Capacity Strengthening to Deliver a New Firstline Treatment for Kala Azar in Eastern Africa: The Leading Role of the LEAP Platform

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Presentation Outline

- Introduction: Neglected VL patients in Eastern Africa
- DNDi and the Idea of the Platform
- The LEAP Platform
- Responding to patient needs – the case of LEAP 0104
- LEAP Achievements & Challenges
- Conclusion
Bridging The R&D Gap: The Reality for Neglected Patients…

- Poorest of the poor
- Living in remote areas
- Socioeconomic burden on family and community
- Marginalized & voiceless patients
VL in Eastern Africa

- VL is a poverty-related disease
- In Africa primarily affects children (over 60%)
- If untreated, VL is fatal
- Population displacements have exacerbated the spread of the disease
- Field-relevant treatments are scarce

(Photo courtesy of Prof. A Hailu)
DNDi – The Idea of The Platforms

Started in 2003

1st DNDi Africa meeting

- 7-9 May 2003, Nairobi: 18 African countries, 71 participants
- Neglected, marginalized, forgotten, invisible diseases
- Consensus conclusion: more action, fewer words
- Desire to collaborate to solve many health crises plaguing Africa
- For diseases urgently needing improvement of treatments: VL, HAT
- DNDi officially created the LEAP Platform in August 2003 in Khartoum, Sudan
60 members. 4 countries. VL experts. Physicians with expertise to run clinical trials. Researchers. Health professionals. Representatives from drug registration authorities in disease endemic areas. NGOs.
LEAP collaborates with DNDi, MSF, IOWH – India, IDA, TDR and industry partners in Visceral Leishmaniasis (VL) R&D work in East Africa.

A group of scientists and institutions working on developing clinical trial capacity to bring new treatments to patients.

SUDAN: 3 sites (Kassab, Dooka, Um El Kher)
Univ. of Khartoum
Federal Ministry of Health

ETHIOPIA: 2 sites (Gondar, Arba Minch)
Addis Ababa Univ.
Gondar Univ.
DACA
Ministry of Health

UGANDA: 1 site (Amudat)
- Makerere Univ.
- Ministry of Health

KENYA: 2 sites (Nairobi, Kimalel)
KEMRI
Ministry of Health
LEAP Members
LEAP Objectives

- Evaluate, validate and register improved treatment options for VL in the Eastern African region (Ethiopia, Kenya, Sudan and Uganda)

- Provide capacity strengthening for treatment, evaluation and clinical studies in the region
Advantages of LEAP

LEAP at inception was envisaged to:

- Be a true example of South-South collaboration
- *Join efforts* with regional health and regulatory authorities, in addressing the high burden of disease through research and community engagement
- Give priority to address the *needs of patients*
- *Develop joint proposals*
- Seek *joint funding* for its activities
Advantages of LEAP Cont’d

Such collaboration allows LEAP to:

- **Strengthen existing capacities** for conducting trials in Eastern Africa
- **Eliminate duplication of effort** – time taken to get meaningful results minimized.
- **Accelerate registration** of much needed new VL drugs in all member countries
- To be a **trusted reference group** by the community and governments
- **Efficiently translate research results into policy**
Responding to patient needs – the case of LEAP 0104 clinical trial
A multi-centre comparative trial of efficacy and safety of sodium stibogluconate (SSG) versus paromomycin (PM) versus combination of SSG and PM as the first line treatment for visceral leishmaniasis in Ethiopia, Kenya and Sudan
1. Kassab Hospital, University of Khartoum, Sudan
2. Um el Kehr centre, MSF-Holland, Sudan
3. Gonder Hospital, Gonder University, Ethiopia
4. Arba Minch Hospital, Addis Ababa University, Ethiopia
5. Amudat Hospital, Makerere University, Uganda
6. Kimalel Hospital, KEMRI, Kenya
7. Centre for clinical Research, KEMRI, Nairobi
LEAP 0104: Objectives of the trial

- To assess the efficacy and safety of SSG 30 days alone in the treatment of patients with VL.
- To assess the efficacy and safety of PM 21 days alone in the treatment of patients with VL.
- To assess the efficacy and safety of SSG and PM as a combination course of 17 days in the treatment of patients with VL.
SSG&PM: Sodium Stibogluconate & Paromomycin

Results
## Analysis of SSG&PM: Efficacy outcomes

<table>
<thead>
<tr>
<th></th>
<th>ITT</th>
<th>PP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SSG (N = 359)</td>
<td>Combination (N = 359)</td>
</tr>
<tr>
<td>Efficacy at 6 months follow-up, n (%)</td>
<td>337 (93.9)</td>
<td>328 (91.4)</td>
</tr>
<tr>
<td>Unadjusted difference between SSG and Combination (95% CI)</td>
<td>2.51% (-1.31 to 6.33%)</td>
<td>2.76% (-1.07 to 6.60%)</td>
</tr>
<tr>
<td>Test of difference between treatment efficacy: p value*</td>
<td>0.198</td>
<td>0.157</td>
</tr>
<tr>
<td>Test of difference across centres, after adjustment for treatment: p value*</td>
<td>0.337</td>
<td>0.286</td>
</tr>
<tr>
<td>Test of difference between adults and children after adjustment for treatment: p Value*</td>
<td>0.122</td>
<td>0.080</td>
</tr>
</tbody>
</table>

