Lessons learnt from **Kaladrug**-R: **New tools** for monitoring drug resistance and treatment response in Visceral Leishmaniasis in the Indian subcontinent

Bart Ostyn, Manu Vanaerschot, Syamal Roy, Poonam Salotra, Chris Carter, Matt Berriman, Martin Eichner, Louis Maes, Gabi Schoenian, Suman Rijal, Shyam Sundar, Marleen Boelaert, Jean-Claude Dujardin.

Abstract

Background: Kaladrug-R project

We present the most relevant findings of four years (2009-2012) of clinical-epidemiological and parasitological research on treatment response and drug resistance in previously treated and new cases of VL in India (Muzaffarpur district, Bihar) and Nepal (Terai region).

Miltefosine (MIL):

- Up to 20% MIL-relapse observed when patients are followed up for 12 months, early treatment failure of MIL is not observed.
- Relapse is not due to re-infection, low-drug quality or under-exposure to the drug.
- Age and gender were risk factors for MIL-relapse.
- Although MIL-resistance is inducible in vitro, true MIL-R strains have as yet not been identified in clinical samples.
- An association between parasite infectivity and MIL-treatment outcome of the patient was observed.

Paromomycin (PMM) and pentavalent antimonials (SSG):

- PMM-R is easily induced in vitro, vigilance is required when implemented in clinical practice
- SSG-R strains, which are still present in the Indian subcontinent, more efficiently manipulate the host's immune system, causing higher parasite burdens: what is their legacy for the efficacy of other treatments?

VL-epidemiology

- *L. donovani* population in the Indian subcontinent is fairly homogeneous, but highly divergent strains circulate in the hilly regions of Nepal.
- Asymptomatics significantly outnumber clinical cases. Mathematical modeling shows that if these are able to transmit parasites to sandflies, this reservoir can be most efficiently tackled through adequate vector control.

VL-control take home messages

- Importance of late treatment outcome monitoring, up to 12 months after treatment.
- Tools for VL-treatment outcome monitoring at primary health care level available.
- Importance of vector control