Real-World Associations Between Smoking Status and Genetic Driver Mutations in Metastatic Lung Cancer in US Community Oncology

RWD148

Lisa Herms, Matthew Whitesell, Zhaohui Su, Jessica Paulus, Robert Reid

Author Affiliations: Ontada, Boston, MA, USA

Disclosure: All authors are employees of Ontada, a McKesson business

Background

- As of 2023, lung cancer in never-smokers (NS) has become the fifth leading cause of cancer mortality worldwide, with rising incidence
- NS patients may harbor distinct genetic driver mutations, differentiating them clinically from ever-smokers (ES) and potentially influencing treatment strategies and outcomes
- This real-world study examined the relationship between smoking status and genetic mutations in metastatic lung cancer patients treated within a large network of US community oncology clinics

Objective

- To examine the relationship between smoking status and genetic mutations in metastatic lung cancer patients in a real-world community oncology setting

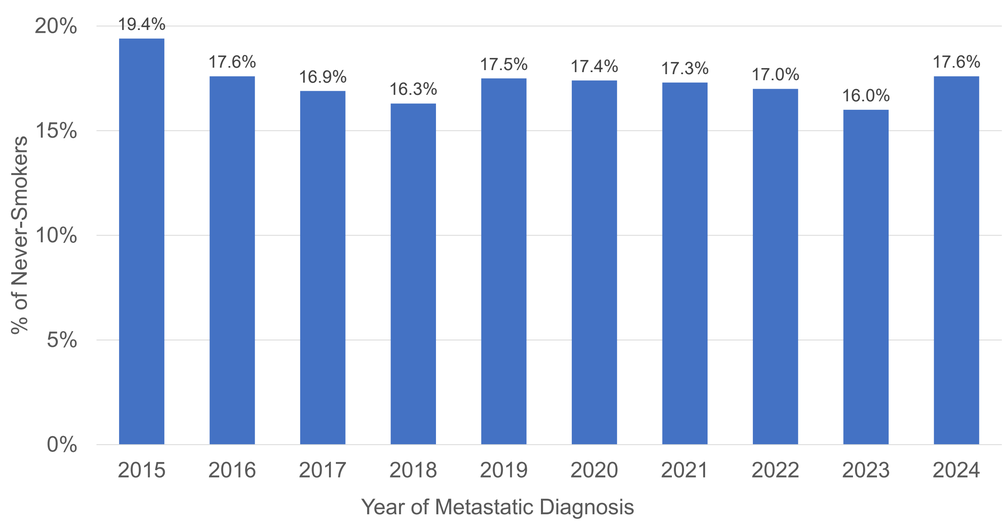
Methods

- Adults diagnosed with metastatic adenocarcinoma and large cell carcinoma between 2015 and 2024 were identified from an oncology-specific electronic health records system used by The US Oncology Network and non-Network practices
- Patients with self-reported tobacco history were classified as ES or NS
- Biomarker testing within 90 days of metastatic diagnosis was described over time. Biomarkers included EGFR, ALK, KRAS, ROS1, PD-L1, NTRK, HER2, RET, MET, BRAF, and NRG1
- The proportion of ES and NS patients with genetic mutations were compared using chi-square tests

Results

- The total study population of 27,263 patients included 4,696 NS, 18,681 ES, and 3,886 with unknown smoking status
- The proportion of LC patients who were NS remained consistent over time (~17-18%) (Figure 1)

Figure 1: Proportion of Never-Smokers among Lung Cancer Patients Over Time



- Higher alteration rates (p<0.01) were observed for NS compared to ES in EGFR (44.3% vs. 11.1%), ALK (11.0% vs. 2.7%), and, to a lesser extent, ROS1 (3.7% vs. 1.8%) (Figure 3)
- Conversely, higher KRAS alteration rates were observed among ES compared to NS patients (40.7% vs. 13.8%; p<0.01)

