**Supplemental Data Tables and Figures for the Diagnosis and Treatment of Leishmaniasis 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Society of Tropical Medicine and Hygiene (ASTMH)**

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| **Score Sheet** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|  | **INTERVENTION** | **NUMBER PER ARM** | **COUNTRY** | **SPECIATION PERFORMED** | **SPECIES 1** | **SPECIES 2** | **DIAGNOSTIC CRITERIA** | **METHODS** | **ORAL TREATMENTS** | **LOCAL TREATMENTS** | **PARENTERAL TREATMENT** | **OUTCOMES** | **CLINICAL ENDPOINT** | **RESULTS** | **AUTHORS' CONCLUSIONS** | **SIMILARITY OF GROUPS** | **LOSS TO FOLLOW-UP & FOLLOW-UP TIME** | **BLINDING** | **RANDOMIZATION** | **TOTAL QUALITY SCORE** | **NUMBER SCORE** | **SPECIATION SCORE** | **DIAGNOSTIC SCORE** | **ENDPOINT SCORE** | **SIMILARITY SCORE** | **FOLLOW-UP SCORE** | **BLINDING SCORE** |
| **NEW WORLD CUTANEOUS LEISHMANIASIS** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Hepburn 1994 [**[**1**](#_ENREF_1)**]** | PRM & SSG | 17 | Belize | Speciation via isoenzyme typing (23/34) | L. braziliensis | L. mexicana | Microscopy and culture | RCT; Participants British soldiers, treated in the UK | N/A | N/A | T1(n=17): paromomycin 14 mg/kg IV daily (max 1 g/day) x 20 days; T2(n=17): SSG 20 mg/kg IV daily x 20 days | Primary: % cure at 1.5 months; Secondary: adverse events | Cure defined as completely re-epithelialized with lack of induration. | paromomycin cured 10 of 17 lesions; SSG cured 15 of 17 lesions. | paromomycin was not as effective as SSG in the treatment of CL from Belize, particularly in cases due to L. braziliensis. It was, however, safe and well tolerated. A single course of SSG can cure 88% of patients. | Differed in lesion duration and size | Loss not mentioned; followed for 6 months | Open | stated but method not explained | 4 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Oster 1985 [**[**2**](#_ENREF_2)**]** | SSG | 12 | Brazil & Panama | Speciation via isoenzyme typing (26/36) | L. braziliensis | L. mexicana, L. chagasi | Microscopy and culture | RCT; Participants were Americans who acquired CL while travelling, aged >18 years | N/A | N/A | T1(n=12): SSG 600mg IV daily x 10 days; T2(n=12): SSG loading dose of 600 mg IV followed by 600mg/day continuous infusion x 9 days; T3(n=12): SSG loading dose of 600 mg IV followed by 200 mg q8h x 9 days | Primary: % cure at 12 months; Secondary: adverse events | Cure defined as complete healing of the lesions and negative aspiration culture after the treatment. "Healing" not defined. | The cure rate after the first course of treatment was 64%, but was higher for T1 (100%) than for T2 (50%) or T3 (42%) (P < 0.01). | Giving the same total amount of sodium stibogluconate in three divided doses or by continuous infusion offers no advantage over standard, once daily treatment | Not compared | Loss not mentioned; followed for 12 months | Not mentioned | Randomized via predetermined randomization schedule | 3.5 | 0 | 1 | 1 | 0 | 0 | 0.5 | 0 |
| **Correia 1996 [**[**3**](#_ENREF_3)**]** | PEN & PRM & MA | 15 | Brazil | Monoclonal antibody and isoenzymes | L. braziliensis | none | Microscopy and intra-dermal skin test | RCT; Participants aged 12-56, lesions < 6 months in duration, mean 1 lesion | N/A | N/A | T1(n=15): Pentamidine 4 mg/kg IM q 2 days x 8 sessions; T2(n=15): paromomycin 20 mg/kg IM daily x 20 days; T3(n=16): MA 10mg/kg IM daily x 20 days | Primary: % cure at 1 year; Secondary: adverse events | Failure of therapy was defined as ulceration of the skin lesion four months after treatment. | One year after treatment, there was no significant difference in cure rates between IM paromomycin and IM Pentamidine. AE were not statistically different between groups. | Statistical significance of the results between the three schedules used was not verified. No conclusion provided in the abstract (article in Portuguese) | Differed in number of lesions | Loss not mentioned; followed for 1 year. | Open | Randomized but method not explained | 3 | 0 | 1 | 1 | 0 | 0 | 0.5 | 0 |
| **Oliveira-Neto 1997 [**[**4**](#_ENREF_4)**]** | MA | 12 & 11 | Brazil | Monoclonal antibody | L. braziliensis (18/23) | none | Microscopy or culture and intra-dermal skin test | RCT; Participants aged 11-66, lesions 1-11 months in duration | N/A | N/A | T1(n=12): MA 5mg/kg IV daily x 30 days; T2(n=11): MA 20mg/kg IV daily x 30 days | Primary: % cure; Secondary: adverse events | Cure was defined as complete re-epithelialisation of the lesion. | Cure was observed in 83% in T1 and 82% in T2. AE included arthralgias and myalgias, mostly observed in T2. | Low-dose and high-dose antimony may be equally effective for treatment of CL | Differed in the number of lesions | Loss not mentioned; followed for 7 years. | Not mentioned | Randomized by the chief-nurse into the 2 treatment groups | 4.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Almeida 1999 [**[**5**](#_ENREF_5)**]** | GM-CSF & SSG | 10 | Brazil | Previous studies | L. braziliensis | none | Microscopy and detection of antigen via serology or intra-dermal skin test | RCT; Participants aged 10-50, presence of single ulcer of < 60 days in duration | N/A | N/A | T1(n=10): GM-CSF 200 mcg weekly x 2 injections & SSG 20mg/kg IV daily x 20 days; T2(n=10): placebo injections & SSG 20mg/kg IV daily x 20 days | Primary: % cure at 20 days; Secondary: none; Tertiary: speed of healing | Cure was defined as complete re-epithelialisation of the lesion. | GM-CSF and antimony-treated patients healed faster than patients who received antimony alone (49 +/- 32.8 vs. 110 +/- 61.6 days, p<0.05). No AE reported. | Combined GM-CSF and antimony significantly increased the chance of lesion healing in 40 days | No significant differences | Loss not mentioned; followed for 180 days | Double blind | Randomized but method not explained | 5 | 0 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| **Figueiredo 1999** | MA | 24 & 19 (mix of patients with CL and MCL) | Brazil | Not performed | N/A | none | Clinically diagnosed by examination | RCT; CL and MCL patients, aged 15-60 | N/A | N/A | T1(n=24): MA 14mg/kg IV daily for 2 cycles of 20 days (CL) or 3 cycles of 30 days (MCL); T2(n=19): MA 28mg/kg IV daily x 10 days followed by placebo x 10 days (7 with MCL and 12 CL). | Primary: % cure at 2 years | N/A | Two years after treatment, there was no significant difference in cure rates between MA 14 mg/kg/day and MA 28 mg/kg/day. | N/A | N/A | 4 out of 43 (9.3%); total follow-up time unknown | Double blind | Randomized but method not explained | 2 | 0 | 0 | 0 | 0 | 0 | 0.5 | 1 |
| **Machado-Pinto 2002 [**[**6**](#_ENREF_6)**]** | Vaccine & MA | 51 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Microscopy and intra-dermal skin test | RCT; Participants aged 5-65, with mean 1 lesion. | N/A | N/A | T1(n=51): L. amazonensis strain vaccine injected daily & MA 8.5 mg/kg IM daily x 10 days with repeat cycles every 10 days if necessary; T2(n=51): placebo vaccine & MA 8.5 mg/kg IM x 10 days with repeat cycles every 10 days if necessary | Primary: % cure; Secondary: adverse events; Tertiary: speed of healing | Cure defined as complete re-epithelialisation of all lesions without relapse | Complete cure occurred in 92% and 7.8% of participants in the respective groups at the end of treatment (short-term primary outcome, excluded from analysis). (p<0.0001); no significant side effects | The combination of a single-strain Leishmania (Leishmania) amazonensis vaccine with a half dose regimen of antimonial was highly effective for the treatment of ACL | Differed in age of participants | 6 out of 102 (6%); followed for 1 year | Double blind | Randomized but method not explained | 5.5 | 1 | 0 | 1 | 1 | 0 | 1 | 1 |
| **Santos 2004 [**[**7**](#_ENREF_7)**]** | GM-CSF & MA | 11 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Microscopy and detection of antigen via serology or intra-dermal skin test | RCT; Participants aged 15-50, lesions < 60 days in duration. | N/A | T1(n=11): GM-CSF 10 mcg/ml ointment 3x/week x 3 weeks & MA 20 mg/kg IV daily x 20 days | T2(n=11): MA 20 mg/kg IV daily x 20 days & placebo ointment | Primary: % cure at 40 days; Secondary: adverse events; Tertiary: speed of healing | Cure was defined as complete re-epithelialisation of the ulcer | Complete cure occurred in 91% (10/11) and 45.5% (5/11) of participants in the respective groups. The mean healing time was 43 +/- 14 days in the GM-CSF group, and 104 +/- 79 days in the placebo group (p=0.043). No significant AE. | Topically applied GM-CSF was effective in the management of CL | No significant differences | 2 out of 22 (9%); followed for 1 year | Double blind | Randomized, by randomization tables performed by a statistician | 6 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| **Lobo 2006 [**[**8**](#_ENREF_8)**]** | RFT & MA | 17 & 20 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Microscopy and detection of antigen via serology or intra-dermal skin test | RCT; Participants aged 18-67, < 2 cutaneous lesions and < 10 cm in size | N/A | T1(n=17): radiofrequency thermotherapy (50°C x 30 sec) x 1 session & MA 20mg/kg IV daily x 20 days | T2(n=20): MA 20 mg/kg IV daily x 20 days | Primary: % cure at 1 month; Secondary: adverse effects | Not defined | At 28 days, 75% of lesions were healing or healed in the heat therapy group and 90% in the control group (p=0.1261); 8 patients complicated with secondary bacterial infection of the lesion in the heat therapy group. | No difference in cure rates between heat therapy and Glucantime and Glucantime alone | Differed in gender allocation and number of lesions | 1 out of 37 (2.7%); followed for 1 month | Not mentioned | Randomized but method not explained | 2 | 0 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Nascimento 2010 *[***[***9***](#_ENREF_9)***]*** | Vaccine & MA | 27 & 8 & 9 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Microscopy | RCT; Participants aged 18-60, lesions < 6 months in duration, mean 1 lesion | N/A | N/A | All patients received MA. T1(n=27): LEISH-F1+MPL-SE vaccine (consisting of 5 (n=9), 10 (n=9), or 20 μg (n=9) recombinant Leishmania polyprotein LEISH-F1 antigen and 25 μg MPL-SE adjuvant monthly x 3 doses; T2(n=8): received adjuvant alone; T3(n=9): received saline placebo | Primary: determine the safety and tolerability of the LEISH-F1 and MPL-SE vaccine; Secondary: evaluate the immunogenicity and the effect of the vaccine on the clinical course of CL. | Cure defined as complete re-epithelialized, the patient was considered clinically cured | The vaccine was safe and well tolerated at all doses. Nearly all vaccine recipients and no adjuvant-alone or placebo recipients demonstrated an IgG antibody response to LEISH-F1 at Day 84. Also at Day 84, 80% of vaccine recipients were clinically cured, compared to 50% and 38% of adjuvant-alone and placebo recipients. | The LEISH-F1+MPL-SE vaccine was safe and immunogenic in CL patients and appeared to shorten their time to cure when used in combination with meglumine antimoniate chemotherapy. | Differed in gender allocation | 3 out of 44 (6.8%); followed for 11 months | Double blind | Randomized but method not explained | 5.5 | 0 | 1 | 1 | 1 | 0 | 1 | 1 |
| **Machado 2010 [**[**10**](#_ENREF_10)**]** | MIL & MA | 60 & 30 | Brazil | PCR | L. braziliensis | none | Microscopy, culture, and intra-dermal skin test | RCT; Participants aged 2-65, lesions < 3 months in duration, no prior treatment | T1(n=60): Miltefosine 2.5mg/kg PO daily x 28 days | N/A | T2(n=30): MA 20mg/kg IV daily x 20 days | Primary: % cure at 6 months; Secondary: adverse events | Cure defined as complete re-epithelialisation, without raised borders, infiltrations or crusts were considered healed | Cure was observed in 53.3% with MA and 75% with miltefosine (p = 0.04). Miltefosine was more effective than MA for 13-65 year olds vs 2-12 year olds (78.9% versus 45%, p = 0.02). AE included GI symptoms with miltefosine and myalgias with MA | This study demonstrates that miltefosine therapy was more effective than standard MA and safe for the treatment of CL caused by Leishmania braziliensis in Bahia, Brazil. | Differed in gender allocation and number of lesions | 3 out of 90 (3%); followed for 6 months | Open | Randomized via computer-generated system | 6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 |
| **Sousa 2011 [**[**11**](#_ENREF_11)**]** | FLU | 8 & 14 & 6 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Microscopy and culture | Not an RCT; Fluconazole used in individuals with contraindications to pentavalent antimonials (elderly, renal or cardiac disease, diabetes), participants aged 2-88 | T1(n=8): Fluconazole 5mg/kg daily x 4-12 weeks; T2(n=14): fluconazole 6.5mg/kg daily x 4-12 weeks; T3(n=6): fluconazole 8 mg/kg daily x 4-12 weeks | N/A | N/A | Primary: % cure; Secondary: time to cure; Tertiary: adverse events | Cure not defined | As the dose of fluconazole increased, the cure rate increased and the time to cure shortened. Those treated with 5 mg/kg/day had a cure rate of 75%, and healing took a mean of 7.5 weeks. Of those treated with 8 mg/kg/day, 100% were cured, and the time to healing was 4 weeks. Fluconazole was well tolerated in all patients. | Fluconazole was used successfully to treat L. braziliensis infection. The cure rate with fluconazole was high. The dosages of fluconazole used were higher than the ones used by others to treat CL | Differed in gender allocation and duration of lesions | Loss and follow-up time not mentioned | Not mentioned | Not randomized | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| **Chrusciak-Talhari 2011 [**[**12**](#_ENREF_12)**]** | MIL & MA | 60 & 30 | Brazil | PCR-RFLP and enzyme electrophoresis | L. guyanensis | none | Microscopy | RCT; Participants 2-65, 1 -5 lesions of < 3 months in duration | T1(n=60): Miltefosine 2.5 mg/kg PO daily x 28 days | N/A | T2(n=30): MA 15-20mg/kg IV daily x 20 days | Primary: % cure at 6 months; Secondary: safety of miltefosine compared to antimony | Cure defined as complete re-epithelialisation of all ulcers and complete disappearance of inflammatory induration. | Cure rates were 71.4% and 53.6% for miltefosine and antimonial respectively. No severe AE occurred. | Miltefosine was safe and relatively well tolerated and cure rate was higher than antimony. | No significant differences | 3.6% in T1 and 3.5% in T2; followed for 6 months | Open | Randomized via 2:1 allocation for miltefosine | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Neves 2011 [**[**13**](#_ENREF_13)**]** | MA & PEN & AMB | 74 & 74 & 37 | Brazil | PCR-RFLP | L. guyanensis (88.7%) | L. braziliensis | Microscopy and culture | RCT Participants aged 5 to 65, primarily men, | N/A | N/A | T1(n=74): MA 15 mg/kg IV or IM daily x 20 days; T2(n=74): Pentamidine 4 mg/kg IM q72hours x 3 doses; T3(n=37): amphotericin B 1mg/kg IV daily x 20 days. | Primary: cure at 6 months; Secondary: adverse events | Cure defined as complete re-epithelialisation of all ulcers and absence of any signs of inflammatory reaction at 2 months. | Intention-to-treat analysis showed efficacy of 58.1% for pentamidine and 55.5% for meglumine (p=0.857). 75% of the Amphotericin group refused to continue the study. AE included arthralgia with meglumine, and local pain with pentamidine. | Pentamidine and meglumine show similar efficacy in the treatment of ATL caused by L. guyanensis. Given the low efficacy of both drugs, there is an urgent need for new therapeutical approaches. | Only differed in gender distribution for AMB group, however this group was excluded from the efficacy analysis. | 75.7% receiving AMB refused to continue in the study; 6.2% loss in the other groups; followed for 6 months | Open | Randomized via list of random distribution | 6.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **Newlove 2011 [**[**14**](#_ENREF_14)**]** | MA | 45 | Brazil | Endemic, speciation not performed | L. braziliensis | none | Intra-dermal skin testing | RCT; Participants aged 13-50, < 4 lesions of 15-60 days in duration. All patients had a helminth infection; study evaluated the difference between early vs deferred treatment of intestinal helminths in the treatment of CL. | T1(n=45): albendazole 400 mg PO, ivermectin 200 μg/kg PO, and praziquantel 50 mg/kg PO at Days 0 and 30 and placebo at Day 60; T2(n=45): placebo on day 0 and 30, and appropriate antihelmintic treatment based on parasitology assay on day 60. | N/A | All patients received MA 20 mg/kg IV daily x 20 days | Primary: % cure at 3 months; Secondary: time to cure | Cure defined as complete re-epithelialisation at 3 months. | At the 90-day study endpoint, 51.1% in the control group had persistent lesions, compared with 62.2% in the treatment group. Patients who received early anthelmintic treatment took longer to heal their lesions than their non-treated counterparts, although this result was not statistically significant (P = 0.13). | Cutaneous leishmaniasis and co-existing helminth infection was associated with poor response to therapy. However, introduction of early anthelmintic treatment in co-infected patients did not lead to improvement in overall cure rates or time to cure for CL and was associated with a tendency for delayed lesion healing. | No significant differences | No losses; followed for 3 months | Double blind | randomization tables | 6.5 | 1 | 0 | 0.5 | 1 | 1 | 1 | 1 |
