67 Real world data of how next-generation sequencing changes treatment strategy and identify hereditary diseases in urology cancers

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Introduction & Objectives: Next generation sequencing (NGS) has been routinely used in urology cancers in order to diagnose hereditary diseases for young age patients or to guide further precision medications for late stage cancers. We conducted this study to investigate how far NGS is changing our treatment strategies from a real world data.

Materials & Methods: We retrospectively reviewed the NGS data of urology cancer (prostate, kidney and urothelial cancer) patients who undergone NGS testing in our institute from December 2017 to December 2018. All of the patients accepted NGS under physicians' advises for detecting either hereditary diseases or to guide further treatments. Advises were given based on clinical purposes during daily clinical practices. The gene panels chosen in the study included known urology hereditary genes, known genes responsible for targeted therapy and known cancer driver genes. Potential pathogenic and likely pathogenic mutations were verified according to ACMG guidelines.

Results: In total, 141 patients undergone NGS for germline mutations, 76 patients undergone NGS for somatic mutations. For prostate cancers, more than 80% were of late stage or of CRPC. 43 pathogenic mutations were found in the 52 somatic samples, among which 9 patients harbor DNA damage repair gene(DRGs) mutations and 1 patient harbor MSH2 mutation. Advises of taking PARP inhibitors were given to patients with DRG mutations. For kidney cancers, 42 patients undergone germline NGS, some of them were young patients less than 46 years old, some of them had typical phenotypes. In total 7 pathogenic mutations were found to be hereditary, including 3 VHL, 1 FH, 1 CHEK2, 1 RAD50 and 1 BRCA2. Of which, RAD50 and BRCA2 were not genes responsible for hereditary kidney cancers, aroused interest for further investigation. Family members of those patients were recruited to the hospital for further genetic counseling. Mutation burden were significantly higher in metastatic urothelial cancer patients compared to the other cancer types. 6 TP53 pathogenic mutations were found in the 9 urothelial cancer patients, the rest were 3KMT2D, 1 PTEN, 1 BRCA2, 1 TSC1, 1 KRAS etc. Some of the patients were suggested to enter clinical trials targeting certain mutations, while some turned to use PD-1 inhibitors.

Conclusions: This study of real world data shows that during clinical practice, NGS for selected patients could alter at least 20% treatment strategies and could discover more hereditary diseases in a more effective way.