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Visceral Leishmaniasis / HIV co-infection: Current challenges and perspectives Experience from the Field

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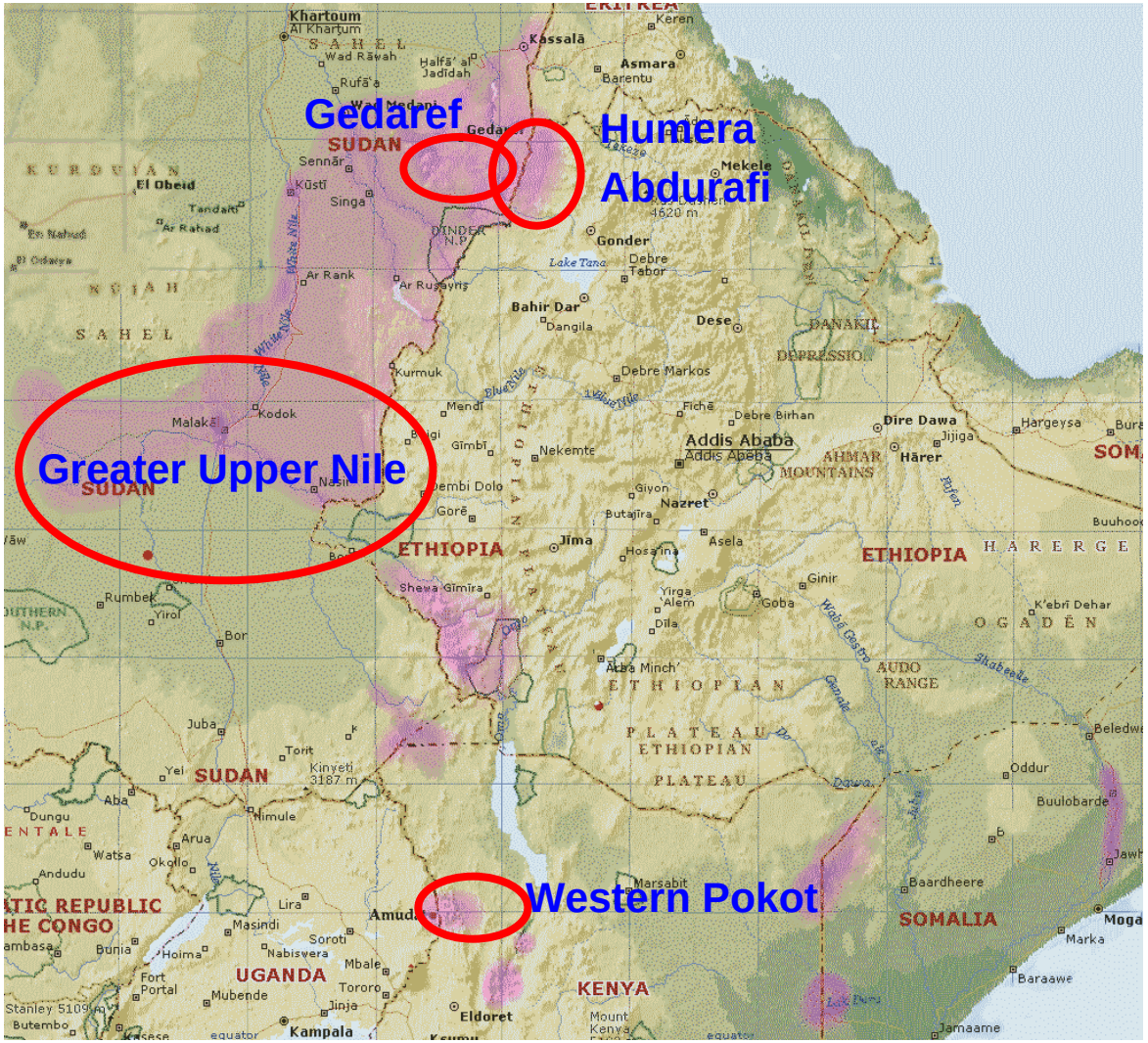
VL endemic areas in East Africa
HIV/VL rates in MSF treatment sites



