Supplemental Table 3. Summary of cohort studies 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	
Prospective cohort studies							
Baki *et al,*[23] 1991 Turkey	92 children (age 2mo to 6y, most <6mo) • neonatal (n=89, 0.05ml) or infant (n=3, 0.1ml) BCG (BCG-Pasteur) • non-supp or supp LD 1 to 8cm FU: until LD recovery (all for ≥12m)	Gp1: non-supp A (n=17): INH (po 10mg/kg/d) 6m B (n=33): No treatment	Gp2: mix supp (n=22) & non-supp (n=20) C (n=26): Surg D (n=16): Surg + INH po (10mg/kg/d) 6m	Gp1 A: 28.2wk B: 29.1wk, p=ns	Gp2 C: 4.4wk D: 4.0wk, p=ns	Spont drainage and sinus tract GpA, C, D (interventions): 0% (0/59) GpB (no treatment): 18% (6/33) p=0.002†	
Bhandari *et al,* [24] 1980 India	40 infants (age range 2 to 15mo) • BCG timing and strain NR • non-supp and supp LD FU: 12m	Gp1: non-supp A (n=5): Placebo B (n=11): ERY po (30mg/kg) 10d C (n=7): INH po (20mg/kg) 6m D (n=3): STR inj. (20mg/kg) 2m + INH po 12m	Gp 2: supp E (n=2): Placebo F (n=5): FNA + ERY po (30mg/kg) 10d G (n=3): Surg + ERY po (30mg/kg) 10d H (n=4): Surg + STR inj. (20mg/kg) 2m + INH po 12m	Gp1 A: 3.6m B: 3.1m C: 3.8m D: 3.0m, p=ns	Gp2 E: 3.5m F: 2.4m G: 1.3m, p<0.05 vs. E,F,H H: 3.5m		Very small numbers per subgroup
Caglayan *et al,*[28] 1991 Turkey	50 children (mean age 3mo) • infant BCG (0.1ml, BCG-Pasteur) • supp LD FU: until discharge dried	Gp1: no previous drainage (n=23) FNA at day 0, and7 if re-accumulation	Gp2: previous drainage (11 incisional, 16 spont) A (n=10): Surg B (n=17): No Surg (families refused Surg)	Gp1; recovery at 1m 87% (20/23), incl. 8 who needed two aspirations	Gp2 A: all recovered after Surg (time NR) B: 8wk	Gp1: 13% (3/23) spont drainage after FNA (larger bores used) and required Surg GpA: 0%, none had discharge during post-operative FU	17/27 (Gp2) and 6/23 (Gp1) had AMB prior to study. 16/27 (Gp2) had ABX for secondary infection during study
Oguz *et al,* 1992[32] Turkey	175 infants (mean age 6.7mo, range 1.5 to 24mo) and 8 children >6y (55 lost to FU, NI) • Infant (n=175) and revaccination >6y (n=8) BCG (dose, strain NR) • LD > 0.5cm diam FU: 3m	Gp1: mix non-supp (n=81) & supp (n=8) A (n=75): INH po (5-10mg/kg/d) 3m B (n=54): No treatment at enrolment	Gp2: LD type not specified C (n=29): Surg D (n=25): Surg + INH po (5-10mg/kg/d) 3m	Gp1; recovery at 3m A: 38.8% (19/49) B: 52.5% (21/40), p=ns	Gp2; improve at 3m C: 100% (19/19) D: 100% (20/20)	Gp1; spont or surgical drainage A: 61.2% (30/49) B: 42.5% (17/40), p=ns Note: surgical drainage if accelerated LD size or >2-3cm diam with induration and oedema	68% had LD <2cm diam at enrolment. 5 (GpA) and 3 (GpD) had LD with drainage at enrolment
Retrospective cohort studies							
