

The genomic landscape of small cell lung cancer in never smoking patients

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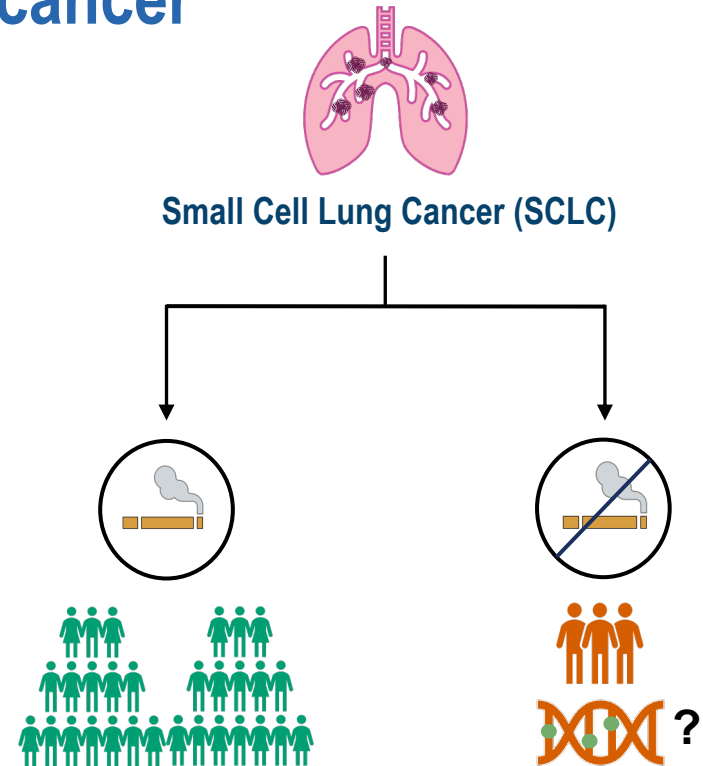
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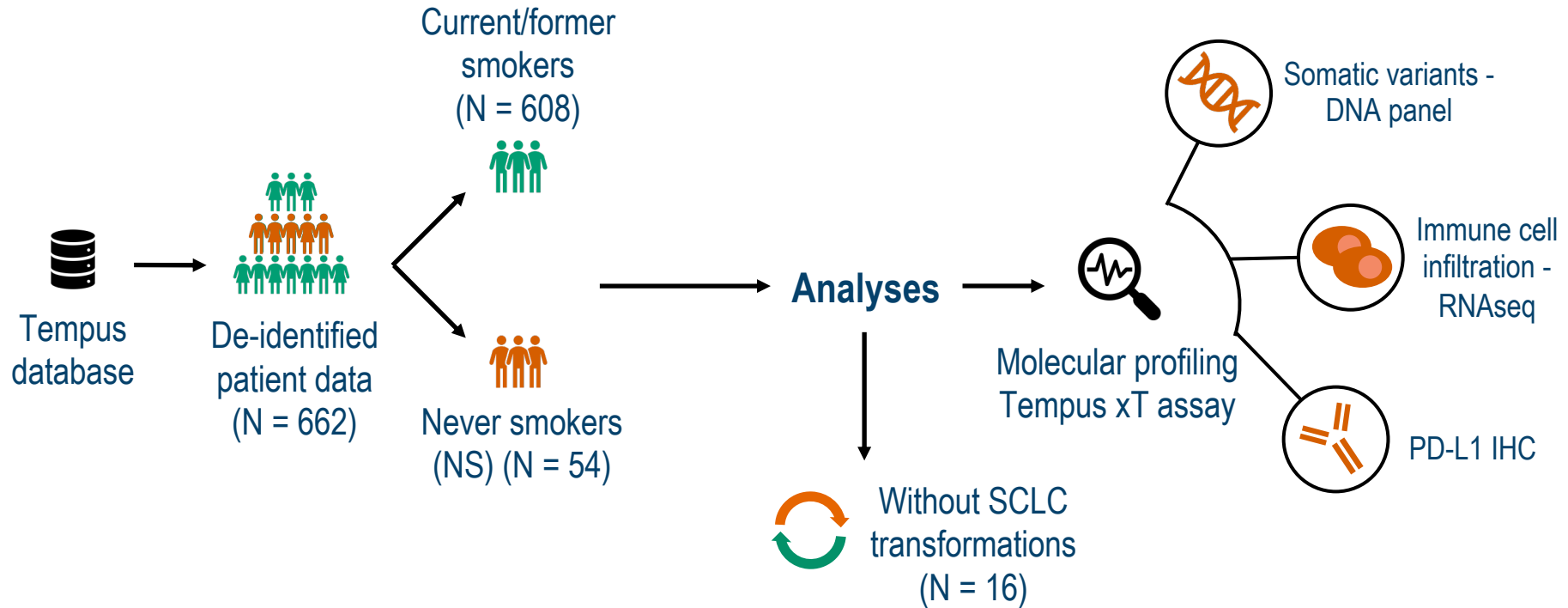


