1704
EFFICACY OF ONE-YEAR MAINTENANCE IN EARLY ADJUVANT CHEMOTHERAPY FOR INTERMEDIATE RISK NON-MUSCLE-INVASIVE BLADDER CANCER. RESULTS AT 24 MONTHS OF A RANDOMIZED TRIAL.

Vincenzo Serretta*, Vincenzo Altieri, Giuseppe Morgia, Darvinio Meloni, Maria Karidi, Pasquale Ameno, Giuseppe Carriero, Maurizio Cacciatore, Nino Dispensa, Alessandra Di Lallo, Giovanni Ruggiero, Federico Niccoli, Mauro Iadevaia, Francesco Vacirca, Francesco Paolo Selvaggi, Rosalinda Allegro. Palermo, Italy, Napoli, Italy, Messina, Italy, Matera, Italy, Foggia, Italy, Partinico (PA), Italy, Campobasso, Italy, Telese Terme (BN), Italy, Catania, Italy, Maddaloni (CE), Italy, Catanzaisetta, Italy, and Bari, Italy.

INTRODUCTION AND OBJECTIVE: The clinical value of early intravesical adjuvant chemotherapy after TUR of intermediate risk non-muscle-invasive bladder cancer (NMI TCCB) is well established. On the other hand, the optimal schedule regimen and the role of maintenance are still debated. The aim of the present study was to evaluate the effectiveness of one-year maintenance schedule in patients submitted to TUR plus adjuvant early intravesical chemotherapy for intermediate risk NMI TCCB.

METHODS: Between May 2002 and August 2003, 577 patients, were recruited. All patients underwent TUR and early (within 6 hours) intravesical chemotherapy with epirubicin at the dose of 80 mg diluted in 60 ml of saline solution. When history was available, 95 patients were excluded from the study since they were harbouring T1G3, Tis or single and primary Ta G1-G2 tumors. Four hundred eighty-two patients with intermediate risk NMI TCCB were randomized according 2 different intravesical instillation schedules: Arm A, 5 more weekly instillations; arm B, 5 more weekly instillations followed by monthly instillations for a total of 16 instillations. All patients were submitted 3-monthly for the first 2-years and then 6-monthly to cytology, cystoscopy and biopsy of every suspicious bladder lesion.

RESULTS: Out of 482 randomized patients, 396 are evaluable for toxicity and 392 for efficacy. The tumours were multiple in 318 patients (66.0%) and recurrent in 192 (39.8%). No difference emerged between the 2 arms in relation to tumors’ characteristics. The median follow-up time was 22 months (range: 3-56). Eighty-two (20.9%) patients recurred at a median time of 9 months from TUR. Four patients progressed (1%). The recurrence rate was 24.4% (47/192) in arm A and 18.5% (35/200) in arm B (p=0.05). No difference was evident between the two arms for recurrence rate at 3 months (p=0.06). However, an advantage in favour of maintenance emerged in terms of recurrence rate at 6 (p=0.01), 9 (p=0.04) and 12 months (p=0.03) and in terms of recurrence-free interval (p=0.03). No difference for toxicity was evident according to treatment schedule.

CONCLUSIONS: A preliminary analysis at 2-years is presented. The role of maintenance is analyzed in patients affected by intermediate risk NMI TCCB treated after TUR with early epirubicin intravesical chemotherapy followed by 5 weekly instillation. The risk of tumour recurrence is significantly reduced by one-year maintenance without enhanced toxicity.

Source of Funding: None

1705
MULTICENTER RANDOMIZED COMPARISON OF BCG WITH OR WITHOUT ALFA 2b INTERFERON (IFN) AND ONCOVITE (ONC) VERSUS RECOMMENDED DAILY ALLOWANCE (RDA) VITAMINS DURING INDUCTION AND EXTENDED 3-WEEK MAINTENANCE.

Donald L Lamm*, Mike A O’Donnell. Phoenix, AZ, and Iowa City, IA.

