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

Dr Ahmed Mudawi Musa
Institute of Endemic Diseases,
University of Khartoum

Chair, LEAP

DNDi
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

DNDi
LEAP

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

DNDi
LEAP

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)

DNDi
LEAP

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

DNDi LEAP

The story begins…

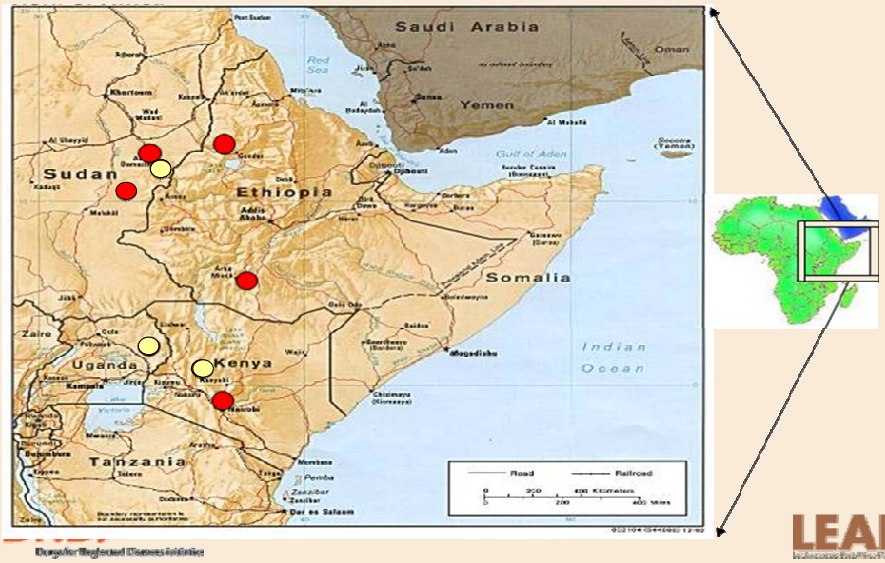
DNDi LEAP

Main challenges

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

DNDi
LEAP

LEAP 0104 study sites



DNDi
LEAP

MSF – Um el Kher, Sudan

(Photo courtesy of Dr M Balasegaram)

(Photo courtesy of Dr C Royce)

DNDi
Drugs for Neglected Diseases initiative

LEAP

Kassab Hospital, Sudan

(Photo courtesy of Dr Musa)

DNDi
Drugs for Neglected Diseases initiative

LEAP

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

DNDi LEAP

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

DNDi LEAP

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

DNDi
LEAP

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.**

DNDi
LEAP

Arba Minch, Ethiopia

(Photo courtesy of Dr C Royce)

Kassab, Sudan

Amudat, Uganda

DNDi
LEAP

Kimalel, Kenya

DNDi
LEAP

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

DNDi LEAP

Planned DND*i* / 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

DNDi LEAP

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

DNDi
LEAP

Acknowledgements

- Patients and communities
- Research teams
- LEAP members
- Ministries of Health, regulatory authorities, cooperating institutes
- Donors

DNDi
LEAP