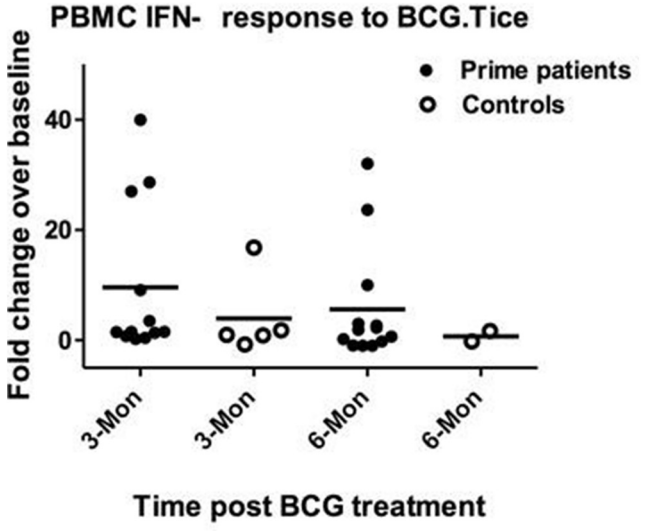
INTRODUCTION AND OBJECTIVES: Intravesical induction immunotherapy with Bacille Calmette-Guerin (BCG) is the standard of care treatment for high risk non-muscle invasive bladder cancer (NMIBC). Despite this, rates of recurrence and progression to muscle-invasion remain unacceptably high. We sought to optimize immunologic response to intravesical induction immunotherapy with standardized BCG intradermal vaccination prior to induction, and herein report our two year outcomes.

METHODS: BCG-naive patients with high-risk NMIBC who were candidates for BCG therapy were prospectively enrolled from 2014-2015. Patients who were PPD-negative were subsequently vaccinated with BCG in standard intradermal fashion, and 3 weeks later, standard induction immunotherapy with Tice BCG was performed. Urinary cytokines, BCG-specific T and mononuclear cells, and clinical outcomes were analyzed.

RESULTS: 15 patients were enrolled and 13 completed the study; 5 controls were also enrolled. The median follow-up was 20.4 months (range: 28.1 to 14.8m). No patient experienced dose-limiting toxicity or a Grade 3+ adverse event. No patients progressed to muscle-invasive disease. 9 patients successfully converted PPD. 9 of 13 patients recurred in the lower tract (69.2%) and all were successfully salvaged. Immunologically, BCG-specific T cell lymphoproliferation was increased, as was IFN-γ secretion, IFN-γ ELISPOT response, and direct ex vivo IFN-γ response. Flow cytometry demonstrated that BCG significantly enhanced CD4+ and CD8+ T cells in most patients. Compared to controls, primed patients exhibited an increase in IFN-γ release in response to BCG ex vivo at both 3 months and 6 months after therapy. Priming resulted in an earlier and more robust increase in urinary IL-2, IL-17, and IL-8 compared to control patients suggesting a potential benefit from earlier and higher activation of local immune response.

CONCLUSIONS: Vaccination with BCG prior to induction immunotherapy results in improved immunologic measurements and increased urinary cytokines associated with control of high-risk NMIBC. Priming may represent a method to increase the efficacy of BCG immunotherapy for high-risk NMIBC. Further study with dedicated multi-center clinical trials and long term follow-up is warranted.



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PD48-07

RECURRENCE AND PROGRESSION ACCORDING TO STAGE AT RE-TUR IN T1G3 BLADDER CANCER PATIENTS TREATED WITH BCG: NOT AS BAD AS PREVIOUSLY THOUGHT

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INTRODUCTION AND OBJECTIVES: The goals of transurethral resection of a bladder tumour (TUR) are to completely resect the lesions and to make a correct diagnosis in order to adequately stage the patient. Persistent disease after TUR is not uncommon and is the reason why re-TUR is recommended in T1G3 patients. When there is T1 tumour in the re-TUR specimen, very high risks of progression (82%) have been reported1 and therefore cystectomy is considered to be mandatory. We analyse the tumour stage at re-TUR and the risk of recurrence, progression to muscle invasive disease and cancer specific mortality (CSM) in T1G3 patients treated with BCG.

METHODS: In our retrospective cohort of 2451 T1G3 patients initially treated with BCG, pathology results for 934 patients (38.1%) who underwent re-TUR are available. There was no residual disease in 267 patients (28.6%) and residual disease in 667 patients (71.4%): Ta in 378 (40.5%) and T1 in 289 (30.9%) patients. 310 patients (33.2%) received more than 6 instillations of BCG. Event rates in the 3 groups were compared using the chi-square statistic on 2 degrees of freedom

RESULTS: Table 1 shows the observed results with a median follow up of 5.2 years and a maximum follow up of 18.7 years. Similar trends were seen in both patients with and patients without muscle in the original TUR specimen.

CONCLUSIONS: Patients with T1G3 tumours treated with BCG and no residual disease or Ta tumour at re-TUR have better recurrence, progression and CSM rates than those with T1 tumour. The 25.3% progression rate of patients with T1 disease after re-TUR is far lower than that previously reported, with a CSM rate of 13.1%.

4¥Residual tumour at re-TUR	Recurrence N (%)	Progression N (%)	CSM N (%)
No residual tumour	112 (41.9)	**38 (14.2)**	16 (6.0)
Ta tumour	193 (51.1)	**55 (14.6)**	31 (8.2)
T1 tumour	207 (71.6)	**73 (25.3)**	38 (13.1)
P value	P < 0.001	**P < 0.001**	P = 0.01

Table 1. Results at mean follow up of 5.2 years

Source of Funding: None

PD48-08

CLINICAL AND PATHOLOGICAL OUTCOMES FOR PATIENTS WITH HIGH RISK T1HG BLADDER CANCER MANAGED WITH EITHER UPFRONT CYSTECTOMY OR PRIMARY BCG AND DELAYED CYSTECTOMY

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INTRODUCTION AND OBJECTIVES: In muscle invasive bladder cancer (BC) there is an increased risk for systemic disease identified for patients with certain high risk features (HRF). We sought to