Smoking status in small cell lung cancer

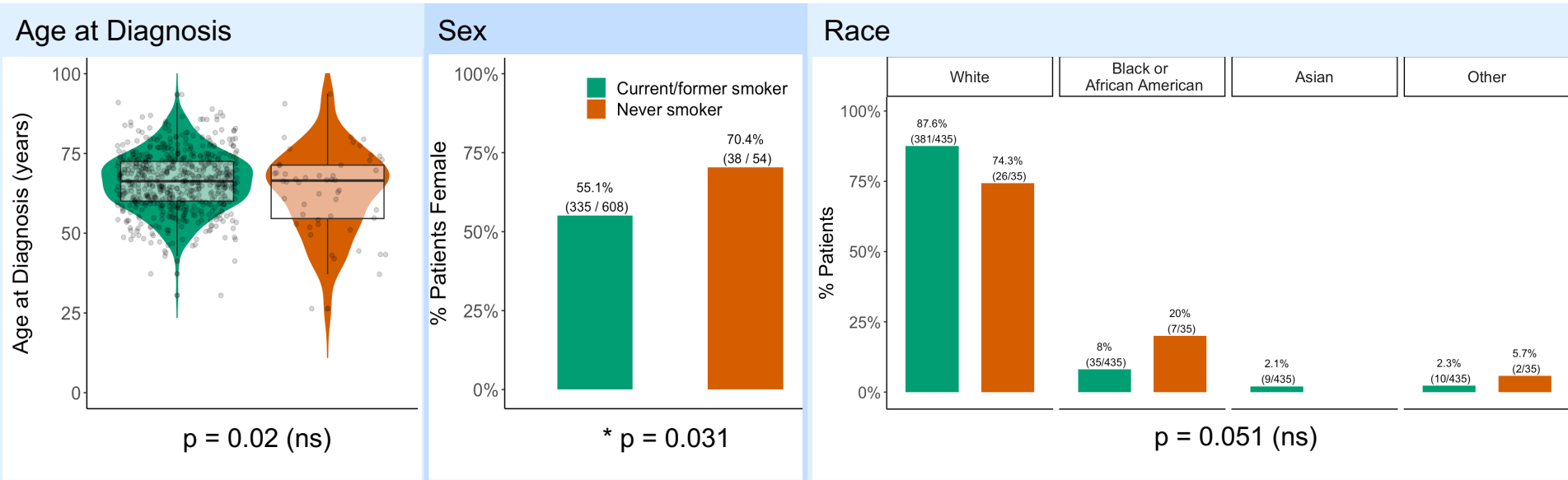
- SCLC typically found in patients with significant tobacco exposure
- Recent trial data suggest more-than-expected patients who have never smoked:
 - **CASPIAN** (Paz-Ares et al, 2019): 6.9%
 - **IMpower133** (Horn et al, 2019): 3.0%



