

Background

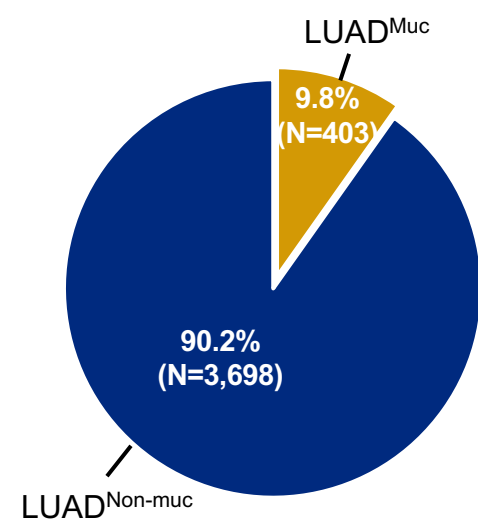
Approximately 10% of lung adenocarcinomas (LUAD) have mucinous features (LUAD^{Muc}). The efficacy of immune checkpoint inhibitors (ICI), chemoimmunotherapy and KRAS inhibitors for these patients is undefined.

Methods

Clinicopathologic, genomic, and outcomes data were abstracted from patients with LUAD at three academic centers. LUAD with any mucinous component as assessed by a thoracic pathologist was classified as LUAD^{Muc} and compared to LUAD without mucinous components (LUAD^{Non-muc}).

Results

Proportion of cases

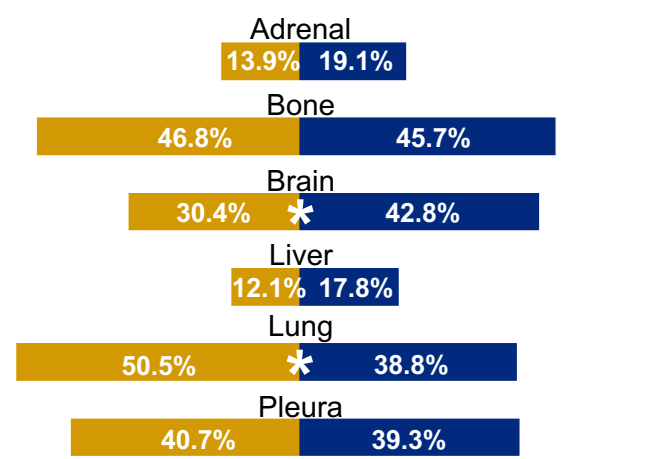


Proportion of LUAD^{Muc} and LUAD^{Non-muc} cases.

Sites of metastasis

■ LUAD^{Muc} (N=137) ■ LUAD^{Non-muc} (N=1,499)

