

# CONSTRUCTING ANTIRETROVIRAL REGIMENS TO OVERCOME IMPERFECT ADHERENCE

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# OBJECTIVES

- Present obstacles to adherence of antiretroviral regimens
- Discuss evidenced based approaches to increasing adherence
- Provide anecdotal case examples of changes in regimens to increase adherence

# REASONS FOR SUBOPTIMAL ADHERENCE

- Characteristics of patients
  - Cognitive and executive function, lack of knowledge, literacy and language barriers, active substance abuse, mental illness, younger age
- Situational conditions
  - food, housing, and transportation issues, stigma, demanding or erratic schedule, healthcare system limitations
- Illness and treatment related attributes
  - Adverse effects, regimen complexity, comorbidities

# OBSTACLES TO ADHERENCE

- Frequency of administration
- Pill burden
- Formulation of solid dosage forms
  - Capsule vs tablet
  - Large vs small
- Inability to tolerate solid dosage forms
- Taste perversion
- Adverse effects

# FREQUENCY OF ADMINISTRATION

- QD vs BID vs TID???
- First line regimens
  - TDF/FTC + ATV/r OR EFV OR DRV/r are ONCE DAILY
  - TDF/FTC + RAL is TWICE DAILY
- QD vs BID
  - 10% higher adherence with QD but BID less likely to have trough concentrations below minimum effective conc
  - LPV/r QD (91%) vs BID (80%) adherence : no difference in outcome but BID better with HIV RNA >100,000 copies/mL
- Data in clinical trials applicable to real life?



# PILL BURDEN

- Fixed dose combinations vs multiple pills per day
- Advantage of not missing one of a regimen if use a fixed dose combination
- Disadvantage of missing one pill miss all meds in regimen
- Bangsberg, et al
  - 26% increased adherence with single vs multiple pills per day in homeless or marginally housed patients
- Sax, et al
  - Single pill per day more likely to reach 95% adherence threshold vs three or more per day (OR 1.59;  $p < 0.001$ )
  - Single pill per day 24% less likely to be hospitalized (OR 0.76;  $p = 0.003$ )

# FORMULATION OF SOLID DOSAGE FORMS

- Capsule vs tablet
- Large vs small
- Shape

Norvir®



Atripla®



Reyataz®



Epivir®



# INABILITY TO TOLERATE SOLID DOSAGE FORMS

- Secondary to thrush, esophagitis, physical or psychogenic disorders
- Available liquids/suspensions/powders
  - AZT, 3TC, FTC, ddI, d4T, ABC, TDF, NVP, FPV, NFV, TPV
  - KAL and RTV have 40+% alcohol
- Splitting, crushing, dissolving solid dosage forms
  - NO for Atripla®, Complera®, Kaletra®, Norvir®\*
  - Etravirine dissolving
  - Raltegravir has a chewable tablet
  - Limited data on other dosage forms
  - [www.tthhivclinic.com](http://www.tthhivclinic.com)

Atripla=tenofovir/emtricitabine/efavirenz; Complera=tenofovir/emtricitabine/rilpivirine; Kaletra=lopinavir/ritonavir; Norvir=ritonavir



# INABILITY TO TOLERATE SOLID DOSAGE FORMS

- G and J tubes
  - Consider location of absorption in GI tract
  - Tenofovir, emtricitabine, etravirine, raltegravir concentrations via G tube
    - Similar concentrations at 2 and 12 hrs post dose as historic data

# TASTE PERVERSION

- Liquids and crushing solid dosage forms
  - “Tastes like gasoline”
  - “I vomit every dose”
- Strategies to mask taste
  - Place powder inside gelatin capsule
  - Peanut butter, jelly, chocolate milk/pudding

# ADVERSE EFFECTS

- Short term vs long term
- Gastrointestinal, CNS effects, fatigue, drowsiness, insomnia, hyperbilirubinemia
- Lypodystrophy, Insulin resistance (or worsening DM)

# CASE EXAMPLES

- 3/2011: CW is a 53 yo AAF who presented to clinic after some time out of care. Dx with HIV in 2005 and in care at our clinic since 2008 when she moved to be near her family.
- On no ARVs at the time
- G tube placed by outside MD in another state for med administration due to difficulty swallowing
- Last known ARVs: AZT/3TC, ABC, TDF, FPV 1400 BID
- HIV RNA 69,000; CD4 76
- Attempted multiple times to restart current regimen
- Over several visits patient reported incorrect administration of medications (ie, QD instead of BID; missing some days of doses, etc)



# INTERVENTIONS

- Weekly visits to the clinic for pill box fills
- Assistance in crushing tablets, placing the powders in the pill boxes with instructions to mix and place in G tube
- Gradually introducing meds with more potential for toxicity (ie, RTV)
- Changing regimen to include as many liquids as possible (AZT, LPV/r, TDF-crush)
- Labeling all medications with a “unique” name
- Indicating the dose of meds on dosage cups
- Move to a location with local resources for her care

# CLINICAL OUTCOME

Date	HIV RNA	CD4
Mar 2011	68,569	76
Oct 2011	12,952	131
Nov 2011	34,138	118
Dec 2011	28,088	N/A
Apr 2012	163,114	141
May 2012	264	168

# SUMMARY

- Multiple reasons for suboptimal adherence
- Including....obstacles related to the antiretroviral regimen
- Can overcome some of these obstacles by considering the needs of the patient and altering the regimen
- Interdisciplinary, individualized, holistic approach to care is ideal