

# Rate of Upstaging in Variant Histology Nonmuscle Invasive Bladder Cancer: Is There Evidence to Support the AUA Guidelines “Expert Opinion”?

Kristian Stensland, David Canes, Harras Zaid

## INTRODUCTION:

Non-urothelial variant bladder cancers may harbor more aggressive behaviors than pure urothelial cell carcinoma. As such, the AUA Guidelines on non-muscle invasive bladder cancer recommend consideration of timely cystectomy in patients with cT1 bladder cancer with variant histology, though this is provided as an “Expert Opinion”. The rationale for this recommendation is supposedly a high rate of upstaging at the time of cystectomy. However, the data on outcomes and upstaging for cT1 variant histologies are limited to small series. Herein, then, we sought to support this guideline statement with population-level evidence.

## METHODS:

The National Cancer Database was queried for non-metastatic, cT1 cN0 bladder cancer patients diagnosed between 2006-2014. Cases were excluded if patients received neoadjuvant chemotherapy. Clinical staging was compared to pathologic staging for variant histologies and compared to conventional urothelial carcinoma. Variant histologies evaluated included the following: adenocarcinoma, small cell, spindle cell, squamous cell, signet ring cell, and micropapillary. Upstaging was defined as pathologic T2-T4 or pathologic node-positive disease. Rates of upstaging for each variant histology were compared to conventional urothelial carcinoma and the null hypothesis of no difference in upstaging tested by the chi-square test.

## RESULTS:

A total of 22,722 cases of bladder cancer were included. A total of 21,855 (96%) cases were urothelial, and 867 (4%) were variant. The most common variant histology was SCC (n=312), followed by adenocarcinoma (n=250), spindle cell (n=96), micropapillary (n=92), small cell (n=78), and signet ring cell carcinoma (n=39). The rates of upstaging from clinical to pathologic staging were significantly higher for all 6 variant histologies evaluated compared to urothelial carcinoma, with rates ranging from 30.8% (adenocarcinoma) to 61.5% (signet ring cell carcinoma); see Table 1.

## DISCUSSION:

These data demonstrate significant rates of upstaging in cT1 bladder cancers with variant histologies, as high as 62%. The information provided here is in line with the “Expert Opinion” set forth in the AUA Guidelines for non-muscle invasive bladder cancer and lend further data for timely cystectomy in this high-risk population.

### Rates of Up/Downstaging

Histology	Upstaged	Same stage	Downstaged
Urothelial	2,552 (11.7%)	18,147 (83.0%)	1,156 (5.3%)
Adenocarcinoma	77 (30.8%)	161 (64.4%)	12 (4.8%)
Small Cell	34 (43.6%)	39 (50.0%)	5 (6.4%)

Spindle Cell	43 (44.8%)	44 (45.8%)	9 (9.4%)
Squamous Cell	154 (49.4%)	148 (47.4%)	10 (3.2%)
Signet Ring Cell	24 (61.5%)	13 (33.3%)	2 (5.1%)
Micropapillary	37 (40.2%)	46 (50.0%)	9 (9.8%)

*All histologies compared pairwise to urothelial rate of upstaging; all  $p < 0.001$*