

BCCA Protocol Summary for Palliative Therapy for BCG-Refractory Superficial High-Grade Transitional Cell Carcinoma Bladder with BCG and Interferon

Protocol Code *GUBCGIFN*

Tumour Group *Genitourinary*

Contact Physician *Chair, GUTG*

ELIGIBILITY:

- Tis and High-Grade Ta, T1 superficial transitional cell carcinoma (TCC) bladder, with recurrence of disease either on maintenance BCG or within 6 months of the last treatment with BCG, who are not suitable surgical candidates.

EXCLUSIONS:

- Those fit for cystectomy
- Concurrent systemic corticosteroids or a specific immunodeficiency syndrome including AIDS
- Severe pre-existing dysuria or hourly urinary frequency
- Concurrent urinary tract infection
- Hypersensitivity to Interferon

TESTS:

- Baseline:
 - Cystoscopic evaluation including biopsy
- Before each treatment: Cystoscopy, cold biopsy of visible lesions to include muscle
 - Transurethral resection of Ta/T1 disease
 - Bimanual examination under anesthesia before and 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
- After each treatment: Re-evaluation of pre-treatment abnormalities (if any) at 4-8 weeks

PREMEDICATIONS:

- Urinary antispasmodic, if required.

TREATMENT:

Drug	Dose	BCCA Administration Guideline
BCG*	1/3 vial	Reconstitute both drugs as directed, combine, and qs to 50 mL with preservative-free NS.*** Administer by catheter into 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.
Interferon-alfa 2b**	50 million units	

*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. One vial = Montréal 120 mg = TICE 50 mg [1 to 8 x 10⁸ CFU] = Connaught 81 mg).

**It is important to use Interferon lyophilized powder, reconstituted with sterile water, as the Interferon ready-to-use solution contains preservatives which destroys BCG.

*** Due to short stability, pharmacy may provide the final preparation OR may provide ingredients necessary for nurse or physician to prepare at bedside.

Induction treatment: repeat every week for 6 weeks.

Maintenance treatment: 3 weekly treatments beginning 3 months after the end of induction and repeated twice at further 6-month intervals at approximately 5, 11 and 17 months after the start of induction. BCG dose may be 1/3 vial for each treatment, or may be 1/3 vial for week 1, then 1/10 vial for weeks 2 and 3.

Discontinue if no response after induction treatment. Those who fail such measures early on will likely not respond to further intravesical therapy, and alternative measures should be considered urgently.

DOSE MODIFICATIONS:

1. Dose decreases of BCG in approximately equal gradations of 1/3 (1/10, 1/30 and 1/100) may be necessary for treatment intolerance. BCG intolerance is defined as fever greater than 39C less than 24 hours in duration, moderate to severe cystitis symptoms persisting beyond 3 days or inability to retain treatment at least 1 hour despite urinary antispasmodics, including narcotics.
2. Interferon-alfa 2b dose is not modified.
3. Dose delays of up to 2 weeks may be necessary for treatment intolerance.

PRECAUTIONS:

1. Patients should be advised to minimise oral fluids (especially those containing caffeine) for 6 hours before each treatment to minimise dilution of drug 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 (ie, systemic BCG infection) should be suspected.

Call Tumour Group Chair at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 1 June 2005

Date revised: 1 May 2009 (unsafe abbreviations and symbols replaced, disclaimer added)

References:

1. O'Donnell, M.A., J. Krohn, and W.C. DeWolf, *Salvage intravesical therapy with interferon-alpha 2b plus low dose bacillus Calmette-Guerin is effective in patients with superficial bladder cancer in whom bacillus Calmette-Guerin alone previously failed.* J Urol, 2001. **166**(4): p. 1300-4, discussion 1304-5.
2. Lam, J.S., et al., *Bacillus Calmete-Guerin plus interferon-alpha2B intravesical therapy maintains an extended treatment plan for superficial bladder cancer with minimal toxicity.* Urol Oncol, 2003. 21(5): p. 354-60.