Efficacy of Miltefosine in the treatment of visceral leishmaniasis in the Indian sub-continent: the current status.

Jean-Claude Dujardin[1], Poonam Salotra[2], Syamal Roy[3], Manu Vanaerschot[1], Bart Ostyn[1], Marleen Boelaert[1], Shyam Sundar[4], Suman Rijal[5]

[1]Institute of Tropical Medicine, Antwerp, Belgium; [2]ICMR, New Delhi, India; [3]CSIR, Kolkata, India; [4]BHU, Varanasi, India; [5]BPKIHS, Dharan, Nepal

Miltefosine (MIL) is the only oral drug available for treatment of Visceral Leishmaniasis (VL) which has shown to be safe and effective. Its unrestricted use has raised concern about its continued efficacy. In the context of a large multidisciplinary study, we recruited and followed two cohorts of VL patients in the Indian subcontinent and found a significant decrease in efficacy of the drug in comparison to earlier reported phase IV studies. In India and Nepal, relapse rates were 7.24 % (6-months follow-up) and 21.8 % (12-months follow-up) respectively. DNA fingerprinting of parasites from relapsing patients demonstrated identical patterns as those obtained at the onset of treatment, excluding the occurrence of re-infections. The MIL-susceptibility of clinical isolates was analyzed *in vitro* using promastigote and amastigote assays and did not show so far any clear-cut MIL-resistance in isolates from relapsing patients. However, isolates with a higher tolerance to the drug were observed in some patients. The latter isolates show residual parasites in the spleen upon MIL treatment in infected hamsters, which was not the case with parasites showing low EC50 values. Data on the virulence of the corresponding parasites will also be presented.