| **Motta 2012 [**[**15**](#_ENREF_15)**]** | AMB & MA | 16 & 19 | Brazil | Monoclonal antibody | L. braziliensis | L. amazonensis, L. viannia | Microscopy, culture, and intra-dermal skin test | Not an RCT, prospective non-randomized study; Participants mean age 25 years, predominantly male, lesions > 6 months in duration, < 7 lesions | N/A | N/A | T1(n=16): Liposomal amphotericin B 1.5 mg/kg IV daily x 5 days; T2(n=19): MA 20 mg/kg IV daily x 20 days. | Primary: % cure | Cure defined as complete re-epithelialisation of the lesion at 3 months. | In T1, 50% experienced a clinical cure. There was 100% clinical cure in T2. AE included myalgia, arthralgia, tachycardia, headache and Hexheimer’s reaction with MA. | Liposomal amphotericin B seemed to be promising and safe for the treatment of American cutaneous leishmaniasis. | Differed in number of lesions and speciation | Loss not mentioned; followed for 12 months | Open | Not randomized | 3.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Toledo 2014 [**[**16**](#_ENREF_16)**]** | AZI & MA | 24 | Brazil | PCR | L. braziliensis | none | Microscopy, culture, and intra-dermal skin test | RCT; Participants aged 14-65, mean 1.6 lesions, mean duration 3 months, treatment-naive | T2(n=24): Azithromycin 500mg PO daily x 20 day | N/A | T1(n=24): MA 15mg/kg IV/IM daily x 20 days | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as complete re-epithelialisation without inflammatory infiltration and erythema until 90 days after the treatment ended. | The study was interrupted due to the high failure rate in the azithromycin group. The MA group had a higher cure rate, with the ITT and PP analyses that were 54.2% vs 20.8% and 72.2% vs 23.8%, respectively. | Azithromycin was ineffective for CL treatment and does not seem to have a role in the therapeutic arsenal for CL. | Differed in lesion duration | 6 out of 48 (12.5%); followed for 6 months | Open | Randomized via 1:1 allocation | 4.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Soto 2008 [**[**17**](#_ENREF_17)**]** | MIL & MA | 41 & 16 | Bolivia | Endemic, speciation not performed | L. braziliensis | none | Microscopy | RCT; Participants aged 25-30, median 1 lesion | T1(n=41): Miltefosine 2.5 mg/kg PO daily x 28 days | N/A | T2(n=16): MA 20mg/kg IM daily x 20 days | Primary: % cure at 6 months; Secondary: adverse events; Tertiary: speed of healing | Cure was defined as complete epithelialisation of all lesions by 6 months after the end of therapy. | Cure rates were of 88% with miltefosine and of 94% with MA. More rapid healing was observed with MA. AE included gastrointestinal side effects with miltefosine and arthralgias with MA. | The two conclusions from this work are that oral miltefosine can be used for cutaneous disease in this part of Bolivia and that miltefosine was more effective for L. braziliensis in this region than for L. braziliensis in Guatemala. | No significant differences between treatment arms | 5 out of 62 (8%); followed for 1 year | Open | Randomized but method not explained | 4.5 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |
| **Solomon 2013 [**[**18**](#_ENREF_18)**]** | AMB & SSG | 34 | Bolivia | PCR | L. braziliensis | none | Microscopy or culture | Not a RCT, prospective study, Mean age 24, mean 2 lesions, most (94% and 88%) acquired in Bolivia | N/A | N/A | T1(n=34): Liposomal amphotericin B 3 mg/kg x 5 days, and a 6th dose on day 10; T2(n=34): SSG 20 mg/kg IV daily x 3 weeks | Primary: % cure; Secondary: adverse outcome | Cure was defined as 100% re-epithelialisation of the ulcer within 3 months of treatment completion | With L-AMB 85% had complete cure compared with 70% in those receiving SSG (though difference not statistically significant). Treatment interrupted in 65% SSG patients because of AE. | Comparison of L-AMB to SSG treatment for L (V) braziliensis showed that the former was effective, better tolerated, and more cost effective. L-AMB should therefore be considered as the first-line treatment option for cutaneous L (V) braziliensis infection | No significant differences | loss not mentioned; followed for mean 29 months (range 10 to 85) | Open | Not randomized; treatment group determine by who had insurance to cover for L-AMB | 5.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **Soto 2004A [**[**19**](#_ENREF_19)**]** | SSG & MA | 48 & 16 & 50 | Bolivia & Colombia | Monoclonal antibody | L. panamensis | none | Microscopy | RCT; Participants aged 18-65, average 1.8 lesions. From La Paz, Bolivia, or Uraba and Carmen de Chucuri, Colombia | N/A | N/A | T1(n=48): SSG (generic) 20 mg/kg IM daily x 20 days; T2(n=16): SSG (Pentostam) 20 mg/kg IV daily x 20 days; T3(n=50): MA 20 mg/kg IM daily x 20 days | Primary: % cure at 6 months; Secondary: adverse events | Cure was defined as complete epithelialisation of all lesions by 6 months after the end of therapy. | There was no significant difference in cure rates between IM SSG and IM MA. Per-protocol cure rates and intention-to-treat cure rates for all pentavalent antimonials were 86% and 79%. More AE were reported with MA | The efficacy and tolerance of inexpensive generic stibogluconate was comparable to branded formulations for the treatment of CL | Differed in gender allocation and ulcer size | 10 out of 114 (8.8%); followed for 6 months | Double blind | Randomized by playing cards | 6 | 0 | 1 | 1 | 1 | 0 | 1 | 1 |
| **Soto 2004B *[***[***20***](#_ENREF_20)***]*** | MIL | 49 & 24 & 40 & 20 | Colombia & Guatemala | Monoclonal antibody and PCR | L. panamensis (100% from Colombia) | L. braziliensis (63% Guatemala) & L. mexicana (37% Guatemala) | Microscopy or culture | RCT; Participants aged >12 years, predominantly male, mean 1 lesion | Colombia: T1(n=49): Miltefosine 50 mg PO x 28 days; T2(n=24): placebo PO x 28 days; Guatemala: T1(n=40): Miltefosine 50 mg PO x 28 days; T2(n=20): placebo PO x 28 days | N/A | N/A | Primary: % cure at 6 months; Secondary: % remission and adverse events | Cure was defined as complete healing of all lesions by 6 months after the end of therapy. | Colombia: per-protocol cure rates for miltefosine and placebo were 91% and 38%. Guatemala: per-protocol cure rates for miltefosine and placebo were 53% and 21%. AE included including creatinine and LFTs | Miltefosine cure rate was lower than historic antimony cure rates of >90%; Miltefosine is a useful PO agent against CL due to L. panamensis in Colombia, but not against L. braziliensis in Guatemala | No significant differences | 8 out of 133 (6%); followed for 6 months | Double blind | Randomized but method not explained | 6.5 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Martínez 1992 [**[**21**](#_ENREF_21)**]** | ALL & MA | 25 & 33 & 35 & 17 | Colombia | Endemic, speciation via isoenzyme typing | L. panamensis | none | Microscopy, culture, and intra-dermal skin test | RCT; Participants aged 11-40, predominantly male, 1-3 lesions | T1(n=25): Allopurinol 20 mg/kg PO daily x 15 days; T3(n=35): Allopurinol 20 mg/kg PO daily x 15 days & MA 20 mg/kg IV daily x 15 days; | N/A | T2(n=33): MA 20 mg/kg IV daily x 15 days; T4(n=17) : no treatment | Primary: % cure at 1 year; Secondary: % remission | Cure was defined as complete epithelialisation at 3 months without recurrence by 1 year. | Cure rate in T2 was 36%. The addition of allopurinol in T3 increased cure rate to 74% (p<0.001). Cure rate with allopurinol alone (T1) was 80% (p<0.001). No cures in T4. Only minor AE were reported. | Cure rates were significantly higher in the oral allopurinol group compared with the MA group. There was no significant difference in cure rates between oral allopurinol alone and oral allopurinol in combination with MA. The efficacy of allopurinol alone appears to be as good as in combination. The validity of these conclusions have been questioned [[21](#_ENREF_21)] | Differed in age of participants | Loss not mentioned; followed for 1 year | Open | Not all groups randomized; Allopurinol alone and the group that received no treatment were self-selected | 4 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Soto 1994 [**[**22**](#_ENREF_22)**]** | PRM | 30 | Colombia | Monoclonal antibody and isoenzyme typing (30/90) | L. panamensis | none | Microscopy or culture (30/90) | RCT; Participants aged 18-60, military personnel | N/A | N/A | T1(n=30): paromomycin sulphate 12 mg/kg IM daily x 7 days; T2(n=30): paromomycin sulphate 12 mg/kg IM daily x 14 days; T3(n=30): paromomycin sulphate 18 mg/kg IM daily x 14 days | Primary: % cure at 1 year; Secondary: adverse effects | Cure defined as healed lesion within 1.5 months, without relapse at 12 months. | Cure rates were 10%, 45%, and 50% respectively for T1, T2, and T3 | Parenteral paromomycin alone was less likely to be successful in the treatment of CL than MCL (for which a 74% cure rate has been reported); further trials might consider the combination of paromomycin with other anti-leishmanial drugs | Not compared | 1 out of 90 (1.1%); followed for 1 year | Not mentioned | Randomized but 3rd group was added later in the study and the final 40 patients were randomly allocated to the three groups in the ratio 5:5:30 | 4.5 | 1 | 1 | 1 | 0 | 0 | 1 | 0 |
| **Martínez 1997 [**[**23**](#_ENREF_23)**]** | ALL & SSG | 51 | Colombia | Speciation via isoenzyme typing | L. braziliensis | none | Microscopy or culture and intra-dermal skin test | RCT; Participants aged 18-57, 47% were farmers, 35% were soldiers | T1(n=51): Allopurinol 20 mg/kg PO daily x 15 days & SSG 20 mg/kg IV daily x 15 days; | N/A | T2(n=49): SSG 20mg/kg IV daily x 15 days | Primary: % cure at 1 year; Secondary: % remission and adverse effects | Cure was defined as complete epithelialisation at 3 months without recurrence by 1 year. | Cure was observed in 39% in T2. The addition of allopurinol (T1) increased the cure rate to 71% (p=0.005). AE included chemical hepatitis with allopurinol. | The combination of allopurinol and SSG was significantly more effective than SSG alone. The data support the use of allopurinol as an inexpensive, orally administered agent that can be used as an adjunct | No significant differences | 3 out of 100 (3%); followed for 1 year | Open | Randomized via master list generated by computer | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Vélez 1997 [**[**24**](#_ENREF_24)**]** | ALL & MA | 56 | Colombia | Monoclonal antibody | L. panamensis (84%) | L. braziliensis (16%) | Microscopy or culture | RCT; Participants aged 6-60, mean 3 lesions. | T1(n=60): Allopurinol 300 mg PO x 28 days; T2(n=56): placebo PO x 28 days | N/A | T3(n=66): MA 20 mg/kg IM daily x 20 days | Primary: % cure at 1 year; Secondary: % remission and adverse effects | Cure was defined as complete epithelialisation at 3 months without recurrence by 1 year. | Cure was observed in 18/55 (33%) in T1, 17/46 (37%) in T2, 52/56 (93%) in T3 (P<0.001). AE included myalgias, arthralgias, anorexia, nausea, and headache in patients receiving MA. | Allopurinol monotherapy had no effect on Colombian cutaneous disease primarily caused by L. panamensis | No significant differences | 30 out of 187 (16%); followed for 1 year | Double-blinded (except patients in MA group) | Randomized but method not explained | 7 | 1 | 1 | 1 | 1 | 1 | 0.5 | 1 |
| **Soto 1998 [**[**25**](#_ENREF_25)**]** | PRM & MA | 30 | Colombia | Isoenzyme typing (in the 69/150 positive cultures) | L. braziliensis (20/69) | L. panamensis (49/69) | Microscopy or culture | RCT; Participants aged 18-60, mean of 1.4 lesions | N/A | T1(n=59): 15% paromomycin sulphate in 12% MBCL x 10 days & MA 20 mg/kg IV daily x 7 days; T3(n=31): 15% paromomycin sulphate in 12% MBCL x 10 days & MA 20 mg/kg IV daily x 3 days | T2(n=30): MA 20 mg/kg IV daily x 7 days & topical placebo x 10 days; T4(n=31): MA 20 mg/kg IV daily x 20 days | Primary: % cure at 1 year | Cure defined as complete re-epithelialisation of all lesions without relapse | Cure rates were 58%, 53%, 20%, and 84% for T1, T2, T3, and T4 respectively. | 10 days of treatment with paromomycin/MBCL did not augment the response of CL compared to a short-course of treatment with meglumine antimoniate | No significant differences | 2 out of 150 (1.3%); followed for 1 year | Double-blinded | Randomized, assigned in unequal allocation (2:1:1:1) | 7.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Palacios 2001 *[***[***26***](#_ENREF_26)***]*** | MA | 68 | Colombia | Monoclonal antibody and isoenzyme typing | L. panamensis (84/88) | L. braziliensis (4/88) | Microscopy or culture | RCT; Participants were predominantly pediatric, with a median of 2 lesions | N/A | N/A | T1(n=68): MA 20 mg/kg IM daily x 10 days; T2(n=68): MA 20 mg/kg IM days x 20 days | Primary: % cure at 1 year | Cure was defined as complete re-epithelialisation of the all lesions at 13 weeks without relapses at 1 year. | Efficacy of MA for a 10 day treatment was 61% compared to 67% for 20 days; there was significantly lower clinical response for children <5 years in both the 10 day(11%) and 20 day (25%) groups, compared with patients aged 5-14 years (67% and 75%) and 15+ years (81% and 83%) | Overall efficacy of 10 day vs 20 day MA was similar; low efficacy rates largely explained by poor response in children compared to adults | Differed in lesion size and presence of adenopathy | 54 out of 136 (39.7%); followed for 1 year | Single-blinded (examiners only) | Randomized via permuted block randomisation | 6 | 1 | 1 | 1 | 1 | 0 | 0.5 | 0.5 |
| **Soto 2002 [**[**27**](#_ENREF_27)**]** | PRM | 33 & 12 | Colombia | Monoclonal antibody (only in 5/45) | L. panamensis (detected in 5/45) | none | Clinically diagnosed by examination, culture (only 5/45 successful) | RCT; Participants were all male soldiers, mean aged 25 years, mean 1.6 lesions, 26% had failed MA | N/A | T1(n=33): Paromomycin in WR279396 x 20 days; T2(n=12): topical placebo x 20 days | N/A | Primary: % cure at 70 days; Secondary: adverse events; Tertiary: speed of healing | Cure was defined as 100% re-epithelialisation of the lesion without relapse by the 6-month follow-up | 17/28 (61%) of T1patients were cured; 5/9 (55%) of T2 patients were cured (p=0.9); mean time to lesion cure was 35 days in T1 and 56 days in T2 (p=0.04); WR-group, 55% had mild local reactions for 3.6 days, while 33% in placebo-group | WR279396 (a topical formulation of aminoglycosides) significantly accelerated cure time, but was not statistically more effective than placebo | Differed in lesion size | 8 out of 45 (17.8%); followed for 6 months | Single-blinded (examiners only) | Randomized via 2:1 allocation | 2.5 | 0 | 0 | 0 | 1 | 0 | 0.5 | 0.5 |
| **Lopez-Jaramillo 2010 [**[**28**](#_ENREF_28)**]** | NO & MA | 90 | Colombia | Endemic, speciation not performed | L. panamensis | none | Microscopy or culture | RCT; Participants aged 19-50 | N/A | T2(n=88): nitric oxide releasing patch & placebo IM x 20 days | T1(n=90): MA 20 mg/kg IM daily and placebo patch x 20 days | Primary: % cure at 3 months; Secondary: adverse events | Cure was defined as complete re-epithelialisation of the ulcer | The cure rates were 94.8% for MA compared with 37.1% for NO. A significantly lower frequency of non-serious adverse events and abnormal serum markers were observed in patients treated with NO. | Treatment of CL with NO resulted in a lower effectiveness compared with Glucantime; however, the low frequency of adverse events and the facility of topic administration justify the development of new generations of NO systems for the treatment of CL. | No significant differences between treatment arms | 35 out of 178 (19.6%); followed for 3 months | Double blind | Randomized via computer-generated system | 6.5 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| **Velez I 2010 [**[**29**](#_ENREF_29)**]** | MIL & MA | 143 | Colombia | PCR-RFLP | L. panamensis (38%) | L. braziliensis (62%) | Culture | RCT; Participants mean age 25 years, male soldiers, mean 1 lesion | T1(n=145): Miltefosine 50 mg PO TID x 28 days | N/A | T2(n=143): MA 20 mg/kg IM daily x 20 days | Primary: % cure of 6 months; Secondary: assess safety of miltefosine compared to meglumine antimoniate | Cure defined as complete re-epithelialisation of all ulcers and complete disappearance of the induration up to 3 months, without relapse at 6 months. | The efficacy of miltefosine by protocol was 69.8% and 58.6% by intention to treat. For meglumine antimoniate, the efficacy by protocol was 85.1% and 72% by intention to treat. | The efficacy of MA was statistically superior to that of miltefosine in the treatment of CL in Colombia (P = 0.003). No differences were found in the response to treatment based on the species responsible | No significant differences between treatment arms | 39 out of 288 (13.5%); followed for 6 months | Open | Randomized via computerized block randomization | 6.