Twelve months outcome in kala-azar patients treated with 3 novel regimens, at public health care facilities in Bihar

Provide **evidence based recommendations** for policy makers

ICID 5th March 2016 Vishal Goyal

DNDi
Drugs for Neglected Diseases *initiative*

Introduction

New treatment regimens developed in the last few years from already existing drugs for VL, specifically - AmBisome®, paromomycin and miltefosine

These new treatment modalities have now been recommended by WHO Expert Committee on the control of leishmaniasis (March 2010) and RTAG (WHO SEARO)

There was need to generate data to make evidence-based recommendations for replacing miltefosine monotherapy with AmBisome and combination therapies in the National Kala-azar Elimination Program

Rationale:

Reducing the duration of therapy will improve compliance, reduce side effects and also prevent the emergence of resistant parasites and thus increase the duration of effectiveness of available drugs.

Objectives

- Determine **effectiveness (including 12 month outcome) and safety profile of 3 new treatment regimens under real field conditions**

- Provide **evidence based recommendations** for policy makers

Pilot Implementation Study - India

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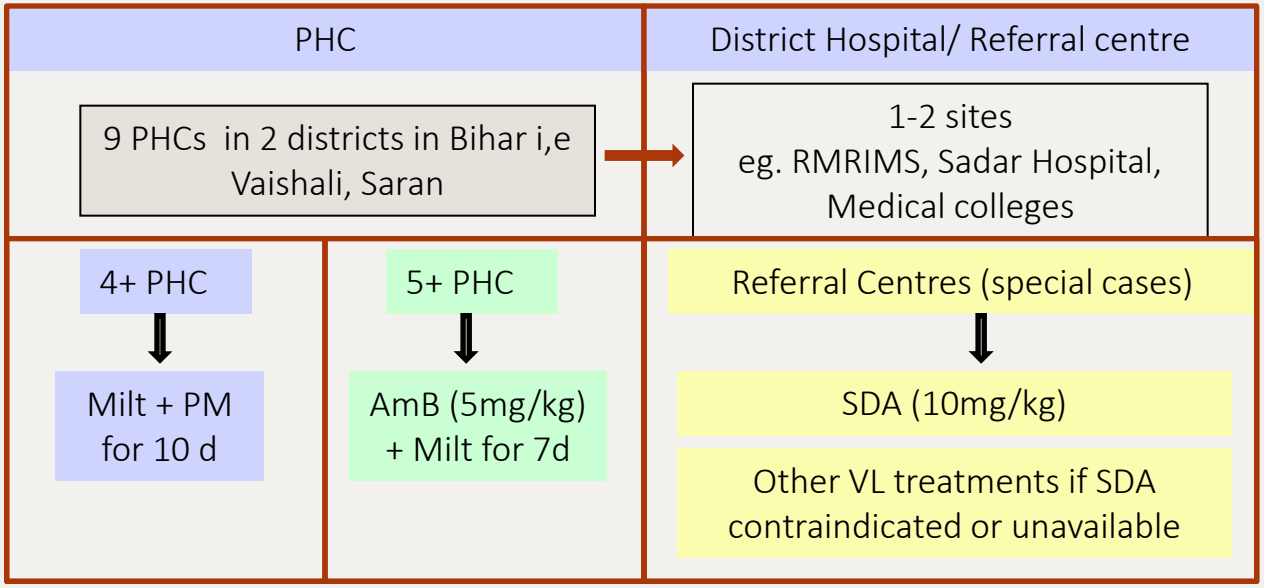
study in p
Regimens: S g
Milt (2.5mg
AmB (5mg/

- Treatment by Government doctors/staff except Hajipur
- Training: GCP + KA case management
- Upgradation of health centers e.g lab, ILR, drugs, diagnostic kits
- IEC team: training of ASHA

