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

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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

(Photograph 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)

Kassab Hospital, Sudan

(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.
Arba Minch, Ethiopia

Kassab, Sudan
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

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