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **Lopez 2012 [**[**30**](#_ENREF_30)**]** | RFT & MA | 149 | Colombia | PCR | L. panamensis | L. braziliensis | Microscopy, culture, and intra-dermal skin test | RCT; Participants all male soldiers (no other demographics provided) | N/A | T1(n=149): Thermotherapy (50°C x 30 seconds) x 1 session & fusidic acid ointment x 10 days | T2(n=143): MA 20 mg/kg IM daily x 20 days | Primary: % cure at 6 months; Secondary: adverse events | Complete re-epithelialisation of all ulcers and complete loss of induration up to three months after the end of treatment | The efficacy of thermotherapy was 64% (86/134 patients) by protocol and 58% (86/149) by intention-to-treat. For the meglumine antimoniate group, efficacy by protocol was 85% (103/121 patients) and 72% (103/143) by intention-to-treat. Significant difference. | Although the efficacy rate of meglumine antimoniate was greater than that of thermotherapy for the treatment of cutaneous leishmaniasis, the side effects were also greater. This makes us consider thermotherapy as a first line treatment for cutaneous leishmaniasis. | No table provided (only mentioned that patients balanced, but data not in article) | 31 out of 292 (10.6%); followed for 6 months | Open | Randomized via generated list in blocks of eight | 5.5 | 1 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Rubiano 2012 [**[**31**](#_ENREF_31)**]** | MIL & MA | 58 | Colombia | Monoclonal antibodies or isoenzyme electrophoresis | L. panamensis (68-76%) | L. guyanensis (20-30%) | Microscopy and culture | RCT; Participants all pediatric (ages 2-12) | T2(n=58): Miltefosine 1.8-2.5 mg PO daily x 28 days | N/A | T1(n=58): MA 20 mg/kg IM daily x 20 days | Primary: % failure at 26 weeks | Cure was defined as complete re-epithelialisation and absence of inflammatory signs for all lesions | By intention-to-treat analysis, failure rate was 17.2% for miltefosine and 31% for meglumine antimoniate (p=0.04); Adverse events were mild for both treatments. | Miltefosine is non-inferior to meglumine antimoniate for treatment of pediatric CL secondary to L. Viannia sp. | Differed only slightly in lymphatic involvement. | 5 out of 116 (4.3%); followed for 6 months | Open | Randomized via computerized balanced block randomization scheme | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Lopez 2013 [**[**32**](#_ENREF_32)**]** | MIL & RFT | 143 & 147 | Colombia | PCR-RFLP | L. braziliensis | L. panamensis | Microscopy | RCT; Participants all male soldiers, aged 19-39, mean 1 lesion, mean 2-3 months duration | T1(n=143): Miltefosine 50 mg PO TID x 28 days | T2(n=147): Thermotherapy (Thermomed®, 50°C x 30 seconds) x 1 session | N/A | Primary: % cure at 6 months; Secondary: adverse events | Cure defined as complete re-epithelialisation of all ulcers and disappearance of induration up to three months following treatment | The efficacy of miltefosine by protocol and by intention to treat was 70% (85/122 patients) and 69% (85/145 patients), respectively. AE included gastrointestinal symptoms for T1 and local pain in T2. | No statistically significant difference was found in the efficacy analysis (intention to treat and protocol) between the miltefosine and thermotherapy. | No significant differences | 35 out of 290 (12.0%); followed for 6 months | Open | Randomized via block of eight | 6.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **Guderian 1991 [**[**33**](#_ENREF_33)**]** | ALL & PRB & SSG | 30 & 30 & 15 | Ecuador | Monoclonal antibody | L. panamensis | L. braziliensis & L. mexicana & L. guyanensis | Microscopy or culture | RCT; Participants mean age 29 years, lesions 3-4 months in duration | T1(n=30): Allopurinol ribonucleoside 1500 mg PO QID & probenecid 500 mg PO QID x 28 days | N/A | T2(n=30): SSG 20mg/kg IM daily x 20 days; T3(n=15): no treatment | Primary: % cure at 1.5 months | Cure defined as >80% re-epithelialisation by 1.5 months | Mean reduction in lesion size for patients in T2 group was 61%, 23% and 11% after 1, 2, and 3 weeks; mean reduction in lesions size for patients in T3 group was 56%, 29%, and 25% after 1, 2, and 3 weeks; 41%, 100%, 75% cure for patients in T1, T2, and T3 groups | Allopurinol will be an oral agent available to augment standard therapy | Not compared | 14 out of 75 (18.67%); followed for 1 year | Not mentioned | Randomized via 2:2:1 allocation | 4.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Armijos 2004 [**[**34**](#_ENREF_34)**]** | PRM & MA | 40 | Ecuador | Not performed | N/A | none | Microscopy or culture | RCT; Participants aged 5-60, 1-3 lesions, lesions > 4 months in duration | N/A | T1(n=40): 15% paromomycin in 12% MBCL ointment daily x 3 months; T2(n=40): 15% paromomycin in 10% urea daily x 30 days | T3(n=40): MA 20 mg/kg IM daily x 10 days | Primary: % cure at 2 months; Secondary: adverse events; Tertiary: speed of healing | The complete healing of all lesions by week 12 after the start of treatment with no relapse observed during the 52-week follow-up period was defined as a clinically cured case. | Cure rates were 47.5%, 47.5% and 70% at 2 months but at 12 weeks were 79.3%, 70%, and 91.7% in T1, T2, and T3 (p>0.05). MA-treated (T3) subjects had a faster healing time (29.5 days vs. 43.1 days). AE included burning, redness, inflammation, and soreness | Although the time required for clinical healing of ulcerated lesions takes longer, topical paromomycin may be an acceptable alternative in endemic areas where meglumine antimoniate is unavailable, too costly, or contraindicated | Differed in lesion size | 25 out of 120 (20.83%); followed for 1 year | Double blinded, except T3 | Randomized via Computer-generated random numbers table | 3.5 | 1 | 0 | 1 | 0 | 0 | 0 | 0.5 |
| **D’Oliveira 1997 [**[**35**](#_ENREF_35)**]** | ALL & MA | 18 & 16 | El Salvador | Unclear if speciated or based on endemicity | L. braziliensis | none | Microscopy and/or culture | RCT; Participants had never received previous treatment | T1(n=18): Allopurinol 20mg/kg PO TID x 20 days; | N/A | T2(n=16): MA 10 mg/kg IV daily x 20 days | Primary: % cure at 70 days; Secondary: recurrence at 3 months | Cure not defined; defined therapeutic failure | Study stopped because 0/9 on Allopurinol showed response at 1 month, and 2/18 developed mucosal disease | Allopurinol should not be used. | Differed slightly in number of lesions | Loss not mentioned; followed for 12 months | Open | Randomized but method not explained | 3.5 | 0 | 0 | 1 | 0 | 1 | 0.5 | 0 |
| **Arana 1994 [**[**36**](#_ENREF_36)**]** | MA & IFN- γ | 22 | Guatemala | Speciation method not mentioned | L. braziliensis | L. mexicana | Culture | RCT; Participants all Guatemalan male soldiers, aged 18-20, mean 1.2 lesions | N/A | N/A | T1(n=22): MA 20 mg/kg IV daily x 20 days; T2(n=22): MA 20 mg/kg IV daily x 10 days followed by placebo IV x 10 days; T3(n=22): MA 20 mg/kg IV daily x 10 days & IFN- γ (1 ml solution containing 0.2 mg of recombinant IFN-γ /ml) S/C every other day x 5 doses | Primary: % cure at 1 year; Secondary: recurrence rate | Cure defined as complete re-epithelialisation of all lesions with no residual erythema. Test-of-cure cultures at the end of therapy and at the 9 week follow-up | Cure was observed in 90% of patients receiving meglumine for 20 days, 90% of patients receiving meglumine for 10 days, and 100% of patients receiving meglumine plus interferon-gamma. | The high efficacy of our 10-day course of meglumine indicates that the currently recommended duration of 20 days may be unnecessary for infections caused by L. braziliensis | No significant differences | 4 out of 66 (4.5%); followed for 12 months | Double blind | Randomized but method not explained | 5.5 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| **Arana 2001 [**[**37**](#_ENREF_37)**]** | PRM | 35 & 33 | Guatemala | Endemic, speciation not performed | L. braziliensis | L. mexicana | Microscopy and culture | RCT; Participants aged 10-60, excluded patient with previous antimony-containing treatments | N/A | T1(n =35): 15% paromomycin in 12% MBCL BID x 20 days; T2(n=33): topical placebo | N/A | Primary: % cure at 1 year | Cure defined as complete re-epithelialisation w/ no inflammation or indurations and no reactivation | Cure was observed in 85.7% in the treatment group and 39.4% in the placebo group (P < or = 0.001). | Our findings show that the combination of paromomycin with methylbenzethonium chloride for 20 days is a good alternative for antimonial treatments of cutaneous leishmaniasis in Guatemala. | No significant differences | 8 out of 76 (10.5%); followed for 12 months | Double blind | Randomized but method not explained | 6 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| **Navin 1990 [**[**38**](#_ENREF_38)**]** | RFT & MA | 22 | Guatemala | Endemic, speciation not performed | L. braziliensis | L. mexicana | Microscopy and culture | RCT Participants all male soldiers, aged 18-60years, mean 1 lesion | N/A | T2(n=22): Thermotherapy (50ºC for 30 sec) weekly x 3 treatments | T1(n=22): MA 850 mg IM daily x 15 days; T3(n=22): placebo treatment | Primary: % cure at 2 months; Secondary: adverse effects | Cure defined as complete re-epithelialisation with no evidence of papules, inflammation or induration | Cure was observed in 73% receiving meglumine antimoniate, 73% receiving heat therapy, and 27% receiving placebo. Speed of healing was slower with heat therapy. | Although neither meglumine antimoniate nor heat therapy proved completely effective, both treatments were more effective than the placebo treatment. Heat treatment was not better than meglumine antimonite. | Not compared | Loss not mentioned; followed for 52 weeks | Single blinded (patient) | Randomized, but method not explained | 3.5 | 0 | 0 | 1 | 1 | 0 | 0.5 | 0.5 |
| **Navin 1992 [**[**39**](#_ENREF_39)**]** | KET & SSG | 40 | Guatemala | Speciation via isoenzyme typing | L. braziliensis | L. mexicana | Microscopy and culture | RCT; Participants Guatemalan civilians and soldiers, aged 19-22, mean 1.5 lesions | T1(n=40): Ketoconazole 600 mg PO daily x 28 days | N/A | T2(n=40): SSG 20 mg/kg IV daily x 20 days; T3(n=40): placebo (either saline infusions or placebo tablets) | Primary: % cure at 2 months; Secondary: recurrence rate within 1 year | Cure defined as complete re-epithelialisation and no evidence of inflammation | Among patients infected with L. braziliensis, 24/25 (96%) receiving SSG but 7/23 (30%) receiving ketoconazole were cured. Among L. mexicana infected patients, 4/7 (57%) receiving SSG but 8/9 (89%) receiving ketoconazole were cured. | These differences emphasize the importance of speciation in the treatment of leishmaniasis. However, the small sample size for each strain limits these results | Differed in lesion size | 7 out of 120 (5.83%); followed for 52 weeks | Single blinded | Randomized via computer algorithm | 6.5 | 1 | 1 | 1 | 1 | 0 | 1 | 0.5 |
| **Neva 1997 [**[**40**](#_ENREF_40)**]** | PRM | 23 & 30 | Honduras | Speciation via isoenzyme typing | L. chagasi | L. mexicana | Culture | RCT; Participants were inhabitants from the municipalities of San Juan Bautista and Coyolito | N/A | T1(n=23): 15% paromomycin in 10% urea TID x 4 weeks; T2(n=30): topical placebo TID x 4 weeks | N/A | Primary: % cure at 3 months; Secondary: recurrence rate after 4-5 months | Cure not defined. | The treatment was not effective | Topical therapy with 15% paromomycin and 10% urea was not better than placebo in treating non-ulcerating cutaneous leishmaniasis. | No table provided (only mentioned that patients balanced, but data not in article) | Loss not mentioned; followed for 11 weeks | Double blind | Randomized by a computer algorithm | 4.5 | 0 | 1 | 1 | 0 | 0 | 0.5 | 1 |
| **Balou 1987** | SSG | 21 & 19 | Panama | Monoclonal antibody (23/40 patients) | L. panamensis | L. chagasi | Microscopy and culture | RCT; Participants were American soldiers on duty in Panama treated in Washington | N/A | N/A | T1(n=21): SSG 10 mg/kg IV daily x 20 days; T2(n=19): SSG 20 mg/kg IV daily x 20 days. | Primary: % cured at 1.5 months; Secondary: adverse events | Cure not defined. | Nine weeks after starting treatment, all 19 patients treated with SSG 20 mg/kg/day were cured but 5/21 patients treated with SSG 10 mg/kg/day had persistent active disease (p < 0.05). | Higher doses of sodium stibogluconate are both safe and efficacious at treating American cutaneous leishmaniasis. Lower doses are inadequate for some patients. | No significant differences | Loss not mentioned; followed for 12 months | Double blind | Randomized but method not explained | 5 | 0 | 1 | 1 | 0 | 1 | 0.5 | 1 |
| **Saenz 1987 [**[**41**](#_ENREF_41)**]** | SSG & MA | 30 & 29 | Panama | N/A | L. panamensis | none | Microscopy and culture | RCT; Participants primarily male inhabitants of the provinces of Panama and Colon | N/A | N/A | T1(n=30): SSG 20 mg/kg IM daily x 20 days; T2(n=30): MA 20 mg/kg IM daily x 20 days. | Primary: % cured; Secondary: recurrence at 1 year & adverse events | N/A | N/A (Article only in Spanish) | N/A (Article only in Spanish) | N/A | 9 out of 59 (15.3%); followed for 12 months | Not mentioned | Randomized, method unknown (article only in Spanish) | 3 | 1 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Saenz 1990 [**[**42**](#_ENREF_42)**]** | KET & MA | 22 & 19 & 11 | Panama | Speciation via isoenzyme typing (31/41) | L. panamensis | L. mexicana | Microscopy and culture | RCT; Participants all male, aged 16-67, mean 2.1 and 2.6 lesions per treatment arm. | T1(n=22): Ketoconazole 600 mg PO daily x 28 days; T3(n=11): placebo PO daily x 28 days. | N/A | T2(n=19): MA 20 mg/kg IM (max 850 mg/day) daily x 20 days | Primary: % cure at 3 months; Secondary: adverse events; Tertiary: speed of healing | Cure defined as complete re-epithelialisation and no clinical relapse in the f/u period | Ketoconazole clinically cured 16/21 (76%). Pentostam cured 13/19 (68%). The placebo group had a 0% cure rate. | Both ketoconazole and Pentostam were more effective than placebo against L. panamensis. Ketoconazole is comparable in efficacy to Pentostam. | Significant difference in lesion size and duration | Loss not mentioned; followed for 12 months | Not mentioned | Randomized via card drawing | 4.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Sosa 2013 [**[**43**](#_ENREF_43)**]** | PRM | 15 | Panama | Isoenzyme electropheresis or PCR | L. panamensis | none | Microscopy and culture | RCT; Participants mean age 25 years, mean 2 lesions, mean 2-3 months duration | N/A | T1(n=15): topical WR 279,396 (15% paromomycin & 0.5% gentamicin) applied daily x 20 days; T2(n=15): 15% paromomycin daily x 20 days | N/A | Primary: % cure at 6 months; Secondary: adverse events | Cure defined as complete re-epithelialisation of index lesion by nominal Day 63 | The index lesion cure rate after 6 months follow-up was 13 of 15 (87%) for WR 279,396 and 9 of 15 (60%) for Paromomycin Alone (P = 0.099). No significant AE. | The increased final cure rate in the WR 279,396 group in this small Phase 2 study suggests that the combination product may provide greater clinical benefit than paromomycin monotherapy. | Differed in lesion duration and size | No losses; followed for 6 months | Double blind | Randomized via 1:1 allocation | 6 | 0 | 1 | 1 | 1 | 0 | 1 | 1 |
| **Andersen 2005 [**[**44**](#_ENREF_44)**]** | PEN & MA | 40 | Peru | Isoenzyme electrophoresis | L. braziliensis | none | Microscopy or culture | RCT; Participants aged 18-60, predominantly male, mean 2 lesions | N/A | N/A | T1(n=40): Pentamidine 2 mg/kg IV on alternate days x 7 doses; T2(n=40): MA 20 mg/kg IV daily x 20 days | Primary: % cure at 6 months; Secondary: adverse events; Tertiary: histopathological cure | Clinical cure was defined as completely re-epithelialized by 6 months. Parasitological cure was defined as the inability to culture or stain parasites from the lesion | 78% cure rate in patients administered Glucantime (T2); 35% cure in patients administered Pentamidine (T1) | Glucantime is more effective than pentamidine for treatment of L. braziliensis CL in Peru based on parasitological as well as clinical criteria | No significant differences | 6 out of 80 (7.5%); followed for 6 months | Open | Randomized via 1:1 allocation | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Miranda-Verástegui 2005 [**[**45**](#_ENREF_45)**]** | IMQ & MA | 20 | Peru | Endemic, speciation not performed | L. braziliensis | L. peruviana | Microscopy, culture, and/or PCR | RCT; Participants aged 1-78, predominantly pediatric; history of one or more failed courses of treatment with MA | N/A | T1(n=20): 5% imiquimod cream applied every other day x 20 days & MA 20 mg/kg IM daily x 20 days; | T2(n=20): MA 20 mg/kg IM daily x 20 days & topical placebo cream | Primary: % cure at 1 year; Secondary: adverse events | Cure was defined as complete re-epithelialisation without signs of inflammation | Lesions resolved more rapidly in imiquimod group: 50% cure at 1 month vs 15% for control group (p=0.02), 61% at 2 months vs. 25% (p=0.03), and 72% cure at 3 months vs. 35% (p=0.02); erythema occurred more often in T1 (p=0.02); One year after treatment, there was no significant difference in cure rates btw both arms | Combined antimony plus imiquimod treatment was well tolerated, accelerated lesion healing, and improved scar quality; this therapy may have particular advantages for subjects with facial lesions | Differed in lesion duration | 2 out of 40 (5%); followed for 1 year | Double blind | Randomized but method not explained | 4.5 | 0 | 0 | 1 | 1 | 0 | 1 | 1 |
