BCCA Protocol Summary for Standard Protocol – INTRALESIONAL BCG

Protocol Code: SMILBCG

Tumour Group: Melanoma

Contact Physician: Dr. Kenneth Wilson

ELIGIBILITY/TESTS:

Intralesional BCG is usually considered for local or regional metastatic disease in lieu of more toxic systemic therapy where such a local approach can provide effective palliation and occasional cure. Such patients can be expected to have a good performance status, ECOG less than or equal to 3. Large lesions, greater than 2 cm are unlikely to respond. This treatment is unlikely to be effective in the face of rapidly progressive disease with the appearance of many cutaneous lesions over a few days or weeks. Consideration should be given to the possible side effects (see below) before recommending treatment.

TREATMENT:

Supply:

BCG is supplied as 1.5 mg of lyophilized powder and an additional diluent vial containing 1.5 ml saline. A separate supply of preservative-free saline is required for the lower doses.

BCG Preparation and Dilution:

Because of volume considerations, the lower doses, beween 0.005 and 0.05 mg, require double dilution. Using the small diluent vial, the initial dilution is as instructed in the package insert to result in a concentration of 1 mg/ml. To make the double dilution, 0.9 ml of preservative-free saline is introduced into the now empty small diluent vial. To this is then added 0.1 ml from the initial dilution to result in a final double dilution concentration of 0.1 mg/ml. Doses of 0.005, 0.01, 0.02 and 0.04 mg can then be delivered in 0.05, 0.1, 0.2 and 0.4 ml, respectively.

Higher doses, beginning at 0.1 mg, can be delivered using a single dilution only, by appropriate adjustment of diluent added to the lyophilized BCG. This is summarized in the following table:

Dose (mg)	Volume of Diluent (ml)	Volume to Deliver (ml)
0.l	1.5	0.l
0.2	1.5	0.2
0.4	1.5	0.4
1.0	0.6	0.4
1.5	0.4	0.4

Administration:

BCG is delivered in a tuberculin syringe fitted with a 25 gauge needle. Injection is into the centre of a small lesion or at multiple sites for a larger lesion. Intracutaneous lesions may not retain fluid injected directly. In such cases it may be better to insert the needle slightly distant from the lesion and advance it into the centre through the deep margin.

In consideration of occasional allergic reactions (see below), the first dose of 0.005 mg is given 30 min after administering intramuscular 50 mg diphenhydramine (BENADRYL®). The antihistamine is not routinely repeated with subsequent doses, but patients should remain under observation for 30 min following each injection.

Dose escalation is usually in the sequence detailed above for 'lower' and 'higher' doses. In each case this is an approximate two fold change between doses. Escalation of weekly injections continues until a dose is identified that causes a local inflammatory reaction or systemic symptoms. Further injections may be given at the same dose level every other week for two doses, then every month. Dose reductions may be indicated with significant increases in local or systemic reactivity. The total dose may be divided among several lesions where more than one is being treated.

Response may not be apparent for 4-6 weeks. After that, use of BCG should be reconsidered with clear evidence of progression of disease.

DOSE MODIFICATIONS:

PRECAUTIONS:

Side Effects:

1. Local:

Local mild discomfort from the injection is to be expected.

Surrounding erythema within a 48 hrs is a sign of delayed cutaneous hypersensitivity. Patients will not respond if they fail to develop this after a period of sensitization. Dose reduction should be considered for erythema more than 6 cm surrounding the injection site, especially if associated with systemic symptoms.

Since BCG is a live vaccine, ulceration and drainage are to be expected after several weeks of treatment. This can be well managed with dry dressings.

2. Systemic:

Fever, malaise muscle aches are common on the evening of the injection in sensitized patients. This can usually be well managed with acetaminophen. Severe or prolonged systemic symptoms may require dose reduction.

While rare, anaphylactic reactions have been reported with intralesional BCG. This is more likely to occur in older patients or those who are PPD positive and have previously been exposed to TB. Patients should remain under observation for twenty minutes after injection. Appropriate medication, including epinepherine, should be at hand in the unlikely event that this might occur. Patients with a history of tuberculosis require additional monitoring as BCG can occasionally reactivate old TB.

Autopsy studies have identified small metastatic granulomas in the liver and lungs of some patients treated with intralesional BCG. This is rarely symptomatic. Occasionally, an increase of liver function studies may be seen following intralesional treatment in the absence of detectable metastatic melanoma in the liver. Such patients respond to discontinuation of BCG and treatment with antituberculosis therapy, such as INH.

BCG can also occasionally reactivate old tuberculosis.

Call Dr. Kenneth Wilson or tumour group delegate at (250) 519 5572 or 1-800-670-3322 local 5572 with any problems or questions regarding this treatment program.

Date activated: N/A

Date last revised: 01 May 2008 (unsafe abbreviations and symbols replaced)