HIV coinfection rates in primary VL

Ethiopia 12% <15 yrs
Humera: 35.2%
Abdurafi; 20.5%

Sudan 62-71% <15 yrs
Gedaref: 1.8%
Gr.Upper Nile: 1.7%

Kenya: 63% <15 yrs
West Pokot: 0.5%

Pentavalent Antimonials (SSG) and HIV
Randomised clinical trial, Ethiopia

Mainstay of VL treatment in east Africa:

sodium stibogluconate (SSG):

20 mg/kg/day x 30 days IM

	HIV neg (n = 112)	**HIV pos** (n = 27)
Initial Cure	96.4%	63.0%
Mortality during treatment	3.6%	33.3%
Final Cure Rate (6m follow-up)	92.1%	43.5%

Ritmeijer et al. *Trans R Soc Trop Med Hyg* 2001

Miltefosine and HIV

Miltefosine vs. SSG randomised clinical trial, Ethiopia

Miltefosine: 100 mg/day PO x 28 days

Outcome	HIV neg (n = 131)	HIV pos (n = 63)	SSG in HIV-positive
Initial Cure	93.8%	77.8%	81.0%
Failure	4.5%	17.5%	0.7%
Death	0.8%	1.6%	15.7%

Ritmeijer et al. *Clin Inf Dis* 2006

AmBisome and HIV/VL
Retrospective evaluation, Ethiopia, 2007-2009

Liposomal amphotericin-B
Non-toxic

Introduced in Ethiopia Oct 2006

Eligible:

- HIV co-infected primary VL
- Severely ill VL
- VL Relapses

Regimen:

- High dose: 30 mg/kg total dose,
- 5mg/kg x 6 IV doses on alternate days
- Test-of-cure (splenic aspirate) on day 28

Ritmeijer et al. *Clin Inf Dis* 2011 *(in press)*

Baseline Characteristics of VL Patients treated with AmBisome monotherapy

	HIV Negative (n = 94)		**HIV Positive** (n = 195)	
	Median	*Range*	Median	*Range*
Age (y)	24	*1.5 – 67*	30	*10 – 56*
Spleen size (cm)	8	*0 – 20*	8	*0 – 20*
Hb (g/dL)	5.7	*2.1 – 14.5*	7.6	*2.5 – 13.1*
BMI (kg/m^2)	16.2	*11.0 – 22.2*	15.9	*10.8 – 25.5*
CD4 count (cells/μL)			116 *	*15 – 576*
	%	*#*	%	*#*
Sex (male)	88.3%	*83*	91.8%	*179*
TB coinfection	7.4%	*7*	29.7%	*58*
VL relapse	10.6%	*10*	40.5%	*79*

** N = 43*

Initial treatment outcome AmBisome mono-therapy according to HIV status

	HIV negative Severe VL (n = 94)		HIV positive (n = 195)		
	#	*%*	#	*%*	*P* value
Initial Cure	87	*92.6*	116	*59.6*	<.001
Death	6	*6.4*	13	*6.7*	.87
Parasitological Failure	0	*0.0*	63	*32.3*	.001
Defaulter / Transfer	1	*1.1*	3	*1.5*	1.00

Initial outcome AmBisome mono-therapy in 195 HIV-Positive VL patients

	Primary VL (n = 116)		**Relapse VL** (n = 79)		
	#	*%*	#	*%*	*P* value
Initial Cure	86	*74.1*	30	*38.0*	<.001
Death	9	*7.8*	4	*5.1*	.67
Parasitological Failure	19	*16.4*	44	*55.7*	<.001
Defaulter / Transfer	2	*1.7*	1	*1.3*	1.00

Rescue treatment with SSG of initial AmBisome failures

- 58 AmBisome failures received rescue treatment with SSG
- SSG regimen: 20mg/kg IM x 30 days
- Initial cure rate 71% (41/58)
- Mortality during treatment: 16% (9/58)

