Supplementary material

Annex S1

We estimated the mortality associated to SB and L-AmB treatment to calculate the health outcome of VL suspects in the cost-effectiveness model. A literature search on mortality associated to both treatments was undertaken to compute the case fatality rate for both regimens by calculating the total number of deaths over the total number of VL patients recorded. A beta distribution based on the reported cases was generated for the cost-effectiveness model. Two-day course L-AmB mortality rate was assumed to be minimum as no death cases were reported in the literature at the moment of the study.

Death cases reported associated to SB treatment:

Articles	Deaths	N	Mortality	SD
Belhadj et al, 1996	3	50	6.00	0.04
Benelbarhdadi et al, 1995	2	6	33.33	757.44
Besbes et al, 1994	20	221	9.05	10.49
Harrat et al, 1992	17	285	5.96	0.02
Hassani et al, 2010	3	31	9.68	14.94
Houda, 2011	3	73	4.11	2.90
Idrissi et al, 2007	6	209	2.87	8.65
Zait et al, 2012	4	71	5.63	0.03
Syriopoulou et al, 2003	0	52	0.00	33.77
	58	998	5.81	828.29

Mortality rate of SB=0.0581 (95% CI 0.0416–0.0772) obtained from a beta distribution with parameters a=46.065 and b=747.28.

Death cases reported associated to six-day course L-AmB regimen treatment:

Articles	Deaths	N	Mortality	SD
Kafetzis et al, 2005	0	4	0	0.58
Cascio et al, 2004	0	164	0	0.58
Syriopoulou et al, 2003	2	30	6.67	34.88
Davidson et al, 1999	0	13	0	0.58
Figueras Nadal et al, 2006	0	20	0	0.58

Minodier et al, 2003	0	32	0	0.58
		263	0.76	37.77

Mortality rate of six-day course L-AmB= 0.0076 (95% CI 0.0069–0.0084) obtained from a beta distribution with parameters a=396.95 and b=51,833.53.

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Table S2 List of input parameters showing their value in the model and the value used for the univariate sensitivity analyses

Input parameter	Value in the model	Modification
BM price	21.40 US$ (17.41 US$–25.79 US$)	5.90 US$
BM sensitivity (SE) and specificity (SP)	SE 77% (95% CI 71.50%–81.50%) SP 99% (95% CI 94.00%–99.70%)	SE 60% (range 50%–90%) SP 100%
RDT sensitivity (SE) and specificity (SP)	SE 83.20% (95% CI 74.10%–90.10%) SP 99.80% (95% CI 99.00%–100.00%)	SE 92.00% (95% CI 91.49%–92.92%) SP 95.00% (95% CI 94.30%–95.48%)
SB price	1.70 US$ (1.20 US$–3.40 US$)	1.70 US$
SB mortality	5.81% (95% CI 4.16%–7.72%)	2.00%
L-AmB efficacy (relapse)	95.06% and 97.72%	100%
VL prevalence	73.46% (95% CI 61.26%–91.77%)	50% and 50%

Table S3 Baseline analysis: expected costs and effects over a 100 VL suspects

Strategy (diagnosis +treatment)	Cost (C)	Deaths
A (BM + SB)*	55,956.35	5.45
B (BM + six-day L-AmB)	113,733.68	1.28
C (BM + two-day L-AmB)	77,474.11	0.39
D (RDT + SB)	50,869.29	5.24
E (RDT + six-day L-AmB)	108,618.00	1.09
F (RDT + two-day L-AmB)	72,288.50	0.29

**Current practices in Morocco; SB: meglumine antimoniate; L-AmB: Liposomal amphotericin B; BM: Bone Marrow and microscopy; RDT: Rapid Diagnostic Test*

Table S4 Probabilistic results: cost-effective analysis of management a 100 VL suspects (subsidised L-AmB at 18US$/vial)

Strategy (diagnosis +treatment)	Cost per 100 suspect VL cases (US$)			Effectiveness per 100 suspect VL cases			C/E ratio	Incremental C/E (ICER)
	Cost (C)	Incremental Cost		Deaths	Deaths averted			
F (RDT + two-day L-AmB)	19,011.35 ± 252.22			0.29 ± 0.00			190.67	
C (BM+ two-day L-AmB)	29,765.53 ± 699.28	**10,754.18**		0.39 ± 0.00	**-0.10**		-298.82	**Dominated**
E (RDT + six-day L-AmB)	38,796.38 ± 447.03	**9,030.85**		1.10 ± 0.01	**-0.71**		-392.27	**Dominated**
B (BM + six-day L-AmB)	49,543.44 ± 819.60	**10,747.06**		1.28 ± 0.01	**-0.18**		-501.87	**Dominated**
D (RDT + SB)	65,556.25 ± 1,496.88	**16,012.81**		5.27 ± 0.04	**-3.99**		-692.04	**Dominated**
A (BM + SB)*	76,289.59 ± 1,624.60	**10,733.34**		5.48 ± 0.04	**-0.21**		-807.10	**Dominated**