Venkata-raman *et al,*[26] 2015 United Kingdom	39 children (72% <6mo) • neonatal BCG (BCG-Denmark) • non-supp and supp LD >1cm diam (all axillary) FU: 6m	Gp1: non-supp A (n=1): INH±RIF + FNA B (n=2): FNA C (n=1): INH±RIF (dose, duration NR) D (n=15): No treatment	Gp2: supp E (n=1): INH±RIF + Surg F (n=2): INH±RIF + FNA G (n=7): FNA H (n=7): INH±RIF I (n=3): No treatment	Gp1; recovery at 6m A: 0% (0/1) B: 100% (2/2) C: 100% (1/1) D: 93% (14/15)	Gp2; recovery at 6m E: 0% (0/1) F: 50% (1/2) G: 29% (2/7) H: 29% (2/7) I: 33% (1/3)	Gp2; sinus tract E:100% (1/1) F: 50% (1/2) G: 0% (0/7) H: 14% (1/7) I: 33% (1/3)	Most children who received AMB had INH alone. Five received INH and RIF (dose and duration NR)
AbuZeid *et al,*[25] 2011 Jordan	89 infants (age 2 to 9mo, <6m post BCG) • infant BCG (BCG-Denmark) • LD size ≥2cm or supp FU: 1y	Gp1 non-supp (n=42): No treatment Gp2 supp (n=27): INH+RIF+EMB 3m (dose NR) Gp3 type not specified (n=20): FNA		Recovery at 1y Gp1:100% (42/42) Gp2: 100% (27/27) Gp3: 95% (19/20)		Sinus tract Gp1-2: 9% (6/69) Gp3: 50% (10/20); all had Surg	4/89 had disseminated infection and diagnosed with SCID (1 died); treatment group NR
Hengster *et al,*[29] 1997 Austria	116 infants (mean 3.8wk post BCG, range 3 to 28w) • neonatal BCG (0.05ml, mostly BCG-Pasteur) • supp LD (1-4cm diam) ref to surgery dept FU: not specified	Gp1 'smaller' LD (n=6): Topical therapy (no detail) Gp2 no criteria for Surg (n=21): INH po (10mg/kg) Gp3 criteria for Surg (n=89): Surg ± INH po (10mg/kg) + vitamin B6 6wk (Note: 30 (34%) already had INH for 1-12wk prior to Surg)		No outcome data reported for Gp1 and Gp2		Spont perforation Gp1-3: 5% (6/116) Required subsequent surg Gp3: 7% (6/89)	Criteria for Surg: fluctuating LD >1.5cm, inflammation infiltrating the skin, spont perforation or fistula
Merry *et al,*[30] 1996 Ireland	17 children (mean 10m post BCG, range 3-29m) • neonatal (n=16) and infant 8mo (n=1) BCG (Denmark, n=13; Glaxo, n=3; Pasteur, n=1) • persistent LD >1cm ref to surgery dept FU: up to 12m (if Surg, FU until recovery)	Gp1 LD abscess (n=4): Drainage of LD abscess Gp2 LD w/o abscess (n=5): Surg + INH for 2 to 3m Groups with no initial Surg (LD type not specified) Gp3 (n=6): INH± vitamin B6 for 4 to 12m Gp4 (n=2): No treatment		Gp1: 100% (4/4) at end of post-op FU Gp2: 100% (5/5) at end of post-op FU Gp3: 17% (1/6) at 12m Gp4: 0% (0/2) at 12m		Supp or skin fixation over LD, or remain unresolved after 4-11m Gp3: 83% (5/6) Gp4: 100% (2/2) These 7/8 subsequently had Surg	Gp1: Method of drainage NR (presumed surgical incision and drainage)

Abbreviations: ABX: antibiotics; AMB, anti-mycobacterial; BCG, Bacille Calmette-Guérin; d, days; dept, department; diam, diameter; EMB, ethambutol; ERY, erythromycin; FNA, fine needle aspiration; FU, follow-up; Gp, group; incl., including; INH, isoniazid; instil., instillation; inj. injection; LD, lymphadenitis; m, months; max., maximum; mo, month-old; NI, not included; NR, not reported; ns, not significant; po, per os; ref, referred; RIF, rifampicin; SCID, severe combined immunodeficiency; spont, spontaneous; STR, streptomycin; sup, suppurative; Surg, total surgical excision; w/o, without; wk, weeks; y, years

†Calculated using Stata V16 (StataCorp, College Station, Texas, USA); not provided in original publication.