



## NORTHWEST AIDS EDUCATION AND TRAINING CENTER

# Acute Side Effects from Antiretroviral Medication

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# Disclosures

- No relationships or financial ties to disclose

# Objectives

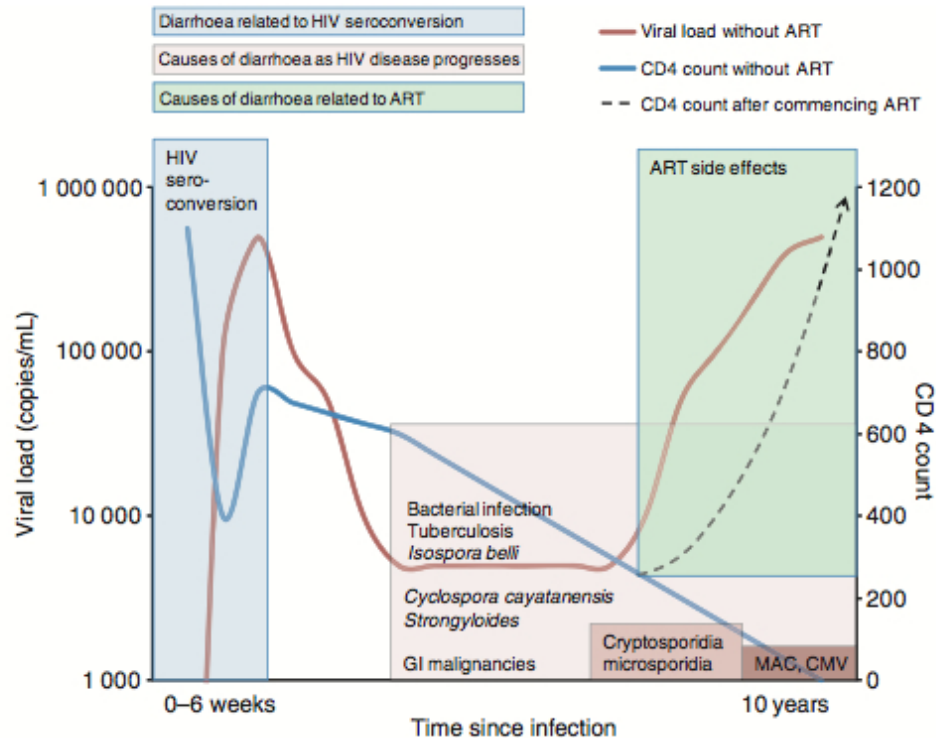
- Properly identify and provide management strategies for
  - Gastrointestinal
    - Diarrhea
    - Nausea and vomiting
    - Hepatotoxicity
  - Dermatologic
    - Stevens-Johnson syndrome
    - Other rashes
  - Central nervous system
    - Headache and dizziness
    - Neuropsychiatric

# Introduction

- Adverse drug effects (ADEs)
  - Most common reasons for switching or discontinuing therapy
  - ADEs have declined with the introduction of newer agents
  - Starting patients with higher CD4 cell counts have fewer side effects than patients with lower counts
  - Higher rates of adverse effects are seen in women, specifically:
    - Rashes (SJS), hepatotoxicity and lactic acidosis
    - Older patients can also experience higher rates of side effects
  - Many medications have overlapping side effects or toxicities
- *Educating patients about what to expect for potential side effects **AND** how to manage them will help get them adjusted to new therapy*

# Gastrointestinal

# Diarrhoea



**Figure 1** | Scheme showing causes of diarrhoea at different stages of HIV disease: following HIV seroconversion, CD4 count recovers to a set point, then falls gradually over 5-10 years. The coloured boxes schematically indicate causes of diarrhoea at different stages of HIV infection based on CD4<sup>+</sup> T-lymphocyte count (blue line). The black dotted line indicates the impact of starting ART on CD4 count and the overlap between different categories after starting ART highlights the potential diagnostic difficulty at that time.

# Diarrhea

- Frequency and severity
  - Spectrum of presentation
- Most commonly associated with the protease inhibitors
  - Lopinavir/ritonavir >> darunavir/ritonavir >> atazanavir/ritonavir
- Ritonavir is the the biggest contributor to diarrhea
  - Original doses were much higher than what we use today
- Post marketing data suggest raltegravir is associated with mild diarrhea

*Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents pages 126-129*

*Norvir and Isentress Package Insert*

# Diarrhea

- Management
  - Taking medications properly
  - Hydration status
  - OTC agents
    - Loperamide
    - Bulking agents / oatbran tablets
    - Calcium tablets
  - Prescription
    - Diphenoxalate / atropine
    - Colesevelam



# Nausea and Vomiting

- Listed as a potential ADE in every class of medications
  - PIs >> NRTIs >> NNRTIs >> Integrase inhibitors
- Nausea
  - Can be minimized by taking medication with food (except efavirenz containing regimens)
  - Prescription antiemetic medications can be used safely
    - Compazine and prochlorperazine
    - Ondansetron
  - If weight loss is an issue, the use of appetite stimulants can be employed
- Vomiting
  - Patients can try antiemetic medication, but in severe cases may need to have their medications switched