| **Arévalo 2007 [**[**46**](#_ENREF_46)**]** | IMQ & MA | 6 | Peru | Endemic, speciation not performed | L. braziliensis | L. peruviana & L. mexicana & L. amazonensi | Microscopy, culture, and/or PCR | RCT; Participants aged 18-87 | N/A | T1(n=6): 7.5% imiquimod cream applied every other day x 20 days; T2(n=7): 7.5% imiquimod cream applied every other day x 20 days & MA 20 mg/kg IV daily x 20 days; | T3(n=7): MA 20 mg/kg IV daily x 20 days | Primary: % cure at 3 months; Secondary: adverse events | Clinical cure was defined as complete re-epithelialisation without signs of inflammation. | Although several patients showed initial resolution with imiquimod alone (T1), all relapsed after treatment discontinuation; 57% of those receiving meglumine alone (T3) and 100% of those receiving combination treatment (T2) were cured; combination treatment was more effective (p<0.05) | Combination therapy with imiquimod and meglumine is a promising regimen for initial treatment of CL and warrants additional larger studies | Differed in lesion size, location, and duration | Loss not disclosed; Followed for 3 year | Not mentioned | Randomized but method not explained | 3 | 0 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Llanos-Cuentas 2008 [**[**47**](#_ENREF_47)**]** | SSG | 127 | Peru | PCR | L. peruviana (49.6%) | L. braziliensis (22.8) & L. guyanensis (21.3%), other sp. (6.3%) | Microscopy, culture, and intra-dermal skin test | Not an RCT, prospective case-control study; Participants aged 2-51, mean 2 lesions | N/A | N/A | T1(n = 127): SSG 20mg/kg IV or IM daily x 20 days | Primary: % failure at 6 months | Clinical cure was defined as complete wound closure and re-epithelialisation without inflammation or infiltration | Failure rate at 6 months was 24.4%, with 96% of the failures occurring in the first 3 months; clinical risk factors associated with failure were younger age, a shorter stay in an area of disease acquisition, shorter duration of disease, additional lesions, and infection with L. peruviana or L. braziliensis | The identification of parasite species and clinical risk factors for antimonial treatment failure should lead to improved management of CL in Peru | Single treatment arm | Loss not mentioned; followed for 6 months | Open | Not randomized | 4.5 | 1 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Miranda-Verastegui 2009 [**[**48**](#_ENREF_48)**]** | IMQ & MA | 39 & 36 | Peru | PCR | L. peruviana | L. braziliensis & L. guyanensis | Microscopy, culture, and/or PCR | RCT; Participants aged 5–65, lesions > 4 weeks in duration, acquired lesions primarily in the jungle | N/A | T1(n=39): Imiquimod cream applied 3x/week x 9 applications; T2(n=36): placebo cream applied 3x/week x 9 applications. | All participants in T1 and T2 also received MA 20 mg/kg IV daily x 20 days | Primary: % cure at 12 months; Secondary: adverse events | cure defined as complete re-epithelialisation with no inflammation assessed during the 12 months post-treatment period. | The cure rate at 12-month for the ITT analysis was 75% (30/40) in T1 and 58% (23/40) in T2 (p = 0.098). Subgroup analyses suggested that combination treatment benefits were most often observed with L. braziliensis infections. Over the study period, only one adverse event (rash) was recorded, in the experimental arm. | The combination treatment of imiquimod plus pentavalent antimony performed better than placebo plus pentavalent antimony, but the difference was not statistically significant. | No significant differences between treatment arms | 5 out of 80 (6.25%); followed for 6 months | Double blind | Randomized but method not explained | 7.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **van der Meide 2009 *[***[***49***](#_ENREF_49)***]*** | PEN | 23 | Suriname | PCR-RFLP | L. guyanensis | none | Microscopy or smear | Not RCT, prospective single arm study; Participants aged 17-65, mean 2 lesions of median 7 weeks in duration | N/A | N/A | T1(n=23): pentamidine isethionate 300 mg IM weekly x 3-4 doses | Primary: patient compliance to treatment; Secondary: % cure at 10 weeks | lesion was judged on the following criteria: re-epithelialisation and degree of contraction, decrease in necrotic tissue, and decrease in border activity. | A lower cure rate (76-78%) was estimated than that obtained previously (90%), and only 50% of the recruited CL patients finished the complete treatment schedule. | As one-half of the CL patients were treated insufficiently, a much shorter treatment protocol should be considered to improve the inadequate follow-up | Single treatment arm | 8 out of 23 (34.9%); followed for 2.5 months | Open | Not randomized | 3.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Convit 1987 [**[**50**](#_ENREF_50)**]** | Vaccine & MA | 124 & 51 | Venezuela | Mono- or poly-clonal antibody and PCR | L. braziliensis | none | Microscopy, culture, and intra-dermal skin test | RCT; Participants aged >12 years, lesions < 12 months in duration | N/A | N/A | T1(n=44): MA 50 mg/kg IM daily x 20 days for 2-3 courses with 15 day intervals; T2(n=58): vaccine (L. mexicana amazonensis with BCG), the amount used in 1st dose depended on response to TBST, a 2nd dose was given at 6-8 weeks, and a 3rd dose at 12-18 weeks | Primary: % cure at 6 months; Secondary: adverse events; Tertiary: speed of healing, development of cell-mediated immunity | Clinical cure defined as complete healing of the lesion without evidence of infiltration or lymphangitis. | The vaccine gave a similar cure rate (94%) to three 20-day courses of MA. AE were few with the vaccine, and with MA. AE included myalgias, headache, fever, hypotension,  cardiac arrhythmia, and paresthesia. | Immunotherapy is a low-cost, low-risk alternative to chemotherapy in localised CL | No significant differences between treatment arms | 8 out of 102 (7.8%); followed for 40 weeks | Single blind (examiner) | Randomized but method not explained | 6 | 1 | 1 | 1 | 0 | 1 | 1 | 0.5 |
| **Convit 1989 [**[**51**](#_ENREF_51)**]** | Vaccine & MA | 124 & 51 & 42 | Venezuela | Mono- or poly-clonal antibody and PCR | L. braziliensis | none | Microscopy and culture | RCT; Participants aged > 12 years, lesions < 12 months in duration | N/A | N/A | T1(n=124): vaccine (L. mexicana amazonensis with BCG) q6-8weeks x 3 doses; T2(n=51): MA 50 mg/kg IM daily x 20 days, for 2-3 courses with 15 day intervals; T3(n=42): intradermal BCG q6-8weeks x 3 doses | Primary: % cure at 6 months; Secondary: adverse events; Tertiary: speed of healing | Clinical cure defined as complete healing of the lesion and absence of peripheral infiltration/inflammation, satellite lesions, adenopathy, lymphangitis, or new lesions. | In T1 and T2, there was a 90% cure rate, with an average time to healing of 16-18 weeks.T3 had significantly lower cure rates. AE included arrhythmia, severe myalgias, colic, paresthesia with MA. | Combined vaccine is efficacious for American CL; provides a strong rationale for studying vaccine effectiveness in prophylactic trials | No significant differences between treatment arms | Loss not mentioned; followed for 2 years | Single blind (examiner) | Randomized via random sequence generation | 6 | 1 | 1 | 1 | 0 | 1 | 0.5 | 0.5 |
| **INTERNATIONAL TRIALS** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0 |  |  |  |  |  |  |  |
| **Wortmann 2010 [**[**52**](#_ENREF_52)**]** | AMB | 20 | Iraq (5), Afghanistan (5), Peru (1), French Guiana (1), Honduras (2), Colombia (6) | Isoenzyme electrophoresis | L. braziliensis (3), L. guyanensis (3) | L. panamensis (4), L. tropica (2), L. major (3) | Microscopy and culture | Not an RCT, retrospective study; Participants predominantly male soldiers, mean age 29 years, mean 1 lesion | N/A | N/A | T1(n=20): Liposomal amphotericin B 3mg/kg IV daily x 10 doses given within a 21-day period | Primary: % cure; Secondary: adverse events | Not defined | 16/19 experienced a cure with the initial treatment regimen. 3 patients needed additional doses to achieve cure. Acute infusion-related reactions occurred in 25%, and mild renal toxicity occurred in 45% of patients. | Although the optimum dosing regimen is undefined and the cost and toxicity may limit widespread use, liposomal amphotericin B is a viable treatment alternative. | Single treatment arm | 1 out of 20 (5%); followed for mean 4 months | Open | Not randomized | 3 | 0 | 1 | 1 | 0 | 0 | 1 | 0 |
| **Harms 2011 [**[**53**](#_ENREF_53)**]** | AMB & MA | 13 & 8 & 2 | Bolivia, Brazil, Costa Rica, Ecuador, French Guiana, Peru | PCR-RFLP | L. braziliensis | none | Microscopy and/or culture | Not an RCT, retrospective study of German travelers to Central and South America, treated in Germany | T2(n=8): miltefosine 2.5 mg/kg PO daily TID x 28 days; | N/A | T1(n=13): Liposomal amphotericin B 3 mg/kg IV on days 1-5 and day 10; T3(n=2): MA 20 mg/kg IV daily x 21 days | Primary: % cure; Secondary: adverse events | Cure defined as completely re-epithelialized without inflammation. | Cure achieved with amphotericin B in 11/13 patients, miltefosine in 5/8, and meglumine antimoniate in 2/2. Of the patients who failed initial therapy, four were cured with meglumine antimoniate and one with amphotericin B. | Amphotericin B, miltefosine, and meglumine antimoniate proved to be effective. Conventional meglumine antimoniate showed high efficacy as a first-line treatment. | Patient demographics individually listed, but not compared | Loss not mentioned; followed for 12 month | Open | Not randomized | 3.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Morizit 2013 [**[**54**](#_ENREF_54)**]** | AMB & MIL & MA | 168 | International | PCR-RFLP | many | many | Microscopy and/or culture | Not an RCT, retrospective analysis of data on returned travelers collected by experts with the French leishmaniasis reference center. | N/A | Treated via a stepwise algorithm: in situation 1, wound care measures are employed; in situation 2, local therapy is employed (cryotherapy, IL MA, or topical paromomycin) | Treated via a stepwise algorithm: in situation 3, systemic therapy is employed (MA, Amphotericin B, or miltefosine) | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as positive outcome at 42-60 days | 23/25 (92%) with wound care alone had positive outcome (mostly L. major, L. tropica, L. aethiopia). 37/47 (79%) had positive outcome with local therapy; 4/19 (21%) with L. braziliensis or L. panamensis. 22/37 (60%) receiving systemic therapy had positive outcome. | Stepwise therapy as per the French guidelines allows for safe and reasonable patient outcome at 42-60 days | Not compared | Loss not mentioned; followed for 2 months | Open | Not randomized | 3.5 | 1 | 1 | 1 | 0 | 0 | 0.5 | 0 |
| **OLD WORLD CUTANEOUS LEISHMANIASIS** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0 |  |  |  |  |  |  |  |
| **Reithinger 2005 [**[**55**](#_ENREF_55)**]** | SSG & RFT | 148 & 144 & 138 | Afghanistan | PCR-RFLP | L. tropica | none | Microscopy | RCT; Participants aged >5, one lesion, no prior treatment | N/A | T1(n=148): SSG IL q 5-7 days over 29 days; T3(n=139): radiofrequency thermotherapy treatment (50°C x 30 sec) x 1 session | T2(n=144): SSG 20 mg/kg (max 850 mg) IM daily x 21 days | Primary: % cure at 2 months; Secondary: speed of healing, adverse effects | Cure defined as complete re-epithelialisation at day 100 | Thermotherapy treatment cured 75/138 (54%), IL SSG 70/146 (48%) and IM SSG 26/117 (22%), by ITT analysis. AE included secondary infection (more frequently with thermotherapy), bradycardia (with SSG), local reactions. | Single session with thermotherapy was as effective as IL SSG and more effective than IM SSG. | No significant differences | 172 out of 431 (40%); followed for 3 months | Open | Randomized via picking pieces out of a hat | 6.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **van Thiel 2010 A [**[**56**](#_ENREF_56)**]** | SSG | 172 | Afghanistan | PCR-RFLP | L. major | none | Microscopy | Not an RCT, case series by the Dutch military | N/A | T1(n=172): SSG IL q 1-3 days until clinical improved. If no improvement, alternative treatments were started | N/A | Primary: % cure at 6 months | Cure defined as complete re-epithelialisation | Satisfactory response to IL SSG +/- cryotherapy in 77%; 19.5% treated with miltefosine. 6 month cure 77%. | Natural evolution played a role in this observational study, which showed cure of all patients at six months. Management of CL was feasible under field conditions. | Single arm study | Loss 9.6%; followed for 6 months | Open | Not randomized | 5 | 1 | 1 | 1 | 1 | 0 | 1 | 0 |
| **van Thiel 2010B [**[**57**](#_ENREF_57)**]** | MIL | 34 | Afghanistan | PCR-RFLP | L. major | none | Microscopy and/or culture | Not an RCT, observational study; Participants aged 19-49, predominantly male Dutch military personnel | T1(n=34): miltefosine 50 mg PO TID x 28 days | N/A | N/A | Primary: % cure; Secondary: adverse event | Cure defined as re-epithelialisation at 6 months | All patients had experienced clinical improvement at the end of treatment, but no cure. At 6 months, 28 patients had definite cure. AE included diminution of ejaculate volume | Miltefosine efficacious for L. major. | Single arm study | No losses; followed for 6 months | Open | Not randomized | 5 | 1 | 1 | 1 | 1 | 0 | 1 | 0 |
| **Safi 2012 [**[**58**](#_ENREF_58)**]** | RFT & ILMA | 195 | Afghanistan | Endemic, speciation not performed | L. tropica | none | Microscopy | RCT; Participants aged 5-75, primarily pediatric | N/A | T1(n=195): radiofrequency thermotherapy (50°C x 30 sec) x 1 session; T2(n=195): MA IL weekly x 5 doses | N/A | Primary: % cure at 6 months | Cure defined as complete re-epithelialisation | Cure was observed in 83% in T1 compared to 74% in T2; outcomes were better if the lesion smaller or nodular | A single treatment with thermotherapy was more effective than 5 days of intralesional Glucantime. It is also more cost-effective and has fewer side effects. | No significant differences | 5 out of 390 (1%); followed for 6 months | Open | Randomized via picking pieces out of a hat | 6 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| **Jebran 2014 [**[**59**](#_ENREF_59)**]** | EC & MWT | 73 & 62 | Afghanistan | PCR-RFLP | L. tropica | none | Microscopy and/or culture | RCT; Participants aged 5-66, lesions 1-12 months in duration | N/A | T1(n=73): Bipolar high frequency electro-cauterization followed by MWT with polyacrylate hydrogel and sodium chlorite applied daily; T2(n=62): Bipolar high frequency electro-cauterization, followed by MWT with polyacrylate hydrogel without sodium chlorite applied daily | N/A | Primary: % cure at 6 months | Cure defined as complete re-epithelialisation | Cure in both groups was more rapid than historical cure time by IL MA, but no different between T1 and T2 (43 and 42 days respectively). | Bipolar high frequency electro-cauterization (EC) followed by daily moist-wound-treatment leads to rapid wound healing. | No significant differences | 22 out of 135 (16.3%); followed for 6 months | Double blind | Randomized via computer algorithm | 7.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 1 |
| **Stahl 2014 [**[**60**](#_ENREF_60)**]** | SSG & EC & MWT | 24 & 32 & 31 | Afghanistan | PCR-RFLP | L. tropica | L. major | Microscopy or smear | RCT; Participants aged 19-40, lesions 7-11 months in duration | N/A | T1(n=24): SSG IL twice weekly x 4 weeks; T2(n=32): high-frequency electro-cauterization and MWT with 0.045% DAC N-055; T3(n=31): MWT with 0.045% DAC N-055 | N/A | Primary: ratio of closed versus open wounds 2.5 months | Cure defined as complete re-epithelialisation | PP analysis of 69 (79%) patients revealed complete epithelialisation before day 75 in 65% in T1, 100% in T2, and 87% T3 (p = 0.004). Re-ulceration occurred 17%, 13%, 30% respectively. | Treatment of CL ulcers with EC followed by MWT with 0.045% DAC N-055 or with DAC N-055 alone showed shorter wound closure times than with the standard SSG therapy. | No significant differences | 10 out of 87 (11.5%); followed for 6 months | Open | Randomized via 1:1:1 allocation | 5.5 | 0 | 1 | 1 | 1 | 1 | 0.5 | 0 |
| **Negera 2012 [**[**61**](#_ENREF_61)**]** | CRY & SSG | 103 & 20 | Ethiopia | PCR-RFLP | L. aethiopica | none | Microscopy and/or culture | Not an RCT, prospective non-randomized study; Participants mean age 20.6 years in T1 and 18.4 years in T2, lesions mean 8.5 months in duration | N/A | T2(n=103): Cryotherapy (liquid nitrogen) x 3-4 sessions/lesion weekly until cure; T3(n=10): untreated lesions, selected among the participants in T2 | T1(n=20): SSG 20 mg/kg (max 850 mg) daily x 30 days | Primary: % cure at 6 months | Cure defined by lesions showing complete scarring and disappearance of inflammatory signs by 3 months | Cure was observed in 83/89 (94%) receiving cryotherapy, and in 85% receiving SSG. | Both methods were equally effective at treating CL due to L. aethiopica. | Not reported | 15 out of 123 (15%); followed for 6 months | Open | Not randomized | 3.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Dogra 1990 [**[**62**](#_ENREF_62)**]** | ITR | 15 & 5 | India | Not performed | N/A | none | Microscopy | RCT; Participants with lesions 4-11 weeks in duration, <6 lesions total | T1(n=15): Itraconazole 4 mg/kg (max 200 mg) PO daily x 6 weeks; T2(n=5): no treatment | N/A | N/A | Primary: % cure at 3 months; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete disappearance of induration or redness if nodular, complete healing of ulcer, and negative smear; definition of healing not specified | Cure observed in 10/15 (67%) receiving itraconazole and 0/5 on no treatment. AE included mild headache with itraconazole | Small study. Itraconazole had some efficacy compared to observed cohort | Not reported | Loss not mentioned; followed for 3 months | Open | Randomized, method unknown (full article not available) | 2 | 0 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Dogra 1991 [**[**63**](#_ENREF_63)**]** | DAP | 60 | India | Not performed | N/A | none | Microscopy | RCT; Participants aged > 12 years, no prior treatment, lesions < 4 months in duration | T1(n=60): Dapsone 100 mg PO BID x 6 weeks; T2(n=60): placebo tablet PO BID x 6 weeks | N/A | N/A | Primary: % cure at 1 month; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete disappearance of induration of nodules or re-epithelialisation if ulcer, and 3 negative smears | Cure was observed in 49/60 (71%) in dapsone treated patients and 0/60 with placebo. AE included dapsone related hemolysis (3 patients), and nausea | Dapsone for 6 weeks had some efficacy in treatment of CL compared to placebo | No table provided (only mentioned that patients balanced) | Loss not mentioned; followed for 1 month | Double blind | Randomized but method not explained | 4.5 | 1 | 0 | 1 | 1 | 0 | 0 | 1 |
| **Dogra 1992[**[**64**](#_ENREF_64)**]** | ITR & DAP | 20 | India | Not performed | N/A | none | Microscopy | RCT; Participants aged 15- >55, no further demographics provided | T1(n=20): Itraconazole 4mg/kg (max 200 mg) PO daily x 6 weeks; T2( n=20): dapsone 4mg/kg PO BID x 6 weeks; T3(n=20): placebo | N/A | N/A | Primary: % cure; Secondary: adverse events | Cure defined as complete disappearance of induration in nodular lesions or re-epithelialisation of ulcer, and 3 monthly negative smears | Itraconazole cured 15/20 (75%), dapsone 18/20 (90%), and placebo 2/20 (10%). AE included nausea and increased LFTs | Dapsone was more efficacious than itraconazole. | Not reported | Loss not mentioned; followed for 3 months | Not mentioned | Randomized, but method not explained | 3 | 0 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Dogra 1996 [**[**65**](#_ENREF_65)**]** | ITR | 10 | India | Not performed | N/A | none | Microscopy | RCT; Participants aged >18 years, no prior treatment, lesion < 4 months in duration | T1(n=10): Itraconazole 200 mg PO daily x 6 weeks; T2(n=10): placebo 2 tablets PO daily x 6 weeks | N/A | N/A | Primary: % cure at 3 months; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete disappearance of nodular lesions or re-epithelialisation of ulcers and 3 negative smears | Itraconazole healed 7/10 (70%) and placebo 1/10 (10%). AE included nausea and increased LFTs | Itraconazole could be a preferred choice over pentavalent antimonials (systemic/peri-lesional) for the initial therapy of CL. | No table provided (only mentioned that patients balanced) | Loss not mentioned; followed for 3 months | Double blind | Randomized, but method not explained | 4 | 0 | 0 | 1 | 1 | 0 | 0.5 | 1 |
