

**A REAL-WORLD RETROSPECTIVE STUDY OF IMMUNOTHERAPY IN NSCLC PATIENTS WITH KRAS MUTATION**

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**Background** KRAS mutations occur in about 15–20% of patients with lung cancer. Due to the small size and smooth surface of KRAS protein, it is difficult to develop KRAS inhibitors. Sotorasib and adagrasib are targeted drugs that have been proven effective and approved for KRAS G12C mutation, but they have not yet entered the Chinese market. For non-small cell lung cancer (NSCLC) patients with KRAS mutations, immune checkpoint inhibitors (ICIs) have been widely used. However, it remains unclear how much those patients benefit from ICIs.

**Methods** A total of 166 NSCLC patients with KRAS mutations who had received immunotherapy at Shanghai Chest Hospital were analyzed retrospectively. The baseline clinical characteristics, whether combined with TP53 or STK11 mutation, PD-L1 expression, and immunotherapy regimen, were evaluated. The correlation between these factors and progression-free survival (PFS), overall survival (OS), and objective response rate (ORR) were also analyzed.

**Results** Among the 166 patients, 129 (77.7%) were lung adenocarcinoma, and 145 (87.3%) were stage IV. The most common KRAS mutation was KRAS G12C (32%), followed by KRAS G12V (19%) and KRAS G12D (17%). Thirty-two patients (19.3%) received ICIs monotherapy, and 134 patients (80.7%) received ICIs combined with chemotherapy or anti-angiogenesis therapy. The ORR of the entire population was 42.8%, while the mPFS and the mOS were 9.0 months and 16.0 months, respectively. The patients were divided into two groups according to their timing of receiving immunotherapy, as 105 patients (63.3%) received first-line treatment (1L) and 61 (36.7%) received second-line and above treatment (2L+). The 1L group had better prognosis than the 2L+ group, reflected in ORR (50.5% vs. 29.5%,  $P=0.001$ ), mPFS (13.5 months vs. 5.0 months,  $P < 0.001$ ), and mOS (20.0 months vs. 11.0 months,  $P=0.004$ ). In the 1L group, patients who received combination therapy had longer survival than who received monotherapy (mPFS: 14.0 months vs. 4.0 months,  $P=0.048$ ; mOS: 20.0 months vs. 10.5 months,  $P=0.013$ ). Moreover, in the entire population, patients with TP53 mutation (11.0 months vs. 8.5 months,  $P=0.038$ ), positive PD-L1 expression (9.0 months vs. 8.5 months,  $P=0.041$ ), or common mutations such as KRAS G12C/G12D/G12V showed better PFS (PFS: 14.5 months vs. 8.0 months,  $P=0.045$ ).

**Conclusions** Bringing immunotherapy to first-line use in NSCLC patients with KRAS mutation might prolong their survival, and combination therapy is a preferable option compared to monotherapy. Positive PD-L1 expression and common KRAS mutations may serve as potential prognostic biomarkers for KRAS-mutated NSCLC patients who receive immunotherapy.

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