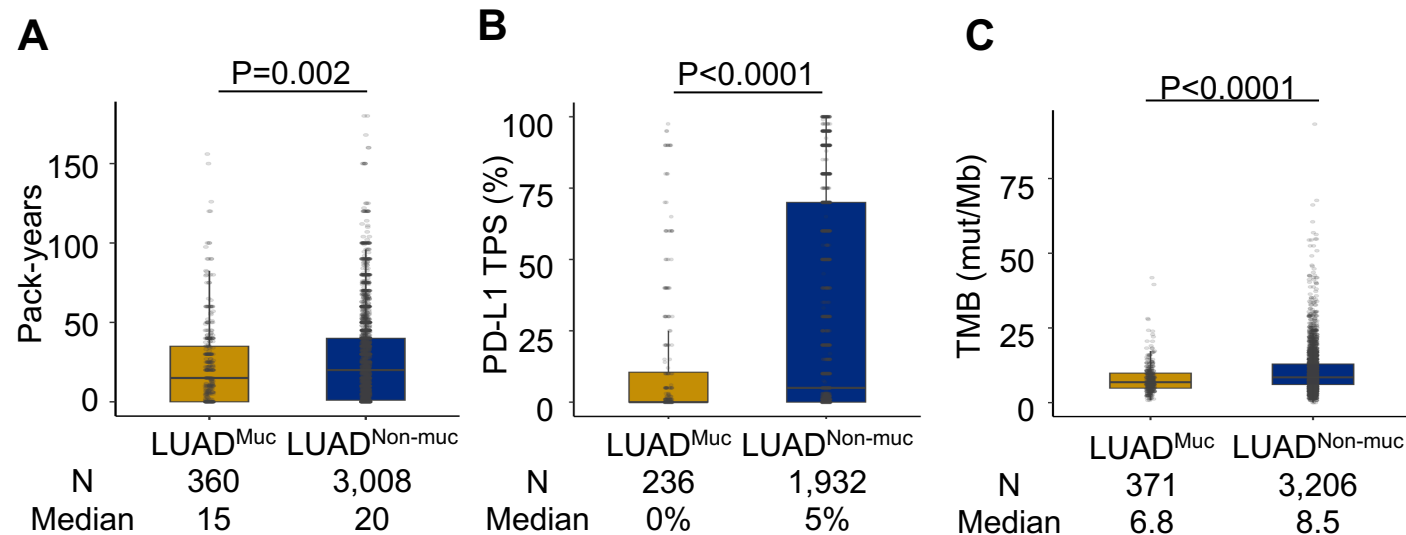
✱ P<0.05



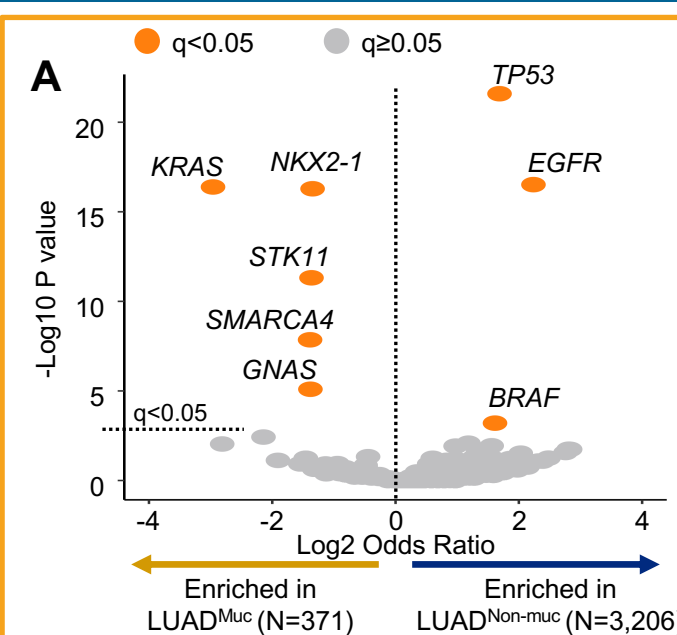
Sites of metastasis at stage IV diagnosis in LUAD^{Muc} vs LUAD^{Non-muc} cases.

Results

Smoking status, PD-L1 and TMB

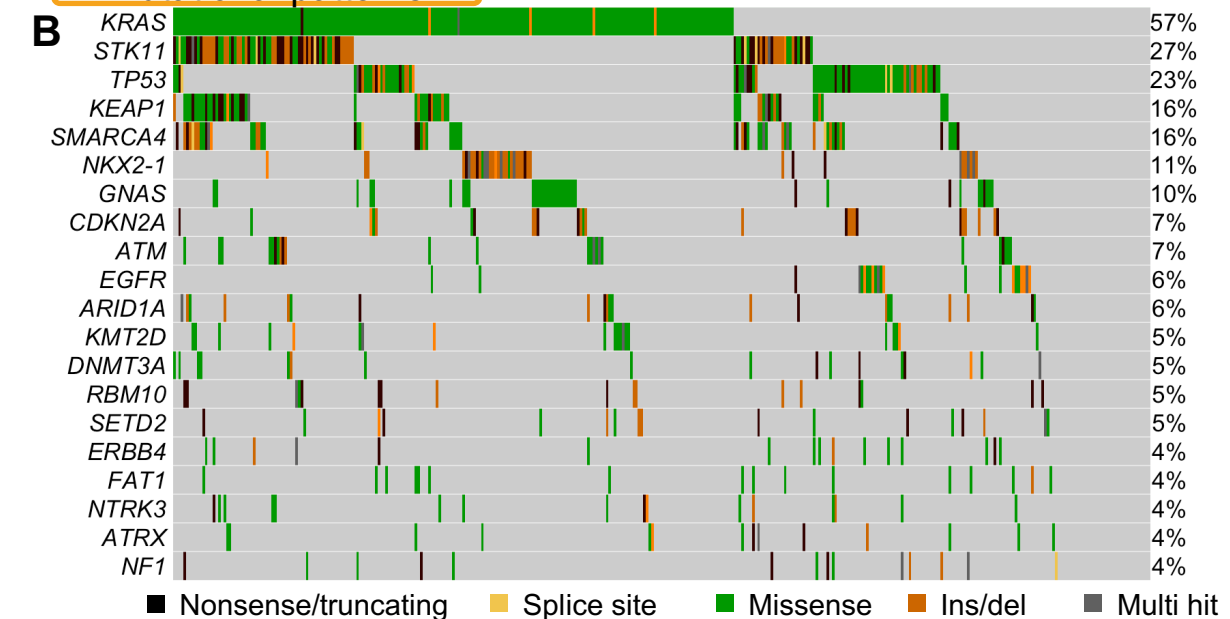


(A) Cigarette smoking history measured as pack-years, (B) PD-L1 tumor proportion score (TPS), and (C) tumor mutation burden (TMB) in LUAD^{Muc} vs LUAD^{Non-muc} cases.

