Strengthening Pharmacovigilance in Africa

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I have no conflict of interest to declare
European & Developing Countries Clinical Trials Partnership (EDCTP)

Clinical research to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against poverty-related infectious diseases in sub-Saharan Africa (HIV/AIDS, TB, malaria, NTDs)

Focus on phase II and III clinical trials

**Call:** strategic actions to strengthen the capacity of health systems to effectively deliver new products and to monitor their post-market safety
Background

- Significant increase in the introduction of new drugs in Africa mainly targeting poverty-related diseases, often based on limited trial data

- Pharmacovigilance processes in most SSA health systems are still inadequately prepared to manage these new products

→ increase readiness of health systems to introduce and absorb new interventions for PRDs

→ increase the coverage, accessibility and effectiveness of evidence-based interventions in sub-Saharan Africa
Estimates 2017, Africa:

- **2.5 million** people fell ill with new (incident) TB
- People living with HIV accounted for **27%**
- **0.65 million** people died from TB, **38%** with HIV
- **90,000** people had incident multidrug-resistant TB
MDR-TB has poor treatment outcomes
20-24 months treatment, pre-2018 guidelines
Revised MDR-TB treatment guidelines (August 2018)

<table>
<thead>
<tr>
<th>GROUP</th>
<th>MEDICINE</th>
<th>Abbreviation</th>
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</thead>
<tbody>
<tr>
<td>Group A: Include all three medicines (unless they cannot be used)</td>
<td>Levofloxacin OR</td>
<td>Lfx</td>
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<tr>
<td></td>
<td>Moxifloxacin</td>
<td>Mfx</td>
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<tr>
<td></td>
<td>Bedaquiline(^1,4)</td>
<td>Bdq</td>
</tr>
<tr>
<td></td>
<td>Linezolid(^2)</td>
<td>Lzd</td>
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<tr>
<td></td>
<td>Clofazimine</td>
<td>Cfz</td>
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<tr>
<td></td>
<td>Cycloserine OR</td>
<td>Cs</td>
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<tr>
<td></td>
<td>Terizidone</td>
<td>Trd</td>
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<tr>
<td>Group B: Add both medicines (unless they cannot be used)</td>
<td>Ethambutol</td>
<td>E</td>
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<tr>
<td></td>
<td>Delamanid(^3,4)</td>
<td>Dlm</td>
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<tr>
<td></td>
<td>Pyrazinamide(^5)</td>
<td>Z</td>
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<tr>
<td></td>
<td>Imipenem-cilastatin OR Meropenem(^6)</td>
<td>Ipm-Cln Mpm</td>
</tr>
<tr>
<td></td>
<td>Amikacin (OR Streptomycin)(^7)</td>
<td>Am</td>
</tr>
<tr>
<td></td>
<td>Ethionamide OR Prothionamide</td>
<td>Eto</td>
</tr>
<tr>
<td></td>
<td>p-aminosalicylic acid</td>
<td>PAS</td>
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TB drugs clinical development pipeline (August 2018)

<table>
<thead>
<tr>
<th>Phase I*</th>
<th>Phase II*</th>
<th>Phase III*</th>
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<tbody>
<tr>
<td>Contezolid (MRX-1)^b</td>
<td>Delpazolid (LCB01-0371)</td>
<td>Bedaquiline (TMC-207)^b</td>
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<tr>
<td>GSK-303656^b</td>
<td>SQ109</td>
<td>Delamanid (OPC-67683)^2</td>
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<tr>
<td>Macozinone (PBTZ169)^b</td>
<td>Sutezolid (PNU-100480)^b</td>
<td>Pretomanid (PA-824)</td>
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<tr>
<td>OPC-167832</td>
<td>Linezolid dose-ranging</td>
<td>Clofazimine</td>
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<tr>
<td>Q203^b</td>
<td>Nitazoxanide</td>
<td>High dose rifampicin for treatment of DS-TB</td>
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<tr>
<td>TBA-7371^b</td>
<td>High dose rifampicin for DS-TB (PANACEA)</td>
<td>Rifapentine for treatment of DS-TB</td>
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<tr>
<td>TBI-166</td>
<td>Bedaquiline and delamanid (ACTG A5343 DELIBERATE trial)</td>
<td>Bedaquiline – Pretomanid – Linezolid (NiX-TB trial)</td>
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<tr>
<td></td>
<td>Bedaquiline – Pretomanid – Moxifloxacin – Pyrazinamide (BPaMZ) regimen</td>
<td>Bedaquiline – Pretomanid – Linezolid (ZeNix trial) – Linezolid optimization</td>
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<tr>
<td></td>
<td>Bedaquiline and pretomanid with existing and re-purposed anti-TB drugs for MDR-TB (TB PRACTECAL Phase 2/3 trial)</td>
<td>Bedaquiline with two optimised background regimens (oral, 9 months; with oral and injectables, 6 months) (STREAM trial)</td>
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<td>Delamanid, linezolid, levofloxacin, and pyrazinamide for quinolone sensitive MDR-TB (MDR-END trial)</td>
<td>Bedaquiline – Linezolid – Levofloxacin with OBR for MDR-TB (NExt trial)</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin with OBR for MDR-TB (OPTI-Q)</td>
<td>Bedaquiline and delamanid with various existing regimens for MDR-TB and XDR-TB (endTB trial)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pretomanid – Moxifloxacin – Pyrazinamide regimen (STAND trial)</td>
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<tr>
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<td></td>
<td>Rifapentine – Moxifloxacin for treatment of DS-TB (TB Trial Consortium Study 31/A5349)</td>
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TB active drug safety monitoring (aDSM)
PAVIA

