Pharmacovigilance – Pilot Project – Lao PDR
Adverse Drug Reaction Monitoring/Targeted Spontaneous Reporting for ARV

Lao PDR
Ministry of Health
Food and Drug Department (FDD)
Center for HIV/AIDS and STI (CHAS)
Lao People's Democratic Republic (Lao PDR)

- Population: 6.7 million
- Capital: Vientiane
- *Lower-middle* economy
- HIV prev. 0.3% (15-49 years)
- PLHIV: #10,000
- #2,560 on ART (coverage 55%)
Project background

• About 2560 patients on ARV (55% of coverage) in 8 centers;
• 75% of the national funding on HIV is from Global Fund;
• Lao PDR had no pharmacovigilance (PV) despite intention of FDD to start such the programme;
• With financial support from The Gates Foundation through WHO, FDD and CHAS started a PV system to monitor ADR of ARV with expectation to expand to other drugs;
• The project includes – FDD, HCD, CHAS, and 5 ARV sites
• Targeted Spontaneous Reporting of ADR for specific toxicities of Zidovudine (AZT) to monitor Anemia and Nevirapine (NVP) to monitor Rash/Steven’s Johnson syndromes and Hepatotoxicity;
• Timeframe – from 1rst Oct 2012 to 31 December 2013
Project Goal

Project goal
• To strengthen a pharmacovigilance (PV) system in Lao PDR: monitor, assess and improve the safety of ARV drugs;

Specific objectives
• Supporting to join the WHO Drug Monitoring Programme;
• Integrating into the monthly reporting M&E ART system to National AIDS Programme (NAP) and share with PV center;
• Developing forms for targeted spontaneous reporting of toxicities (AZT and NVP);
• Advocating and train clinicians in ART centers to the toxicity monitoring and report of adverse reactions;
• Defining and analyzing data;
• Disseminating results including regular feedback to ART sites;
• Setting up the system of report to the WHO Drug Monitoring Programme;
• Working with FDD to setup an efficient and ongoing system of reporting (National PV committee);
• Monitoring and evaluating the feasibility of TSR for ARVs and its integration into routine care;
• Seeking further funding to expand the system to other drugs i.e. Global Fund.
Project outputs

• Agreement on an establishment of a management and coordinating committee for Pharmacovigilance for ARV drugs, MoH – Minister decree number 767, 17 May 2012;
• Targeted Spontaneous Reporting form for ADR of ARV developed;
• SOP for ADR in five pilot ARV sites developed;
• 10 clinicians from five ARV hubs trained on SOP and TSR form reporting;
### ADR definition

<table>
<thead>
<tr>
<th><em>Anemia/เลือดจูบ</em></th>
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<tr>
<td><strong>Haemoglobin</strong></td>
<td>8.5–10.0 g/dl</td>
<td>7.5–&lt;8.5 g/dl</td>
<td>6.5–&lt;7.5 g/dl</td>
<td>&lt;6.5 g/dl</td>
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<tr>
<td>(เด็ก &gt;60 days of age)</td>
<td>1.32–1.55 mmol/l</td>
<td>1.16–&lt;1.32 mmol/l</td>
<td>1.01–&lt;1.16 mmol/l</td>
<td>&lt;1.01 mmol/l</td>
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### Rash

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<thead>
<tr>
<th><em>Rash</em></th>
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<tr>
<td>ปากนิ้วนิ้วสิ้นเนื้อมะน**</td>
<td><strong>Diffuse macular, Macula papular, or morbilliform rash OR target lesions</strong></td>
<td><strong>Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to one site</strong></td>
<td><strong>Extensive or generalized bullous lesions OR Stevens-Johnson syndrome OR ulceration of mucous membrane involving two or more distinct mucosal sites OR toxic epidermal necrolysis (TEN)</strong></td>
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### Hepato-toxicity

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</tr>
<tr>
<td>ALT (SGPT)</td>
<td>1.25–2.5 x ULN</td>
<td>2.6–5.0 x ULN</td>
<td>5.1–10.0 x ULN</td>
<td>&gt;10.0 x ULN</td>
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## ADR Form

