Many studies, now including 3 meta-analyses, show that BCG intravesical therapy provides superior protection from tumor recurrence, and with maintenance schedules reduces disease progression, metastasis and mortality. No other intravesical treatment has achieved these results. Data from the EORTC now show that even patients with intermediate risk disease, when given my 3 week maintenance schedule, have significant reduction in recurrence, progression to metastasis, and cancer death. Despite this good news there remain patients who fail to respond to BCG therapy. Here are my current recommendations for optimal BCG therapy and management of BCG failure patients.

**Patient Selection:** While BCG is effective in low grade, Ta tumors, these patients are at low risk of disease progression. Chemotherapy is more effective in low grade than high grade tumors. Immediate postoperative chemotherapy reduces tumor recurrence by about 20% and in my double blind study Oncovite (Mission Pharmacal) 2 tabs twice a day, reduced recurrence by 40%. Oncovite was most effective in patients with low grade, low stage disease. With multiple recurrences of low grade tumor, however, changing from chemotherapy to BCG is appropriate because 25% of patients who develop muscle invasion begin with low grade, Ta disease. For patients with CIS, high grade, or T1 TCC maintenance BCG is indicated.

**Before BCG** care should be taken to resect all visible tumor and cauterize CIS. Immediate postoperative chemotherapy is given to further reduce tumor burden, which has been shown to be important in BCG therapy. Two to four weeks later, BCG is begun.

**BCG Technique:** Patients are asked to minimize fluids after midnight so they will be able to hold BCG for two hours. One vial of TheraCys or TICE BCG is diluted in 50cc preservative-free normal saline and instilled in the carefully emptied bladder. Both preparations are highly effective, but randomized comparison has found the TheraCys (ImmuCys outside of the US) to be more effective than TICE. Patients are asked to lie on their abdomen for 15 minutes during the two hour retention period. Treatments are given weekly for a total of 6 weeks. Do not give BCG if catheterization causes bleeding or patients have cystitis.

**Maintenance** is given weekly for 3 weeks at 3, 6, 12, 18, 24, and 36 months. I have omitted the 30 month treatment, but in high risk patients continue at 4, 5, 6, 8, 10 and 12 years to reduce the risk of late disease recurrence and progression. We recommend 1/3 dose BCG during maintenance and I would recommend further reducing to 1/10, 1/30, and 1/100th dose in 50cc in any patient with increased side effects. The benefit of BCG is gone 10 years after the last treatment.

**BCG Failure** may be caused by occult invasive or extravesical disease, inadequate immune response, or BCG resistance. Extravesical and invasive disease should be sought and treated. Percutaneous BCG can be given to improve response, especially in PPD skin test negative patients. A second 6 week course of BCG should not be given unless interferon is added because immunosuppression may otherwise be induced. 50 MU is added directly to BCG, often using the reduced BCG dose. Mitomycin 40mg/20cc, Adriamycin 50mg/25cc, Thiopeta 30mg/15cc, docetaxel 20mg/10cc or Gemcitabine 200mg/10cc water can be used in patients who are not candidates for cystectomy. If that doesn’t work call me- we are looking at new therapies such as Eoquin, Chemophage plus Mitomycin, hyperthermic chemotherapy, combination chemotherapy, KLH, Regressin, and GMCSF producing adenovirus gene therapy.

**Side Effects** can be reduced by lowering the dose, giving Ofloxacin 200mg 6 hours after instillation and the following morning, or retaining BCG for only 30 minutes. BCG infection is treated with INH 300mg/d and Cipro 500mg bid. Serious reactions require triple antibiotics and steroids.