| **Kochar 2000 [**[**66**](#_ENREF_66)**]** | RIF | 23 | India | Not performed | N/A | none | Microscopy | RCT; Participants aged 1-60, mean 2 lesions, median duration 2 months duration | T1(n=23): Rifampin 600 mg PO BID x 4 weeks; T2(n=23): placebo | N/A | N/A | Primary: % cure; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete healing at 4 weeks; definition of healing not specified | Rifampin cured 73.9% while placebo cured on 4%. There were no AE | Rifampin demonstrated better cure rates than placebo, however it needs to be studied over a longer time period. | Significant differences in lesion size, number and duration | 4 out of 50 (8%); followed for 1 month | Double blind | Not randomized | 2.5 | 0 | 0 | 1 | 0 | 0 | 0.5 | 1 |
| **Kochar 2006 [**[**67**](#_ENREF_67)**]** | RIF | 25 | India | Not performed | N/A | none | Microscopy | RCT; Participants predominantly pediatric, lesions < 3 months in duration, 50% with nodular lesions | T1(n=25): Rifampin 600 mg PO BID and omeprazole 20 mg PO daily x 6 weeks; T2(n=25): placebo x 6 weeks | N/A | N/A | Primary: % cure; Second: adverse events | Cure defined as complete healing and disappearance of lesion; definition of healing not specified | Rifampin cured 6/25 (24%) while placebo cured 3/25 (12%) by ITT. No AE reported | Only modest cure rates were observed with rifampin as compared to placebo. | No significant differences | 6 out of 50 (12%); followed for 1.5 months | Double blind | Randomized, but method not explained | 5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 1 |
| **Aara 2013 [**[**68**](#_ENREF_68)**]** | RIF & ILSSG & RFT & CRY | 361 & 297 & 185 & 96 & 19 | India | PCR-RFLP | L. tropica | none | Microscopy | Not an RCT, consecutive case series presenting to hospital in Rajasthan over 10 years; Treated on a case to case basis. | T4(n=96): Rifampin PO x 4-6 weeks | T1(n=361): SSG IL biweekly x 5-7 sessions; T2(n=297): SSG IL weekly x 5-7 sessions; T3(n=185): Thermotherapy (50°C x 30–60 sec) x 1 session; T5(n=19): Cryotherapy | N/A | Primary: % cure at 6-24 weeks | Cure defined as total re-epithelialisation and absence of amastigotes on smear | T1 cure 92% at 24 weeks, T2 92% at 24 weeks, T3 98% at 24 weeks, T4 84% at 6 weeks, and T5 84% at 24 weeks | Most modalities are associated with cure by 16-24 weeks | Not reported | 406 out of 1379 (29%); followed for 18 months | Open | Not randomized | 3.5 | 0 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Bumb 2013 *[***[***69***](#_ENREF_69)***]*** | RFT & ILSSG | 50 | India | PCR-RFLP | L. tropica | none | Microscopy | RCT; Participants aged 4-60, ≤ 4 lesions, 1-18 months in duration | N/A | T1(n=50): Thermotherapy (50°C x 30-60 sec) x 1 session; T2(n=50): SSG IL biweekly x 7 sessions | N/A | Primary: % cure at 6 months; Secondary: time to cure; Tertiary: adverse events | Cure defined as complete re-epithelialisation | Cure rates in the heat therapy and SSG groups were 98% and 94% respectively. AE included local infections with heat therapy | A single application of radiofrequency heat therapy is safe, cosmetically acceptable and effective in inducing a long-term cure of CL. | No significant differences | No losses; followed for 12 months | Open | Randomized via 1:1 allocation | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Agarwal 2014 [**[**70**](#_ENREF_70)**]** | RIF & DAP & ILSSG & RFT | 58 & 14 & 50 & 3 & 5 | India | PCR | L. tropica | N/A | Microscopy, culture, and/or PCR | Not an RCT, case series of 151 pediatric patients. Participants aged 0-5 years, mostly single facial lesions, mean 4.5 months in duration, mean 2.4 cm in size | T3(n=50): Rifampin 20 mg/kg PO daily x 4-6 weeks; T4(n=3): Dapsone 20 mg/kg daily PO x 4-6 weeks; T5(n=11): Rifampin 20 mg/kg PO daily & Dapsone 20 mg/kg PO daily x 4-6 weeks | T1(n=58): SSG IL once to twice per week x 5-7 session; T2(n=14): Thermotherapy (50°C x 30 seconds); T6(n=12): SSG IL once to twice per week x 5-7 session & rifampin 20 mg/kg PO daily x 4-6 weeks | N/A | Primary: % cure at 3 months | Cure was defined as total re-epithelialisation of the lesion and a negative skin smear. | Complete cure with local therapies (SSG IL and RFT) was observed in 84.4% and 91.8%, respectively. Rifampicin, dapsone, and a combination of both, complete healing was recorded in 82%, 66.67%, and 90.1% respectively. The combination of SSG IL and rifampicin was effective in 100% of cases. | Relatively good success rates with variable treatment regimens. | Not compared | 9 out of 151 (6.0%); followed for 3 months | Open | Not randomized | 4 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |
| **Aronson 2010 [**[**71**](#_ENREF_71)**]** | RFT & SSG | 27 | Iraq & Kuwait | PCR-RFLP and enzyme electrophoresis | L. major | none | Microscopy | RCT; Participants aged 18-57, predominantly male, median 2-3 lesions of median 4 months duration | N/A | T2(n=27): Thermotherapy (50°C x 30 sec) x 1 session | T1(n=27): SSG 20 mg/kg IV daily x 10 days | Primary: % cure at 2 months; Secondary: adverse events | Cure defined as complete re-epithelialisation | In an ITT analysis, the per subject efficacy was 54% SSG and 48% TM (p = 0.78), and the per lesion efficacy was 59% SSG and 73% TM (p = 0.053). Local AE were recorded with TM, and myalgias, increased LFTs and cytopenias with SSG. | L. major treated with heat by TM had similar cure rates as IV SSG, and was associated with fewer side effects | No significant differences | No losses; followed for 12 months | Single blind (examiner) | Randomized via computer algorithm | 7.5 | 1 | 1 | 1 | 1 | 1 | 1 | 0.5 |
| **Asilian 1995 [**[**72**](#_ENREF_72)**]** | PRM | 126 & 125 | Iran | Not performed | N/A | none | Microscopy | RCT; participants with lesions < 4 weeks in duration, children > 2 years, size < 5cm, single lesion | N/A | T1(n=126): 15% paromomycin in 10% urea ointment BID x 14 days; T2(n=125): placebo ointment BID x 14 days | N/A | Primary: % cure at 2.5 months; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete re-epithelialisation of ulcer by day 45 or 105 | Paromomycin ointment cured 80/126 and placebo ointment 79/125, RR 1 | Paromomycin ointment for 14 days was no better than a placebo petrolatum ointment | No significant differences | 16 out of 251 (6.4%); followed 3.5 months | Double blind | Randomized, but method not explained | 6.5 | 1 | 0 | 1 | 1 | 1 | 1 | 1 |
| **Zerehsaz 1999 [**[**73**](#_ENREF_73)**]** | HRB & MA | 86 & 85 | Iran | Not performed | N/A | none | Microscopy | RCT; participants with lesion < 4 months in duration, mean < 2 lesions | N/A | T1(n=86): Herbal extract in black paste to lesion daily x 5 days & placebo saline injections daily x 20 days | T2(n=85): MA 15-20 mg/kg IM daily x 20 days & placebo black paste to lesions daily x 5 days | Primary: % cure at 6 weeks; Secondary: adverse events | Cure defined as complete healing and re-epithelialisation of lesion | Herbal extract paste healed 64/86 (74%) and MA 23/85 (27%). Adverse events included urticarial and generalized pruritus in the MA cohort | Herbal extract paste was more effective for healing of CL than MA in this study | Not reported | Loss not mentioned; followed for 6 months | Double blind | Randomized, but method not explained | 5 | 1 | 0 | 1 | 1 | 0 | 0.5 | 1 |
| **Gholami 2000** | Garlic | 96 & 75 | Iran | Not performed | N/A | none | Not specified | RCT; Participants aged > 5 years, lesions < 100 days in duration, no facial lesions included | N/A | T1(n=96): 5% garlic cream BID q3days x 40 days; T2(n=75): placebo | N/A | Primary: % cured at 40 days | Cure defined as complete healing; definition of healing not specified | Garlic cream healed 18/96 and placebo 15/75 | 5% garlic cream was not effective in the treatment of CL | No significant differences | 26 out of 197 (13.2%); followed for 2 months | Double blind | Randomized, method unknown (full article not available) | 4 | 1 | 0 | 0 | 0 | 1 | 0.5 | 1 |
| **Salmanpour 2001 *[***[***74***](#_ENREF_74)***]*** | KET & ILMA | 64 & 36 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged > 3 years | T1(n=64): Ketoconazole 600 mg (adults) or 10 mg/kg (children) daily x 30 days | T2(n=36): MA IL q2weeks x 6-8 sessions | N/A | Primary: % cure at 6 weeks; Secondary: adverse events | Cure defined as complete re-epithelialisation of ulcer with little or no scar | Ketoconazole healed 57/64 (89%) of lesions, and ILMA healed 23/32 (72%). AE included elevated LFTs with ketoconazole and local irritation with ILMA. | Ketoconazole was more effective than ILMA in this study | No table provided (only mentioned that patients balanced, but data not in article) | Loss not mentioned; followed for 6 months | Not mentioned | Randomized, but method not explained | 4 | 1 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Esfandiarpour 2002 [**[**75**](#_ENREF_75)**]** | ALL & MA | 50 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants mean age 14, mean 1 lesion, mean 8 months duration | T1(n=50): Allopurinol 15 mg/kg PO divided TID x 3 weeks; T3(n=50): allopurinol 15 mg/kg PO divided TID x 3 weeks & MA 30 mg/kg IM x 2 weeks | N/A | T2(n=50): MA 30 mg/kg IM daily x 2 weeks | Primary: % cure; Secondary: adverse events | Cure defined as reduction of inflammation, edema, and flattening on scar | Allopurinol was associated with cure in 9/50 (18%), MA in 12/50 (24%) and Allopurinol & MA in 23/50 (46%). AE in allopurinol included nausea, heartburn, and elevated LFTs | Combined allopurinol and MA was more effective than either therapy alone, however none of these treatments demonstrated good efficacy | No significant differences | Loss not mentioned; followed for 1 month | Not mentioned | Randomized but method not explained | 3.5 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| **Momeni 2002 [**[**76**](#_ENREF_76)**]** | ALL & MA | 36 | Iran | Monoclonal antibodies or isoenzyme electrophoresis | L. major | none | Microscopy | RCT; Participants aged > 5, no prior treatments, lesion < 4 months in duration | T1(n=36): Allopurinol 20 mg/kg daily & MA 30 mg/kg IM daily x 20 days | N/A | T2(n=36): MA 60 mg/kg IM daily x 20 days | Primary: % cure at 2 months | Cure defined as all lesions healed and negative amastigotes on smears; definition of healing not specified | Low dose MA with allopurinol cured 25/36 (72%) while MA alone cured 26/36 (75%). AE included abdominal pain, nausea, skin eruption, myalgias | Combination low dose MA with allopurinol showed similar efficacy compared to full dose MA, and had less toxicity | No significant differences | 6 out of 62 (9.7%); followed for 2 months | Open | Randomized but method not explained | 5.5 | 1 | 1 | 1 | 0 | 1 | 1 | 0 |
| **Faghihi 2003 [**[**77**](#_ENREF_77)**]** | PRM & ILMA | 48 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 1–48, mean 16 years old, ≤ 3 lesions, no ulcerating lesions included | N/A | T1(n=48): 15% paromomycin sulfate in 10% urea ointment BID x 45 days; T2(n=48): MA 15g/5ml IL weekly x maximum 12 injections | N/A | Primary: % cure after 2 months; Secondary: % relapses over 1 year | Cure defined as return to normal tissue texture in < 2 months | Topical paromomycin ointment healed 8/48 (17%) of lesions at 2 months and ILMA healed 20/48 (42%). | Neither performed well, but ILMA was superior than topical paromomycin. | Groups not compared, only listed number of lesions in each group and location | loss not mentioned; followed for 12 months | Open | Randomized via a stratified blocked randomization method | 3.5 | 1 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Momeni 2003A [**[**78**](#_ENREF_78)**]** | KET | 49 & 55 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged > 5 years, lesion < 4 months in duration | N/A | T1(n=49): 2% ketoconazole cream BID x 21 days; T2(n=55): placebo cream BID x 21 days | N/A | Primary: % cure at 2 months; Secondary: adverse events | Cure defined as healed lesions by day 51 and negative amastigotes on smear | Ketoconazole cream healed 11/49 (22%) and placebo cream 6/55 (11%). AE included pruritus at lesion site. | The low response rate in patients receiving ketoconazole cream indicates that it cannot be used as the single agent. | No significant differences | 17 out of 90 (17.9%); followed for 1.5 months | Open | Randomized but method not explained | 5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 1 |
| **Momeni 2003 *B[***[***79***](#_ENREF_79)***]*** | ITR | 70 | Iran | Isoenzyme electrophoresis | L. major | none | Microscopy and/or culture | RCT; Participants aged >12 years, no prior treatment, no facial lesions, < 4 months in duration | T1(n=70): Itraconazole 7 mg/kg (max 400 mg) PO daily x 3 weeks; T2(n=70): placebo x 3 weeks | N/A | N/A | Primary: % cure at 2 months; Secondary: adverse events | Cure defined as all lesions healed with negative smears; definition of healing not specified | Cure observed in 36/51 (59%) receiving itraconazole and in 27/61 (44%) receiving placebo. | Itraconazole was not significantly more effective than placebo when given for 3 weeks | No significant differences | 9 out of 140 (6.4%); followed for 1.5 months | Double blind | Randomized, method unknown | 7 | 1 | 1 | 1 | 0 | 1 | 1 | 1 |
| **Asilian 2004B [**[**80**](#_ENREF_80)**]** | CO2 & MA | 123 & 110 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 7-70, < 5 lesions, < 4 months in duration | N/A | T1(n=123): CO2 laser (Sonic 500 machine) x 1 session & topical 2% erythromycin | T2(n=110): MA 50 mg/kg IM daily x 15 days, rest 5 days, resume for additional 15 days | Primary: % cure at 1.5 months; Secondary: speed of healing; Tertiary: scar prevention; Quaternary: adverse events | Cure defined as complete re-epithelialisation, flattening and negative amastigotes on smear | CO2 laser cured 104/111 lesions while MA cured 176/210 lesions, RR1.12 | Similar efficacy between a single session of CO2 laser and a 30 day treatment of MA | Differed in number of lesions | 59 out of 233 (25%); followed for 6 months | Not mentioned | Randomized via coin flip | 4.5 | 1 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Asilian 2003 [**[**81**](#_ENREF_81)**]** | PRM | 117 & 116 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants with single lesion, < 4 months in duration, < 5 cm in size, no prior treatment | N/A | T1(n=117): 15% paromomycin in 10% urea ointment BID x 4 weeks; T2(n=116): 15% paromomycin BID x 2 weeks followed by paraffin ointment BID x 2 weeks | N/A | Primary: % cure at 2.5 months; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete epithelialisation of lesion | 4 weeks of topical paromomycin ointment healed 58/117, while 2 weeks healed 43/116. RR 1.34. No AE reported | Higher healing rates and parasite cure were observed with 4 weeks of topical paromomycin in urea ointment | No significant differences | 87 out of 233 (37%); followed for 3.5 months | Double blind | Randomized but method not explained | 6.5 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| **Asilian 2004A [**[**82**](#_ENREF_82)**]** | CRY | 100 & 200 & 160 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants with lesions < 8 weeks in duration | N/A | T1(n=100): cryotherapy and MA IL q2weeks x 6 weeks; T2(n=200): cryotherapy q2weeks x 6 weeks; T3(n=160): MA IL q2weeks x 6 weeks | N/A | Primary: % cure at 6 months; Secondary: adverse events, remission duration, relapse rate; Tertiary: parasite cure | Cure defined as complete re-epithelialisation of ulcer with loss of edema, induration and absence of amastigotes on smear | Cryotherapy & ILMA healed 120/149 (91%) of lesions; cryotherapy healed 120/230 (57%) of lesions; ILMA healed 84/160 (56%) of lesions | Combined cryotherapy and intralesional meglumine antimoniate was more effective than either cryotherapy or ILMA alone | No significant differences | 30 out of 400 (7.5%); followed for 6 months | Not mentioned | Randomized, but method not explained | 5.5 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| **Iraji 2004 [**[**83**](#_ENREF_83)**]** | ILMA & ZnSO4 | 35 & 31 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 2-67, lesions < 12 weeks in duration, < 4 lesions | N/A | T1(n=35): MA IL q2weeks x 6 weeks; T2(n=31): 2% ZnSO4 IL q2weeks x 6 weeks | N/A | Primary: % cure at 1.5 months; Secondary: adverse events | Cure defined using the Sharquie grading system, where 4 represented total clearance of lesion and parasite | Healing at 6 weeks was noted in 84% IL Zinc Sulfate and in 60% of ILMA. AE included pain and vasovagal episodes with Zinc Sulfate and local irritation with ILMA. | No statistical difference in efficacy between IL Zinc Sulfate and ILMA. | No significant differences | 38 out of 104 (36.5%); followed for 1.5 months | Double blind | Randomized, but method not explained | 6 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| **Nilforoushzadeh 2004 (source only cochrane review)** | PRM & ILMA & CRY | 81 & 76 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 1-20, lesion < 2 months in duration, max 3 lesions | N/A | T1(n=81): MA IL biweekly x 6 weeks; T2(n=76): MA IL biweekly x 6 weeks & 15% paromomycin in 10% urea ointment BID x 4 weeks & cryotherapy q 2 weeks x 3 sessions | N/A | Primary: % cure at 2 months | Not defined | Triple therapy healed 68/81 (89.5%) while ILMA healed 57/76 (70%) at 6 