The purpose of this study was to compare two new urinary tumor markers: Nuclear Matrix Protein (NMP22) and Bladder Tumor Antigen (BTA Stat) in the screening and monitoring of patients at risk for bladder cancer. A cohort of 278 patients at risk for bladder cancer (these include patients who present with either gross (n = 77) or microscopic hematuria (n = 112), chronic voiding symptoms (n = 89) submitted a single voided urine sample. Each sample was divided into three parts for NMP22 test, BTA Stat, and for cytological examination. Of the 278 patients evaluated in this study, 34 (12%) patients had histologically confirmed bladder cancer. Out of these 34 tumors, BTA Stat detected 23 cases with a sensitivity of 67.6% and NMP22 detected 28 cases with a sensitivity of 82.3%, however, the sensitivity of cytology was low at 29.4% as it was positive in only 10 cases. In the 72 patients with elevated NMP22 values, 28 cancers were detected (specificity: 81%; positive predictive value (PPV): 39%), the remaining 44 were false positives. Similarly, in the 66 patients with a positive BTA Stat test, 23 cancers were detected (specificity: 82%; PPV: 35%), the remaining 43 were false positives. Overall, a high negative predictive value was seen for both tumor markers and cytology (>90%). Both tumor markers, BTA Stat and NMP22 provide similar results (sensitivity and specificity) in the screening and monitoring of patients with bladder cancer. The high sensitivity of these two tumor markers as compared to the cytology should allow us to implement their use in our clinical practice.