ANTIRETROVIRAL THERAPY IN NAMIBIA

SAHIVCS CONFERENCE CAPE TOWN 25-28-NOVEMBER 2012

DR. F. MUGALA – MUKUNGU
M.MED (INT.MED)
SPECIALIST PHYSICIAN
KATUTURA STATE HOSPITAL
WINDHOEK NAMIBIA
Current status in Namibia

- Population, 2.3M
- Surface area (sq. km) (thousands 823.4
- GDP (current US$) (billions) 12.3 GDP per capita growth (annual %) 3.8
- Life expectancy at birth, 62.3 years
- Mortality rate, infant 29.6 per 1,000 live births
- Prevalence of HIV, 18.8% ANC Sero survey 2010
HIV Prevalence Rate in Pregnant Women in Namibia 1992 - 2010

Source: MOHSS report of the 2010 National HIV Sentinel Survey, November 2010
Implementation of ARV therapy in Namibia

- ARV therapy was implemented in the Private Sector in 1997 by Government Medical Aid as approved by cabinet.
- There were no ARV guidelines
- The HIV Clinicians Society Namibia was founded by a group of doctors from both Private and state sectors.
- The initial draft guideline was made by this group in 2002 and later became the framework for the initial ARV guidelines of Namibia in 2003.
- The latest draft of Namibia guidelines is the 2010 document.
- This is the third edition
CURRENT STATUS OF ARV THERPAY IN NAMIBIA

• 80% patients in need of ART are receiving ARV Medicines
  64% are women
  16% are children

• Complete nation wide coverage of ART Service delivery.

• Introduction of Integrated Management of Adolescent and Adult illnesses (IMAI) strategy by MOHSS.

• Introduction of quality management program (HIV QUAL) has taken place successfully
Minimum requirement to start ARV therapy

1. Trained Medical Practitioner
   To be able to assess and stage HIV positive Individual.

2. Access to Laboratory facility with minimum tests of full blood count, kidney function, HBSAg, ALT and a CD4 count.
   Trained support staff especially a Nurse and a community counselor

No baseline virology studies required.
Requirement for HIV positive Adult to start on HAART therapy.

1. WHO clinical stage 3 or 4, irrespective of CD4 count or
2. If WHO stage 1 or 2, CD4 Count < 350 cells /mm³
3. It is anticipated that from April 2013, all pregnant women will be eligible irrespective of WHO Clinical stage or CD4 count. (Option B+)
4. All HIV/HBV Co-Infected patients with ALT > 2X ULN or HBeAg-positive.
Considerations to improve HAART Adherence.

1. Assessment, Counselling and Information given 2 weeks before ARV therapy.
2. Adherence supporter encouraged but not mandatory.
3. Using the Simplest regimens.
4. Improving Provider related skills.
5. Dialogue with the community include NGOs peer educator and linkages to the TB Control program.
7. Standardised definitions of a defaulter.
Recommended HAART in Namibia in Adults

1. First line regimen: TDF 300mg + 3TC 300mg OD plus NVP 200mg twice day.

2. HIV-TB Co-Infection: TDF/3TC/EFV

3. Chronic active TDF/3TC/NVP or TDF/3TC/EFV

**Second line**
4. Second line Regimen: AZT/TDF/3TC/LPV/r.

**Third line**
Third line regimen: Is always to be discussed with an HIV Specialist taking into consideration results of HIV resistance testing.
Eligibility criteria for children

1. All HIV infected Infants less than 24 months age.
2. HIV infected Children between 24 – 59 months with
   - WHO Paediatric stage 3 or 4
   or stage 1 and 2, if CD4 ≤ 25%
3. HIV infected Children ≥ 5 years of age.
   - WHO Paediatric stage 3 or 4
   or WHO Paediatric stage 1 or 2 if CD4 <350/mm³.
First line regimens available for children.

1. HIV + Infants < 24 months with known prior exposure to NVP or to maternal NVP-containing HAART or PMTCT prophylaxis – LPV/r + D4T/3TC FDC
   - d4T used because there currently there is no infant AZT-containing FDC available

2. HIV + Infants < 24 months old without prior exposure to NVP and children > 24 months old but < 14kg – NVP/D4T/3TC FDC.

3. Children ≥ 24 months ≥ 14kg and Tanner stage I – III AZT/3TC/NVP.
   - These children can use the adult AZT-containing FDC

4. Tanner stage IV or post pubertal Adolescents TDF/3TC/NVP.
Second line Regimens in Children

1. Second line HAART for children (Tanner stage I – III) first line: (ABC + AZT + 3TC + LPV/r)

2. Second line HAART for children Tanner stages I - III who had PI-based first line ABC + AZT + 3TC + (NVP or EFV).

3. The second line HAART Regimen for children who are Tanner stage IV or V is the same as Adults. If the first line regimen included Tenofovir, seek advice of an HIV Specialist.
HAART REGIMENS IN CHILDREN ON RIFAMPICIN BASED REGIMES

1. ≥ 3 years and weight ≥ 10kg
   - AZT or d4T + 3TC + EFV if sexual maturity Tanner stage I-III
   - TDF + 3TC + EFV if sexual maturity Tanner stage IV/V.