weeks post treatment. | Combined cryotherapy, topical paromomycin and ILMA was more effective than ILMA alone. | No table provided (only mentioned that patients were balanced) | 53 out of 210 (25%); followed for 1.5 months | Open | Randomized, method unknown | 3.5 | 1 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| Shazad 2005 [[84](#_ENREF_84)] | PRM & ILMA | 30 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants all male soldiers, no prior treatment, 1-3 lesions total, 77% ulcerating lesions | N/A | T1(n=30): 15% paromomycin in 10% urea ointment BID x 20 days; T2(n=30): MA IL daily x 20 days | N/A | Primary: % cure at 1 month; Secondary: adverse events | Cure defined as complete re-epithelialisation of all lesions | 18/30 (60%) receiving topical paromomycin and 20/30 (66%) receiving ILMA were cured. AE included urticarial, pain, lymphadenitis, not specified to which groups | Topical paromomycin and ILMA showed similar effectiveness | Only differed in number of lesions | 38 out of 104 (36.5%); followed for 1.5 months | Open | Randomized, method unknown (full article not available) | 4 | 1 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| Asilian 2006 [[85](#_ENREF_85)] | 5-ALA & PRM | 20 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 5-59, ≤ 2 lesions of < 2 months duration, no prior treatments | N/A | T1(n=20): 10% 5-aminolaevulinic acid (5-ALA) hydrochloride cream followed by irradiation via visible red light at 100 J/cm weekly x 4 weeks; T2(n=20): 15% paromomycin in 12% MBL ointment BID x 28 days; T3(n=20): placebo ointment BID x 28 days | N/A | Primary: % cure at 2 months; Secondary: adverse events; Tertiary: parasite cure | Cure defined as loss of induration, complete re-epithelialisation, negative amastigotes smear | Cure at 2 months post-treatment occurred in 29/31(93.5%) receiving PDT, 14/31 (41%) receiving topical paromomycin, and 4/30 receiving placebo. AE included itch, burning, redness, edema, pain | PDT was more effective than topical paromomycin; both treatments were better than placebo ointment | No significant differences | 3 out of 60 (5%); followed for 2 months | Double blind | Randomized via computer-based randomization | 6 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| Firooz 2006 [[86](#_ENREF_86)] | IMQ & MA | 59 & 60 | Iran | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants age 12-60, lesion < 6 months in duration, < 5 lesions total | N/A | T1(n=59): 5% imiquimod cream 3x/week x 28 days & MA 20 mg/kg IM daily x 14 days; | T2(n=60): MA 20 mg/kg IM daily x 14 days & placebo petrolatum cream 3x/week x 28 days | Primary: % cure at 3.5 months; Secondary: adverse events | Cure defined as >75% re-epithelialisation of lesion compared to baseline | In the imiquimod/MA group 26/59 lesions were healed, while in the MA/placebo arm 24/60 were healed, RR 1.10 | No beneficial effect of combining a 4-week course of treatment with 5% imiquimod cream and a standard course of meglumine antimoniate. | No significant differences | 30 out of 119 (25%); followed for 3.5 months | Double blind | Randomized via a simple randomization block design | 6.5 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| Nilforoushzadeh 2006 [[87](#_ENREF_87)] | TCA & ILMA | 40 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 5-75, lesions < 12 weeks in duration, < 5 lesions total, no prior treatment | N/A | T1(n=40): 50% trichloroacetic acid applied q2weeks x 3 sessions; T2(n=40): MA IL weekly x 6 weeks | N/A | Primary: % cure at 6 weeks; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete re-epithelialisation of lesion | Healing at 6 weeks was 26/38 (68%) with trichloroacetic acid , 23/35 (66%) with IL MA. AE included pruritus and mild erythema with MA | Similar effectiveness between trichloroacetic acid and IL MA in this study | No significant differences | 7 out of 80 (8.7%); followed for 3 months | Open | Randomized, but method not explained | 5.5 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| Sadeghian 2006 A [[88](#_ENREF_88)] | NS & ILMA | 36 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged > 5 years, no facial lesions | N/A | T1(n=36): 5% NS IL weekly x 6-10 weeks; T2(n=36): MA IL weekly x 6-10 weeks | N/A | Primary: % cure at 6 months; Secondary: adverse events | Cure defined as re-epithelialisation, decreased induration, ulcer size, negative smear | Cure at 6 weeks was 33% with ILMA, 25% with 5% NS; cure at 6 months was 52% with ILMA and 25% with 5% NS | At end of treatment neither ILMA or IL NS was very effective; at 6 months ILMA had better efficacy than IL 5% NS | No significant differences | Loss not mentioned; followed for 6 months | Double blind | Randomized, but method not explained | 6 | 1 | 0 | 1 | 1 | 1 | 0.5 | 1 |
| Sadeghian 2006B [[89](#_ENREF_89)] | PTX & MA | 32 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 14-46, lesions < 2 months in duration | T1(n=32): Pentoxifylline 400 mg PO TID x 20 days & MA 20 mg/kg IM daily x 20 days; | N/A | T2(n=32): MA 20 mg/kg IM daily x 20 days & placebo PO TID x 20 days | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as complete improvement 3 months after treatment; definition of improvement not specified | Complete cure was observed in 81.3% in the trial group and 51.6% in the control group. No AE resulted from pentoxifylline. | Combined therapy with Glucantime and pentoxifylline is more effective than Glucantime alone (P < 0.05). | No significant differences | 1 out of 64 (1.5%); followed for 3 months | Double blind | Randomized but method not explained | 5.5 | 1 | 0 | 1 | 0 | 1 | 1 | 1 |
| Salmanpour 2006 | CRY & ILMA | 20 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged > 3 years | N/A | T1(n=20): Cryotherapy weekly x 6 weeks; T2(n=20): Cryotherapy & MA IL weekly x 6-8 weeks; T3(n=20): MA IL weekly x 6-8 weeks | N/A | Primary: % cure, time not reported | Not defined | ILMA healed 15/20 patients (75%), Cryotherapy healed 14/20 (68%) and Cryotherapy & ILMA healed 18/20 (89%) | Combined cryotherapy and ILMA had higher effectiveness than either treatment alone | Not reported | Loss not mentioned; follow-up duration not mentioned | Not mentioned | Randomized, but method not explained | 1.5 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Layegh 2007 [[90](#_ENREF_90)] | AZI & MA | 22 & 27 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 4-70, lesion < 6 months in duration | T1(n=22): Azithromycin 500 mg PO x 5 days/month, repeat monthly up to 4 months (pediatric dose 10mg/kg) | N/A | T2(n=27): MA 60 mg/kg IM daily x 20 days | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as decreased induration by >75%, full re-epithelialisation, or negative amastigotes on smear | Cure observed in 3/35 (10%) recieving azithromycin and 20/58 (34%) receiving IMMA. AE included myalgias and local erythema with IMMA, and GI intolerance with azithromycin | IMMA was more effective than azithromycin | No significant differences | 2 out of 49 (4.1%); followed for 3 months | Open | Randomized, but method not explained | 4.5 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |
| Mohebali 2007 [[91](#_ENREF_91)] | MIL & MA | 32 & 31 | Iran | PCR-RFLP and enzyme electrophoresis | L. major | none | Microscopy | RCT; Participants mean ages 20.2 and 16.8 between groups, mean < 2 lesions, no prior treatments | T1(n=32): Miltefosine 2.5 mg/kg PO daily x 28 days | N/A | T2(n=31): MA 20 mg/kg IM daily x 14 days | Primary: % cure at 3 months; Secondary: % relapse at 6 months; Tertiary: adverse events | Cure defined as complete re-epithelialisation and disappearance of induration at 3 months | Miltefosine cured 26/32 (81%) and MA cured 25/31 (81%), RR 1.01. AE included nausea, vomiting with miltefosine; mild elevation in LFTs in both groups | Both drugs are equally effective in treating CL, but early nausea and vomiting with miltefosine led to >10% withdrawal from the study. | Differed in lesion size | 5 out of 63 (8%); followed for 6 months | Open | Randomized via balanced block method | 5 | 1 | 1 |  | 1 | 0 | 1 | 0 |
| Nilforoushzadeh 2007 [[92](#_ENREF_92)] | Honey & ILMA | 50 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 7-70, lesion < 3 months in duration, no prior treatment | N/A | T1(n=50): topical honey soaked in gauze BID and MA IL weekly x 6 weeks; T2(n=50): MA IL weekly x 6 weeks | N/A | Primary: % cure at 2.5-3 months; Secondary: speed of healing | Cure defined as disappearance of induration and complete re-epithelialisation of ulcers and negative smear | Honey and ILMA healed 23/50 and ILMA healed 32/50, with RR 0.72 for the combination. | The combination of honey and ILMA was less effective than ILMA alone | No significant differences | 23 out of 100 (23%); followed for 4 months | Open | Randomized via Random allocation software | 6 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| Sadeghian 2007 [[93](#_ENREF_93)] | RFT & ILMA | 57 & 60 | Iran | Not performed | N/A | none | Microscopy | RCT, aged >5 years, no facial lesions, no prior treatment | N/A | T1(n=57): Thermotherapy weekly x 4 weeks; T2(n=60): MA IL weekly x 4 weeks | N/A | Primary: % cure at 6 months; Secondary: % relapse and adverse events | Cure assessed by examining for flattened lesion, no induration, re-appearance of epidermal creases | Heat therapy healed 46/57 (81%) of lesions, ILMA healed 52/94 (55%). AE included erythema, edema and pruritus with ILMA | Heat therapy was more effective than 4 doses of ILMA | No significant differences | Loss not mentioned; followed for 6 months | Single-blinded (examiners only) | Randomized via random number list | 5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 0.5 |
| Layegh 2009 [[94](#_ENREF_94)] | CRY & ILMA | 40 & 39 | Iran | Not performed | N/A | none | positive smear | RCT; Participants all children ≤ 13 years, lesions < 12 weeks in duration | N/A | T1(n=40): Cryotherapy weekly x 3-6 weeks; T2(n=39): MA IL x 4-6 weeks | N/A | Primary: % cure | Cure defined as complete re-epithelialisation and negative amastigotes on smear | ITT analysis: cryotherapy better than ILMA. Cryotherapy cured 52.5% vs 25% with ILMA. | Because of its simplicity, lower cost, low rate of serious complications, and greater tolerability, cryotherapy is an appropriate treatment for children | No significant differences | 7 our of 79 (8.8%); followed for 6 months | Open | Randomized, but method not explained | 5.5 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| Emad 2011 [[95](#_ENREF_95)] | FLU | 60 | Iran | PCR-RFLP | L. major | none | Method not mentioned | RCT; Participants aged > 12, lesions < 4months in duration | T1(n=60): Fluconazole 100 mg PO BID x 6 weeks; T2(n=60): fluconazole 200 mg PO BID x 6 weeks | N/A | N/A | Primary: % cure at 1.5 months; Secondary: adverse events | Cure defined as complete re-epithelialisation | In T1, no patients showed cure at 4 weeks, but 29 of 60 patients (48.3%) were cured by 6 weeks. In T2, 38 of 58 patients (65.5%) were cured in 4 weeks and an additional 9 patients (15.5%) at 6 weeks. AE included increased LFTs, GI symptoms in T2. | Higher doses of fluconazole demonstrated better efficacy in the treatment of CL. | No significant differences | 2 out of 120 (1.7%); followed for 1.5 months | Open | Randomized but method not explained | 5.5 | 1 | 1 | 0 | 1 | 1 | 1 | 0 |
| Layegh 2011 [[96](#_ENREF_96)] | MA | 56 | Iran | Endemic, speciation not performed | L. tropica | none | Microscopy | Not an RCT, prospective observational study; Participants divided into groups based on age (< or > 15 years), lesions < 3 months in duration | N/A | N/A | T1(n=56): MA 20 mg/kg IM daily x 20 days (all participants aged ≤ 15 years); T2(n=56): MA 20 mg/kg IM daily x 20 days (all participants aged > 15 years) | Primary: % cure at 1.5 months | Cure defined as complete re-epithelialisation with negative amastigotes on smear | Per-protocol analysis showed a significantly lower response in the children group 20 and 45 days after initiation of the treatment (P = 0.0001) | Children with CL do not respond as well as adults when treated with IMMA | Significant difference in age between treatment arms | 12 out of 112 (11%); followed for 1.5 months | Open | Not randomized | 3.5 | 1 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| Meymandi 2011 [[97](#_ENREF_97)] | CO2 & CRY & ILMA | 80 | Iran | Endemic, speciation not performed | L. tropica | none | Microscopy | RCT; Participants aged 7–60 years | N/A | T1(n=80): CO2 laser therapy x 3-5 sessions; T2(n=80): Cryotherapy biweekly x 12 weeks & MA IL biweekly x 12 weeks | N/A | Primary: % cure; Secondary: adverse event | Cure defined as total re-epithelialisation of the lesion with negative amastigotes on smear | Cure rates in T1 were 97% vs 78% in T2. Similar rates AE | CO2 laser was more effective for CL than combined MA IL with cryotherapy | No significant differences | 31 out of 160 (19.3%); followed for 4 months | Not mentioned | Randomized via randomization tables | 5.5 | 1 | 0 | 1 | 1 | 1 | 0.5 | 0 |
| Dastgheib 2012[[98](#_ENREF_98)] | AZI & ALL & MA | 36 & 35 | Iran | Endemic, PCR on only negative smears | L. major | none | Microscopy | RCT; Participants aged > 12, lesion < 3 months in duration, < 5 lesions total | T1(n=36): Azithromycin 10 mg/kg (max 500 mg) PO daily and allopurinol 10 mg/kg (max 800 mg) PO daily x 2 months | N/A | T2(n=35): MA 20 mg/kg IM daily x 20 days | Primary: % cure at 2 months | Cure defined as complete re-epithelialisation | Cure observed in 39% in T1 and 40% in T2 at 2 months post end of treatment. AE included GI intolerance | Comparable efficacy with both regimens, neither highly efficacious. | No significant differences | 14 out of 86 (16%); followed for 2 months | Open | Randomized via even and odd number allocation | 5.5 | 1 | 0 | 1 | 1 | 1 | 0.5 | 0 |
| Jowkar 2012 [[99](#_ENREF_99)] | CRY & NaNO2 | 36 & 27 | Iran | PCR-RFLP | L. tropica (89%) | L major (11%) | Microscopy | RCT; Participants aged > 11 years, lesions < 4 months in duration | N/A | T1(n=36): Cryotherapy weekly and 2 creams (3% salicylic and 3% Na nitrite); T2(n=27): Cryotherapy weekly and 2 creams (3% salicylic with placebo) | N/A | Primary: % cure; Secondary: adverse events | Cure defined as complete re-epithelialisation of the lesion | 83% cure in T1 vs 74% with placebo. More local AE in the Na nitrite group | No more effectiveness from combining a 12-week treatment with 3% nitric oxide cream and weekly cryotherapy in comparison with cryotherapy and placebo | No significant differences | 37 out of 100 (37%); followed for 3 months | Double blind | Randomized, but method not explained | 7 | 1 | 1 | 1 | 1 | 1 | 0.5 | 1 |
| Khatami 2012 [[100](#_ENREF_100)] | MIL & ILMA | 63 & 75 | Iran | Not performed | N/A | none | Microscopy | RCT; Participants aged 12-50 | T1(n=63): Miltefosine 2.5 mg/kg PO daily x 4 weeks; | T2(n=75): MA IL x 14 days | N/A | Primary: % cure at 2 months; Secondary: adverse events | Not defined | No difference in cure rates. More AE in T1 (p=0.001) | Cure with miltefosine vs ILMA not different. Miltefosine has more AE | Not reported | 73 out of 138 (53%); followed for 2 months | Open | Randomized, method unknown (full article not available) | 3.5 | 1 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| Maleki 2012 [[101](#_ENREF_101)] | ZnSO4 & ILMA | 24 & 10 | Iran | Not performed | none | none | Microscopy | RCT; Participants aged 7-60, ≤ 3 lesions, < 12 weeks in duration, only "dry" lesions | N/A | T1(n=24): 2% ZnSO4 IL 2x/week x 2 weeks; T2(n=10): MA IL weekly x 6 weeks | N/A | Primary: % cure at 8 weeks | Cure defined as per the Sharquie score: 1-5 with 5 representing complete healing and negative smear, and 1 representing partial reduction of erythema and edema | Complete cure observed in 33% receiving ZnSO4, and 80% in those receiving ILMA. Many local AE. | ILMA is superior to IL ZnS04. AE seen with both modalities | No significant differences | 11 out of 45 (24%); followed for 2 months | Open | Randomized, but method not explained | 4 | 0 | 0 | 1 | 1 | 1 | 0.5 | 0 |
| Nilforoushzadeh 2012 [[102](#_ENREF_102)] | TCA | 16 | Iran | Endemic, speciation not performed | L. major | none | Microscopy | Not an RCT, case series; Participants aged 6-60, lesions < 5 cm, < 12 weeks in duration | N/A | T1(n=16): 5% trichloroacetic acid (TCA) cream applied BID x 8 weeks | N/A | Primary: % cure at 8 weeks | Cure defined as complete re-epithelialisation and negative amastigotes on smear | 16/16 cured at 8 weeks. No withdrawals due to AE | Decreasing the scar size and the low cost are two promising aspects in introducing 5% TCA cream as a potential alternative for intralesional Glucantime. | Single arm study | Loss not mentioned; followed for 2 month | Open | Not randomized | 2.5 | 0 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Khatami 2013 [**[**100**](#_ENREF_100)**]** | ILMA | 26 & 26 & 31 | Iran | Endemic, speciation not performed | L. major | none | Microscopy and/or culture | RCT; Participants aged 12-60, lesions < 3 months in duration, < 5 lesions, < 5 cm | N/A | T1(n=26): MA IL x 6 weeks; T2(n=26): MA IL & non-silver dressing x 6 weeks; T3(n=31): MA IL & silver dressing x 6 weeks | N/A | Primary: % cure a 5 months; Secondary: adverse events | Cure defined as >75% re-epithelialisation of the lesion | Overall cure at 10 weeks after initiation of therapy was 36-42%. Only relapse was in ILMA & silver dressings. AE included local pruritus, burning, edema. | It could not be demonstrated that the efficacy of ILMA was improved by either dressing. | Differed in male/female distribution | 10 out of 83 (12%); followed for 5 months | Double blind | Randomized via computer generated randomization | 5.5 | 1 | 0 | 1 | 1 | 0 | 0.5 | 1 |
