

## SENSITIVITY AND PROGNOSTIC IMPLICATIONS OF CYCLOOXYGENASE-2 (COX-2) MONOCLONAL ANTIBODY STAINING IN CYSTECTOMY SPECIMENS OF PATIENTS WITH 5 YEAR FOLLOW-UP

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**INTRODUCTION AND OBJECTIVES:** Cyclooxygenase-2 is an inducible enzyme, which plays a major role in inflammation, angiogenesis, and oncogenesis. Its expression is up-regulated in colon, bladder, and prostate cancer but previous reports have not correlated survival in bladder cancer patients with COX-2 levels. COX-2 staining intensity of cystectomy patients was examined and results correlated with tumor grade, clinical stage, and survival.

**METHODS:** Paraffin embedded specimens from 20 patients who each had a radical cystectomy in 1995 were retrieved and their clinical and pathologic data reviewed. Sixteen patients had various grades and stages of transitional cell carcinoma while four patients were used as negative controls. Colon cancer slides were used as positive controls with each immunostaining batch. The monoclonal antibody, AS66, recognizes the native COX-2 and does not cross react with COX-1. The slides were immunostained using AS66 and a standard avidin-biotin-horseradish peroxidase kit without antigen amplification or retrieval. A pathologist graded the staining results 0-3+ (no staining to most intense) in a blinded fashion.

**RESULTS:** All four patients with normal urothelium stained 0 with minimal epithelial staining while 13 of 16 patients with TCC stained positive (81%). Five out of six (83%) grade 2 tumors stained positive while seven out of ten grade 3 tumors (70%) stained positive. Clinical staging when correlated to staining showed that 5 of 6 T3b (83%) stained positive while 2 of 4 (50%) T3a stained positive. Finally, intensity of staining was correlated to tumor grade. Ten patient specimens stained 2+. Four of these ten were grade 2 and three of four (75%) were alive and with no evidence of disease (NED) at 5 years. The other six patients were grade 3 and three of six (50%) were alive at 5 years. Four patients with TCC had 0 staining with one grade 2 who was alive and NED (100%) but three had grade 3 and only one was alive (33%) and NED at 5 years.

**CONCLUSIONS:** AS66 can be utilized for immunostaining of paraffin embedded bladder tissue. Grade 2 tumors and clinical stage T3b tumors had the highest (83%) positivity. Staining intensity is correlated to tumor grade and survival, it appears that survival is higher with higher staining intensity and lower grade tumors, while no staining and high grade tumors reflect a poorer prognosis. COX-2 staining when correlated to tumor grade may have prognostic implications.

Presented at the 2001 Annual Meeting of the [American Urological Association](#). June 2–7, 2001, Anaheim, CA