Figure 3: Frequency of Genetic Mutations, by Smoking Status

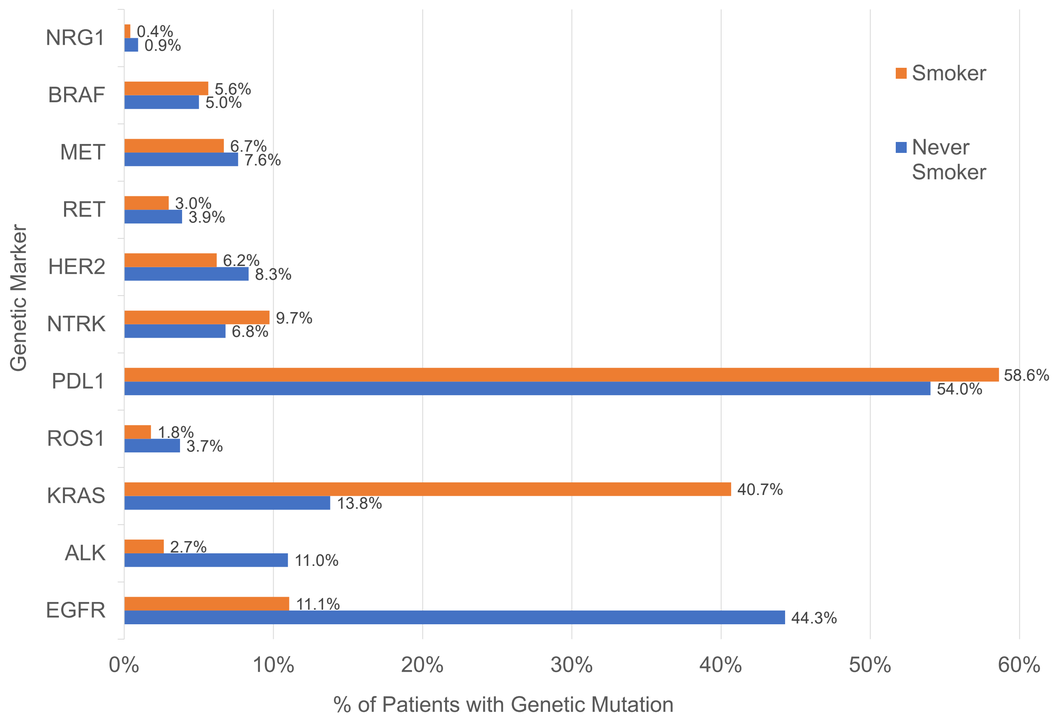
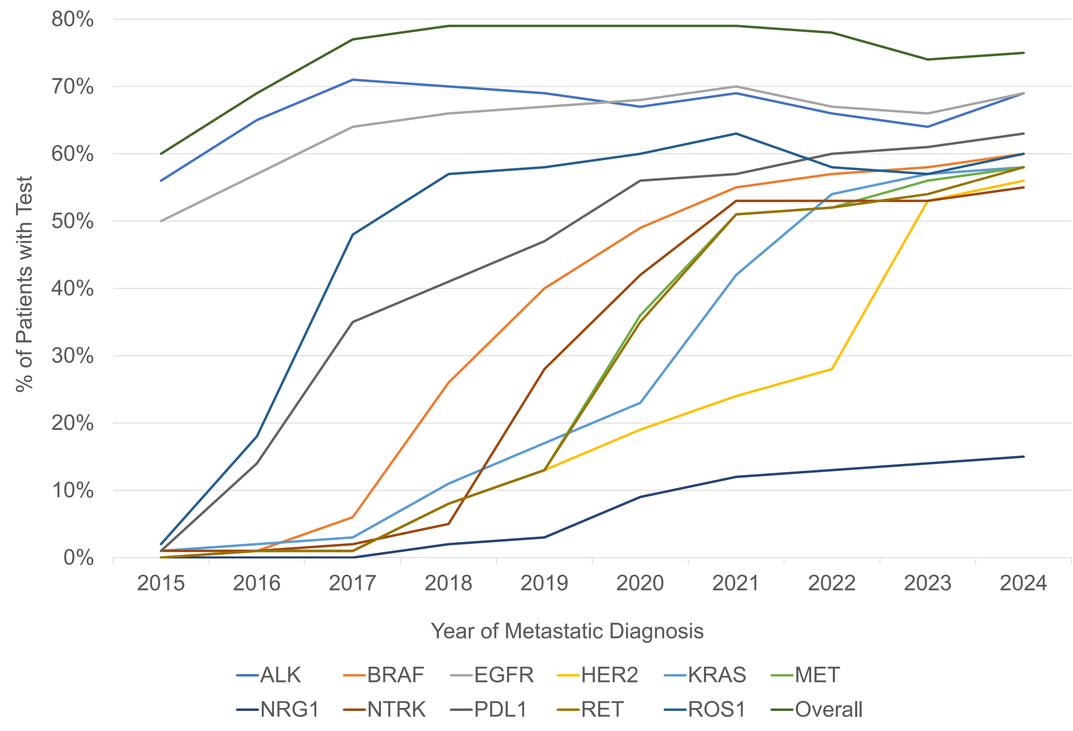
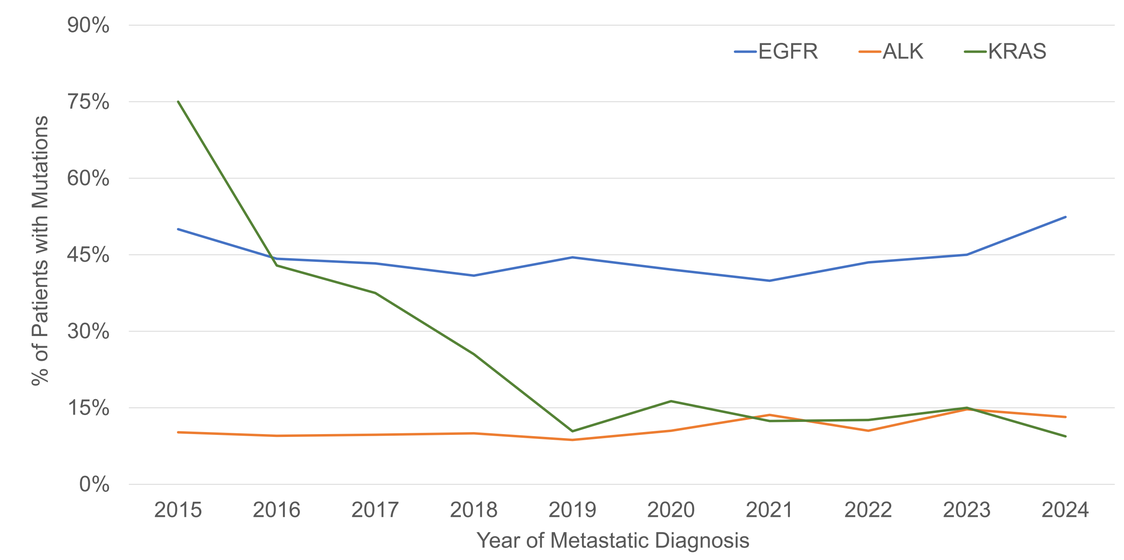


Figure 2: Annual Genetic Testing between 2015 and 2024



- Between 2015 to 2024, cumulative biomarker testing rates increased from 59.8% to 75.3% of the overall population, with variation across specific genes in alignment with the approvals of corresponding targeted therapies (Figure 2)

Figure 4: Frequency of Genetic Mutations in Never-Smokers between 2015 and 2024



- The frequency of EGFR mutations observed among NS patients dropped over time, from 75.0% in 2015 to 9.5% in 2024, while ALK and KRAS mutations were relatively stable (Figure 4)

Conclusions

- This large-scale real-world analysis supports the unique pattern and prevalence of metastatic lung cancer driver mutations in NS compared to ES in the community oncology setting.
- NS showed distinct biomarker profiles, reinforcing the relevance of smoking history in guiding molecular testing and personalized treatment strategies
- As new therapies increasingly rely on specific genetic alterations, the identification of the driver genetic mutations in lung cancer and their pattern by smoking history is a prerequisite for appropriate diagnosis and treatment.