INTRODUCTION AND OBJECTIVE: 6-week induction BCG with 3-week maintenance is currently the best treatment of high-risk bladder cancer but only 16% of patients tolerate the full schedule. Patients failing BCG are frequently salvaged with interferon (IFN) plus BCG at a lower dose. Previously, in a double blind trial, high doses of vitamins A, B6, C and E plus zinc reduced tumor recurrence by 40%. To evaluate the added benefits, if any, of IFN and high dose vitamins, BCG naive patients were treated with standard induction and 3-week reduced dose maintenance BCG along with vitamins and IFN in 2x2 factorial design randomized clinical trial.

METHODS: Patients with Ta, T1, or in situ TCC who had resection within 8 weeks were randomized by central computer to receive BCG or BCG plus IFN and also randomized to receive RDA vitamins or the high-dose antioxidant vitamin preparation Oncovite (Mission Pharmacal, San Antonio, TX). 50mg TICE BCG in 50ml saline +/- 50 million units (MU) of Alfa 2b interferon (Intron A, Schering-Plough, Kenilworth, NJ) was given weekly for 6 weeks, Maintenance BCG was reduced to 1/3 (16.6mg/50ml) given at 4, 7, 13, 19, 25, and 37 months +/- 50 MU IFN. Matched, blinded vitamins were given in a dose of 2 tablets twice daily throughout the study. Each RDA tablet contained 25% of the recommended total daily dose. Vitamin D and folate were increased in this new Oncovite formulation due to reported antitumor benefit. Each Oncovite tablet contained Vitamins A (8,000 IU), B6 (25mg), C (500mg), D3 (400 IU), folate (0.4mg), and E (100 IU), as well as Zinc (7.6mg). Patients were followed with quarterly cystoscopy for 2 years, then semiannually through year four, then annually. The primary end point was biopsy-confirmed tumor recurrence.

RESULTS: 610 of 671 patients accrued between September 1999 and December 2003 were eligible and had at least one follow-up cystoscopy. Tumor recurrence was documented in 64 of 163 BCG RDA patients (39%); 35/154 (22.7%) with BCG Onc; 30/142 (21.1%) with BCG IFN RDA; and 33/151 (22%) with BCG IFN Onc (P<0.000 vs. RDA, Chi Square).

CONCLUSIONS: Oncovite or alfa 2b interferon added to BCG significantly reduced tumor recurrence compared with 3 week BCG maintenance therapy plus RDA vitamins. Oncovite, a high dose vitamin supplement, was as effective as adding interferon to BCG. Interferon has been shown to enhance the efficacy of BCG, however there was no additive effect of combining interferon with Oncovite.

Source of Funding: Schering-Plough, Mission Pharmacal.

1706
A RETROSPECTIVE ANALYSIS OF THE EFFECT OF STATIN USE ON THE EFFICACY OF BCG TREATMENT FOR TCC OF THE BLADDER.


INTRODUCTION AND OBJECTIVE: BCG is an effective immunotherapy for carcinoma in situ of the bladder, and it reduces recurrences from resected papillary TCC of the bladder. Many patients undergoing BCG therapy are concurrently taking oral statin agents, which have known immunomodulatory properties which may alter the performance of BCG. Some data has suggested that patients concurrently taking a statin while undergoing BCG therapy have reduced clinical efficacy.

METHODS: A retrospective review of 952 consecutive patients from 1978 through 2006 was conducted. Time to recurrence and progression to surgery were compared between those taking and not taking a statin by Kaplan-Meier methods and multivariable Cox regression controlling for stage and grade.

RESULTS: A total of 245 (26%) patients were taking a statin prior to BCG therapy and 707 were not (74%). Patients taking statins were more likely to be older (median 69 vs 65 years), male (85% vs 78%), and have higher grade tumors (52% vs 45%). A total of 796 patients recurred overall, with 214 patients in the statin group and 582 in the other. The median time to recurrence was similar between those who did and did not use a statin (see Figure 1). On multivariable analysis, statin use was not significantly associated with recurrence (hazard ratio 1.04; 95% CI 0.81, 1.34; p=0.7) or progression to surgery (hazard ratio 0.77; 95% CI 0.52, 1.13; p=0.17) following BCG therapy.