2. < 3 years or weight < 10kg give either
   D4T or AZT + 3TC + ABC OR
   D4T or AZT + 3TC + super-boosted LPV/r.
Post Exposure Prophylaxis

1. Low risk exposure: TDF plus 3TC fixed dose combination for 28 days within 24 hours of Exposure.

2. High Risk exposure: TDF + 3TC + LPV/r or EFV for 28 days within 24 hours of Exposure.

3. Because the background prevalence of HIV is high, there is no differentiation in management depending on whether the source is high or low HIV risk.
Overview of ARV Therapy in Namibia (April – June 2012)

50 sites in Namibia give ART therapy
No. of patients on ART AS OF June 2012 108 687.
No. of Adults 90.4%
Paediatrics (<14 years old) 9.6%
Top ARV used in Namibia Public sector:
  3TC + TDF   fixed dose
  3TC + AZT + NVP – fixed dose
  NVP
  EFV
  LPV/r  200/50.
Overview of ARV Therapy in Namibia (April – June 2012)

ARVs in the Public Sector-NNRTIs vs PIs March -June 2012

- Nevirapine, 74%
- Efavirenz, 21%
- Protease inhibitors, 5%
ARV IN THE PUBLIC SECTOR

Consumption Trend for the Top Five ARVs,
Jul'11 - Jun'12
ARVs in the Public Sector -

Nucleoside Analogues March-June 2012

- AZT BASED 54,867, 47%
- Tenofovir 44,256, 38%
- Stavudine based 16,790, 14%
- Abacavir 1%
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia

- Dr Ishmael Katjite, Principal Investigator
- and
- Catherine Corbell, BPharm, MSc
- Andy Stergachis, PhD, RPh
- Global Medicines Program
- University of Washington
- October 2010
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia: Background

• 2007: Namibia switched first-line treatment from d4T- to AZT-based HAART

• 2008: ~50% (22,050/43,329) of HAART users on AZT-based regimens in 2008

• 2008: Anemia in HAART users most commonly reported adverse event in 2008 (106 of 256 spontaneous ADR reports to TIPC)

• 2009: TAC requested MSH-SPS to provide technical assistance in the adverse event monitoring of ARVs
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia: Specific Aims

Primary Aim:

To determine the incidence of and risk factors for anemia in adults on AZT-based HAART

Secondary Aim:

To demonstrate the feasibility of using automated databases and records linkage as a sustainable platform for assessing the safety and use of HAART to help support evidence-based decision-making in Namibia
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia: Results

• Of 12,358 persons who initiated HAART between January 2007 and June 2008, 7,206 started on AZT- and 5,152 on d4T-based HAART.

• 4,746 (38%) individuals had baseline Hb values available.
  ➢ 63% of persons with baseline Hb values were in AZT cohort.

• Total of 828 persons (6.7%) developed any anemia, and 151 persons (1.2%) developed severe anemia during follow-up.

• 293 deaths and 12 lost to follow-up.
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia: Characteristics of HAART Cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>AZT (N=7,206)</th>
<th>d4T (N=5,152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% female</td>
<td>61.1</td>
<td>61.5</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>35.7</td>
<td>36.7</td>
</tr>
<tr>
<td>% started their HAART regimen in 2007</td>
<td>43.3</td>
<td>89.7</td>
</tr>
<tr>
<td>Mean baseline weight, kg</td>
<td>56.7</td>
<td>53.8</td>
</tr>
<tr>
<td>Mean baseline CD4 count</td>
<td>157.1</td>
<td>155.0</td>
</tr>
<tr>
<td>% Baseline WHO stage 3 and 4</td>
<td>34</td>
<td>41</td>
</tr>
<tr>
<td>Mean baseline hemoglobin, g/dl</td>
<td>11.8</td>
<td>11.8</td>
</tr>
<tr>
<td>Hb measurements in first year of HAART, median (IQR)()</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>Median time to first Hb measurement, days (IQR)</td>
<td>37 (14-70)</td>
<td>146 (55-258)</td>
</tr>
<tr>
<td>Mean follow-up time, years</td>
<td>1.26</td>
<td>1.76</td>
</tr>
</tbody>
</table>
Results

Prevalence of anemia at the start of HAART

- Of 4,852 with baseline Hb values, 672 (13.8%) had any anemia at start of HAART.

