



Leishmaniasis East African Platform (LEAP): Preparing the field for implementation

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Chair, LEAP



Presentation outline

- Introduction to VL in East Africa
 - Patients' burden
 - current treatments and delivery challenges
- Research activities of LEAP
 - ongoing
 - planned
- How will we get these treatments to patients?
 - Preparedness for registration





VL in East Africa

- Sudan
 - estimated annual incidence: 15 000 – 20 000 cases
 - PKDL occurs in up to 50% of VL patients
- Ethiopia
 - estimated annual incidence: 4 000 cases
 - VL is prevalent mostly in arid lowland areas
 - up to 40% of cases reported in Ethiopia are HIV co-infected
- Kenya
 - estimated annual incidence of 4 000 cases
- Uganda
 - up to 200 cases

Impact of VL in East Africa

- Mainly disease of children (over 60%)
- Malnutrition is common
- Prevalent among the poor
- Population mortality of VL can be up to 36%
- Low economic and agricultural activity



(Photo courtesy of Prof. A Hailu)



Determining Regional Needs - Leishmaniasis

- Current treatment options in use in the East Africa are far from satisfactory.
- Either toxic (antimonials) or expensive (AmBisome).
- The risk of emerging resistance is there.

Rationale for the objective of LEAP: Evaluate, validate and register improved treatment options for VL in East African region

The story begins...

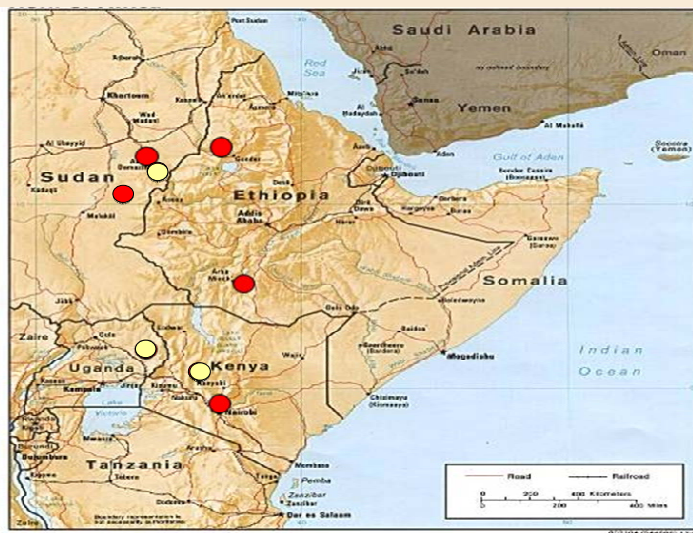


Main challenges

- Poor infrastructure
- Different regulatory environments
- Importation of trial equipment and drugs

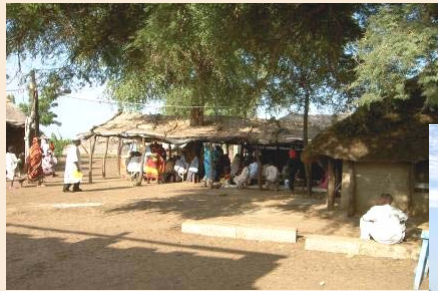


LEAP 0104 study sites





MSF – Um el Kher, Sudan



(Photo courtesy of Dr M Balasegaram)



(Photo courtesy of Dr C Royce)

Kassab Hospital, Sudan



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(Photo courtesy of Dr Musa)



LEAP 0104 clinical trial design

- A randomised, open-label, multicentre, comparative Phase III trial of efficacy and safety of:
 - sodium stibogluconate (SSG)
 - paromomycin (PM)
 - combination of SSG and PM
- Sample size: 705, 90% power, between treatment difference of no more than 10%
- Countries:
 - recruiting: Ethiopia, Kenya, Sudan

Treatment regimens

- SSG 20mg/kg/day for 30 days iv/im
- PM 15mg/kg/day for 21 days im
- Combination
 - SSG 20mg/kg/day for 17 days iv/im
 - PM 15mg/kg/day for 17 days im

**PM dose was selected based on
the dose used in the Indian trial**



Summary

- Trial feasible in a rural setting
- Comparatively few safety concerns
- Efficacy of PM (15 mg/kg/d at 21 d) inadequate in Eastern Sudan

Dose-ranging study

- Two-armed sub-study in Sudan
- Increased the PM dosage by 33%:
 - 15 mg/kg/d for 28 days (n=21).
 - 20 mg/kg/d for 21 days (n=21).
- Pharmacokinetics (PK) was performed on a subset of patients.
- Other LEAP sites continued recruitment.

Actions:

- **0104B: 20 mg/kg/d for 21 days into the original trial.**



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LEISHMANIASIS RESEARCH & TREATMENT CENTRE

Arba Minch, Ethiopia



DNDi

Drugs for Neglected Diseases initiative

(Photo courtesy of Dr C Royce)

LEAP

Leishmaniasis Endemic Areas Programme

Kassab, Sudan



DNDi

Drugs for Neglected Diseases initiative

LEAP

Leishmaniasis Endemic Areas Programme



Amudat, Uganda



Kimalel, Kenya





Moving forward...

- Complete ongoing LEAP 0104B study in 2009
 - recruiting: Ethiopia, Kenya, Sudan, Uganda
- Open-Label, Sequential Step, Safety and Efficacy Study to Determine the Optimal Single Dose of AmBisome® for VL
 - just started in Ethiopia and ready to start in Sudan

Planned DNDi / LEAP studies in Africa

“A Phase II, randomized, 3-arm parallel group, open-labeled clinical trial to assess the safety and efficacy of the combination of:

- SSG plus single dose AmBisome®
- Miltefosine plus single dose AmBisome®
- Miltefosine alone.

For the treatment of VL in Eastern Africa



Registration of new treatments

- Beyond doubt, there is an utmost need for new better treatments
- Regulatory authorities were involved from the beginning
- They are:
 - members of the LEAP
 - facilitate importation of trials medications and equipments
 - identifying new treatments is becoming part of the mandate of MoH

**Registration of much needed, newer VL drugs
in all member countries will be feasible**

Acknowledgements

- Patients and communities
- Research teams
- LEAP members
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- Donors