Adverse Events of Antiretroviral drugs
Clinician’s Perspective

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AEs IN ART IN ZIMBABWE

- Few systematic studies
- Clearly common as seen in clinical trials and national programs
  - DART, A5175, A5208, HPTN 052, Others
- Renal dysfunction in a TDF containing triple nuc regimen-published (IAC, Toronto 2006)
- Lipodystrophy & lipid changes-on-going study
Baseline characteristics

3316 participants (accrual completed Oct 2004)

- Sex 65% women
- Median age 37 years (IQR: 32-42)
- Median CD4 86 cells/mm³ (IQR: 31-140)
- WHO stage 23% WHO 4 56% WHO 3
- Median Hb 11.4 g/dl (IQR: 10.3-12.7)
- Anaemia 12% <9.5g/dl (grade 1)
- Median BMI 21.2 (IQR: 19.2-23.6)
- Median follow-up 48 weeks (IQR: 25-60, max: 96)

Data to 15 January 2005 (trial ongoing)
Incidence of anaemia

- Most severe new episode:

<table>
<thead>
<tr>
<th>Grade</th>
<th>n</th>
<th>%</th>
<th>cumulative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 4 (&lt;6.5 g/dl)</td>
<td>220</td>
<td>6.6%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>38</td>
<td>1.2%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>136</td>
<td>4.1%</td>
<td>11.9%</td>
</tr>
<tr>
<td>Grade 1</td>
<td>407</td>
<td>12.3%</td>
<td>24.2%</td>
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</tbody>
</table>

- 14 patients had >1 grade 4 episode
Weight and serum creatinine change after baseline

- Weight increase up to week 48 but stabilisation thereafter

Weeks from ART initiation

Weight (kg) vs S-Crea (mg/dl)
Prevalence of impaired GFR* and raised S-Creatinine** (grade 3 or 4)

% with grade 3 or 4 reduction

* National Kidney Foundation; ** ACTG criteria
Patients with mild renal impairment at baseline showed greater improvements than those without impairment - changes were within the normal range.
Common AEs-Zim

- Common AEs well known and part of ART training
  - Nevirapine
    - Rash, hepatitis-less well known hypersensitivity
  - Efavirenz
    - CNS side effects
  - Stavudine
    - Peripheral neuropathy, metabolic AEs-lactic acidosis, lipodystrophy
  - Zidovudine
    - Anaemia, lactic acidosis, myositis
  - Tenofovir
    - Renal dysfunction
  - Protease Inhibitors
    - Lipid abnormalities, lipodystrophy
AEs-Issues

• Issues
  • Clinical trials
    • Reported to regulatory authorities according to standard definitions and guidelines eg DAIDS toxicity tables and MRCZ and MCAZ requirements
  • Programs
    • Reports according to national requirements MCAZ and National Drugs & Therapeutic Control Authority (NDTPAC)
AEs-Issues

- Knowledge
  - Clinical trials-excellent knowledge of DAIDS tables
  - Programs-lack of standard reporting
    - Coding
    - Definitions
    - Grading
    - Relatedness information
AEs

- Recognition-needs
  - Standardized reporting systems
  - Training
  - Opportunities for reporting
    - Routine pharmacovigilance
    - Targeted-clinical trials, program, etc
- Accuracy ie full description
  - Concomitant medication including TB medicine, antimalarials, Cotrimoxazole
  - Traditional medicines/herbs
  - Over the counter medications-antiacids and H2 antagonists
AEs

- Diagnosis
  - Presumptive/confirmed
  - Clinical descriptions/laboratory data
  - Symptomatic/asymptomatic
- Reporting
  - Emphasized in ART guidelines
  - Included in national formulaty
Thank you