- Prevalence of anemia significantly higher in:
  - women than men (14.9% vs. 12.2%, p=0.01)
  - d4T cohort than AZT cohort (18.3% vs. 11.3%, p <0.001)
## Incidence of anemia

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Persons with baseline Hb values (n=4,746)*</th>
<th>Persons with no baseline Hb values (n=7,506)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Incidence rate (per 100 PYs)</td>
</tr>
<tr>
<td>AZT cohort</td>
<td>379</td>
<td>11.85</td>
</tr>
<tr>
<td>d4T cohort</td>
<td>234</td>
<td>9.31</td>
</tr>
<tr>
<td>p value</td>
<td>0.004</td>
<td></td>
</tr>
</tbody>
</table>

### Any anemia

### Severe anemia

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Events</th>
<th>Incidence rate (per 100 PYs)</th>
<th>Events</th>
<th>Incidence rate (per 100 PYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT cohort</td>
<td>73</td>
<td>2.28</td>
<td>20</td>
<td>0.34</td>
</tr>
<tr>
<td>d4T cohort</td>
<td>45</td>
<td>1.79</td>
<td>13</td>
<td>0.20</td>
</tr>
<tr>
<td>p value</td>
<td>0.5</td>
<td></td>
<td>0.16</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AZT, zidovudine; d4T, stavudine; Hb, hemoglobin; PYs, person-years

* 106 individuals excluded for having severe anemia at baseline.
Risk of severe anemia: retrospective cohort analysis

• **No statistically significant difference** in the risk of severe anemia in AZT vs. d4T cohort.
  - Relative risk adjusted: 0.73; 95% CI: 0.43, 1.24
  - Adjusted for age, gender, baseline weight, CD4 count, WHO clinical stage, baseline hemoglobin, clinical status and year of starting HAART.
  - Does not take duration or timing of use into account

• **Statistically significant risk factors** for severe anemia:
  - Persons with 1 g/dl lower baseline hemoglobin had a 12% increased risk of severe anemia.
  - Persons with 1 kg lower baseline weight had a 3% increased risk of severe anemia.
Assessment of the risk of anemia associated with zidovudine-based HAART in Namibia: Nested case-control results

• Included 11 ART facilities country-wide.

• Records for 82 cases* of severe anemia and 246 persons without severe anemia (controls) abstracted.

* 82/151 cases of severe anemia
Antiretroviral treatment in the Private sector in Namibia

- 280,000 Namibians (17% of the total population) are covered by private medical insurance.
- The Medical insurance for government employees covers over 70% of all members of the private sector.
Antiretroviral treatment in the Private sector in Namibia

- The medical insurance companies in Namibia agreed to make anonymous data on ARV dispensing available to the Society for analysis and feedback in the years 2003, 2004, 2005 and 2008. The Society uses this information to provide feedback to the Ministries of Health and finance, and medical insurance industry. The information
Antiretroviral treatment in the Private sector in Namibia

• Cross sectional ARV dispensing for the last quarters of 2003, 2004, 2005 and the second quarter of 2008 were compiled and analysed.

• ART regimens were compared with the most recent national and international guidelines and classified into
  – recommended (NNRTI-based and boosted PI-based),
  – not recommended (non-boosted PI-based or d4T/ddI containing regimens),
  – ineffective (dual therapy) and second line or salvage regimens.
Antiretroviral treatment in the Private sector in Namibia

NUMBER ON TREATMENT

- Not classified
- Second line/salvage
- Ineffective
- Not recommended
- Recommended

2003: 1527
2004: 2355
2005: 4868
2008: 6375
Antiretroviral treatment in the Private sector in Namibia

NUCLEOSIDE ANALOGUES IN THE PRIVATE SECTOR 2012

- TDF: 52%
- AZT: 45%
- ABC: 2%
- D4T: 1%
Antiretroviral treatment in the Private sector in Namibia

Nevirapine 20%
Efavirenz 66%
Protease inhibitors 631, 14%
27, 0%

Nevirapine Efavirenz - Protease inhibitors DARUNAVIR Private Sector

Efavirenz 66%
Nevirapine 20%
Protease inhibitors 631, 14%
Antiretroviral treatment in the Private sector in Namibia

• The available data give an accurate picture of the significant contribution of the private sector to ART access in Namibia.

• Adherence to recommended ARV regimens has overall improved. There is a significant increase in second line regimens.

• Standard protocols for analysing ARV dispensing could identify practices in need for training and supportive supervision.
Acknowledgements

• Dr Laura Brandt ITECH-Namibia
• Dr Fred Van Der Veen
• Mr Ongeri, B. M- Senior Technical Advisor, Management Sciences for Health/SIAPS Project