

BCCA Protocol Summary for Therapy for High Risk Superficial Transitional Cell Bladder Cancer using BCG

Protocol Code	<i>GUBCG</i>
Tumour Group	<i>Genitourinary</i>
Contact Physician	Chair, GUTG

This protocol is primarily for the guidance of the individual patient's consulting urologist. Some additional details are provided to assist any other physicians involved in administering the treatment. (see references 1-3 for reviews) The protocol should be read in conjunction with the BCCA Cancer management Manual available on-line at <http://www.bccancer.bc.ca>.

Topical BCG may also be used for treatment of non-invasive transitional carcinoma of the upper urinary tract in selected patients. Consultation with a member of the BCCA GU Tumour Group is advised.

Adjuncts: patients who smoke should be advised to quit. Evidence that megadose vitamin supplements may improve the quality of remissions induced with intravesical (Ive) BCG is considered inconclusive.⁴

ELIGIBILITY:

- Pure transitional cell bladder carcinoma
- Any of the following:
 - Therapy of stage Tis (carcinoma-in-situ of the high grade flat type), or
 - Therapy of truly unresectable Ta (papillary TCC), or
 - Prophylaxis of resected T1 disease (superficial invasion of submucosa), or
 - Prophylaxis of high risk Ta (multiple recurrences or multiple high grade).
- Treatment is permitted for relapse after previous chemotherapy or after BCG given at least 12 months previously (this is distinct from 6-monthly maintenance BCG described below).

EXCLUSIONS:

Any of the following:

- Presence of non-transitional histologies
- TCC invading bladder muscle, prostate or other organ
- Biopsy proven relapse or progression in bladder within 12 months of previous IVE BCG (note: positive urine cytology alone may be originating in the upper tracts and does not necessarily constitute failure)

- TURB or urethral trauma within 4 weeks
- Concurrent systemic corticosteroids or a specific immunodeficiency syndrome including AIDS
- Severe pre-existing dysuria or hourly urinary frequency

TESTS:

- Pre-treatment:
 - Cystoscopy, cold biopsy of visible lesions to include muscle
 - Transurethral resection of Ta/T1 disease
 - Bimanual examination under anesthesia before especially *after* resection
 - Upper tract assessment (i.e., IVP and/or retrograde studies)
 - Urine cytology; bladder capacity measurement
 - High grade disease on cytology or biopsy: random biopsies of bladder and prostate
- Post-treatment:
 - Re-evaluation of pre-treatment abnormalities (if any) at 4-8 weeks post BCG
 - Regularly scheduled follow-up to include cystoscopy

TREATMENT:

- BCG strain: the reimbursable strain and supplier may change from time to time: contact a BCCA Cancer Centre pharmacy if necessary. There is no evidence of any clinically significant difference between the strains currently available in Canada.
- Dose: 1 vial (see under Dose and Dose Modification) in 50 mL normal saline.
- Technique: administer by catheter into an empty bladder as soon as possible after reconstitution (within 2 hours) with a dwell time in the bladder of 2 hours. Some investigators have recommended the patient remains recumbent and turns every fifteen minutes.
- Schedule: weekly for 6 consecutive weeks.
- After reassessment (see below), patients who demonstrate response but have residual disease on cystoscopy or cytology may benefit from immediate retreatment with a second 6-week course.

MAINTENANCE BCG:

- If maintenance BCG is to be used to prolong remissions,⁵ give I Ve BCG one vial (see under Dose and Dose Modification) weekly for 3 consecutive weeks every 6 months i.e., three weekly instillations at 6, 12, 18, 24 months.
- Other schedules such as monthly BCG have not been found effective in controlled trials.

DOSE AND DOSE MODIFICATION

- The full dose (mg) will depend on the reimbursable product but is generally supplied in one vial (i.e., Montréal 120 mg = TICE 50 mg [1 to 8×10^8 CFU] = Connaught 81 mg).

- Some symptoms of cystitis are to be expected. If these are severe, exclude non-BCG bacterial infection and wait 1-4 weeks until symptoms improve, then continue with 50% of the previous dose.
- The dose-response relationship of BCG is unclear. Dose increase is not recommended.

PRECAUTIONS:

1. Patients should be advised to minimise oral fluids (especially those containing caffeine) for 6 hours before each treatment to minimise dilution of BCG in the bladder.
2. BCG is a live bacterial preparation. Granulomas in bladder biopsies are expected. If patients experience persistent fever with or without a pulmonary infiltrate, BCGosis, systemic BCG infection, should be suspected.⁶

BENEFITS:

Therapeutic first-line use: complete response in about 70% of patients (pooled data), with a median time to relapse of 1-2 years. There is evidence of reduced long term risk of muscle-invasive disease progression and of improved disease-specific survival in one series with prolonged follow-up.⁷ For prophylactic use, risk of recurrence is reduced by about 2-fold but long term risk of relapse remains.

Call Chair, GU tumour group @ (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: Jan 1989

Date last revised: 16 Jan 2007 (physician contact)

References:

1. Lamm DL, et al. Maintenance BCG immunotherapy for recurrent Ta, T1 and CIS transitional cell carcinoma of the bladder: a randomized SWOG study. *J Urol* 2000; 163: 1124-9.
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3. Alexandroff AB et al. BCG immunotherapy of bladder cancer: 20 years on. *Lancet* 1999;353:1689-94.
4. Pagano F, Fair WR (eds). Superficial bladder cancer. *Isis* (Oxford) 1997. 228 pp.
5. Lamm DL et al. Megadose vitamins in bladder cancer: a double-blind clinical trial. *J Urol* 1994;151:21-6.
6. Lamm DL et al. Maintenance BCG of superficial bladder cancer: a randomized prospective SWOG study. *Proc ASCO* 1992;11:203, A627.
7. Lamm DL et al. Incidence and treatment of complications of BCG intravesical therapy in superficial bladder cancer. *J Urol* 1992;147:596-600.
8. Herr HW et al. Intravesical BCG therapy prevents progression and death from superficial bladder cancer. *J Clin Oncol* 1995;13:1404-8.