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The mutational burden of targeted genes significantly correlated with overall survival after targeted therapy in metastatic renal cell carcinoma

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Abstract

This study aimed to find the correlation between tumour mutation burden and systemic first-line therapeutic response in metastatic tissue samples from patients with metastatic renal cell carcinoma (mRCC). Between 2005 and 2017, 168 triplet-tissue block samples (with at least one tissue block having passed their quality checks) from 56 mRCC patients were selected for targeted gene sequencing (TGS) using the 88 targeted genes from the National Cancer Center, Korea (NCC) kidney cancer panel. The patients' medical records, including therapeutic responsive profiles with overall survival (OS) to first-line targeted therapy, were evaluated with the mutational burden of triplet tissue samples using 88 TGS. The OS was defined as the time interval between the diagnosis of metastasis and death. A few significant target genes associated with the therapeutic response towards targeted therapy were identified after comparing the mutational burden of positive for all three blocks and one or two positive blocks (p-value < 0.05).The median PFS for the first-line targeted therapy and OS were 8.7 and 42 months, respectively. MSKCC and Heng risk criteria showed 28.9/65.8/5.3% and 26,3/57.9/15.8% for favourable, intermediate, and poor-risk groups, respectively. Also, 55.3% and 52.6% of patients received metastasectomy and nephrectomy, respectively. The clinical T stage comprised T1 26.8%, T2 16.1%, T3 8.9%, T4 1.8%, Tx 46.4% and N stage 26.3% of N1. The histopathology showed 50.0%, 1.8%, and 48.2% of clear, non-clear, and unknown cells, respectively. Eighteen (32.1%) patients had all triplet blocks passed for quality check, whereas 21 (37.5%) and 17 (30.4%) patients had two or one passed tissue blocks, respectively. Among the 18 patients with triplet-block, TP53, URB4, PTK2, and SGO2 genes had significant discrimination power for OS on comparing their mutational burden in the three blocks positive group (N=7) and two or fewer blocks positive groups (N=11) (p<0.05). Among the 39 patients with either doublet or triplet blocks passed for quality check, TP53, URB1, PTK2, SGO2, BRAF, NEDD4, PDXDC1, CDH1, FGFR2, RET, RUNX1, and SDHB genes had significant discrimination power for DFS when comparing their mutational burden in the three blocks positive group (N=7) and two or fewer blocks positive groups (N=14) (p<0.01).

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Biography

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