PROJECT DESIGN

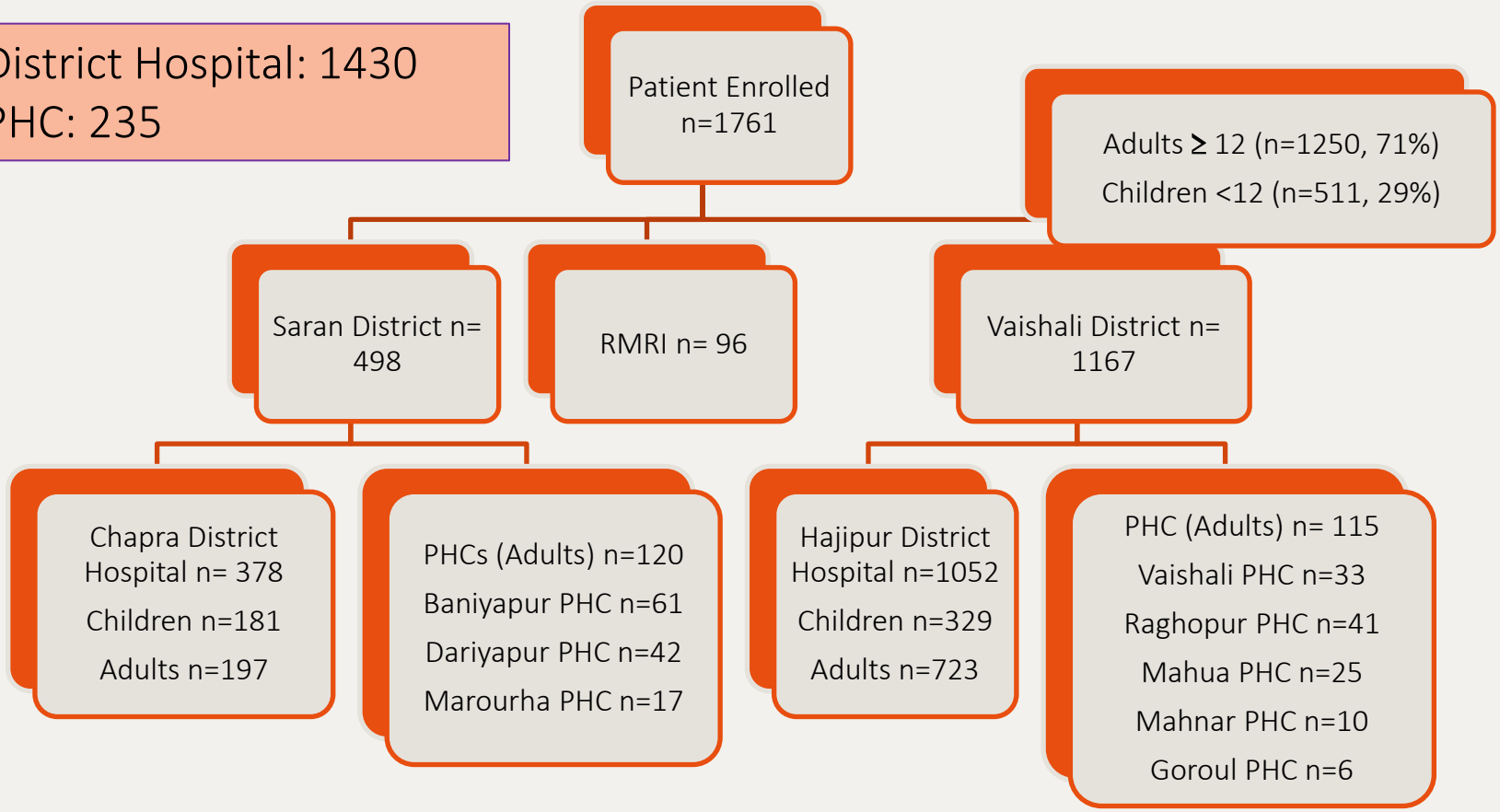


Ethical clearance:
RMRIEC, MSF-ERB, LSHTM

Assessment at 6 months and 12 months

Enrolment (n=1761)
Study Duration Aug 2012-Sep 2015

District Hospital: 1430
PHC: 235



Results – Initial Outcome (n = 1761)

	SD AmB	AmB+MF	MF + PM
Number of patients started on treatment (n=1761)	891	358	512
Initial cure at day 10 (%) (95% CI)	884 (99.2%) (95%CI-98.6-99.8)	354 (99.0%) (CI-98.3 – 100.0)	508 (99.2 %) (CI-98.4- 99.9)

Results- Final Outcome (Worst Case Analysis)

	SD AmB	AmB+MF	MF + PM
Number of patients followed up at 6 mnth(n=1761)	891	358	512
Cure at 6 month Relapse rate (n=64) Defaulter Lost to Follow Up (n=66) Treatment stopped by doctor for side effects	810 (90.9%) (95%CI-89.0-92.8) 43 (4.8%) 0 34 4	314 (88.0%) (95%CI-85.5-92.1) 19 (5.3%) 1 22 2	496 (97.0%) (95%CI-95.6-98.5) 2 (0.4%) 4 10 0
Number of patients followed up at 12 months (n=1457)	755	314	388
Relapse Rate (n =11) PKDL(n=15) Lost To Follow Up (n= 96)	2 (0.3%) 02 (0.2%) 50	6 (2%) 01(0.3%) 21	3 (0.8%) 12 (3.0%) 25

Adverse Events

	SD AmB N=891	LAmB + MF N=358	MF + PM N=512
Total Adverse Events Reported	174 (19.5%)	137 (38.4%)	123 (24%)
No. of subjects with at least one AE n(%)	133 (14.9%)	90 (25.2%)	92 (18%)
Drug Related Serious Adverse Events n(%)	2* (0.5)	0 (0)	0 (0)
Non-Drug Related Serious Adverse Events n(%)	3** (0.7)	0 (0)	0 (0)

AE captured during start of treatment to EOT
All SAE resolved

Limitations of Study

- Children **not** treated at Primary Health Centre level and treated at District Hospital only as per regulatory recommendation
- Patients admitted and provided treatment at Saran District Hospital for MF/PM
- Patients referred from PHC/Saran District Hospital to higher centre for parasitology
- Biochemistry tests done only at District Hospital

Conclusion and Recommendations

- Combination regimens and SDA are safe and effective treatment in public health sector at field level and feasible to implement at large scale to facilitate VL elimination
- Indian National program revised policy in Sep 2014
  - Single Dose Ambisome as first option
  - MF/PM Combination as second option
- Combination regimen to be choice of treatment at sites where cold chain cannot be deployed
- Relapses continue to occur after 6 month post treatment, need to Follow up patients for 12 month within national program in region to generate further evidence on relapse
- Cohort Event Monitoring should be strengthened at all sites in India to document long term outcome data and adverse drug reaction to identify relapse, PKDL, treatment failure, ADRs

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- National Vector Borne Disease Control Programme
- All Government Doctors, staff involved in study

State Health Society Bihar

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NVBDCP


Thank you
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