**Current practices in Morocco; SB: meglumine antimoniate; L-AmB: Liposomal amphotericin B; BM: Bone Marrow and microscopy; RDT: Rapid Diagnostic Test*

Table S5 Impact of the univariate change of input parameters on the incremental costs and effects of each strategy and in the cost-effectiveness analysis conclusions: expressed as percentage increase or decrease for costs and survivals of each strategy respect the mean cost of the baseline analysis. IC: increases costs; DC: decreases costs; IS: increases survivals; DC: decreases survivals.

Input parameter	Strategy A	Strategy B	Strategy C	Strategy D	Strategy E	Strategy F	CE conclusions
BM price	DC=3% IS<1%	DC<1% IS<1%	DC=1% IS<1%	DC=2% IS<1%	DC<1% IS<1%	DC<1% IS<1%	Non-modified
BM SE&SP	DC=3% DS<1%	DC=1% DS<1%	DC<1% DS<1%	DC=3% IS<1%	DC<1% IS<1%	DC<1% IS<1%	Non-modified
RDT SE&SP	DC=4% IS<1%	DC=1% IS<1%	DC<1% IS<1%	DC=4% IS<1%	IC<1% IS<1%	IC<1% IS<1%	Non-modified
SB price	DC=2% DS<1%	IC<1% IS<1%	IC<1% IS<1%	DC=3% DS<1%	DC<1% IS<1%	DC<1% IS<1%	Non-modified
SB mortality	DC=2% IS=3%	DC<1% IS<1%	IC<1% IS<1%	DC=3% IS=3%	DC<1% IS<1%	DC<1% IS<1%	Non-modified
L-AmB efficacy*	DC=3% IS<1%	DC<1% IS=1%	DC<1% IS=1%	DC=4% IS<1%	DC=1% IS<1%	DC=1% IS=1%	Non-modified
50% VL prevalence	DC=27% IS=2%	DC=28% IS<1%	DC=26% IS<1%	DC=32% IS=2%	DC=30% IS<1%	DC=29% IS<1%	Non-modified
100% VL prevalence	IC=25% DS=2%	IC=31% DS<1%	IC=29% DS<1%	IC=28% DS=2%	IC=33% DS<1%	IC=32% DS<1%	Non-modified

*Efficacy referred to relapse cases only

Table S6 Detailed results of the threshold analysis. Montecarlo simulations outcomes of the probabilistic sensitivity analysis for different prices of Liposomal amphotericin B (L-AmB), including the proposed subsidised price of 18 US$/vial. The table compares the introduction of six-day course L-AmB as treatment (strategy B) and the introduction of two-day course L-AmB as treatment (strategy C) to current practices. Negative incremental costs represent cost-savings respect to current practices, strategies are considered cost-effective at prices with an associated ICER below 9,571 US$, while strategies are considered highly cost-effective at prices with an associated ICERs below 3,190 US$.

	Strategy A vs B							Strategy A vs C						
Price L-AmB	Incremental costs	Lower CI	Upper CI	Deaths averted	ICER	Lower CI	Upper CI	Incremental costs	Lower CI	Upper CI	Deaths averted	ICER	Lower CI	Upper CI
0	-34,740	-37,466	-32,015	4	-8,424	-9,086	-7,761	-52,836	-55,751	-49,921	5	-10,498	-11,068	-9,929
5	-28,176	-30,530	-25,823	4	-7,283	-7,904	-6,663	-46,824	-49,314	-44,335	5	-9,723	-10,249	-9,197
10	-30,144	-32,793	-27,495	4	-7,473	-8,129	-6,817	-49,294	-52,104	-46,483	5	-10,008	-10,570	-9,446
15	-28,468	-31,246	-25,690	4	-7,112	-7,803	-6,420	-48,363	-51,284	-45,442	5	-9,814	-10,398	-9,229
18	-26,746	-29,325	-24,167	4	-6,631	-7,285	-5,978	-46,524	-49,263	-43,785	5	-9,410	-9,966	-8,853
20	-22,972	-25,523	-20,422	4	-5,736	-6,373	-5,098	-43,175	-45,872	-40,478	5	-8,742	-9,279	-8,206
25	-20,363	-22,825	-17,902	4	-5,140	-5,752	-4,527	-40,392	-42,968	-37,815	5	-8,306	-8,826	-7,785
30	-20,790	-23,583	-17,997	4	-5,204	-5,915	-4,492	-42,286	-45,229	-39,342	5	-8,613	-9,213	-8,014
35	-17,636	-20,437	-14,835	4	-4,501	-5,237	-3,765	-39,614	-42,577	-36,650	5	-8,139	-8,758	-7,521
40	-13,367	-16,008	-10,725	4	-3,263	-3,914	-2,612	-36,221	-38,995	-33,447	5	-7,296	-7,847	-6,745
45	-13,970	-16,749	-11,192	4	-3,412	-4,097	-2,728	-37,167	-40,126	-34,207	5	-7,430	-8,015	-6,846
50	-8,533	-11,194	-5,873	4	-2,146	-2,782	-1,509	-32,379	-35,158	-29,601	5	-6,515	-7,054	-5,975
55	-7,024	-9,644	-4,405	4	-1,780	-2,431	-1,129	-31,764	-34,541	-28,986	5	-6,467	-7,021	-5,913

