Comprehensive genomic profiling (CGP) of upper-tract (UTUC) and bladder (BUC) urothelial carcinoma reveals opportunities for therapeutic and biomarker development

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RESULTS

Comparison of TMB in BUC and UTUC by site of biopsy

Comparison of genomic alterations in BUC and UTUC

Comparison of mutations detected by genomic profiling of tissue and blood samples as a function of time.

A. Unmatched tissue (N=2463) and blood samples with detected ctDNA (N=93) from patients with urothelial cancer were evaluated for FGFR3 mutation frequency. The distribution of FGFR3 mutations identified in tissue and blood are shown. ns, not significant.

B. For the 21 patients with matched tissue and blood samples with detected ctDNA, mutations were classified into those found in tissue-only, blood-only, or shared (found in both tissue and blood). Concordance was evaluated as positive-percent agreement (PPA) with tissue as a reference and as % of all detected mutations that were shared.

C. Comparison of TMB in BUC and UTUC. Overall (median 232 days).

CONCLUSIONS

Against a background of 50% actionability in UC with opportunities for immunotherapy, TT, or combinations thereof, the UTUC cohort is enriched for FGFR3 and HRAS SV relative to BUC in the renal pelvis, that warrants further investigation into the distinct modes of oncogenesis for UC as stratified by anatomic origin.

Liquid biopsy-based genomic profiling identified targetable FGFR3 alterations. 73% of mutations present in matched tissue samples were also detected in paired liquid biopsy samples (>180 days time interval).

These results argue strongly for the routine incorporation of CGP prior to systemic therapy initiation in metastatic UC.

REFERENCES