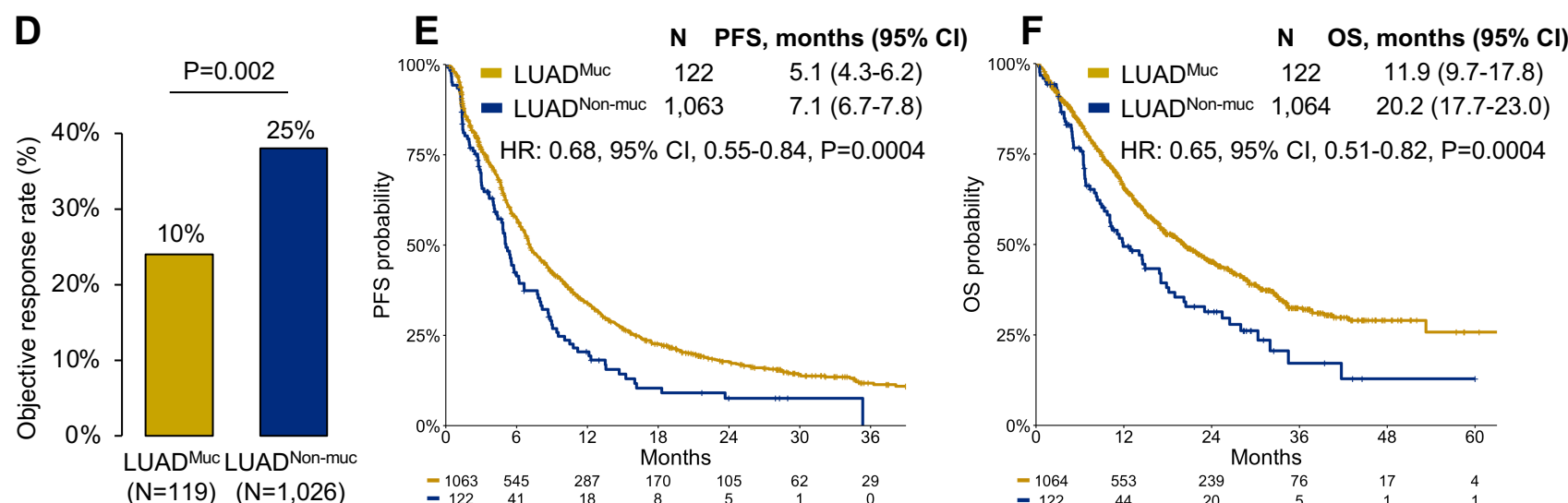
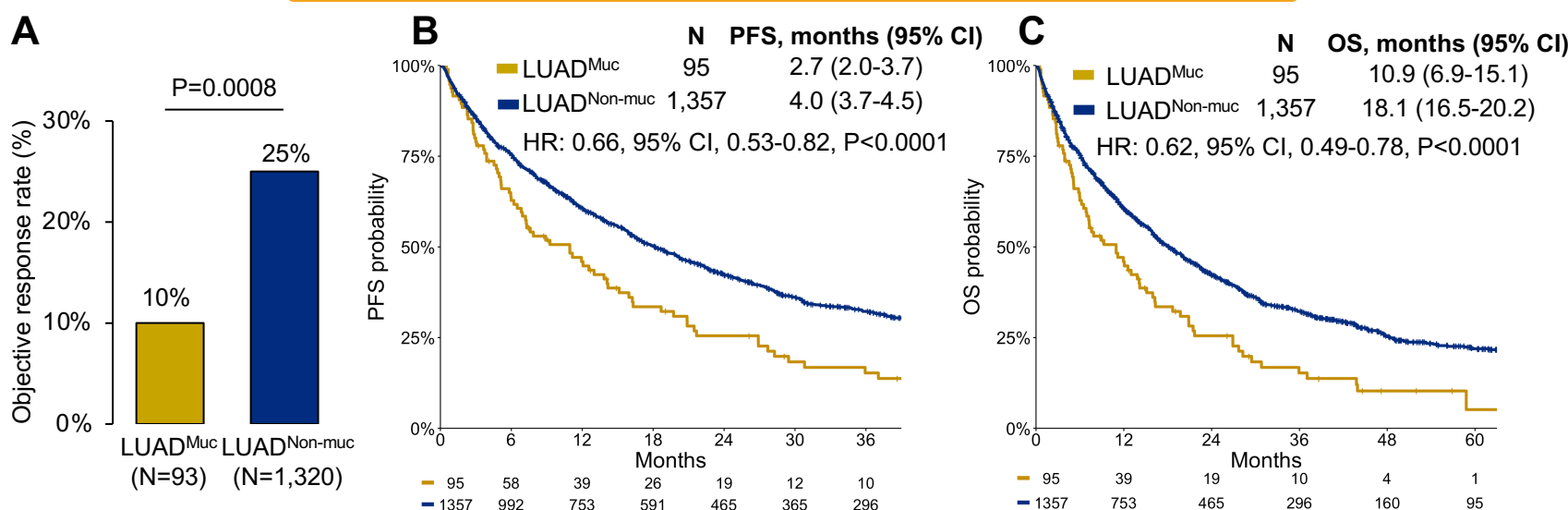


(A) Pathogenic mutations enriched in LUAD^{Muc} vs LUAD^{Non-muc}. (B) Top 20 mutated genes in LUAD^{Muc} cases (N=371).

