Adult ART guidelines

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Topics

- ART in Pregnancy
- Abacavir Hypersensitivity reaction
- Adverse effects from Atazanavir
Ms XB

• 24 Year old Nursing student
  – HIV positive CD4$^+$ Count of 450 cells/μL
  – On ART for the past 3 years
    • Regimen of FDC (TDF/FTC/EFV)
    • Last viral load –LDL 6 months ago
  – 14 weeks pregnant
  – No other medical conditions & clinically well
  – **What do you do next?**
  – **When does she return to the clinic?**
Box 1: Changes specific to pregnant/breastfeeding women

- Immediate initiation of lifelong ART for all HIV-positive women who are pregnant, breastfeeding or within 1 year post-partum, regardless of CD4 cell count

- Use of EFV as part of the first-line regimen, regardless of the gestation of the pregnancy

- Use of maternal lifelong ART throughout pregnancy and breastfeeding to reduce MTCT

- Viral load testing for women on ART ≥3 months at confirmation of pregnancy to direct management

- Repeat HIV testing for HIV-negative women 3-monthly during pregnancy, at labour/delivery, at the 6 week Expanded Programme on Immunisation (EPI) visit and 3-monthly throughout breastfeeding. This should be done during routine antenatal care, postnatal care and EPI/child health follow-up visits

- Women with contraindications to FDC should be considered high-risk pregnancies. They should be initiated on AZT immediately and referred urgently for initiation on to three single ART drugs

- Provision of birth HIV PCR for all HIV exposed neonates

- Use of extended 12 weeks NVP or dual post-exposure prophylaxis with NVP and AZT for infants where maternal viral load suppression may be inadequate
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  – What do you do next?
  – When does she return to the clinic?

| Viral Load | 15 000 copies/ml |
Algorithm for management of pregnant women already on ART for > 3 months

1. **Woman on ART with confirmed pregnancy**
   - Perform viral load at the same visit (Irrespective of when last done)
   - Emphasise importance of adherence

2. **Review viral load result within 2 weeks**

3. **Viral load <1000 copies/ml**
   - Continue current ART regimen
     - If appropriate, switch from 3 individual ARVs to FDC to allow integrated follow up at local ANC clinic
   - Viral load undetectable or ≥1 log drop in viral load

4. **Viral load >1000 copies/ml**
   - Provide comprehensive adherence counselling
   - Repeat viral load one month after initial test
   - Review repeat viral load result
   - Viral load unchanged OR <1 log drop OR increased
     - Switch to second line regimen as per adult ART guidelines
     - Infant requires prophylaxis with AZT plus NVP and birth PCR testing

*NDOH ART Guidelines 2015*
**NEWLY DIAGNOSED HIV / KNOWN HIV POSITIVE BUT NOT YET ON ART**
- Initiate FDC the same day, if no contraindications
- If contraindications to Tenofovir or Efavirenz, initiate alternative regimen

**ART-EXPERIENCED CLIENT DEFAULTING ART**
- Re-start previous regimen on same day
- Emphasize importance of adherence

**CLIENT ON ART**
- Perform VL at the same visit unless documented evidence of VL in the last 12 weeks.
- Emphasize importance of adherence

**VL AFTER 3 MONTHS ON ART**
- VL < 400 copies/ml
  - Repeat 3 months later
  - Continue current ART regimen
- VL 400-1000 copies/ml
  - Provide urgent adherence counselling
  - Repeat 3 months later
- VL > 1000 copies/ml
  - Provide urgent adherence counselling

**VL MONITORING IN PREGNANCY**
- Proposed Western Cape Guideline - Courtesy Rosie Burton

**VL < 1000 copies/ml OR ≥ 1 log drop* in VL**
- Repeat 3 months later
- Continue current ART regimen

**VL > 1000 copies/ml**
- If <14 weeks gestation:
  - Repeat VL 3 months after previous test
- If ≥ 28 weeks gestation:
  - Repeat VL at 1 month after intensive adherence counselling

**Review VL result within 1-2 weeks**
• If <14 weeks gestation:
  Repeat VL 3 months after previous test
• If ≥28 weeks gestation:
  Repeat VL at 1 month after intensive adherence counselling

• Review VL result within 1-2 weeks

• If failing on 1st line regimen, switch to 2nd line regimen as per adult ART guidelines
  • If failing on 2nd line regimen, consult an expert for advice as soon as possible.

