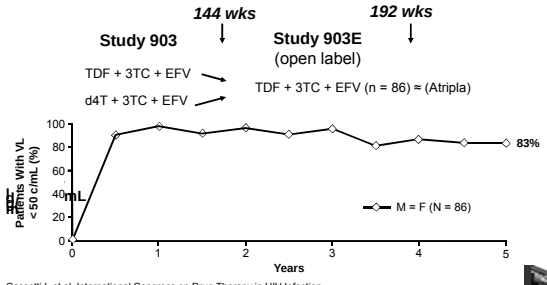
NNRTI More Forgiving of Suboptimal Adherence Than Unboosted PI

- 109 indigent patients in San Francisco
  - 56 unboosted PI, 53 NNRTI regimen
- VL < 400 reliably seen with NNRTI if adherence > 54%, but with unboosted PI, only with very high adherence



Bangsberg DR, et al. CROI 2005. Abstract 616.

GS 903E: Percent of Patients With VL < 50 c/mL Through 5 Years

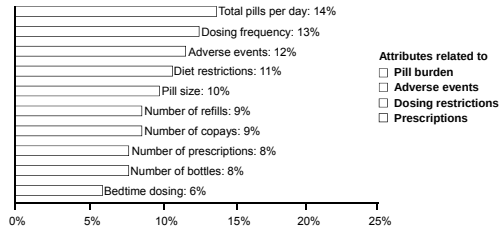


Cassetti I, et al. International Congress on Drug Therapy in HIV Infection Glasgow, Scotland 2006. Poster P152.

Strategies to achieve Treatment Goals

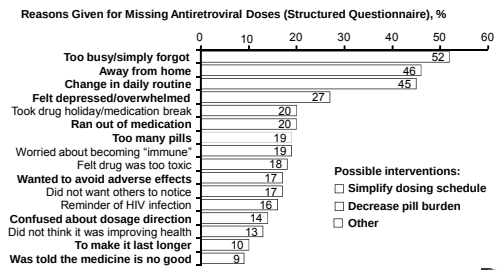
- Regimen selection- tailored to the pt
  - A regimen tailored to the pt allows for better adherence.
- Tailoring regimen includes:
  - Expected side effects
  - Convenience
  - Comorbidities
  - Drug interactions and other concomitant meds
  - Pretreatment genotype

Regimen Attributes With Impact on Adherence: Patient Perceptions



Stone VE, et al. J Acquir Immune Defic Syndr. 2004;36:808-816.

Why Do Patients Miss Doses?



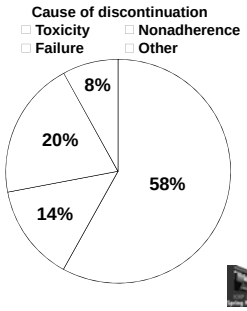
Gifford AL, et al. J Acquire Immune Defic Syndr. 2000;23:386-395.

What Do We Know Now About Regimen Predictors of Adherence ?

- What are the characteristics ARV regimens that are associated with better adherence?
  - Less complex regimens
  - Regimens with fewer side effects. Side effects are the most common reason patients discontinue their ARV regimens.
- What is the evidence?

Toxicity Is a Major Reason for Discontinuation of First-Line HAART

- ICONA Study Group
  - Median follow-up: 45 weeks
  - Study population: 862 ARV-naive patients
  - 84.3% receiving **unboosted PI** + NRTIs
  - **Discontinuations: n = 312 (36%)**



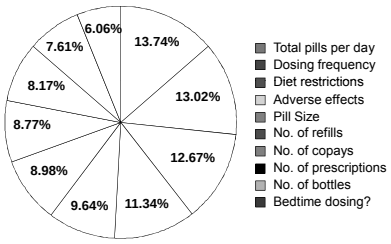
d'Arminio Monforte A, et al. AIDS. 2000;14:499-507.

PASPORT: Study Objectives

- Evaluate relative impact of regimen characteristics on patient adherence
  - Different HAART regimen characteristics (i.e., dosing frequency)
  - Strata within each regimen characteristic (i.e. BID, QD all at once, QD different times, mixed QD/BID)

Stone VE, et al. JAIDS. 2004;36:808-816.

PASPORT: Impact of Regimen Characteristics on Adherence



Stone VE, et al. JAIDS. 2004;36:808-816.

PASPORT: Conclusions

- Many regimen characteristics contribute to adherence, but pills per day, dosing frequency, diet restrictions, and side effects contribute more than others
- Once daily 'QD' regimens only provide an adherence benefit over other HAART regimens if they can be taken all at 1 time, contain few pills and no dietary restrictions.
- Underscores the adherence benefit of new compact regimens using co-formulated pills.

Stone VE, et al. JAIDS 2004;36:808-16.

Goals of Therapy for Treatment-Experienced Patients

- "In those with prior treatment and drug resistance, the goal is to resuppress HIV RNA levels maximally and prevent further selection of resistance mutations, if possible." – US DHHS Guidelines, October 10, 2006[1]
- "Trials with newer antiretroviral agents have shown that it is possible to achieve plasma HIV-1 RNA levels below 50 copies/mL even in highly treatment–experienced patients." – IAS-USA Guidelines, August 2006[2]

1. DHHS. Available at: http://aidsinfo.nih.gov. Accessed August 27, 2007.
2. Hammer SM, et al. JAMA. 2006;296:827-843.

Role for the Pharmacist

- Ensure that the regimen fits the patients lifestyle.
  - Can you simplify?
- Recognizing drug interactions with ART
- **Adherence counseling/assessment at each encounter.**
  - Early detection of poor adherence and prompt intervention can greatly reduce the chance of virologic failure and development of viral resistance.

Barriers to Adherence

- What can the Pharmacist do?
  - Educate pt about the regimen, the disease, and its tx
    Too busy? Use medication handouts
    Internet resources: www.aidsinfonet.org
    www.aidsmeds.com
    www.hivpositive.com
  - Reinforce pt knowledge of pharmacy resources and provide adequate access
  - Ensure correct Rx and that meds are taken as directed
  - Assess for simplification
  - Be aware of potential drug-drug interactions

Access to Pharmaceutical Care
(Health-System Barriers)

- Factors to consider include:
  - Pharmacists knowledge of therapeutic agents and strategies used to treat HIV infection.
  - Assistance in processing 3rd party payment for meds and/or access to drug-assistance programs (ADAP)
  - Pharmacy schedules that include PM or weekend hours for counseling pts or other obligations that prevent daytime visits.
  - Delivery services for ART medications
  - Offering adherence tool devices (pill boxes)

Summary

- HAART regimens, including regimens for tx-experienced pts have become increasingly convenient over the last few years.
  - Pts prefer compact regimens
  - Better adherence on compact regimens
- Pharmacists are a valuable resource:
  - Medication education
  - Recommendations for treatment of side effects
  - Refill records
  - Monitor drug-drug interactions