Aim
To strengthen national PV systems in a collaborative effort with Public Health Programmes, including National TB Programmes (NTPs)

Objectives
In this context:
1. strengthen governance and financial capacity of PV systems in enforcing PV activities
2. improve the efficiency and effectiveness of national surveillance systems in capturing and processing reports
3. build PV capacity and skills to exercise safety-monitoring activities throughout the country
4. create an enabling environment to implement and sustain PV activities
PAVIA – Key outcomes

✓ Country-specific frameworks supported by guidance and documentation for implementation.

✓ Financial sustainability models for exploitation of PV activities.

✓ Overall strengthened PV surveillance system.

✓ In country trained and skilled cohorts of local PV personnel.

✓ Collaborative models of implementation adoptable to specific national environments.
PAVIA – Participating Institutions

- AIGHD
- LAREB
- KNCV
- IHVN
- NAFDAC
- University of Benin
- The Netherlands
- University of Verona
- Italy
- Nigeria
- Ethiopia
- Tanzania
- Swaziland
- Baylor
- MoH-S
- MoH

Involvement of NTPs through KNCV Country Offices
Project activities & deliverables

Key activities
1. Assessments
2. Triangle
3. Training & capacity building
4. System strengthening

Key deliverables
1. Country roadmaps
2. Blended-learning courses
3. Data tools
4. Policy frameworks
5. Blueprint (lessons learned)

Publicly available wherever possible
Assessments

Situational analysis at baseline and end-of-project in each project country
Using standard tools & indicators (including WHO indicators)
Identify the gaps and deficiencies in the PV system & improvements over the project lifetime

Components:
1. Policy, Law and Regulation
2. Systems Structure and Stakeholder Coordination
3. Signal Generation and Data Management
4. Risk Assessment and Evaluation
5. Risk Management and Communication
+ Public Health Programme and Healthcare Facilities
Utilisation of assessment results to define country roadmaps so as to highlight and further enable the countries to address country-specific issues

- Framework and strategies with a clear action plan to realise set objectives
- Builds on, or provides the basis for, a national strategic PV plan
- Draft discussed in country stakeholder workshop
- Actions can be taken up by PAVIA or by other projects or stakeholders

Country ownership is key!
PV activities for tuberculosis as the “building and training ground” for strengthening collaboration with Public Health Programmes

Expand to other disease area/Public Health Programme in second half of the project
Training & capacity building

Strengthen PV-relevant skills and competencies of PV staff and healthcare professionals:

1. Hands-on training of PV staff at national regulatory authority

2. Generic PV blended-learning course for general health care workers

3. TB-specific PV blended-learning course for health care workers treating (MDR) TB
Blended learning package

One-day face-to-face introduction
Baseline test

Individual e-learning

E-learning module on memory stick, interactive

One-day face-to-face finalization
Follow-up test
Certificate

Train-the-trainer approach
System strengthening

Strengthen functional regulatory and organizational structures

1. Define clear roles and responsibilities for stakeholders towards ensuring the safety of medicines, in particular for new PRD products
2. Develop models for financial sustainability
3. Implement tools and technologies for event detection, reporting, analysis and dissemination
4. Advocate for political good will from the government with a view to ensuring support for and good governance of the PV system
5. Obtain commitment from all levels of Government and other stakeholders to ensure a multistakeholder engagement towards realising set goals and objectives to promote PV
6. Sensitize and promote awareness of medicine safety issues in the psyche of Government and all other stakeholders
### Stakeholders and target groups (1)