• Infant must be managed as high-risk HIV exposure post-delivery – eligible for dual PEP and birth PCR

• VL <1000 copies/ml
  or
  ≥ 1 log drop* in VL

• Continue current ART regimen

• Repeat 3 months later

* log drop means a 10 fold drop i.e. divide the VL count by 10

Proposed Western Cape Guideline - Courtesy Rosie Burton
Mr ABC

• 41 year old
  – Diagnosed HIV positive 10 years ago CD4⁺ nadir of 100
  – Initiated on FDC (TDF/FTC/EFV) in 2005
  – Defaulted ART in 2014
  – Admitted on 2nd April with diarrhoea & renal dysfunction
  – Restarted ART in May
    • Regimen Abacavir/ lamivudine/ Efavirenz
3 weeks later

**Symptoms**
- Fever
- Headache
- Vomiting
- Abdominal pain
- Easy fatigability
- Rash on the back

**Examination**
- T 38°C, BP 120/80 mmHg
- P 110
- Maculopapular exfoliative rash on back
- No hepatomegaly
- All other systems normal
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<thead>
<tr>
<th>Laboratory Results</th>
<th>Value</th>
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<tr>
<td>WCC</td>
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<tr>
<td>Hb</td>
<td>10.0 g/dl</td>
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<tr>
<td>PLT</td>
<td>90 X 10⁹/L</td>
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<tr>
<td>Total Bilirubin</td>
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<tr>
<td>GGT</td>
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<td>Creatinine</td>
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Abacavir Drug Hypersensitivity (1)

• Features
  – Fever (usually 39-40 degrees)
  – Rash in 70% (maculopapular or urticarial)
  – Fatigue, malaise
  – GI symptoms (N&V, diarrhoea, abdominal pain)
  – Arthralgias
  – Cough, dyspnoea, pharyngitis
  – Usually > 1 system
  – Temporally related to taking dose

• Timing
  – Median onset 9 days
  – 90% in first 6 weeks
Abacavir Drug Hypersensitivity (2)

- Incidence
  - 4-8% in people of European descent
  - Much less common in people of African descent
  - Strongly associated with HLA-B5701
    - White Americans 8%
    - African-Americans 2.5%
    - Africa < 1%

- Can be fatal
  - 3/10,000 people on abacavir-based ART (trial data)
  - Rechallenge is an important risk
Ms AT

- 33 year old mother of 2 children
  - Diagnosed HIV positive 2013
  - Started ART July 2013- FDC (TDF/FTC/EFV)
  - Nov 2013 CD4$^+$ 635 VL-LDL
  - Sept 2014 develops DILI- EFV
  - Oct 2014 Switched to
    - Truvada + Atazanavir/ Ritonavir
    - CD4$^+$ 743 VL-LDL
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Adverse effects of Atazanavir (1)

• Most common and recognized
  – Hyperbilirubinemia
    • Results in visible jaundice or scleral icterus
    • Due to inhibition of UGT1A1 enzyme
    • Occurs in 30-49% of patients in clinical trials
    • ~40% will experience >2.5 times ULN elevation (grade 3)
    • ~5% will experience >5 times ULN (grade 4)
  – Nausea
  – Diarrhoea
Adverse effects of Atazanavir (2)

- **Lipid profile and body fat composition**
  - ATV increases lipid levels less than other PIs
  - No associated with AEs related to glucose & insulin
  - Changes in body fat composition similar to other ARTs

- **Nephrolithiasis**
  - Obstructive uropathy
  - Acute renal failure
  - Incidence 23.7 cases per 1000 person-years

Adverse effects of Atazanavir (3)

• Cholelithiasis
  – Association between exposure & increased risk
  – Mechanism not fully understood
  – Hamada et al reported a low incidence of 2.23 per 1000 person-years
  – Nishijima et al report that risk increased with > 2 years

Hamada Y et al. PLOS ONE 8(7): e69845
Nishijima et al. JAC 2013