| **Mohammadzadeh 2013 [**[**103**](#_ENREF_103)**]** | ILMA & MA | 38 & 95 | Iran | Endemic, speciation not performed | L. major | L. tropica | Microscopy | Not an RCT, case series; Participants mean age 30.8. T1 included lesions < 3 cm, ≤ 3 lesions. T2 included lesions > 3 cm, >3 lesions, or lesions located on the face or joints. | N/A | T1(n=38): MA IL 2x/week x 6-15 sessions | T2(n=95): MA 10-20 mg/kg IM in 2-3 divided doses x 14 days (L. major) or x 20 days (L. tropica) | Primary: % cure at 1 month | Cure defined as negative smear, and reduced induration | The failure rate for patients treated with one course of Glucantime was 22.6% overall. | The only association with failure was previous exposure to MA | Differed in lesion size and number | 16 out of 133 (12%); followed for 1 month | Open | Not randomized | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |
| **Goyonlo 2014 [**[**104**](#_ENREF_104)**]** | ILAMB | 93 | Iran | Not performed | N/A | none | Microscopy or smear | Not an RCT, prospective study. Participants mean age 20.8 years, lesions mean ≥6 months in duration, 85% unresponsive to MA IL | N/A | T1(n=93): Amphotericin B IL weekly until lesion cure | N/A | Primary: % cure; Secondary: adverse events | Cure defined as more than 90% reduction in size and induration of the lesions. | At 12 weeks, 61.4% were recovered completely, 21.6% had partial remission, and 17% had less than 60% reduction. Recurrence in 9%. No significant AE's. | Weekly intralesional injection of amphotericin B looks promising, considering that most of the patients in this study were resistant to antimoniates. | Single treatment arm | Loss not mentioned; followed for 3 months | Open | Not randomized | 2.5 | 1 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Jaffary 2014 [**[**105**](#_ENREF_105)**]** | Yarrow & ILMA | 30 | Iran | Endemic | L. major | none | Microscopy and culture | RCT; participants mean age 25 years, predominantly male, mean 1.5 lesions, 3 months in duration | N/A | T1(n=30): 5% yarrow (Achilles millefolium) gel BID & MA 20mg/kg IL weekly x 4 weeks; T2(n=30): placebo gel BID & MA 20mg/kg IL weekly x 4 weeks | N/A | Primary: % cure at 3 months; Secondary: adverse events | Not defined, only mentioned that cure was assessed by visual analog scale | No significant difference in complete and relative cure rates between the two groups (P = 0.35) using Visual Analog Scale (VAS). AE included local erythema, pruritus, and increased wound secretion in T1. | There is no significant difference in cure rates of lesions between yarrow and placebo topical gels as an adjuvant drugs with intralesional Glucantime. | No significant differences | Loss not mentioned; followed for 3 months | Double blind | Randomized via a random allocation computer software | 5.5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 1 |
| **Nilforoushzadeh 2014 [**[**106**](#_ENREF_106)**]** | CO2 | 60 & 60 | Iran | Not performed | N/A | none | Not specified | RCT; Participants age 6-45 (mean 27), mean 1 lesion | N/A | T1(n=60): Ablative CO2 laser x 1 session; T2(n=60): Fractional CO2 laser q3weeks x 6 sessions | N/A | Primary: % cure at 6 months; Secondary: adverse events | Scar depth was monitored, with a reduction of >75% consistent with very good improvement. | Use of ablative CO2 demonstrated 44% improvement at 6 months vs. 76.7%  with the fractional laser. AE were similar (rash). | Fractional CO2  laser therapy  is better than ablative CO2  laser in diminishing size of leishmaniasis scars. | Not compared | Loss not mentioned; followed for 6 months | Single blinded | Randomized but method not explained | 2.5 | 1 | 0 | 0 | 0 | 0 | 0.5 | 0.5 |
| **Sharquie 1997 *[***[***107***](#_ENREF_107)***]*** | ZnSO4 & NS | 19 & 17 & 18 & 9 | Iraq | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants aged 3 months to 65 year, lesions < 12 weeks in duration, mean 2 lesions | N/A | T1(n=19): 2% ZnSO4 IL; T2(n=17): 7% NS IL; T3(n=18): SSG IL; T4(n=9): no intervention | N/A | Primary: % cure at 1.5 months; Secondary: speed of healing, scar prevention, adverse events | Cure defined as marked and total clearance: total clearance defined as negative smear, and marked defined as reduction of 60% in lesion and negative smear | IL ZnS04 healed 36 lesions (96%), IL hypertonic NS healed 34 (85%), IL SSG healed 31 (89%) and the no intervention group was associated with no healing. | The results show that the three treatments gave comparable cure rates by the end of the follow-up period. However, zinc sulphate gave a high cure rate (94.8%) usually with a single injection. | No significant differences | 22 out of 85 (26%); followed for 2 months | Open | Randomized via simple random distribution | 4.5 | 0 | 0 | 1 | 1 | 1 | 0.5 | 0 |
| **Sharquie 2011** | CRY & ILMA | 100 & 200 & 160 | Iraq | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants with lesions < 12 weeks in duration, > 5 lesions, size > 4 cm, no prior treatment | N/A | T1(n=100): Cryotherapy and MA IL q2weeks x 6 weeks; T2(n=200): Cryotherapy q2weeks x 6 weeks; T3(n=160): MA IL q2weeks x 6 weeks | N/A | Primary: % cure; Secondary: adverse events; Tertiary: parasite cure | Cure defined as complete re-epithelialisation of lesion with loss of edema, induration and absence of amastigotes | Cryotherapy and ILMA healed 120 of 149 (91%) lesions, cryotherapy healed 120 of 230 (57%) lesions and ILMA healed 84 of 160 (56%) lesions. | Combined cryotherapy and intralesional meglumine antimoniate was more effective than either cryotherapy or ILMA alone | No significant differences | 30 out of 400 (7.5%); followed for 6 months | Not mentioned | Randomized, method unknown | 6 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| **Sharquie 2001 [**[**108**](#_ENREF_108)**]** | ZnSO4 | 39 & 37 & 39 & 15 | Iraq | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants aged 4 months to 65 years, lesion < 3 months in duration, size > 4 cm, no prior treatment | T1(n=39): ZnSO4 2.5 mg/kg PO divided TID x 45 days; T2(n=37): ZnSO4 5 mg/kg PO divided TID x 45 days; T3(n=39): ZnSO4 10 mg/kg PO divided TID x 45 days T4(n=15): no intervention | N/A | N/A | Primary: % cure at 2 months; Secondary: speed of healing, scar prevention, adverse events | Cure defined as total clearance of lesion, negative amastigotes on smear; definition of clearance not specified | ZnSO4 2.5mg/kg cured 16/39 (41%), 5mg/kg cured 23/37 (62%), and 10mg/kg cured 29/39 (74%). T4 had no participants who had cured lesions. AE included nausea, vomiting with higher doses, macular rash | There appeared to be a dose effect using ZnSO4 with higher doses associated with higher rates of cure (74% ITT), but more GI toxicity. | No significant differences | 26 out of 130 (20%); followed for 1.5 months | Open | Randomized, but method not explained | 3 | 0 | 0 | 1 | 0 | 1 | 0.5 | 0 |
| **Enk 2014 [**[**109**](#_ENREF_109)**]** | 5-ALA & PDT | 31 | Israel | PCR | L tropica | L major | Microscopy or smear | Not an RCT, case series. Participants with > 1 lesion, < 1.5 cm in size | N/A | T1(n=31): 16% methyl aminolevulinate applied to lesion followed by Daylight-activated photodynamic therapy (administered either at home or in hospital) for 2.5 hours weekly until cure | N/A | Primary: % cure | Cure defined as flattening of lesion with complete epithelialisation, and microbiological confirmation. | The overall cure rate for hospital-based and self-administered DA-PDT was 88.9% (ITT cure rate 77.4%); hospital-based treatment demonstrated 85.7% cure, and self-administered treatment 92.3% cure. | DA-PDT is effective in the treatment of CL caused by L. major and L. tropica. The majority of the patients were treated according to a self-administered protocol, suggesting that DA-PDT can be adopted in areas lacking technological infrastructure. | Data not yet available [Epub ahead of print] | 4 out of 33 (12%); followed for 18 months | Open | Not randomized | 4.5 | 1 | 1 | 1 | 1 | 0 | 0.5 | 0 |
| **Solomon 2014 *[***[***110***](#_ENREF_110)***]*** | AMB & ILSSG | 21 & 24 | Israel | PCR | L. tropica | none | Microscopy | Not an RCT, retrospective case series. Participants aged 1-15 years, mean 2.6 lesions, 36 had received topical therapy prior to systemic therapy | N/A | T1(n=21): SSG IL x 1-5 injections | T2(n=24): Liposomal amphotericin B 3-5 mg/kg IV daily x 5 days with 6th dose on day 10 of treatment | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as 100% re-epithelialisation of the ulcer (or of the non-ulcerative lesions, regression of the lesion) within 3 months after treatment. | Of those receiving IL SSG, 14/21 (66.6%) were cured within 3 months. AE included injection site erythema and edema. Among the L-AMB-treated patients, 18 (75%) showed a complete response and 2 (8.3%), a partial response. AE included increased LFTs and leukopenia. | In our experience, liposomal amphotericin B treatment in children is safe and effective and is required for a considerably shorter duration than treatment with pentavalent antimony. | Not compared | No losses; followed for 3 months | Open | Not randomized | 4 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |
| **Al-Fouzan 1991 [**[**111**](#_ENREF_111)**]** | ITR | 15 & 9 | Kuwait | Not performed | N/A | none | Microscopy | RCT; Participants aged 12-52, lesion duration 1-14 months | T1(n=15): Itraconazole 200 mg PO BID x 6-8 weeks; T2(n=9): placebo PO BID x 6-8 weeks | N/A | N/A | Primary: % cure at 2 months; Secondary: AE, % recurrence | Not defined | Cure observed in 11/15 (73%) receiving Itraconazole, and in 0% receiving placebo, RR 14.38. AE included nausea, headache, mild increased LFTs | In this small study, itraconazole was markedly superior to placebo, and associated adverse effects were mild | Partially reported | Loss not mentioned; followed for 2 months | Not mentioned | Randomized, method unknown (full article not available) | 2 | 0 | 0 | 1 | 0 | 0 | 0.5 | 0 |
| **Alsaleh 1995 [**[**112**](#_ENREF_112)**]** | KET | 18 & 15 | Kuwait | Not performed | N/A | none | Microscopy | RCT; Participants aged 14-66, 1 to 8 lesions | T1(n=18): Ketoconazole 600 mg PO x 6 weeks or until cure; T2(n=15): Ketoconazole 800 mg PO x 6 weeks or until cure | N/A | N/A | Primary: % cure; Secondary: % recurrence, adverse events | Cure defined as >90% re-epithelialisation, decreased size and inflammation | Ketoconazole 600 mg/day cured 80% and Ketoconazole 800 mg/day cured 82%. AE included elevated triglycerides, nausea, vomiting | In this small study, ketoconazole was well tolerated and there was no difference in efficacy between dosages | Differed in lesion duration | 7 out of 33 (21%); followed for 6 months | Open | Randomized, but method not explained | 3 | 0 | 0 | 1 | 1 | 0 | 0.5 | 0 |
| **Mujtaba 1999 [**[**113**](#_ENREF_113)**]** | ILMA | 49 & 55 | Pakistan | Not performed | N/A | none | Microscopy | RCT; Participants predominantly pediatric, average 1-2 lesions, ≤5 lesions total | N/A | T1(n=49): MA IL weekly x 8 weeks or until cure; T2(n=55): MA IL q 2 weeks x 8 weeks or until cure | N/A | Primary: % cure at 2 months; Secondary: speed of healing, adverse events, scar prevention | Cure defined as 100% improvement; improvement not specified | Healing at 2 months post treatment was 102/11(92%) for weekly ILMA, and 89/104 (86%) for every 2 weeks ILMA; RR 1.07 | ILMA is effective and can be given at 2 week intervals with similar Responses to weekly. AE included transient pain at the injection site | No significant differences | 8 out of 104 (7.7%); followed for 2 months | Open | Randomized, but method not explained | 4.5 | 1 | 0 | 1 | 0 | 1 | 1 | 0 |
| **Mashood 2001 [**[**114**](#_ENREF_114)**]** | ALL & SSG | 20 | Pakistan | Not performed | N/A | none | Microscopy | RCT; Participants all male soldiers, aged 20-40, no prior treatment | T1(n=20): allopurinol 20 mg/kg divided TID or QID x 15 days | N/A | T2(n=20): SSG 20 mg/kg IV daily x 15 days | Primary: % cure at end of treatment; Secondary: adverse events | Cure defined as 80% decrease in size of lesion or re-epithelialisation | Cure observed in 17/20 (85%) receiving SSG and 14/20 (70%) with allopurinol. AE included nausea, vomiting, anorexia, myalgias, increased LFTs, and rash | Both treatments were associated with good efficacy. Allopurinol is an effective treatment of CL in Pakistan | No significant differences | Loss not mentioned; followed for 3 months | Not mentioned | Randomized, method unknown (full article not available) | 4 | 0 | 0 | 1 | 1 | 1 | 0.5 | 0 |
| **Munir 2008 [**[**115**](#_ENREF_115)**]** | ILMA & MA | 20 | Pakistan | Speciation method not mentioned | L. tropica | none | Microscopy | RCT; Participants aged 12-55, lesions < 2 months in duration, no prior treatment | N/A | T2(n=20): MA IL daily x 21 days & MA 20 mg/kg IM daily x 21 day | T1(n=20 each): MA 20 mg/kg IM daily x 21 days; T3(n=20): untreated controls | Primary: % cure at 3 months | Cure defined as absence of exudate, erythema, induration, or amastigotes on smear | Cure was observed in 55% in T1, 75% in T2, and 10% in T3. AE included a case of cardiomyopathy secondary to IMMA | Combination treatment with IL and IM MA is more efficacious than IM MA alone | No significant differences | No losses; followed for 3 months | Open | Randomized but method not explained | 3.5 | 0 | 0 | 1 | 0 | 1 | 1 | 0 |
| **Larbi 1995 [**[**116**](#_ENREF_116)**]** | MIC & CLO | 27 & 31 | Saudi Arabia | Not performed | N/A | none | Microscopy | RCT; Participants aged 1-52, lesions mean 2 month duration | N/A | T1(n=27): 2% miconazole cream BID x 30 days; T2(n=31): 1% clotrimazole cream BID x 30 days | N/A | Primary: % cure; Secondary: adverse events | Cure defined as lesions completely healed and parasite smear negative; definition of healing not specified | Cure occurred with 0/62 in those receiving 2% miconazole cream, and 14/89 (16%) with 1% clotrimazole cream. No AE. | Neither topical antifungal cream was effective. | No significant differences | 4 out of 58 (6.9%); followed for 1 month | Double blind | Randomized via a table of random numbers | 5.5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 1 |
| **Alkhawajah 1997 [**[**117**](#_ENREF_117)**]** | MA | 40 | Saudi Arabia | Not performed | N/A | none | Microscopy | RCT; Participants aged 13-42, predominantly male, 1-3 lesions, ≤ 6 months in duration, no prior treatment | N/A | T2(n=40): MA IL q 2 days x 30 days | T1(n=40): MA 15 mg/kg (max 850 mg) IM daily x 6 days/week for a total of 12 injections | Primary: % cure at 1 month; Secondary: adverse events, scar prevention | Cure defined as lesions completely healed and negative amastigotes on smear; definition of healing not specified | 46 (68%) of the 68 lesions of those treated with IMMA had healed completely, compared to 48/66 (73%) lesions of those treated with ILMA | Similar efficacy was observed using 12 doses of IMMA or daily ILMA for a month | No significant differences | 13 out of 80 (16%); followed for 1 month | Single blind (examiner) | Randomized but method not explained | 4 | 1 | 0 | 1 | 0 | 1 | 0 | 0.5 |
| **Alrajhi 2002 [**[**118**](#_ENREF_118)**]** | FLU | 106 & 103 | Saudi Arabia | Isoenzyme electrophoresis | L. major | none | Microscopy and/or culture | RCT; Participants aged > 12, predominantly male, no facial or ear lesions | T1(n=106): Fluconazole 200 mg PO daily x 6 weeks; T2(n=103): placebo 200 mg daily x 6 weeks | N/A | N/A | Primary: % cure at 3 months; Secondary: adverse events | Cure described as complete healing; definition of healing not specified | Fluconazole cured 59% vs 22% with placebo. Time to healing was 8.5 weeks in fluconazole and 11.2 weeks for placebo. AE were not described | Fluconazole was safe and hastened healing in 37% as compared to placebo. | No significant differences | 64 out of 209 (31%); followed for 12 months | Double blind | Randomized via random-number table | 6.5 | 1 | 1 | 1 | 0 | 1 | 0.5 | 1 |
| **Jaffar 2006 [**[**119**](#_ENREF_119)**]** | RIF | 46 & 16 | Saudi Arabia | Not performed | N/A | none | Microscopy | RCT; Participants aged 3-65, lesions mean 2.6 months in duration, 30% facial lesions | T1(n=46): Rifampin 10 mg/kg divided BID x 4-6 weeks; T2(n=16): placebo BID x 4-6 weeks | N/A | N/A | Primary: % cure at 3 months; Secondary: % recurrence, adverse events | Cure defined as complete healing at the end of 3 months; definition of healing not specified | Rifampin cured 46% and placebo cured 19%, RR 2.43. AE included elevated LFTs | Rifampin compared to placebo showed modest efficacy. | Not reported | 21 out of 62 (34%); followed for 3 months | Double blind | Randomized, but method not explained | 3 | 0 | 0 | 1 | 0 | 0 | 0.5 | 1 |
| **Ranawaka 2010 [**[**120**](#_ENREF_120)**]** | NS & ILSSG | 87 & 67 | Sri Lanka | PCR, culture not routinely done | L. donovani | none | Microscopy | RCT, study of safety and efficacy of IL NS 7% vs ILSSG; Participants mean age 32 years | N/A | T1(n=87): 7% NS IL weekly x 3 weeks, then q 2 weeks x 2 sessions, then monthly until cure; T2(n=67): SSG IL weekly x 3 sessions, then q 2 weeks x 2 sessions, then monthly until cure | N/A | Primary: % cure | Cure defined as clearance of lesion without palpable lesion | 100% cure with IL SSG (1-6 injections) vs 61% cure with hypertonic saline (1-10 injections). No systemic AE; local pain and hyperpigmentation | IL SSG was more efficacious than IL hypertonic saline. | No significant differences | 7 out of 154 (4.5%); followed for 18 months | Double blind | Randomized, but method not explained | 6 | 1 | 0 | 1 | 0 | 1 | 1 | 1 |
| **Ranawaka 2011 [**[**121**](#_ENREF_121)**]** | NO | 65 | Sri Lanka | Endemic, speciation not performed | L. donovani | none | Microscopy | Not an RCT, single arm study; Participants aged 6-71, lesions 1-36 months in duration | N/A | T1(n=65): Liquid nitric oxide weekly x 1-3 weeks, then q2weeks x 4-5 weeks, then monthly until cure | N/A | Primary: % cure; Secondary: time to cure; Tertiary: adverse events | Cure defined as clearance of lesion without palpable lesion; definition of clearance not specified | 91.7% cure within 1-7 sessions, mean 3.5 sessions. AE included local pain, ulceration and secondary infection | Liquid nitric oxide is an effective alternative to the historical use of IL antimonials | Single arm study | 5 out of 65 (8%); followed for 6 months | Open | Not randomized | 3 | 1 | 0 | 1 | 0 | 0 | 1 | 0 |
