

Short Communication

Post-operative Intrapleural BCG in Lung Cancer

M.R. LAW,* W.K. LAM† and M.E. HODSON†

*Department of Environmental and Preventive Medicine, The Medical College of St Bartholomew's Hospital, London EC1M 6BQ, U.K. and †Cardiothoracic Institute, Brompton Hospital, Fulham Road, London SW3 6HP, U.K.

Table 1. Survival at 2 and 5 years after surgery in BCG-treated and control patients

	Total No.	Stage 1 No. surviving		Total No.	Stage 2-3 No. surviving	
		2-year	5-year		2-year	5-year
Control	22	16 (73%)	12 (55%)	17	6 (35%)	5 (29%)
All BCG treated	22	10 (45%)	6 (27%)	17	1 (6%)	1 (6%)
BCG alone	12	5 (42%)	3 (25%)	10	1 (10%)	1 (10%)
BCG + isoniazid	10	5 (50%)	3 (30%)	7	0	0

IN A TRIAL of immunotherapy in lung cancer using a single intrapleural injection of BCG after surgical resection, McKneally *et al.* [1, 2] reported statistically significantly longer survival of BCG-treated patients with localized disease than of controls. This result generated enthusiasm for such treatment, and several other trials of post-operative intrapleural BCG for lung cancer were established. We now report 5-year survival in a randomized controlled trial with two treated groups. In one the methods of McKneally *et al.* [1] were reproduced exactly, but isoniazid after 2 weeks was not given in the other in order to achieve a more prolonged immune stimulus. Details of our methods have been published previously [3].

Table 1 shows the number of patients alive 2 and 5 years after surgery. Survival was worse in the 39 BCG-treated patients than in the 39 con-

trols. For all stages combined, compared with controls, 11 and 22 respectively survived 2 years ($P = 0.012$), 7 and 17 five years ($P = 0.014$). Among BCG-treated patients survival was similar in the groups given and not given isoniazid. Fifty of the 54 deaths were from lung cancer recurrence, three from surgical complications, and one from Hodgkin's disease.

Our trial was small, because the occurrence of severe side-effects necessitated its termination, but 5-year survival is clearly inconsistent with a favourable effect of intrapleural BCG. Survival to 2-3 years in six other trials [4-9] was similar in BCG-treated and control patients.

We observed wound infections, empyema and prolonged chest pain in BCG treated patients [3]. Side-effects were also observed in two other trials which used Tice BCG [10, 11] and in one which used Pasteur BCG [12]. Taken as a whole, the evidence indicates that intrapleural BCG does not prolong survival and causes side-effects. It also illustrates that caution is needed when the early results of a trial of potentially toxic therapy suggest benefit.

Accepted 4 May 1988.

Address for correspondence: Dr M.E. Hodson, Cardiothoracic Institute, Brompton Hospital, Fulham Road, London SW3 6HP, U.K.

REFERENCES

1. McKneally MF, Maver C, Kausel HW. Regional immunotherapy of lung cancer with intrapleural BCG. *Lancet* 1976, **i**, 377-379.
2. McKneally MF, Maver C, Lininger L *et al.* Four year follow up on the Albany experience with intrapleural BCG in lung cancer. *J Thorac Cardiovasc Surg* 1981, **81**, 485-492.
3. Law MR, Lam WK, Studdy PR, Pugsley WB, Hodson ME. Complications of intrapleural BCG in the treatment of operable non-small cell bronchial carcinoma. *Br J Dis Chest* 1982, **76**, 151-156.
4. Wright PW, Hill LD, Peterson AV *et al.* Preliminary results of combined surgery and adjuvant BCG plus levamisole treatment of resectable lung cancer. *Cancer Treat Rep* 1978, **62**, 1671-1675.
5. Jansen HM, The TH, Orie NGM. Adjuvant immunotherapy with BCG in squamous cell bronchial carcinoma. *Thorax* 1980, **35**, 781-787.
6. Lowe J, Iles PB, Shore DF, Langman MJS, Baldwin RW. Intrapleural BCG in operable lung cancer. *Lancet* 1980, **i**, 11-14.
7. Mountain CF, Gail MH. Surgical adjuvant intrapleural BCG treatment for Stage 1 non-small cell lung cancer. *J Thorac Cardiovasc Surg* 1981, **82**, 649-657.
8. Bakker W, Nijhuis-Heddes JMA, Wever AMJ, De la Riviere AB, Van der Velde EA, Dijkman JH. Post-operative intrapleural BCG in lung cancer: lack of efficacy and possible enhancement of tumour growth. *Thorax* 1981, **36**, 870-874.
9. Roeslin N, Lang JM, Morand G, Wihlm JM, Witz JP. Regional immunotherapy in resectable squamous cell lung carcinoma. *Cancer Immunol Immunother* 1982, **13**, 174-175.
10. Ludwig Lung Cancer Study Group. Adverse reactions to intrapleural BCG. *N Engl J Med* 1981, **305**, 167-168.
11. Gail MH, Oldham RK, Holmes EC *et al.* Early side-effects of intrathoracic BCG therapy in patients with stage I squamous cell carcinoma, adenocarcinoma or large cell lung cancer. *Cancer Immunol Immunother* 1981, **10**, 129-137.
12. Bakker W, Nijhuis-Heddes JMA, De la Riviere AB, Dijkman JH. Complications of post-operative intrapleural BCG in lung cancer. *Ann Thorac Surg* 1982, **33**, 267-272.