80P - The analysis of ROS1 fusions characteristics in Chinese solid tumor patients

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BACKGROUND

- Based on the approvals of crizotinib and entrectinib by the Food and Drug Administration for the treatment of ROS1 positive non-small lung cancer (lung cancer), we sought to analysis of ROS1 fusions characteristics in Chinese solid tumor patients to explore the possibility of therapeutic intervention in solid tumors.

METHODS

- In this study, we retrospectively analyzed ROS1 fusion using next-generation sequencing(NGS). For the purposes of this study we excluded any ROS1 fusions where the ROS1 kinase domain wasn't predicted to be preserved based on DNA sequencing results. From May 2019 to April 2022, 50543 patients were detected.

RESULTS

- A total of 296 unique cases (92.9% (275/296) lung cancer and 7.1% (21/296) non-lung cancer with ROS1 fusions were identified. The non-lung cancer cohort consisted up mainly brain tumors (33.3%, 7/21) ,gastric tumors (14.3%, 3/21) , colorectal tumors (9.5%, 2/21) , melanoma (9.5%, 2/21) and biliary tumors (9.5%, 2/21) .
- The top five fusions partners identified in the lung cancer cohort were CD74 (43.1%), EZR (23.1%), SDC4(13.0%), SLC34A2 (5.0%), and TPM3 (2.5%). On the other hand, the most common fusions partners were GOPC（30.4%）and DST (8.6%) in the non lung cancer cohort.
- Nine novel partners, DST, CABYR, CRYBG1, ETV1, MBNL2, MICAL2, UNC13A,CTNNA1 and PPP1R10 were identified across both cohorts of patients. Interestingly, in the lung cancer ROS1 fusion positive cohort, the breakpoints most frequently occurred in ROS1 introns 33, 32, and 31, while in the non-lung cancer ROS1 fusion-positive cohort, more than half of the breakpoints occurred in ROS1 intron 34.
- 79 patients in the lung cancer ROS1 fusion-positive cohort and 14 patients in the non-lung cancer ROS1 fusion-positive cohort could be evaluated for concurrent mutations and microsatellite instability (MSI) status. Overall, fewer other diver mutations/fusions was found in both cohorts of patients and no cases had an MSI-H status.

Fig 1. Prevalence of diagnosis in ROS1 fusion positive cohort

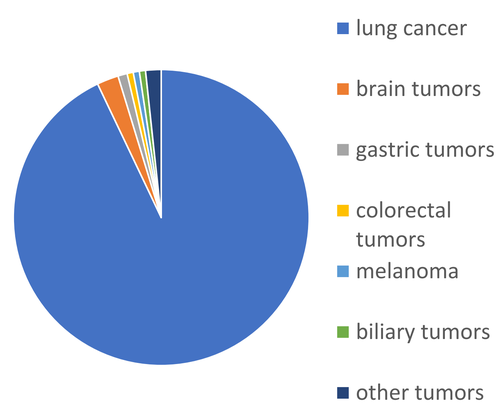

Table 1. The fusion partner prevalence in the NSCLC ROS1 fusion positive cohort and non-NSCLC ROS1 fusion positive cohort

NSCLC *ROS1* fusion^{pos} cohort	non-NSCLC *ROS1* fusion^{pos} cohort
CD74-ROS1(43.1%)	GOPC-ROS1(30.4%)
EZR-ROS1 (23.1%)	DST-ROS1 (8.6%)
SDC4-ROS1 (13.0%)	ROS1 Fusion(other)(61%)
SLC34A2-ROS1 (5.0%)	
TPM3-ROS1(2.5%)	
ROS1 Fusion(other)(13.3%)	

CONCLUSIONS

- ROS1 fusions were detected in 0.59%(296/50543) of Chinese solid tumor patients. 92.9% of ROS1 fusion positive cases were diagnosed with lung cancer and 7.1% were diagnosed with non-lung cancer. Nine novel ROS1 fusion partners were discovered.
- ROS1 fusion is an important driver genomic alteration in both the lung cancer and non-lung cancer cohorts. ROS1 targeted therapies should be further explored in non-lung cancer in clinical studies.

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