Cohort observational study to estimate the prevalence of post-kala-azar dermal Leishmaniasis (PKDL) in visceral leishmaniasis (VL) patients treated with three regimens in Bihar

Presented by:

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Background and Rationale

Objectives:

- Safety and effectiveness of new treatment modalities at field level in India (2012-2015)
- Provide evidence based recommendations for policy makers

- By MoH staff
- Training: GCP
- PHCs Upgraded
- IEC team: ASHA

Assessment at 6 and 12 months

Final Cure ITT at 6 months follow-up

<table>
<thead>
<tr>
<th>Number of patients started on treatment (n=1761)</th>
<th>SD AmB</th>
<th>AmB+MF</th>
<th>MF + PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>891</td>
<td>358</td>
<td>512</td>
<td></td>
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</tbody>
</table>

| Cure at 06 Month n (%)                         | 813 (91.3%) (CI-89.2 - 93.0) | 318 (88.8 %) (CI-85.1-91.9) | 496 (96.9 %) (CI-95.0-98.2) |

PROJECT DESIGN

<table>
<thead>
<tr>
<th>PHC</th>
<th>District Hospital/ Referral centre</th>
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<tbody>
<tr>
<td>9 PHCs in 2 districts in Bihar i.e Vaishali, Saran</td>
<td>RMRIMS, District Hospital</td>
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<tr>
<td>4 PHC</td>
<td>5 PHC</td>
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<tr>
<td>Milt + PM for 10 d</td>
<td>AmB (5mg/kg) + Milt for 7d</td>
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<tr>
<td>Referral Centres (special cases)</td>
<td></td>
</tr>
<tr>
<td>SDA (10mg/kg)</td>
<td></td>
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<tr>
<td>Other VL treatments if SDA contraindicated or unavailable</td>
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Indian National Program recommended to provide evidence to policy makers of the occurrence of Post-Kala-Azar Dermal Leishmaniasis (PKDL) in this large cohort
Study Objectives

Primary Objective:
- To determine the prevalence rate of post-kala-azar dermal leishmaniasis (PKDL) during or more than 24 months post treatment in kala-azar treated cases for the treatment of primary VL with any of the three treatment regimens: single dose AmBisome®, combination of miltefosine and paromomycin for 10 days, combination of AmBisome® and miltefosine for 8 days.

Secondary Objective:
- To determine the average time of occurrence of PKDL after each treatment
- To compare occurrence of PKDL in different treatment arms

All VL cases (n=1,761) treated between Aug 2012 and Oct 2014 in 2 districts (Vaishali and Saran) of Bihar and at RMRI in the pilot implementation study with any one of new treatment regimens were followed up:
  i) Single dose AmBisome® (n=891)
  ii) Miltefosine and paromomycin combination for 10 days (n=512)
  iii) AmBisome® and miltefosine combination for 8 days (n=358)
Rationale

• Burden
  – Little information on natural history of PKDL
  – PKDL cases present after VL treatment (Interval between VL and PKDL is long - median 2 years)

• Morbidity
  – PKDL typically without any physical impairment
  – PKDL thought not to be self healing

• Reservoir
  – PKDL patients may play important role in transmission of VL
  – Public Health concern
Appearance of macules, papules, nodules, macular hypopigmentation AND

Lived in or travelled to VL endemic area AND/OR Past History of VL Treatment

Suspected PKDL

rK39 test AND Dermatological exam
Positive test No loss of skin sensation

Probable PKDL

If loss of skin sensation: Investigate leprosy

Treatment: all PKDL cases (elimination context)
Regimen to be used as per National Program Guidelines

Confirmed PKDL

Referral Hospital RMRI

Skin slit smear (microscopy) and qPCR

Positive

Clinical opinion by expert for differential diagnosis

Negative
<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Suspected PKDL n (%) 95% CI</th>
<th>Probable PKDL n (%) 95% CI</th>
<th>Confirmed PKDL n (%) 95% CI</th>
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<tr>
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<tr>
<td>SDA (n=611)</td>
<td>25 (4.1%) (2.7%, 6.0%)</td>
<td>22 (3.6%) (2.3%, 5.4%)</td>
<td>13 (2.1%) (1.1%, 3.6%)</td>
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<tr>
<td>A+M (n=220)</td>
<td>12 (5.5%) (2.9%, 9.3%)</td>
<td>11 (5%) (2.5%, 8.8%)</td>
<td>05 (2.3%) (0.07%, 5.2%)</td>
</tr>
<tr>
<td>M+P (n=439)</td>
<td>39 (8.9%) (6.4%, 11.9%)</td>
<td>32 (7.3%) (5%, 10.1%)</td>
<td>28 (6.4%) (4.3%, 9.1%)</td>
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<td>Total</td>
<td>76</td>
<td>65</td>
<td>46</td>
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Conclusions and Recommendations

• Preliminary results show that PKDL was observed in 3.6% of patients at least 24 months after treatment of VL

• Measuring the burden of PKDL, the rates according to the drug used in the VL episode, mapping cases, and getting them treated is important for the control of VL, especially given the VL elimination program target of 2017 in the Indian subcontinent.
Acknowledgement and Funders

• State Health Society Bihar
• Rajendra Memorial Institute of Medical Sciences
• National Vector Borne Disease Control Programme
• All Government Doctors, staff involved in study
• Patients

• This work was conducted with the support of Bill & Melinda Gates Foundation, USA; Department for International Development (DFID), UK; Dutch Ministry of Foreign Affairs (DGIS), The Netherlands; Médecins Sans Frontières
Thank you