# Hepatotoxicity

- NNRTIs
  - Nevirapine carries the largest risk in this group
  - Often associated with a rash or hypersensitivity symptoms
  - Greatest risk in treatment naïve women with CD4 cells >250 and men >400
  - Dose titrate over initial two weeks with 200 mg once daily
- Protease Inhibitors
  - Drug-induced hepatitis and hepatic decompensation have been observed with all PIs to varying degrees
  - Jaundice is frequently reported as an adverse effect with atazanavir due to indirect hyperbilirubinemia

# Hepatotoxicity

- NRTIs
  - Older agents >>> newer agents
  - Coinfection with hepatitis B
- Management
  - Abdominal pain and elevated LFTs should be addressed promptly and drugs should be high on the differential
  - Asymptomatic hyperbilirubinemia

# Dermatologic

# Skin Reactions

- NNRTIs
  - Skin rashes are common within this class of agents
  - Spectrum includes minor single erythematous lesions to SJS
  - Treatment
    - Minor reactions can be treated with antihistamines
    - For SJS or more severe reactions, remove all agents and treat supportively
  - To lessen the likelihood, dose escalate nevirapine



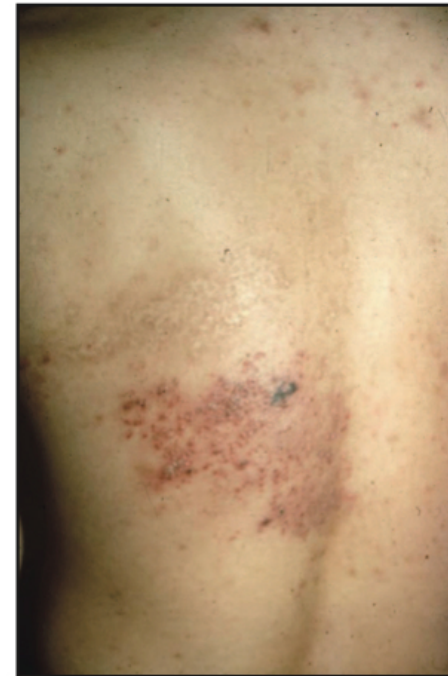
**Fig. 1.** Diffuse, morbilliform rash in an HIV-infected patient with onset  $\approx$ 10 days after initiating nevirapine therapy (photograph courtesy of Toby Maurer, MD).

# Skin Reactions

- Protease Inhibitors
  - Atazanavir, darunavir and fosamprenavir all can cause rashes
  - Caution in patients with a sulfonamide allergy
  - SJS has been reported
- NRTIs
  - Abacavir is known to induce a “hypersensitivity reaction” that may include a diffuse maculopapular, nonpruritic rash in addition to other symptoms
    - Can be head to toe and include palmar surfaces of the hands
    - Occurs usually in the first 6 weeks of therapy
    - Screen with HLA-B 5701 test
    - Management include discontinuing therapy to see if the rash resolves
  - Tenofovir, emtricitabine and zidovudine may also cause mild reactions

# Skin Reactions

- Immune reconstitution
  - 25% of patients who have IRIS present with a skin reaction
  - Usually seen within the first three months of starting medications
  - Management
    - Mild symptoms – NSAIDs and continuation of HAART
    - Severe symptoms – steroids



**Fig. 4.** Dermatomal herpes zoster in an HIV-infected patient who initiated antiretroviral therapy 8 weeks previously. Scarring from a prior episode of zoster is evident superior to the active lesions (photograph courtesy of Toby Maurer, MD).

# Central Nervous System



# CNS Adverse Effects

- Headache
  - Seen in all classes of ARVs
  - Effects may be additive and identifying offending agent may be difficult
  - Management
    - Mild – OTC acetaminophen or NSAIDS as needed
    - Moderate – prescription NSAIDS or mild narcotics
    - Severe – change regimen or treat with stronger narcotics
- Neuropsychiatric
  - Efavirenz crosses the blood brain barrier and can cause more adverse effects
    - Dizziness, insomnia, vivid dreams, impaired concentration, drowsiness
  - Most effects are relatively short-lived
  - Risk of activating psychiatric problems

# First Line Regimens

- Efavirenz based regimens
  - CNS effects and rash
- Atazanavir
  - Nausea, rash, abdominal discomfort, elevated bilirubin
- Darunavir
  - Diarrhea, nausea and potential sulfonamide rash
- Tenofovir and Emtricitabine
  - Headache, fatigue and nausea
- Ritonavir
  - Nausea and diarrhea

# Summary

- Acute adverse effects are common amongst antiretroviral medication
- Identify patients who may be at higher risk for adverse effects and select appropriate regimens
- Proper patient education along with strategies to treat common side effects can help patients overcome problems