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<tr>
<td>AZT (Zidovudine)</td>
<td>NVP (Nevirapine)</td>
<td>Rash/Runny, स्त्री: 1□ 2□ 3□ 4□</td>
<td>Fever/Sweat, स्त्री: 1□ 2□ 3□ 4□</td>
<td>Rash/Runny, स्त्री: 1□ 2□ 3□ 4□</td>
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<tr>
<td>Anemia/Leukemia</td>
<td>Hemoglobin:</td>
<td>SGPT level</td>
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Project outcome

• Lao PDR has been accepted as an associated member of UPPSALA monitoring center;
• Pharmacovigilance unit under FDD is being established to monitor all ADR;
• ADR from AZT and NVP are now routinely reported.
Project results

• From October 2012 until end of September 2013, in 5 ART centers, 421 new patients have been put on ARV;

• 64 cases of ADR reported among these patients, 33 cases from AZT and 40 cases from NVP.
### Reported ADR during the pilot project

<table>
<thead>
<tr>
<th></th>
<th>Patients on ART</th>
<th>Total reported ADR</th>
<th>Reported ADR for AZT</th>
<th>Reported ADR for NVP</th>
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<tbody>
<tr>
<td>Female</td>
<td>219</td>
<td>34</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Male</td>
<td>202</td>
<td>30</td>
<td>15</td>
<td>19</td>
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<tr>
<td>Total</td>
<td>421</td>
<td>64</td>
<td>33</td>
<td>40</td>
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Patients with adverse reactions
Total of patients who initiated ART from Oct. 2012 to Sept. 2013, with ADR reported during the period.
Reported ADR by sites during the pilot project

Number of cases

- Savannakhet
- Luangphabang
- Mahosot
- Champasak
- Setthathirat
- No. cases

ADR of AZT
ADR of NVP
Reported ADR by grading during the pilot project

Number of cases

Grade 1 | Grade 2 | Grade 3 | Grade 4 | No. cases
--- | --- | --- | --- | ---
Anemia | 10 | 15 | 20 | 35
Rash | 5 | 10 | 15 | 30
Hepatotoxicity | 5 | 10 | 15 | 25
Reported ADR for AZT during the pilot project

Number of cases

Number of patients on AZT

Anemia
Anemia+Rash
Anemia+Rash+Hepatotoxicity
Reported ADR for NVP during the pilot project

Number of cases

ADR Cases

Number of patients on NVP

Rash

Hepatotoxicity

Rash+Hepatotoxicity
Lessons learned

• **Strengths**
  – First ever project in Lao PDR on Pharmacovigilance;
  – Support from MoH, FDD, CHAS and relevant key implementers;
  – Gaining evidence on ADR of ARV specifically from AZT and NVP;
  – Increase on safety on the use of ARV for patients;
  – Strong commitment of medical practitioners;
  – Adherence is improved;
  – Enhancing capacity of ARV sites in reporting;
  – Experience from this project could be used to institutionalize the Pharmacovigilance in MOH;
  – This is the base and model to expand the project to cover more ARV drugs;

• **Challenges**
  – Standardized format to have denominators for data analysis is required for future implementation on PV of ADR of other drugs;
  – Timely manner of report submission requires focal point to have close monitoring and follow up;
  – Capacity and focal point for data validation and analysis need effective support;
  – Immediate responsiveness on ADR site supervision and investigation is required;
  – Funding for sustainability is critical;
Conclusion

• This project has greatly achieved each main objectives despitessmall budget and limited time;
• The project has improved the safety for patients by providing early warning on ADR;
• The close monitoring from clinicians have prevented further seriousness of the ADR;
• All ARV sites have gained knowledge and capacity in Pharmacovigilance that could be used to expand the coverage and scope of ADR;
• This is the model project that MOH could use to establish the national Pharmacovigilance in Lao PDR;
• There is a willingness of high decision makers of MOH and practitioners to support the continuation of the project;