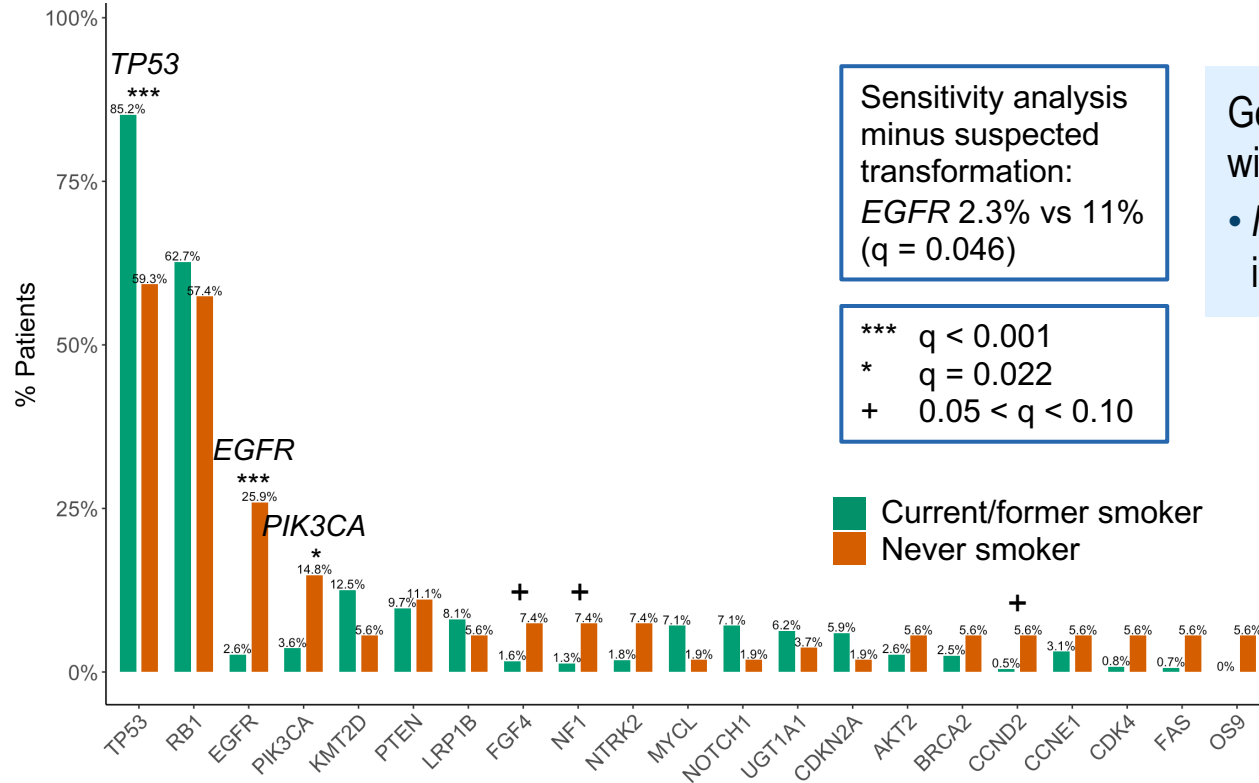
Molecular analysis in SCLC based on smoking status



Demographic composition of SCLC cohort



NS patients exhibit unique somatic variant landscape



Sensitivity analysis
minus suspected
transformation:
EGFR 2.3% vs 11%
($q = 0.046$)

