NTRK3 mutation affects the efficacy of immune checkpoint inhibitors in patients with advanced cancer

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Abstract 2951

BACKGROUND

- Immune checkpoint inhibitors (ICIs) can improve the survival of cancer patients. Nevertheless, ICIs are only effective for some patients.
- Neurotrophin tyrosine kinase receptor 3 (*NTRK3*) acts as a tumor suppressor or oncogene in the development of various cancers. However, the efficacy of *NTRK3* mutation in immunotherapy for patients with cancer is unknown.
- Herein, we aimed to analyze the association between *NTRK3* mutation and the efficacy of ICIs.

METHODS

- We screened 1661 patients with advanced cancer in the MSKCC cohort who had complete information, received at least one dose of ICI, and whose tumors underwent next-generation sequencing (NGS).
- The patients were divided into *NTRK3* mutant type (*NTRK3*-MT) group and *NRTK3* wild type (*NTRK3*-WT) group according to *NTRK3* mutation status.
- We analyzed the differences in overall survival (OS) and TMB between the two groups. Pooled hazard ratios (HR) and 95% confidence intervals (CI) for OS were calculated by Cox regression models, and P values were calculated by Wilcoxon's sign test for TMB.

RESULTS

- Among 1661 advanced cancer patients, 75 (4.5%) *NTRK3*-MT and 1586 (95.5%) *NTRK3*-WT. *NTRK3*-MT group had significantly longer OS (p=7.0e-5; HR=0.42; 95% CI: 0.27-0.65) and higher TMB (p<2.2e-16). In total 1661 patients, 350 (21.1%) were non-small cell lung cancer (NSCLC), including 20 (5.7%) *NTRK3*-MT and 330 (94.8%) *NTRK3*-WT. *NTRK3*-MT group also had significantly longer OS (p=0.01; HR=0.36; 95% CI: 0.16-0.81) and higher TMB(p=1.1e-5) in NSCLC.

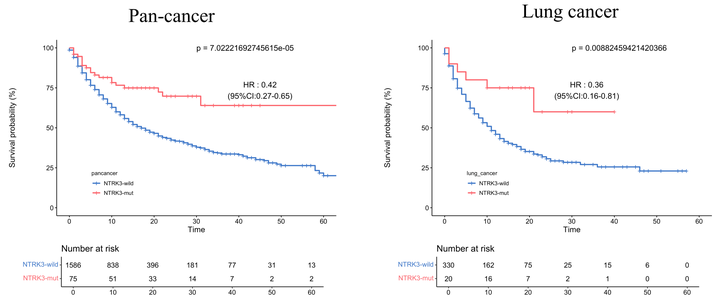

Fig.1 Relationship between survival and *NTRK3* in MSKCC cohort patients

- Moreover, the 1661 patients were further divided into 4 groups according to *NTRK3* status and TMB (TMB-H, TMB top 25%; TMB-L, other TMB) and found that TMB-H_*NTRK3*-MT group had the best OS (p=3.9e-12; HR=0.22; 95% CI: 0.94-4.62). The same outcome trends were reflected in the NSCLC cohort (p=0.01; HR=0.22; 95% CI: 0.70-4.63).

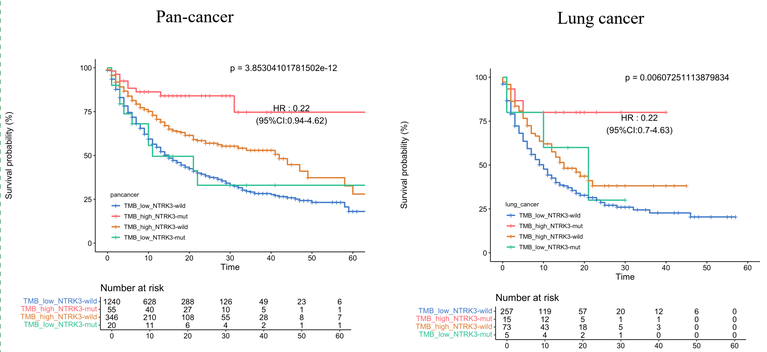

Fig.2 Relationship among survival , TMB and *NTRK3* in MSKCC cohort patients

CONCLUSION

- Our study founded that patients with cancer harboring *NTRK3* mutation tended to have higher TMB and longer OS for the first time. In the future, relevant prospective clinical trials need to be designed to verify this conclusion.

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