| **Ranawaka 2015 *[***[***122***](#_ENREF_122)***]*** | NS & ILSSG | 170 & 192 & 82 | Sri Lanka | Not performed | L. donovani | none | Microscopy or smear | RCT; Participants aged 14 months to 88 years (mean 32.7), mean 1 lesion | N/A | T1(n=170): SSG IL up to 7 injections; T2(n=192): 10% NS IL weekly up to 10 injections; T3(n=82): 15% NS IL weekly up to 10 injections | N/A | Primary: % cure at 18 months; Secondary: adverse effects; Tertiary: duration of treatment | Cure defined as >80% re-epithelialisation of the lesion and parasitological cure. | IL SSG demonstrated 96.3% cure with 3.6 injections (6 weeks of treatment), 10% NS demonstrated 93.0% cure with mean 5.28 injections (9.3 weeks of treatment), and 15% NS demonstrated 93.6% cure with mean 5.3 injection (11 weeks of treatment). AE included cutaneous necrosis in 30.6% receiving 15% hypertonic saline. | This study found 10% HS to be an effective and safe alternative to SSG. Treatment with HS at concentrations of 15% or above was not safe as a result of cutaneous necrosis. | Data not yet available [Epub ahead of print] | 17 out of 444 (3.8%); followed for 18 months | Single blinded | Randomized via 2:2:1 ratio | 5.5 | 1 | 0 | 1 | 1 | 0 | 1 | 0.5 |
| **Lynen 1992 [**[**123**](#_ENREF_123)**]** | BER & SAV | 35 | Sudan | Not performed | N/A | none | Microscopy | RCT; Participants all school children, ulcerating lesions, predominantly lower extremity lesions | N/A | T1(n=35): Berelin (1.05g diminazene aceturate in 2.36 granulate) applied daily except Fridays x 50 days; T2(n=35): Savlan (cetrimide 15% & chlorhexidine 1.5%) applied daily except Fridays x 50 days | N/A | Primary: % cure; Secondary: adverse events | Cure defined as skin lesion closed with scar tissue | Healing was seen in 28/35 (80%) with Berelin and 20/35 (57%) with Savlan. AE included extreme drying of skin and ulceration with Berelin, and slight burning and drying with Savlan | Berelin demonstrated better cure rates over wound care with Savlan washing. | No significant differences | 8 out of 70 (11.4%); followed for 2.5 months | Single blind (examiner) | Randomized, but method not explained | 5 | 1 | 0 | 1 | 0 | 1 | 0.5 | 0.5 |
| **Harms 1991 *[***[***53***](#_ENREF_53)***]*** | ILMA & IFN-γ | 20 | Syria | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants aged 6-60, up to 3 lesions | N/A | T1(n=20): MA IL weekly x 5 weeks; T2(n=20): Lyophilized rIFN-γ 25ug (1 mL) IL weekly x 5 weeks | N/A | Primary: % cure at 1 month; Secondary: adverse events; Tertiary: parasite cure | Cure defined as lesions completely healed with smooth scar and parasite smear negative; definition of healed not specified | Cure observed in 29/38 lesions (76%) receiving ILMA and 1/37 lesions (3%) for rIFNγ . AE with ILMA included pain and local. AE with IFN include pain and headache (1/20) | ILMA was more effective than rIFNγ, which had no treatment effect | No significant differences | Loss not mentioned; followed for 2.5 months | Open | Randomized via random numbers table | 3.5 | 0 | 0 | 1 | 0 | 1 | 0.5 | 0 |
| **Dandashli 2005 [**[**124**](#_ENREF_124)**]** | FLU | 46 & 19 | Syria | Performed, but method not mentioned | L. tropica | none | Not specified | RCT; no participant demographics provided | T1(n=46): fluconazole 200 mg PO daily x 6 weeks; T2(n=19): placebo PO daily x 6 weeks | N/A | N/A | Primary: % cure; Secondary: adverse events | Cure defined as complete recovery; definition of recover not specified | Fluconazole cured 28.4% and placebo cured 9.8%. AE were mild | A six week course of fluconazole is a safe and useful treatment for CL caused by *L. tropica*. | Not reported | 14 out of 79 (18%); unknown follow-up time | Double blind | Randomized, but method not explained | 2 | 0 | 0.5 | 0 | 0 | 0 | 0 | 1 |
| **Ben Salah 1995 [**[**125**](#_ENREF_125)**]** | PRM | 57 & 58 | Tunisia | Isoenzyme electrophoresis | L. major | none | Microscopy and/or culture | RCT; Participants aged 2-60, single lesion, no prior treatment, lesions <5cm size and <4 months in duration | N/A | T1(n=57): 15% paromomycin in 10% urea BID x 14 days; T2(n=58): placebo ointment (10% urea in soft white paraffin) BID x 14 days | N/A | Primary: % cure at 2.5 months; Secondary: adverse events | Cure defined as 50% reduction in lesion, some re-epithelialisation by day 45, and complete re-epithelialisation by day 105 | Cure was seen in 40/57 receiving paromomycin and 40/58 receiving placebo, RR1. AE included local inflammation, rash, pain, redness in the paromomycin arm. | Topical paromomycin was no better than placebo. There appeared to be high rates of self cure in this study | No significant differences | 17 out of 132 (13%); followed for 3.5 months | Double blind | Randomized via random numbers allocation | 7.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 1 |
| **Ben Salah 2009 [**[**126**](#_ENREF_126)**]** | PRM | 49 & 41 | Tunisia | Isoenzyme electropheresis or PCR | L. major (97%) | L. tropica, L. infantum | Microscopy and/or culture | RCT, multi-center study; Participants aged 5-75, ulcerating lesions, no previous treatments in last 3 months, < 5 lesions | N/A | T1(n=49): Paromomycin in gentamicin ointment applied BID x 20 days; T2(n=41): placebo cream applied BID x 20 days | N/A | Primary: % cure at 6 months | Cure defined as complete re-epithelialisation by day 50 or >50% re-epithelialisation at day 50 with full epithelialisation by day 100 | Cure observed in 94% receiving paromomycin with gentamicin ointment, vs 71% in those receiving placebo. No significant AE. | Paromomycin with gentamicin ointment is a simple, safe, and effective option for CL due to L. major. | Differed in age | 2 out of 92 (2.2%); followed for 6 months | Double blind | Randomized via 1:1 computer algorithm | 7 | 1 | 1 | 1 | 1 | 0 | 1 | 1 |
| **Ben Salah 2013 [**[**127**](#_ENREF_127)**]** | PRM | 125 | Tunisia | Performed, but method not mentioned | L. major | none | Microscopy and/or culture | RCT; Participants aged 5-65, ulcerating lesions, < 5 lesions | N/A | T1(n=125): Paromomycin in gentamicin (WR279,396) applied daily x 20 days; T2(n=125): Paromomycin alone applied daily x 20 days; T3(n=125): Vehicle control daily x 20 days | N/A | Primary: % cure | Cure defined as at least 50% decrease in size of index lesion by day 42, with complete re-epithelialisation by day 98 | Cure observed in 81% for T1, vs 82% for T2, vs 58% for T3. Similar cure rate between T1 and T2 at 42 days. AE mostly local site irritation | Paromomycin alone or paromomycin combined with gentamicin are both effective for ulcerative CL due to L. major | No significant differences | 5 out of 375 (1.3%); followed for 6 months | Open | Randomized but method not explained | 6 | 1 | 0.5 | 1 | 1 | 1 | 1 | 0 |
| **Ozgoztasi 1997 [**[**128**](#_ENREF_128)**]** | KET & PRM | 40 & 32 | Turkey | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants aged ≤ 10 years, predominantly facial lesions | T2(n=32): Ketoconazole 400 mg PO daily x 30 days | T1(n=40): 15% paromomycin in 12% MBCL in soft white paraffin BID x 15 days | N/A | Primary: % cure at 1 month; Secondary: adverse events | Cure defined as complete healing of lesions; definition of healing not specified | Cure observed in 15/35 (43%) receiving paromomycin and in 0/32 receiving ketoconazole. No AE mentioned. | In this study topical paromomycin was more effective that oral ketoconazole, although both treatments were poorly effective | No significant differences | Loss not mentioned; followed for 1 month | Open | Randomized but method not explained | 3.5 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| **El-Sayed 2010 [**[**129**](#_ENREF_129)**]** | KET & ILSSG & SSG | 10 | Yemen | Not performed | N/A | none | Microscopy and/or culture | RCT; Participants aged 12-50, lesions 2-8 months in duration | T3(n=10): Ketoconazole 200 mg PO TID x 4 weeks & SSG IL q 2 days x 3 sessions | T1(n=10): SSG IL q 2 days x 3 sessions | T2(n=10): SSG 20 mg/kg IM q 2 days x 3 sessions & SSG IL q 2 days x 3 sessions | Primary: % cure at 3 months; Secondary: adverse events | Cure defined as complete re-epithelialisation, no edema, induration and negative amastigotes on smear | Cure observed in 58% in T1, 93% in T2, and 92% in T3. AE included local irritation. | Combination of IL SSG and either ketoconazole or SSG is better than IL SSG alone. | No significant differences | No losses; followed for 6 months | Open | Randomized but method not explained | 4.5 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Explanation for each Section** | | | | | | | | | |
| **Study Title** | **Intervention** | **Study Publication Date** | **Number** | **Number Score** | **Country** | **Speciation Performed** | **Speciation Score** | **Species 1** | **Species 2** |
| Study title. Studies are listed alphabetically by country and chronologically by year of publication. | Abbreviations of all treatments for easier search through the table. | Year of publication. | Number of patients per treatment arm. If the number of patients per arm is not the same, then each arm is listed separately. | Full point (1) if each treatment arm has at least 25 patients. If one arm had < 25 patients, no point was allocated. | Country where participants contracted CL, not necessarily the country where they were treated. | Method by which the parasite was speciated. | Full point (1) if speciation was performed and method employed was mentioned in the study. No point if not speciated or if speciation method not described. | Primary organism studied. | Any secondary organisms studied. |
|  |  |  |  |  |  |  |  |  |  |
| **Diagnostic Criteria** | **Diagnostic Score** | **Methods** | **Oral Treatment** | **Local Treatment** | **Parenteral Treatment** | **Outcome** | **Clinical Endpoint** | **Endpoint Score** | **Results** |
| Method by which the diagnosis of cutaneous leishmaniasis was made. | Full point (1) if diagnostic method was mentioned. No point if method not mentioned. | Type of trial and information on the population studied, including age range, number of lesions, size, duration, and location. | Description of the treatment arms where the intervention employed was an oral agent. If more than one route was given to a single arm, that treatment arm was classified according to the primary modality being studied. | Description of the treatment arms where the intervention employed was a local treatment (local injections, creams, ointments, etc.). If more than one route was given to a single arm, that treatment arm was classified according to the primary modality being studied. | Description of the treatment arms where the intervention employed was an intravenous agent. If more than one route was given to a single arm, that treatment arm was classified according to the primary modality being studied. | List of the primary, secondary, and tertiary outcomes (if applicable) of the study. | Definition of cure as provided in the study. | Full point (1) if definition includes the mention of at least 75% re-epithelialization of the lesions. No point if no or incomplete definition provided. | Brief summary of the efficacy of the treatments studied and any significant adverse events (AE). |
|  |  |  |  |  |  |  |  |  |  |
| **Conclusions** | **Similarity of Groups** | **Similarity Score** | **Loss to Follow-up and Follow-up Time** | **Follow-up Score** | **Blinding** | **Blinded Score** | **Randomization** | **Randomization Score** | **Quality** |
| Concluding statement of the study, typically as provided in the abstract. | A review of Table 1 to determine if the participants were successfully randomized or if significant differences existed between treatment arms. If significant differences, these were mentioned. | Full point (1) is treatment arms were successfully randomized. No point (0) if the arms differed after randomization, or groups were not compared or the study only had a single treatment arm. | Number of participants lost to follow-up (if mentioned), and the total number of months the participants were followed. | Full point (1) if < 10% of participants lost to follow-up and participants followed for at least 1 month after the end of treatment. Half point (0.5) if only one of these categories is met, and no point (0) if neither are met. | Whether the study was an open study, single blinded study, or double blinded study. If single blinded, the group that was blinded was mentioned. | Full point (1) if double blinded, half point (0.5) if single blinded, and no point (0) if not blinded. | Whether the study was randomized, and by what method. | Full point (1) if the study was randomized and the method used was mentioned. Half point (0.5) if the randomization method was not mentioned. No point (0) if the study was not randomized. | Total score |

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| **List of Acronyms** | |
| **Miscellaneous Abbreviations** | |
| BCG | Bacillus Calmette–Guérin |
| BID | Twice per day |
| DA-PDT | Daylight-activated photodynamic therapy |
| DAC N-055 | Pharmaceutical sodium chlorite solution |
| IL | Intra-lesional |
| ILHS | Isochorismatase-related hydrolases |
| IM | Intra-muscular |
| IV | Intra-venous |
| LCF-RF | Localized current field-radio frequency |
| MBCL | Methylbenzethonium chloride |
| MPL-SE | Monophosphoryl lipid A plus squalene |
| PCR | Polymerase chain reaction |
| PCR-RFLP | Polymerase Chain Reaction - Restriction Fragment Length Polymorphism |
| PO | Per os |
| q | Every |
| qd | Daily |
| QT-NASBA | Real-time quantitative nucleic acid sequence-based amplification |
| Rx | Medications |
| S/C | Subcutaneous |
| TBST | Tuberculin skin test |
| TID | Three times per day |
| **Abbreviations of Medications** | |
| 5-ALA | 5-aminolaevulinic acid |
| ALB | Albendazole |
| ALL | Allopurinol |
| AMI | Aminosidine - (paromomycin) |
| AMB | Amphotericin B |
| AZI | Azithromycin |
| BER | Berelin |
| CLO | Clotrimazole |
| CO2 | CO2 laser |
| CRY | Cryotherapy |
| DAP | Dapsone |
| EC | Electro-cauterization |
| FLU | Fluconazole |
| Garlic | Garlic |
| GM-CSF | Granulocyte-colony stimulating factor |
| Honey | Honey |
| HRB | Herbal extract |
| IFN-γ | Interferon gamma |
| ILAMB | IL Amphotericin B |
| ILMA | IL Meglumine antimoniate |
| ILSSG | IL Sodium Stibogluconate |
| IMQ | Imiquimod |
| ITR | Itraconazole |
| IVM | Ivermectin |
| KET | Ketoconazole |
| MA | Meglumine antimoniate |
| MEF | Mefloquine |
| MIC | Miconazole |
| MIL | Miltefosine |
| MWT | Moist wound treatment |
| NS | Sodium Chloride/Normal Saline |
| NaNO2 | Sodium Nitrite |
| NO | Nitric oxide |
| PDT | Photodynamic therapy |
| PEN | Pentamidine |
| PRA | Praziquantel |
| PRB | Probenecid |
| PRM | Paromomycin (aminosidine) |
| PTX | Pentoxifylline |
| RFT | Radiofrequency thermotherapy |
| RIF | Rifampin |
| SAV | Savlan |
| SSG | Sodium Stibogluconate |
| TCA | Trichloroacetic acid |
| Vaccine | Vaccine |
| Yarrow | Yarrow (Achilles millefolium) |
| ZnSO4 | Zinc sulfate |
| **Measurement** | |
| d | Day |
| kg | Kilograms |
| mcg/ml | Microgram per mililiter |
| mg | Milligrams |
| mg/kg | Miligrams per kilogram |
| mg/kg/d | Miligram per kilogram per day |
| min | Minutes |
| mos | Months |
| wks | Week |
| yrs | Years |
| **Laboratory measures** | |
| CBC | Complete blood count |
| Creat | Creatinine |
| ECG | Electrocardiogram |
| LFTs | Liver function tests |
| Plts | Platelets |
| WBC | White blood cells |
| **Various** | |
| abnl | Abnormal |
| ACL | American cutaneous leishmaniasis |
| ADL | Adenolymphangitis |
| AE | Adverse events |
| ATL | American tegumentary leishmaniasis |
| BFing | Breastfeeding |
| btw | Between |
| bx | Biopsy |
|  |  |
| CCR | Complete clinical response |
| CL | Cutaneous leishmaniasis |
| CN8 | Cranial nerve 8 |
| decr | Decreased |
| div | Divided |
| Dx | Diagnosis |
| Excl | Excluded |
| GI | Gastro-intestinal |
| Grp | Group |
| Hx | History |
| incl | Included |
| infx | Infection |
| ITT | Intention to treat |
| lact | Lactatating |
|  |  |
| Lb | L. braziliensis |
| leish | Leishmania |
| max | Maximum |
| MCL | Mucocutaneous leishmaniasis |
| N | Number of participants |
| N/A | Not applicable |
| pos | Positive |
| PP | Per-protocol |
| prg | Pregnant |
| px | Patients/Participants |
| RCT | Randomized clinical trial |
| re-ep | Re-epithelialization |
| RR | Relative risk |
| SE | Side effects |
| Sig | Significant |
| signif | Significant |
| sx | Symptoms |
| T | Treatment arm |
| tx | Treatment |
| UK | United Kingdom |
| vs | versus |
| WHO | World Health Organization |
| w/in | Within |
| w/o | Without |
| WRAMC | Walter Reed Army Medical Center |
| ZCL | Zoonotic cutaneous leishmaniasis |

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| **List of Treatment** |
| **Oral treatments** |
| Allopurinol |
| Allopurinol ribonucleoside |
| Azithromycin |
| Dapsone |
| Ketoconazole |
| Itraconazole |
| Mefloquine |
| Miltefosine |
| Probenecid |
| Rifampin |
| ZnSO4 |
| **Topical treatments** |
| 0.045% DAC N-055 |
| Berelin |
| Clotrimazole cream |
| CO2 laser |
| Garlic |
| Herbal extract |
| high frequency electrocauterization |
| Imiquimod |
| lyophilized rIFNγ |
| Ketoconazole |
| Meglumine antimoniate |
| Miconazole cream |
| Sodium Chloride 5% solution |
| Sodium Chloride 7% solution |
| Sodium nitrite cream |
| Nitric oxide |
| Paromomycin |
| Savlan |
| Silver dressings |
| Sodium stibogluconate |
| Thermotherapy |
| Topical honey |
| Trichloroacetic acid |
| Yarrow (Achilles millefolium) |
| Zinc sulfate (ZnSO4) |
| **Parenteral treatments** |
| Aminosidine |
| Aminosidine sulphate |
| Amphotericin B |
| GM-CSF |
| IFN- γ |
| Meglumine antimoniate |
| Sodium stibogluconate |
| Pentamidine |
| Vaccine |

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