Challenges and opportunities for the development of new treatments for leishmaniasis

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There are significant differences in the progress and approaches to drug development for visceral leishmaniasis (VL) and cutaneous leishmaniasis (CL). VL, caused by *L. donovani* and *L. infantum*, is potentially fatal and is the primary focus for drug R & D. The need for new drugs is urgent as the standard pentavalent antimonials are now almost obsolete in the key endemic area in Bihar state, India due to resistance. A number of amphotericin B lipid formulations have proved effective in the treatment VL, although only the liposomal formulation, AmBisome®, has become a standard treatment and demonstrated efficacy in single dose treatment and in combination therapy. Major challenges remain for VL treatment due to regional differences in response rates, and co-infections with HIV. Despite extensive screening and evaluation projects, few safe, oral, short course, cheap drugs are close to clinical development.

There are limited treatment options for CL. One problem is the variation in drug effectiveness across the different *Leishmania* species that cause CL. Two recent Cochrane analyses of clinical trials of CL emphasized that most clinical studies did not meet standards of randomized placebo controlled trials. One promising approach has been the development of topical formulations, so far most successful for paromomycin. Another approach to CL treatment is to accelerate self-cure through the use of immunomodulators as adjunct therapies, for example, imiquimod.

All attempts to discover and develop novel drugs for neglected infectious diseases depend on a network of partnerships, upon involvement of PDPs and the pharmaceutical industry and the involvement of key players in disease endemic countries. The issues of changing patterns of funding and involvement of different sectors all play a part in bringing new treatments to patients.