60	-5,241	-8,032	-2,450	4	-1,148	-1,824	-472	-29,588	-32,550	-26,625	5	-5,922	-6,496	-5,347
65	-103	-2,542	2,337	4	64	-563	691	-25,104	-27,672	-22,535	5	-5,069	-5,599	-4,539
70	-960	-3,642	1,722	4	-17	-670	635	-26,618	-29,455	-23,782	5	-5,210	-5,765	-4,655
75	2,443	-318	5,204	4	421	-301	1,143	-23,992	-26,886	-21,098	5	-4,897	-5,507	-4,286
80	4,855	2,190	7,520	4	1,378	710	2,046	-21,717	-24,533	-18,902	5	-4,355	-4,920	-3,790
85	9,600	7,057	12,142	4	2,431	1,787	3,074	-17,362	-20,014	-14,711	5	-3,534	-4,077	-2,991
90	7,490	4,566	10,415	4	2,033	1,342	2,723	-20,467	-23,526	-17,408	5	-3,981	-4,563	-3,399
95	**10,456**	**7,744**	**13,167**	**4**	**2,751**	**2,072**	**3,429**	-18,380	-21,220	-15,539	5	-3,629	-4,197	-3,060
100	15,024	12,340	17,708	4	3,865	3,182	4,548	-14,228	-17,045	-11,411	5	-2,850	-3,425	-2,274
105	19,905	17,383	22,427	4	5,030	4,408	5,653	-9,776	-12,385	-7,166	5	-1,945	-2,466	-1,425
110	21,708	19,226	24,191	4	5,690	5,085	6,295	-8,222	-10,805	-5,640	5	-1,554	-2,056	-1,051
115	22,924	20,337	25,511	4	5,794	5,124	6,463	-7,851	-10,550	-5,153	5	-1,590	-2,147	-1,033
120	25,181	22,384	27,979	4	6,364	5,676	7,052	-6,645	-9,572	-3,719	5	-1,282	-1,859	-706
125	30,196	27,637	32,755	4	7,605	6,977	8,232	-1,707	-4,347	932	5	-299	-825	226
130	30,977	28,380	33,574	4	7,815	7,150	8,480	-1,226	-3,904	1,451	5	-280	-837	277
135	31,183	28,243	34,123	4	8,097	7,409	8,785	-1,761	-4,842	1,320	5	-154	-728	420
140	**34,757**	**32,165**	**37,350**	**4**	**8,845**	**8,207**	**9,484**	1,502	-1,151	4,155	5	406	-120	932
145	38,083	35,362	40,805	4	9,844	9,168	10,520	4,229	1,421	7,036	5	1,038	481	1,595
150	42,098	39,541	44,654	4	10,646	9,996	11,295	7,524	4,908	10,139	5	1,600	1,069	2,130
155	41,425	38,644	44,205	4	10,391	9,685	11,097	6,055	3,202	8,908	5	1,263	687	1,839
160	45,288	42,710	47,865	4	11,587	10,947	12,228	9,748	7,100	12,395	5	2,065	1,541	2,588

165	46,843	44,190	49,497	4	11,932	11,246	12,618	10,366	7,632	13,101	5	2,272	1,719	2,826
170	52,200	49,546	54,853	4	13,082	12,426	13,739	14,901	12,234	17,567	5	3,086	2,558	3,613
175	52,369	49,671	55,067	4	13,107	12,436	13,778	**15,076**	**12,327**	**17,824**	**5**	**3,073**	**2,527**	**3,619**
180	55,111	52,140	58,082	4	13,790	13,072	14,508	16,947	13,869	20,026	5	3,507	2,921	4,093