<table>
<thead>
<tr>
<th><strong>Target audience</strong></th>
<th><strong>Collaborators and implementing institutions</strong></th>
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<tbody>
<tr>
<td></td>
<td>• Regulators such as National Drug Safety Advisory Committees</td>
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<tr>
<td></td>
<td>• PHP, Healthcare Executives and Managers (also private sector)</td>
</tr>
<tr>
<td></td>
<td>• International and local pharmaceutical industry; Marketing Authorisation Holders</td>
</tr>
<tr>
<td></td>
<td>• Universities, professional and regulatory bodies for education</td>
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<table>
<thead>
<tr>
<th><strong>Key messages</strong></th>
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</thead>
<tbody>
<tr>
<td>• provide safety information on newly introduced drugs</td>
</tr>
<tr>
<td>• engage stakeholders in PV activities</td>
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<table>
<thead>
<tr>
<th><strong>Clinical</strong></th>
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<tbody>
<tr>
<td>• Professional (clinical) associations</td>
</tr>
<tr>
<td>• Individual clinicians</td>
</tr>
<tr>
<td>• Community pharmacists and patent medicine dealers</td>
</tr>
<tr>
<td>• Traditional medicine practitioners</td>
</tr>
<tr>
<td>• Patient and consumer organisations/patient advocacy groups</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Key messages</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• create awareness about importance PV activities</td>
</tr>
<tr>
<td>• improve knowledge on detection and reporting</td>
</tr>
<tr>
<td>• inform about safety signals generated and policy decisions</td>
</tr>
</tbody>
</table>
### Stakeholders and target groups (2)

<table>
<thead>
<tr>
<th>Target audience</th>
<th>Key messages</th>
</tr>
</thead>
</table>
| **Policy and decision makers** | • inform about current situation (baseline assessment)  
• engage in PV activities (country specific roadmaps)  
• safety information to inform policy decisions  
• align initiatives |
| • Ministry of Health (departments and agencies) |  |
| • Development partners, NGOs, FBOs etc. |  |
| • Government –finance, education, commerce and industry |  |
| • Members of the National Legislature |  |
| • AMRH/AMA |  |
| • African regional economic communities (RECs) |  |
International alignment

Alignment with relevant global and regional initiatives

Utilize the linkage with the regional and global partners to leverage resources and technical capacities with all PV initiatives in SSA

Through representation of regional and global partners within the PAVIA Advisory Board

- World Health Organization
- Uppsala Monitoring Center (WHO CC)
- International Society of Pharmacovigilance
- African Medicines Regulatory Harmonization, NEPAD
- African Medicines Agency
- East African Community
- Southern Africa Development Community
Project timeline

COUNTRY LEVEL
- Country kick-off
- Roadmap workshop
- Midterm workshop
- Dissemination workshop

assessments triangle training system

PROJECT LEVEL
- Joint kick-off
- Annual meeting
- Annual meeting
- Annual meeting
- International dissemination workshop
PAVIA organization

Country (‘triangle’) teams in each of the 4 project countries supported by a country project coordinator
Who is Who

The PAVIA project is lead by the Amsterdam Institute for Global Health and Development where the project lead is based. A team of experienced researchers and project managers oversees all activities through Workpackage 1. The following people are part of PAVIA:

- Overall project lead: Famed Colkn
- Project manager: Caroline Fleur
- Assistant project manager: Hames Tumelo

A steering board was formed by several members from the African, Italian and Dutch institutions involved. These are:

- Workpackage 2 lead: Annet Margriet
- Workpackage 3 lead: Guido Merlo
- Workpackage 3 lead: Brigitte 3 Thomas

Other steering board members are:

- Pietro Baranzini
- Laszlo Nagy
- Charles Dikoko

Each of the four Sub-Saharan African countries has a national PV coordinator. These are:

- Yacuba Elia Mairi
- Ephraim Joa Kotekwu
- Alphonse Constant Ebuya
- Gueidi Njiwee

https://pavia-project.net/
Complementary projects

- Joint assessments and country plans in Ethiopia and Tanzania
- Joint annual meetings and trainings (2x)
- Joint publications
- Joint training activities, making use of each other’s training modules
- Joint Advisory Board recommendations
THANK YOU

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