CLINICAL MONITORING IN ADULTS ON ART

Presented at the CHASS workshop, Chimoio by Dr Maureen Masha
Know what to expect when…

**Early ART side effects**
- Rash, N&V
- Hepatitis
- Anaemia
- Vivid Dreams

**Later ART side effects**
- Peripheral neuropathy
- Lipodystrophy
- Hyperlactataemia

**TDF Induced Renal toxicity**
Golden Rule of ART

• Adherence
• Adherence
• Adherence
How would you define Adherence?

• Taking medication correctly i.e. taking the right drugs the right way and at the right time
• 100% adherence to ARVs is required for them to work properly
• Miss 3 or more doses (less than 95% adherence) – can lead to resistance
Goals of Adherence

- Improve quality of life
- Effective PMTCT
- VL suppression
- Avoid drug resistance
- Prevent mortality
- Strong immune system
Predictors of poor adherence

- Non-disclosure
- Lack of Psychosocial support
- Poor doctor/patient relationship
- Lack of understanding
- Low literacy – creative counselling needed
- Medication side effects
- Domestic violence
- Religious and traditional beliefs
- Stock-outs
- Stigma & Discrimination
- Mental illness
- Supporting other sick family members
- Active drug and alcohol use
- Mobile lifestyle
- Travel away for holidays
- Knowledge of HIV
- Housing
- Undiagnosed OIs
Clinical Failure

Immunological Failure (CD4)

Virological Failure (Detectable Viral Load)

- Poor Adherence
  - Social/Personal Issues
  - Regimen Issues
  - Toxicities

- Insufficient Drug Level
  - Wrong dose
  - Drug interactions
  - Poor absorption

- Resistant Virus
  - Viral Replication in the Presence of Drug
ART Side-effects
HOW TO MONITOR FOR SIDE EFFECTS
- SUMMARY

1. **IDENTIFY**
   Ask specific questions and check blood results

2. **GRADE**
   Minor or serious

3. **WHICH DRUG IS THE CULPRIT ?**
   e.g. ARV or something else

4. **MANAGE ( use algorithms)**
Commonly used Antiretrovirals

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
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<tbody>
<tr>
<td>Tenofovir (TDF)</td>
<td>Efavirenz (EFV)</td>
<td>Lopinavir</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>Nevirapine (NVP)</td>
<td>Ritonavir</td>
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<tr>
<td>Emtricitabine (FTC)</td>
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<tr>
<td>Zidovudine (AZT)</td>
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<tr>
<td>Abacavir (ABC)</td>
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<td>Stavudine (D4T)</td>
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<td>Didanosine (DDI)</td>
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</table>
## SIDE EFFECTS – BRIEF SUMMARY

<table>
<thead>
<tr>
<th>ARV</th>
<th>SIDE EFFECT</th>
<th>QUESTIONS TO ASK</th>
<th>LABS/ OTHER TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir</td>
<td>Nephrotoxicity, GIT</td>
<td>1. Pain or tenderness over kidney/flank area ?</td>
<td>1. Creatinine clearance</td>
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<td>2. Recent tiredness, blood in urine ?</td>
<td>2. Urine dipstick</td>
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<td>3. Nausea, vomiting ?</td>
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<tr>
<td>Efavirenz</td>
<td>1. CNS Neuro-Psychiatric symptoms, 2. Rash</td>
<td>Nightmares, vivid dreams, dizziness, depression, loss of concentration, sleep disturbances, psychosis.</td>
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<tr>
<td></td>
<td></td>
<td>When did it start, where on body, type of rash ? Itchy?</td>
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<tr>
<td>Nevirapine</td>
<td>1. Rash, Steven Johnson Syndrome (can be fatal)</td>
<td>When did it start? What does it look like? Where on the body? Itchy? NB. If rash is associated with fever, mucous membrane involvement or rash has vesicles, moist desquamation or is exfoliative – REFER URGENTLY</td>
<td></td>
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<tr>
<td></td>
<td>2. Hepatotoxicity (can be fatal)</td>
<td>Right upper quadrant pain/tenderness? Yellowing of eyes/skin? Yelloeing of eyes/skin etc - REFER</td>
<td>ALT – if raised (plus rash) REFER</td>
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When did it start?  What does it look like? Where on the body? Itchy? NB. If rash is associated with fever, mucous membrane involvement or rash has vesicles, moist desquamation or is exfoliative – REFER URGENTLY.

Right upper quadrant pain/tenderness? Yellowing of eyes/skin etc - REFER.
A Dangerous drug rash

