Introduction

- Use of neoadjuvant cisplatin-based chemotherapy (NAC) in UTUC is based on evidence of survival benefit in urothelial carcinoma (UC) of the bladder.
- However, concerns regarding toxicity and lack of efficacy have prevented its widespread adoption.
- We aim to analyze the genomic profiling data of UTUCs from patients who received NAC to identify predictors of chemo-sensitivity.

Methods

- We reviewed data on all ≥cT2anyNM0 high-grade UTUC patients who underwent genomic profiling prior to cisplatin-based NAC.
- We evaluated 14 of the most commonly altered genes in UTUC (≥10%) identified by the MSK-IMPACT assay in a recently published study (FGFR3, KMT2D, KDM8A, KMT2C, STAG2, CDKN2A, TP53, CDKN2B, CREBBP, TSC1, PIK3CA, ARID1A, CCND1 and HRAS), Figure 1. We also looked at ERCC2 and Bcl-2, which have been linked with response to chemotherapy in bladder UC.
- We assessed the association between alterations and pathologic response (<pT2 at Radical nephroureterectomy) using univariate logistic regression.

Results

- 62 (9.1%) received cisplatin-based NAC and 22 underwent MSK-IMPACT sequencing of pre-treatment tumor tissue.
- Of these patients, 16 (73%; 95% CI 50%, 89%) achieved <pT2 response to NAC, Table 1.
- Three patients had CCND1 amplification, one of whom had pathological NAC response. CCND1 amplification was associated with non-significant lower odds of NAC response on pathology (OR 0.13; 95% CI 0.01, 1.87).
- 15/19 (79%) patients without CCND1 amplification had NAC response on pathology compared to 1/3 (33%) patients with CCND1 amplification had NAC response on pathology (difference 46%, 95% CI -11%, 100%).

Conclusions

- CCND1 amplification was found to be non-significantly associated with lack of response following cisplatin-based NAC.
- Similar findings in cancers of the head and neck, colon, breast and bladder suggest the importance of CCND1 as a prognostic marker and potential actionable target in cisplatin-resistant high risk UTUC; however, larger studies are needed for confirmation.