

Supplemental Table 2. Summary of randomised controlled trials on BCG-associated lymphadenitis management

| Source Country | Population (age at lymphadenitis onset) • Timing of BCG vaccine (dose, strain) • Lymphadenitis description, FU period | Study comparator groups | Outcomes | | Comments |
|--|--|--|--|---|---|
| | | | Recovery: time (mean) or rate (%) | Rate of complication | |
| Ayazi <i>et al</i> , ²⁰ 2014 Iran | 40 children (mean age 5.8mo) • infant BCG (0.05ml, BCG-Pasteur) • non-suppl LD ≥0.5cm diam (max 3cm) FU: until LD recovery | Gp1 (n=20): LEX po (50mg/kg/d in 4 doses) 10d Gp2 (n=20): No treatment Note: FNA also done if LD fluctuance during FU | mean±NR Gp1: 16.1±6.5wk Gp2: 15.8±5.7wk, p=ns | <u>Fluctuance, indication for FNA</u> Gp1: 10% (2/20) Gp2: 15% (3/20), p=ns | |
| Banani <i>et al</i> , ²⁷ 1994 Iran | 77 children (mean age 10.6mo, range 1 to 36mo) • neonatal (0.05ml) or infant (0.1ml) (BCG-Pasteur) • suppl (sonographic) LD (size range 1.5-5cm) FU: until LD recovery or stable for 3-4m | Gp1 (n=43): FNA, re-aspiration every 1-2m if needed Gp2 (n=34): No treatment | At 6m FU: Gp1: 95% (41/43) Gp2: 65% (22/34), p<0.002 | <u>Sinus tract at 6m</u> Gp1: 7% (3/43) Gp2: 44% (15/34), p<0.002 | Re-aspiration in 6 patients (2 patients had FNA 3 times) |
| Caglayan <i>et al</i> , ²¹ 1987 Turkey | 120 children (<8m from vaccination) • neonatal (0.05ml) or infant (0.1ml) (BCG-Pasteur) • LD ≥ 1.5cm diam FU: up to 6m | Gp1 (n=21): INH po (10mg/kg/d) 2m Gp2 (n=21): INH + RIF po (10mg/kg/d) 2m Gp3 (n=36): ERY po (30mg/kg/d in 4 doses) 1m Gp4 (n=42): No treatment Surg advised for treatment 'failure' (spont drainage) | Gp1: 52% (11/21) Gp2: 62% (13/21) Gp3: 67% (24/36) Gp4: 67% (28/42), p=ns (rate of improvement or stabilisation) | <u>Spont drainage in early (within 2m) vs. late onset LD (2-8m post BCG)</u> Gp1-3: 48% (13/27) vs. 33% (17/51), p=ns Gp4: 53% (10/19) vs. 17% (4/23), p<0.05 | 16 of original 136 were excluded from study: 6 lost to FU, 10 'untoward' reactions (Gp NR) |
| Close <i>et al</i> , ³¹ 1985 West Indies | 18 infants (age NR) • infant BCG (dose and strain NR) • LD (size NR). Some (n<9) with LD abscess FU: until LD recovery | Gp1 (n=8): INH (po 10mg/kg/d) Gp2 (n=10): No treatment | LD persisted for 2-7m in both groups, no significant difference (further detail NR) | <u>Abscess</u> Gp1: 63% (5/8) Gp2: 40% (4/10) | Abscesses were drained in both Gps, with subsequent healing |
| Kuyucu <i>et al</i> , ¹⁰ 1998 Turkey | 45 infants (mean age 3.8±0.2(SD)mo) • neonatal or infant BCG (BCG-Denmark) • non-suppl LD ≥1.5cm diam FU: until LD recovery | Gp1 (n=15): ERY po (40mg/kg/d in 4 doses) 1m Gp2 (n=15): STR inst. 1 dose (20mg/kg) into node Gp3 (n=15): No treatment FNA also done for LD fluctuance during FU in all Gp1-2 | mean±SE Gp1: 9.4±0.5wk, p=0.01 (vs. Gp2) Gp2: 7.14±0.5wk, p=0.009 (vs. Gp3) Gp3: 11.87±1.5wk | <u>Abscess</u> Gp1: 100% (15/15) Gp2: 100% (15/15) Gp3: 80% (12/15) | <u>Sinus tract</u> Gp1: 0% (0/15) Gp2: 0% (0/15) Gp3: 40% (6/15) |
| Noah <i>et al</i> , ²² 1993 Jamaica | 96 infants (mean age 4.3mo, range 1 to 11mo) • neonatal BCG (BCG-Pasteur) • LD ≥2cm diam, w/o (Gp1) or with (Gp2) abscess FU: until LD recovery | <u>Gp1 (n=69): LD w/o abscess at presentation</u> A (n=35): ERY po (50mg/kg/d in 4 doses) 1m B (n=34): Placebo po (sugar water) 1m <u>Gp2 (n=27): LD with abscess at presentation</u> C (n=14): FNA + ERY po (50mg/kg/d in 4 doses) 1m + 0.5ml saline instil. into abscess cavity D (n=13): FNA + INH instil. (50mg) 1 dose into abscess cavity + placebo po (sugar water) 1m | mean±SD <u>Gp1 (incl. Gp3) n=69</u> A: 4.1±1.48m B: 3.5±1.4m p=ns <u>Gp2</u> FNA+ERY po: 5.2±1.3m FNA+INH instil: 3.9±1.1m p<0.001 | <u>Gp1 (excl. Gp3) n=33</u> 5.1±1.7m 5.7±1.3m p<0.01 <u>Gp3</u> 6.0±1.6m 4.3±1.3m p<0.001 | <u>Abscess</u> Gp1: 52% (36/69) → became Gp3 - GpA: 46% (16/35) - GpB: 59% (20/34), p=0.14 vs. GpA |

Abbreviations: BCG, Bacille Calmette-Guérin; d, days; diam, diameter; EMB, ethambutol; ERY, erythromycin; excl., excluding; FNA, fine needle aspiration; FU, follow-up; Gp, group; incl., including; INH, isoniazid; instil., instillation; LD, lymphadenitis; LEX, cephalixin; m, months; max., maximum; mo, month-old; NR, not reported; ns, not significant; po, per os; RIF, rifampicin; SD, standard deviation; SE, standard error; spont, spontaneous; STR, streptomycin; suppl, suppurative; Surg, total surgical excision; TB, tuberculosis; w/o, without; wk, weeks; y, years;