NVP Rash Danger signs
• Blistering
• Mucosal involvement
• Elevated Temperature
• Systemic signs e.g. malaise, myalgia
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<tr>
<td>Zidovudine</td>
<td>1. GIT SYMPTOMS (frequent short term side effect)</td>
<td>Do you have nausea, vomiting or diarrhoea? (TREAT SYMPTOMATICALLY)</td>
<td></td>
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<tr>
<td></td>
<td>2. Myelosuppression</td>
<td>Have you recently felt tired?</td>
<td>Hb (refer if less than 7g/dl OR IF UNSURE WHAT IS CAUSING THE ANAEMIA) Low Hb, exclude TB and Malaria</td>
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<tr>
<td></td>
<td>• Anaemia</td>
<td></td>
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<tr>
<td></td>
<td>• Neutropenia</td>
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<td></td>
<td>May be severe</td>
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<td></td>
<td>3. Hyperpigmentation of skin, nails and mucous membranes</td>
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<td></td>
<td>4. Prolonged use of AZT may lead to myopathy</td>
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<tr>
<td>Lamivudine and emtricitibine</td>
<td>Generally well tolerated</td>
<td>Do you have nausea or vomiting or headaches?</td>
<td></td>
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<tr>
<td></td>
<td>HeadachesGIT symptoms</td>
<td></td>
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</tr>
<tr>
<td>Didanosine</td>
<td>1. GIT symptoms</td>
<td>Do you have bloating, nausea, vomiting or diarrhoea?</td>
<td>Lactic acid Amylase Lipase</td>
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<tr>
<td></td>
<td>2. Lactic acidosis</td>
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<tr>
<td></td>
<td>3. Pancreatitis</td>
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<tr>
<td>Abacavir</td>
<td>1. GIT</td>
<td>Do you have nausea or vomiting?</td>
<td></td>
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<td></td>
<td>2. Headaches</td>
<td></td>
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<td></td>
<td>3. Hypersensitivity reaction (HSR)</td>
<td>Do you have a rash? (check if also have fever, nausea, fatigue or cough) – REFER URGENTLY</td>
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<td></td>
<td>N.B Do not re-introduce ABC (may be fatal)</td>
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<tr>
<td>Stavudine</td>
<td>1. Peripheral neuropathy</td>
<td>Do you have burning/ tingling/ pain in both feet ?</td>
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<td></td>
<td>2. Lipoatrophy</td>
<td>Have you seen changes in your body shape (loss of fat in face, buttocks, top of arms and legs ?)</td>
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<td></td>
<td>3. Lactic acidosis or symptomatic</td>
<td>Loss of weight, tiredness, stomach pains, vomiting, diarrhoea, shortness of breath, muscle aches, enlarged liver</td>
<td>Blood lactate (use portable device) and <strong>refer urgently</strong> if lactate is above 3mm/L WITH SYMPTOMS</td>
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<td></td>
<td>hyperlactataemia N.B. Know who are your</td>
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<td></td>
<td>high risk patients</td>
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**Note:**
- Blood lactate (use portable device) and refer urgently if lactate is above 3mm/L WITH SYMPTOMS.
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<td>Lopinavir/ritonavir (Aluvia for adults and Kaletra syrup for children)</td>
<td>1. GIT symptoms</td>
<td>Do you have diarrhoea? Loose stools? How many times per day?</td>
<td>Fasting cholesterol and triglycerides</td>
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<td></td>
<td>2. Lipid abnormalities</td>
<td>Have you seen any changes in your body shape?</td>
<td>Blood glucose</td>
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<td>3. Lipodytrophic changes</td>
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<td></td>
<td>3. Insulin resistance</td>
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<td>N.B. 2,3 and 4 plus a high BMI from part of the &quot;metabolic syndrome&quot;, &amp; increases the risk of diabetes, hypertension, stroke, and cardiovascular disease</td>
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Grading of side-effects

- Mild
- Moderate
- Severe
- Life threatening

Check Pages 101 – 112 in your guidelines (Mozambique ART Guidelines)
Management of side-effects

- Identify the culprit
- Check for drug interactions and overlapping side-effects
- Grade side-effect
- If mild or moderate, treat symptomatically. Reassure patient. Side-effects may resolve within 2 weeks
- If severe or life-threatening: STOP ALL ART

In case of NVP adverse reaction, stop NVP first and continue with the other 2 ARVs for 7 days (NVP has long half life)

- Record and report adverse reaction
CASE STUDIES
Case 1

• 32 year old male, HIV+ CD4 count 289. Screened for TB and other OIs. Started on TDF/3TC/EFV one week ago. Now complaining of nightmares and dizziness.

• Diagnosis/Management?
Case 2

• Spot diagnosis of side-effect?

• This patient has been on CTX for 2 months and AZT/3TC/NVP for 6 days.

• How do you manage this patient?

Courtesy of Tanzania MOHSW
Case 3

- Spot diagnosis?
- Which ARVs can cause this?
- Which TB drugs can cause this?
- How do you manage this patient?
IRIS

• Immune
• Reconstitution
• Inflammatory
• Syndrome
UNMASKING of undiagnosed infection

Can be prevented by screening for OI before starting ART

TREATMENT
Continue ART
Start OI treatment
Steroids only if severe

PARADOXICAL REACTION to an infection that is being appropriately treated

Incidence 8-45% for TB
Incidence up to 30% for CM

TREATMENT
Continue ART and OI treatment
Steroids if severe
• OIs excluded before starting ART
• Developed enlarged lymph nodes after starting ART
• What is your diagnosis?
• Will you stop ART?
• HIV+ and was diagnosed with TB lymphadenitis. He was started on TB treatment and 4 weeks later ART was commenced. Swollen lymph nodes became worse.
• What is your diagnosis?
• Will you stop ART?
Monitoring patient on ART

- Full history: Medical/Social
- Clinical Examination
  - vital signs
  - JACCOLD
  - All systems
- Investigations
- Diagnosis
- Treatment
OBRIGADO