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

Protocol Code *GUBCG*

Tumour Group *Genitourinary*

Contact Physician *Dr. Kim Chi*

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 IVe BCG one vial (see under Dose and Dose Modification) weekly for 3 consecutive weeks at 3, 6, 12, 18, 24, 30, 36 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 x 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 Dr. Kim Chi or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: Jan 1989

Date last revised: 01 April 2012 (maintenance treatment interval revised)

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.
2. Lamm DL. BCG immunotherapy for transitional-cell carcinoma in situ of the bladder. Oncology 1995;9:947-65.
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.