Preceding AmBisome treatment and management of complications does not improve SSG tolerability

AmBisome + Miltefosine combination in HIV/VL

Retrospective evaluation, Ethiopia, 2010-2011

AmBisome 5mg/kg IV x 6 doses (30mg/kg total dose)
+ Miltefosine 100mg PO x 28 days

HIV Positive	**AmBisome + Miltefosine** (n = 35)		**AmBisome monotherapy** (n = 195)		
	#	*%*	#	*%*	*P* value
Initial Cure	29	*82.9*	116	*59.6*	.014
Death	2	*5.7*	13	*6.7*	1.00
Parasitological Failure	3	*8.6*	63	*32.3*	.008
Defaulter / Transfer	1	*2.9*	3	*1.5*	0.49

Initial outcome AmBisome + Miltefosine combination in 14 Relapse HIV/VL

AmBisome 5mg/kg IV x 6 doses (30mg/kg total dose)
+ Miltefosine 100mg PO x 28 days

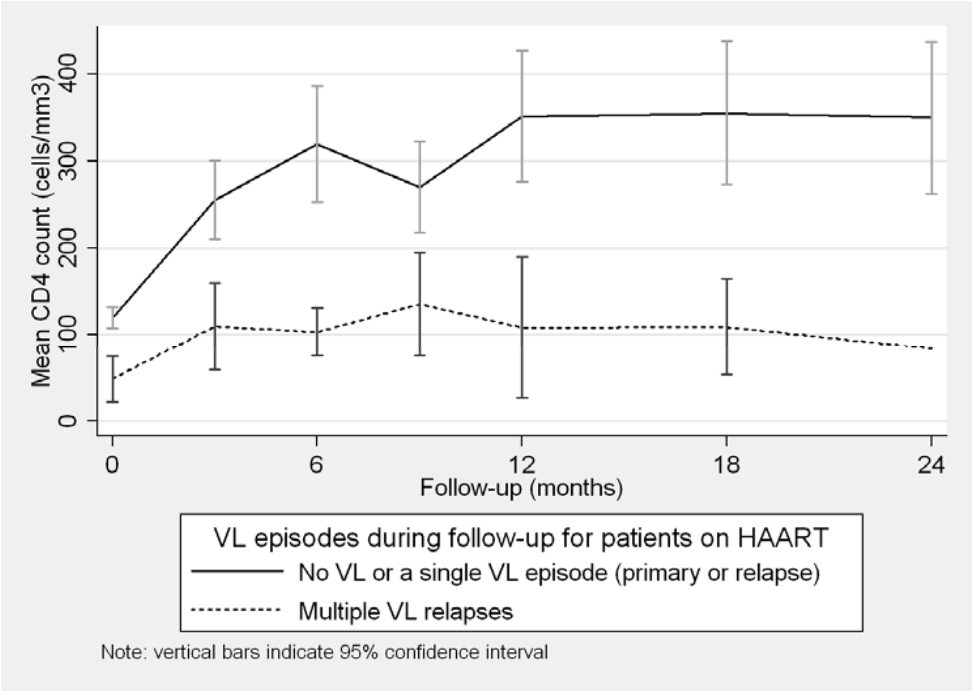
HIV Positive relapse	**AmBisome + Miltefosine** (n = 14)		**AmBisome monotherapy** (n = 79)		
	#	*%*	#	*%*	*P* value
Initial Cure	12	*85.7*	30	*38.0*	.003
Death	1	*7.1*	4	*5.1*	.6
Parasitological Failure	1	*7.1*	44	*55.7*	.002
Defaulter / Transfer	0	*0.0*	1	*1.3*	1.00

Impact of ART on HIV/VL treatment outcome

Retrospective study of 356 HIV/VL co-infected Ethiopian patients , including 600 episodes of VL *(Ter Horst et al. Clin Inf Dis, 2008)*

