ROS1 aberrations without rearrangements in non-small cell lung cancer patients: Clinical and molecular Characteristics

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Background

Fusions in the *ROS1* proto-oncogene are among the best treatable genetic aberrations in Non-small cell lung cancer (NSCLC). Besides the occurrence of solvent-front mutations (SFM) in acquired resistance to targeted therapy, little is known about *ROS1* aberrations other than fusions. We analyzed molecular and clinical characteristics of *ROS1* mutations in NSCLC patients without activating *ROS1* fusions or SFMs.

Methods

Next-generation sequencing (NGS) was performed on tissue samples from NSCLC patients within the National Network Genomic Medicine (nNGM). Patients with activating *ROS1* fusions detected by fluorescence in-situ hybridization (FISH) were excluded. We analyzed the mutations' frequencies and clinical characteristics as well as co-occurring mutations.

References

[1]Bergethon, Kristin et al. "ROS1 rearrangements define a unique molecular class of lung cancers." *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* vol. 30,8 (2012): 863-70

Results

Of 8072 patients analyzed by NGS between 2018 and 2021, 118 (1.5%) patients harbored *ROS1* mutations. Most patients were male (76.3%) and had adenocarcinoma histology (57.6%). The median age at diagnosis amounted to 68 years. Nearly all of the patients (96.5%) had a smoking history, amassing 40 pack-years on average. The most frequent *ROS1* mutations were transversions (53.6%), without defining a genomic hotspot region. Besides *TP53* mutations (61.0%), *KRAS* (25.4%), *EGFR* (7.6%), *PIK3CA* and *FGFR1-4* mutations (5.9% each) co-occurred most frequently. In 12 (10.2%) patients, *ROS1* mutation was the only detected aberration.

Figure 2 - Molecular Characteristics

Co-occurring Mutations and Histology comparing Mutations(above) to Fusions[1](below)

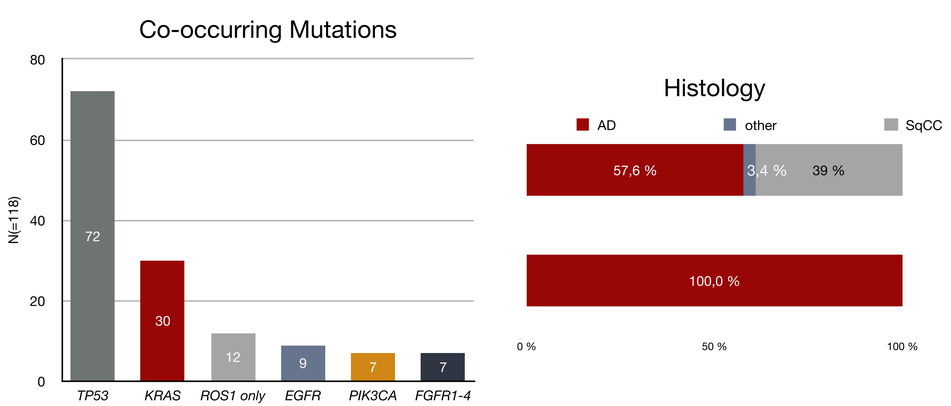
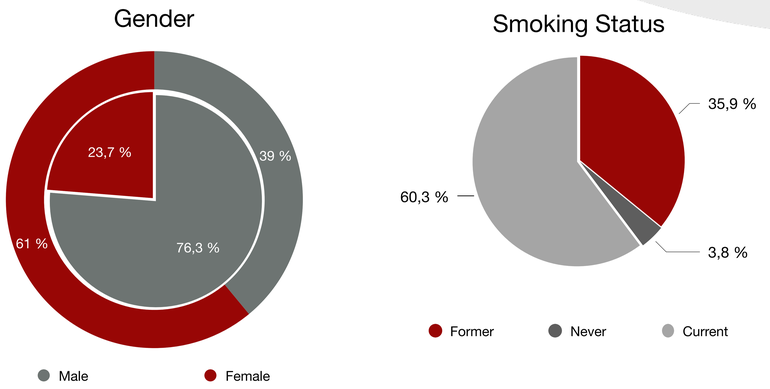


Figure 1 - Clinical Characteristics

Gender comparing Mutations(inner) to Fusions[1](outer) and smoking status in patients with *ROS1* Mutations



Conclusion

Our cohort opposites the clinical characteristics of patients with *ROS1* fusion regarding sex[1], smoking history, age and histology[1]. Further research is warranted to characterize their biological impact and their potential to act as a drug target.

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