

Michael Lin-Brande BS<sup>1</sup>, Daniel Zainfeld MD<sup>1</sup>, Saum Ghodoussipour MD<sup>1</sup>, Jie Cai MS<sup>1</sup>, Gus Miranda BS<sup>1</sup>, Hooman Djaladat MD<sup>1</sup>,

Anne Schuckman MD<sup>1</sup>, Sarmad Sadeghi MD<sup>2</sup>, Tanya Dorff MD<sup>2</sup>, David Quinn MD<sup>2</sup>, Siamak Daneshmand MD<sup>1</sup>

<sup>1</sup>Institute of Urology <sup>2</sup>Department of Medical Oncology, University of Southern California/Norris Comprehensive Cancer Center, Los Angeles, CA

## Background

- Neoadjuvant chemotherapy (NAC) provides a survival benefit for muscle-invasive bladder cancer
- Variant histology (VH) of urothelial carcinoma has gained attention for its aberrant characteristics
- Our objective was to assess the ability of NAC to downstage VH and pure urothelial carcinoma (PUC) and to quantify variant subtypes and overall survival

## Materials and Methods

- We identified 1,440 patients from our prospectively maintained database with urothelial carcinoma of the bladder who underwent radical cystectomy at our tertiary referral center between 2003 and 2016
- Histology was categorized as pure urothelial carcinoma (PUC) or variant histology (VH)
- Neuroendocrine variants were excluded
- Multivariable Cox proportional hazards model was used to analyze impact of VH on overall survival (OS)

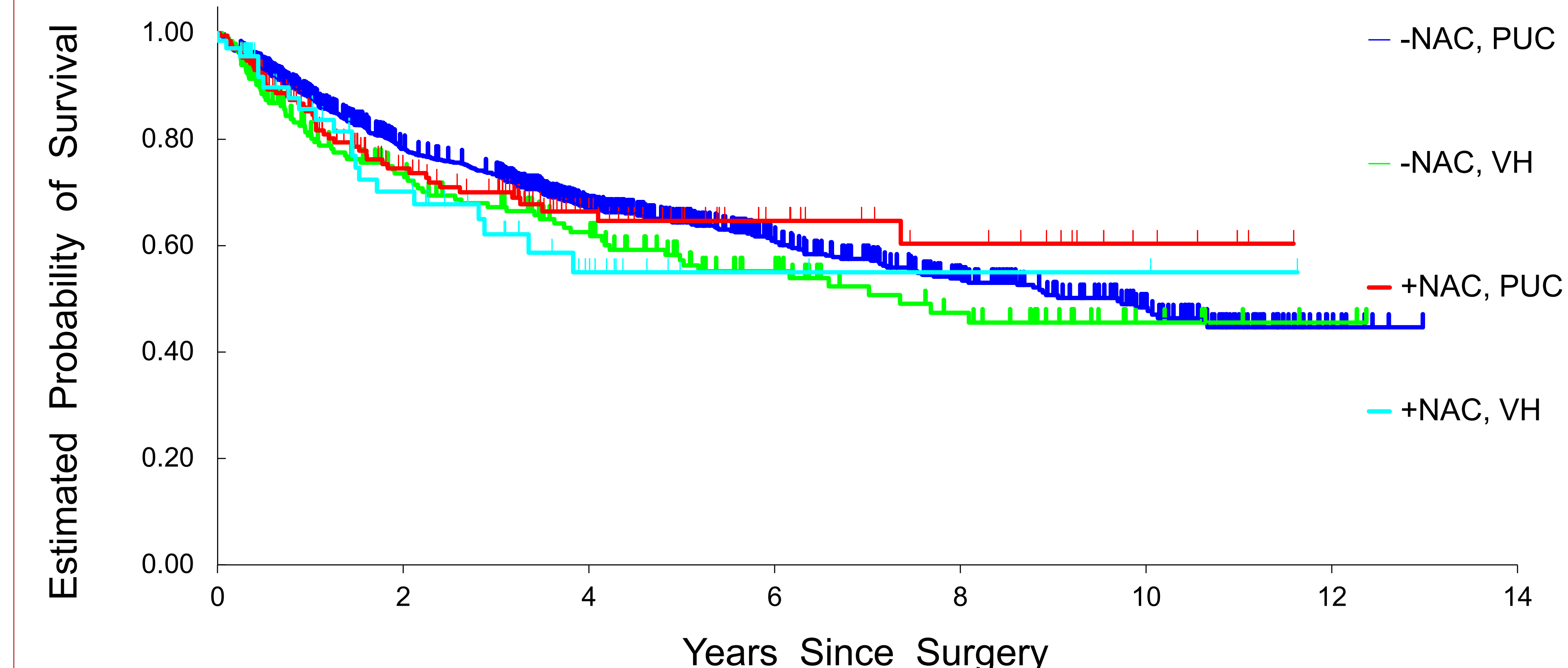
## Results

**Table 1. Variant histology characteristics**

No. patients	269			
Squamous	121 (44.9)	Nested	10 (3.7)	
Glandular	54 (20.0)	Clear cell	5 (1.9)	
Micropapillary	30 (11.2)	Rhabdoid	3 (1.1)	
Sarcomatoid	14 (5.2)	>1 variant	28 (10.4)	

- 1,171 (81.3%) patients were PUC, 269 (18.7%) were VH
- Variant histology was more likely to:
  - Present with extravesical extension (20.8%) vs PUC (13.3%),  $p < 0.01$
  - Receive NAC (27.7%) vs PUC (16.4%),  $p < 0.01$
  - Be downstaged after receiving NAC (62.3%) vs PUC (54.4%),  $p < 0.01$
- On multivariable Cox regression, extravesical extension (HR=2.3,  $p < 0.01$ ), positive lymph node (HR=4.7,  $p < 0.01$ ), LVI (HR=1.6,  $p < 0.01$ ), and age (HR=1.03,  $p < 0.01$ ) were associated with worse OS
- Clinical VH (HR=1.04,  $p = 0.76$ ) and pathologic VH (HR=0.79,  $p = 0.70$ ) had no effect on OS
- 5-year overall survival for VH + NAC was 55% and VH - NAC was 57%,  $p = 0.33$

**Overall survival estimates based on histology and neoadjuvant chemotherapy**



## Conclusions

- Variant histology was more likely to present with extravesical disease, receive neoadjuvant chemotherapy, and be downstaged at cystectomy compared to pure urothelial carcinoma
- Despite the tumor response to NAC, there was no effect on overall survival
- Within variant histology, there are differences in clinical characteristics. Future directions include assessing each variant histology's response to neoadjuvant chemotherapy