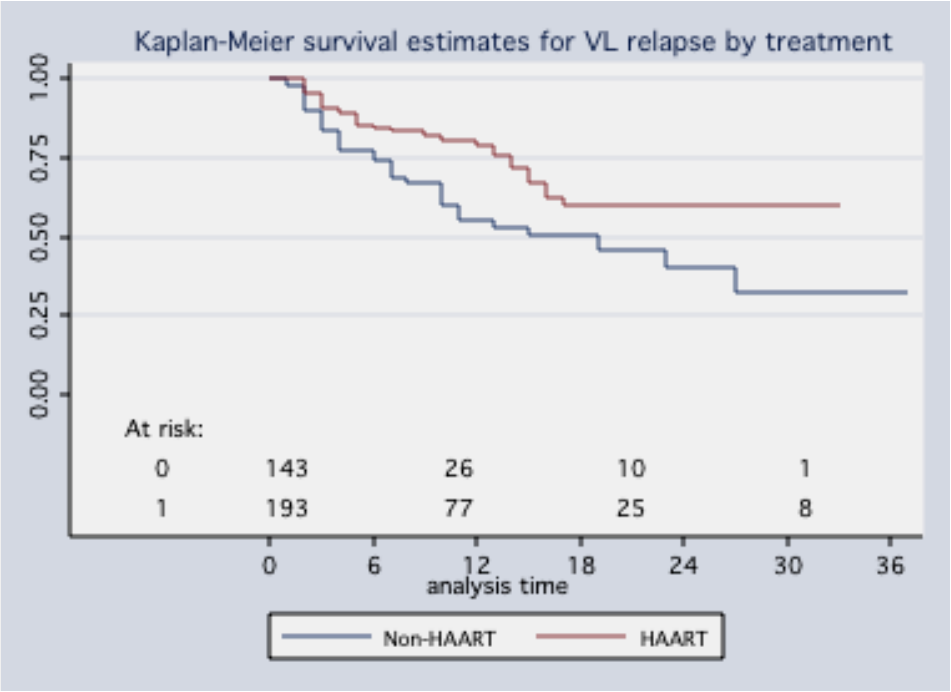
Can ART improve immune-status?

Only partially



Can ART protect against relapse?

Only partially



Liposomal amphotericin B for visceral leishmaniasis in HIV-coinfected patients in Bihar, India

MSF VL treatment program in Bihar since 2007

- Primary VL: AmBisome 20 mg/kg IV (4x5 mg/kg) 4-10d
- Relapse VL: AmBisome 25 mg/kg IV (5x5 mg/kg) 15d

Retrospective cohort study

Baseline characteristics

Characteristic (N = 55)	Median (IQ range) or N (%)
Male	48 (83.6%)
Age (years)	35 (30 – 40)
CD4 count (cells/μL)	66 (38 – 112)
VL relapse	27 (49%)

Sinha et al. Clin Inf Dis, 2011

Initial and two-year treatment outcome after AmBisome mono-therapy in 55 HIV-Positive VL patients

Initial treatment outcome	
Initial cure	52 (94.5%)
Mortality during treatment	3 (5.5%)
Initial treatment failure	0 (0%)
Two-year Follow up	
VL free and alive	41 (74.5%)
Mortality	6 (10.9%)
Relapse	8 (14.5%)

All relapses responded well to AmBisome 25mg/kg

Conclusions

- AmBisome monotherapy is effective in Indian HIV/VL
- All anti-leishmanial drugs lack efficacy in African HIV/VL patients.
- Avoid SSG. Safer drugs are recommended: AmBisome & Miltefosine.
- Combination treatment with AmBisome + Miltefosine seems to enhance treatment effectiveness, and may delay onset of drug-unresponsiveness. Further research is needed.
- ART improves longer-term survival. Yet ART alone is not adequate to prevent VL relapse.
- Secondary prophylaxis (maintenance treatment) should be explored for patients with high risk of relapse (pentamidine)

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