Mutational patterns

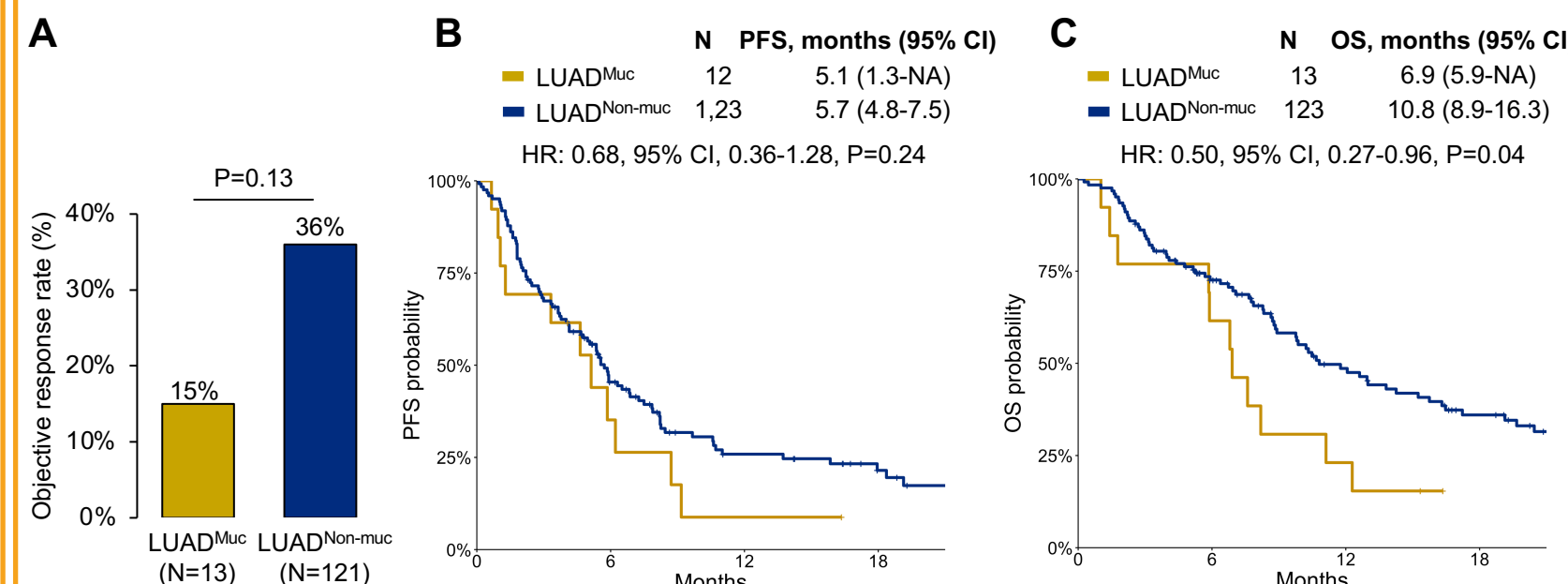


Outcomes to immunotherapy and chemoimmunotherapy



(A) Objective response rate, (B) progression-free survival (PFS), and (C) overall survival (OS) to immunotherapy alone. (D) Objective response rate, (E) PFS, and (F) OS to chemoimmunotherapy.

Outcomes to KRAS G12C inhibitors



(A) Objective response rate, (B) progression-free survival, and (C) overall survival to KRAS G12C inhibitors.

Conclusion

LUAD^{Muc} accounts for approximately 10% of all LUAD cases and, compared to LUAD^{Non-muc}, is characterized by:

- Lighter smoking history
- More common contralateral lung metastases and less common brain metastases
- Lower PD-L1 expression and tumor mutation burden
- Higher frequency of *KRAS*, *NKX2.1*, *STK11*, *SMARCA4*, and *GNAS* mutations
- Lower frequency of *TP53*, *EGFR*, and *BRAF* mutations
- Worse outcomes to immunotherapy, chemoimmunotherapy, and KRAS G12C inhibitors

No conflict of interest to declare

alessandrodifederico1@gmail.com
[@DiFedericoMD](https://twitter.com/DiFedericoMD)