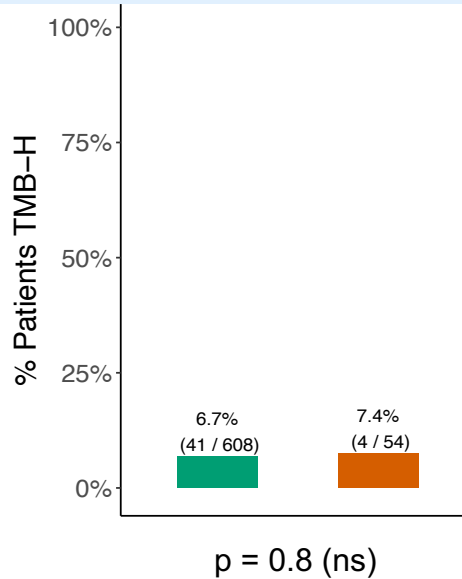
*** $q < 0.001$
 * $q = 0.022$
 + $0.05 < q < 0.10$

Gene fusions infrequent
with no differences

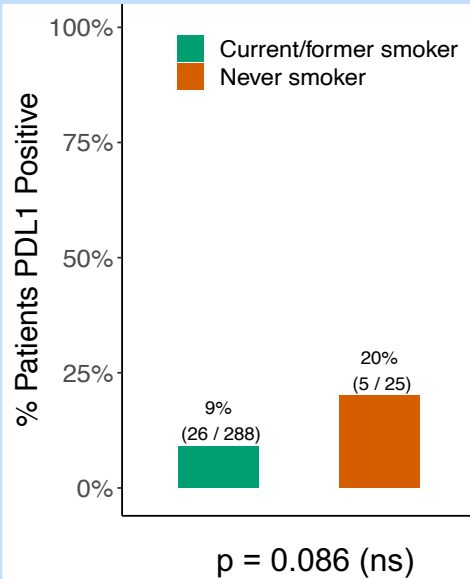
- *NRG1* fusions found
in 2 NS patients

Immune microenvironment by smoking status

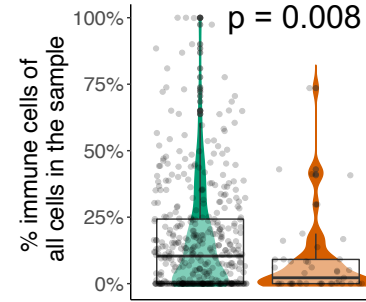
Tumor Mutation Burden



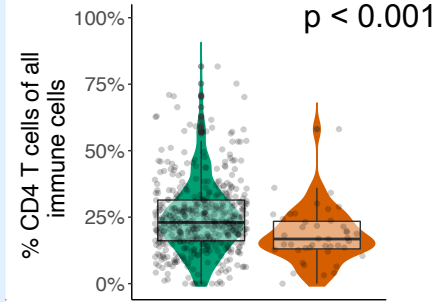
PD-L1 Status



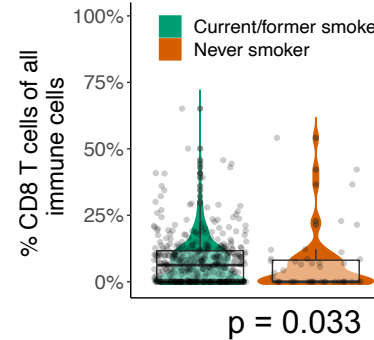
Immune Cell Infiltration



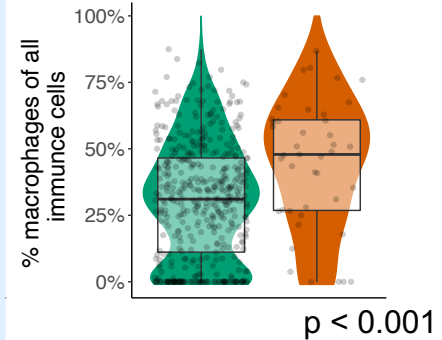
CD4+ T Cells



CD8+ T Cells



Macrophages



Conclusions

- Mutational landscape of SCLC differs based on smoking status
- Tumors of NS more likely to harbor variants in *EGFR* and *PIK3CA*
- Potential differences seen in the immune microenvironment
- Future need to explore possible treatment implications

Thank you!

To Patients and Families

UCLA Thoracic Oncology

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