

# Can Imaging Response following Neoadjuvant Chemotherapy in Upper Tract Urothelial Cancer be a Surrogate for Pathologic Response?

Nirmal Thampi John, Amy Tin, Daniel D Sjoberg, Nicole E Benfante, A Ari Hakimi, Paul Russo, Jonathan Coleman

Memorial Sloan Kettering Cancer Center, New York, NY

## Introduction

- Pathological response following neoadjuvant chemotherapy (NAC) has been shown to be an excellent surrogate for survival in bladder cancer.
- Preoperative endoscopic and pathologic assessment of response is difficult in upper tract urothelial cancer (UTUC).
- The aim of this study was to see whether imaging response following NAC predicted the final pathologic stage and outcomes following radical nephroureterectomy (NU).

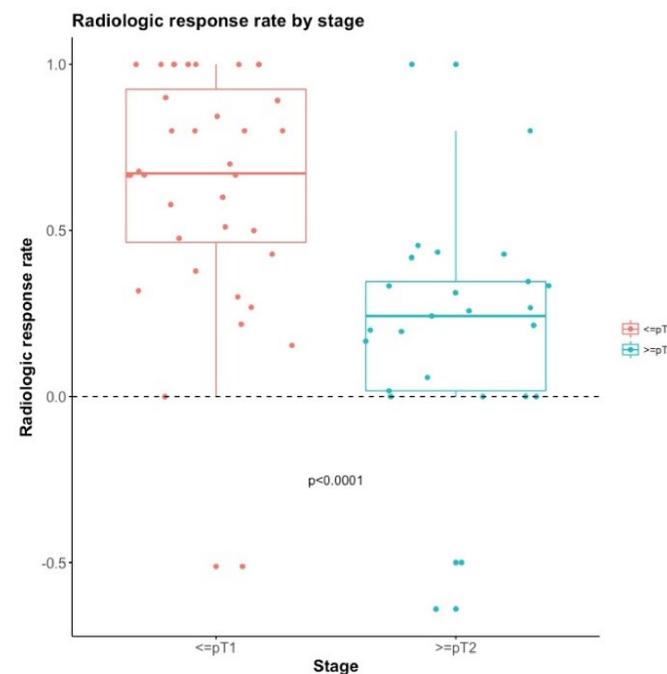
## Methods

- Of the 685 NUs, cytology and/ biopsy proven,  $\geq cT2anyNM0$  high grade UTUC patients who underwent NAC with cisplatin based chemotherapy from Jan 1997 – Jul 2017 were analyzed.
- CT/MR urography was available both before and after NAC. Radiological response rate (RRR) was estimated using the RECIST criteria and pathologic response was defined as  $< pT2$ .
- We assessed the association between response on radiology and final pathology using Fisher's exact test. Multivariable Cox proportional hazard regression model was used to assess association between RRR and overall survival.

## Results

- 62 (9.1%) underwent cisplatin based NAC prior to surgery.
- 16% of patients had complete response on imaging, 52% had partial response, 27% had stable disease, and the remaining 5% progressed. Thirty-six patients (58%; 95% CI 45%, 70%) responded to NAC on pathology.
- The median radiological response rate was 0.44 (0.22, 0.80). The mean RRR stage for responders was 0.64 and 0.21 for the non-responders ( $p < 0.0001$ ), Figure 1.
- Radiological response was significantly associated with pathological response on both univariate (OR 8.45; 95% CI 2.49, 28.74;  $p = 0.001$ ) and multivariable (9.14; 95% CI 2.57, 32.56;  $p = 0.001$ ) analyses, Table 1.
- Pathological response was associated with significant better overall survival (HR 0.20; 95% CI 0.06, 0.64;  $p = 0.007$ ), Figure 2.
- On multivariable analysis, radiological response was associated with non-significant better overall survival (HR 0.48; 95% CI 0.17, 1.31;  $p = 0.2$ ).

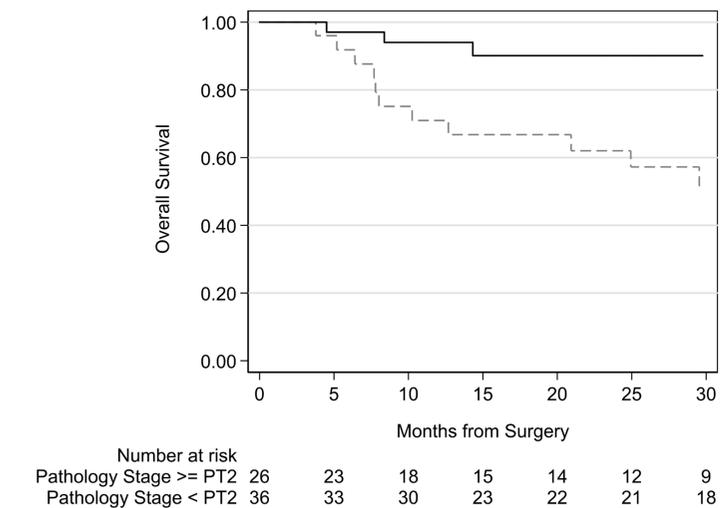
**Figure 1** Mean RRR for responders vs. non-responders



**Table 1** Patients based on response on radiology scans and pathology (Fisher's exact  $p = 0.0004$ )

Response to Chemotherapy		Pathological response	
		Yes	No
Radiological response	Yes	31	11
	No	5	15

**Figure 2** Kaplan-Meier estimated overall survival probability for patients with response on pathology (solid black line) and no response on pathology (dashed grey line)



## Conclusions

- Radiological response rates following NAC in UTUC is significantly associated with pathologic response and non-significantly associated with better overall survival following NU.
- Unlike bladder cancer, there is lack of level I evidence recommending NAC in UTUC. Moreover, toxicity and overtreatment are major concerns.
- Therefore, RRR could be used as a preoperative tool to predict prognosis and identify the "chemo-resistant" cohort who could then be counseled for alternate treatment modalities.