Abstract B11: Whole-exome sequencing analysis of urine transrenal tumor DNA in metastatic colorectal cancer patients

Whole-exome sequencing analysis of urine transrenal tumor DNA in metastatic colorectal cancer patients

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Background: The analysis of circulating free tumor DNA (ctDNA) in blood, commonly referred to as liquid biopsy, is being used to characterize patients with solid cancers. Tumor-specific genetic variants can also be present in DNA isolated from other body fluids such as urine. Unlike blood, urine sampling is noninvasive, can be self-performed, and allows recurrent longitudinal monitoring. The features of tumor DNA that clears from the glomerular filtration barrier (transrenal tumor DNA, hereafter trtDNA) are largely unexplored.

Patients and Methods: Specimens were collected from 24 patients with KRAS or BRAF mutant metastatic colorectal cancer (mCRC). Driver mutations were assessed by droplet digital PCR (ddPCR) in ctDNA from plasma and trtDNA from urine. Whole-exome sequencing (WES) was performed in DNA isolated from tissue, plasma, and urine.

Results: Out of the 24 CRC cases, only four had sufficient DNA to allow WES analyses in urine and plasma. We found that tumor alterations reside primarily in low-molecular-weight fragments. In patients where trtDNA was more than 2.69% of the urine-derived DNA, cancer-specific molecular alterations, mutational signatures, and copy number profiles identified in urine DNA are comparable with those detected in plasma ctDNA.

Conclusions: With current technologies, WES analysis of trtDNA is feasible in a small fraction of mCRC patients. Tumor-related genetic information is mainly present in shorter DNA fragments. Although the limited amounts of trtDNA pose analytical challenges, enrichment of low-molecular-weight DNA and optimized computational tools improve detection of tumor-specific genetic information in urine.