- Reasons for exclusions from PP analysis include: Low HB, Low WCC, incorrect treatment given, expired medication given

*p-value from likelihood ratio test, comparing models with and without variable being tested
Achievements

Clinical Trials

- **SSG+PM; a new improved combination treatment** for VL

- **Completion of LEAP 0104A & B** SSG+PM multi-centre clinical trial; including PK for SSG & PM

- **Single high dose of AmBisome** for the treatment of primary VL (AmBi 0106); including PK/PD for AmBisome
Clinical Trials

- AmBisome combination trial in Eastern Africa (LEAP 0208 SSG+PM, SSG+AmB, MILT+AmB Including PK/PD)
- Study of rapid diagnostic tests
- SSG +PM (combo) PV study completed
- Safety and efficacy of Fexinidazole Phase II for primary VL, ongoing in Sudan
Achievements Cont’d

- **Capacity Strengthening**
  - *Research capacity strengthening* in Ethiopia, Kenya, Sudan and Uganda in the following domains: *(Clinical trials, Communications, Infrastructure)*
Achievements Cont’d

- Capacity Strengthening

- *Training across the LEAP* (Short-term and post graduate)
## Trainings: Short-term

<table>
<thead>
<tr>
<th>Training</th>
<th>No. of Participants</th>
</tr>
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<tbody>
<tr>
<td>Good Clinical Practice (GCP)</td>
<td>354</td>
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<tr>
<td>Pharmacovigilance (PV) Training</td>
<td>104</td>
</tr>
<tr>
<td>PPD GCP/GCLP</td>
<td>95</td>
</tr>
<tr>
<td>Audiometry</td>
<td>26</td>
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<tr>
<td>VL Guideline (Kenya)</td>
<td>55</td>
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<tr>
<td>Urine LEISH Antigen Elisa standardization training</td>
<td>15</td>
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<tr>
<td>Lab Safety &amp; Refresher Parasitology Course</td>
<td>14</td>
</tr>
<tr>
<td>From Molecule to Medicine</td>
<td>4</td>
</tr>
<tr>
<td>Human Subjects Protection (HSP/GCP) TOT Programme</td>
<td>5</td>
</tr>
<tr>
<td>Clinical Monitors course – “Back to Basics”</td>
<td>2</td>
</tr>
<tr>
<td>DSMB &amp; Monitor’s training</td>
<td>30</td>
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</tbody>
</table>
## Trainings: Post Graduate

<table>
<thead>
<tr>
<th>Training</th>
<th>No. of Participants</th>
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</thead>
<tbody>
<tr>
<td>Diploma in Medicine</td>
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</tr>
<tr>
<td>Bachelors (Lab, Nursing, Pharmacy)</td>
<td>10</td>
</tr>
<tr>
<td>MSc</td>
<td>12</td>
</tr>
<tr>
<td>MPH</td>
<td>1</td>
</tr>
<tr>
<td>PhD</td>
<td>2</td>
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South-South & North-South Collaboration

- Bringing together research institutions, academia, MoH and NGO’s (Key players)
- Influencing policy at both national and international levels
Achievements Cont’d

- **Data Center**
  - Developed off-line OpenClinica
  - Facilitate DM for multiple clinical trial

- **Community Benefit**
  - Over 7,000 VL patients treated
  - Increased awareness in the *community*, improved access reduction in *morbidity*, early *reporting* to health facilities

- **Financial**
  - Implementation of Good Financial Practice (GFP)
Achievements Cont’d

PUBLICATIONS


- **Stibogluconate (SSG) & Paromomycin Combination Compared to SSG for Visceral Leishmaniasis in East Africa: A Randomised Controlled Trial**, Ahmed Musa, Eltahir Khalil et al., *PLoS NTDs*, 6(6): e1674, June 2012


Policy Change
Kenya’s VL guidelines launched September 2012

Uganda VL guidelines
LEAP: Advocacy
Events

Promised support for our activities by committing funding for NTDs in the 2014/2015 Health Budget

Prof. Fred Segor, PS Health, Kenya
Challenges
Challenge to Conduct Clinical Trials in Very Difficult Settings

- Access to Sites
- Status of Infrastructure
- Staff Limitations

Dr. Jannin, WHO
Conclusion

- Treatment for VL not yet optimal. Need more research
- Patient needs of efficacious, safe oral drug for VL is still unmet
- LEAP Platform’s 10 years have been a success. The next 10 years will be even greater delivering oral treatment to neglected patients

- **South-South, South-North** collaboration is possible
- **Equal partnerships** is key to success
- VL disease endemic areas in Africa can pull **resources, infrastructure, expertise** for the benefit of the neglected communities
- Clinical Research at **international standards** is possible in remote disease endemic areas in Africa
- **Early involvement of MOH** in clinical trials leads to faster policy change.
Thank You to All Our Partners & Donors

www.dndi.org
THANK YOU! ASANTE SANA

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