



# 2639: Genomic and clinical differences between pulmonary and extrapulmonary small cell carcinomas.

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## INTRODUCTION

- Small cell lung cancer (SCLC) is a well-defined entity with established treatment guidelines.
- Extrapulmonary small cell carcinoma (EPSCC) is a rare malignancy lacking site-specific management recommendations.
- Consequently, treatment strategies for EPSCC are commonly extrapolated from SCLC despite limited evidence of biological equivalence.
- To determine whether EPSCC represents a distinct disease entity, we compared the clinical characteristics and genomic profiles of patients with SCLC and EPSCC.

## METHODS

### Design:

- Clinical and genomic data were extracted from the **GENIE v18.0 public cohort** using **cBioPortal**.
- Patients were classified into:
  - **Small Cell Lung Cancer (SCLC), and Extrapulmonary Small Cell Carcinoma (EPSCC)**, including tumors of the gastrointestinal tract, esophagus, hepatobiliary system, prostate, bladder, cervix, and ovary.
- Demographic characteristics (age, sex, and race) and genomic alterations were evaluated.
- Comparisons between groups were performed using **Chi-squared tests** , **Wilcoxon rank-sum tests**.
- Statistical significance was defined as **p < 0.05**.

## DISCUSSION AND CONCLUSION

### Conclusion:

- SCLC and EPSCC demonstrate distinct clinical and genomic characteristics, supporting EPSCC as a separate disease entity rather than a pulmonary counterpart.
- SCLC exhibited a higher mutational burden and more frequent **TP53** and **RB1** alterations.
- EPSCC showed distinct genomic alterations, including **CDKN1A**, **SETDB1**, **FANCC**, and **SMARCA4**.

### Future Direction for Research:

- Further studies are needed to validate these genomic differences and identify actionable therapeutic targets in EPSCC.
- Prospective, site-specific clinical trials are warranted to develop tailored treatment strategies for EPSCC.

## REFERENCES & ACKNOWLEDGEMENTS

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## RESULTS

- A total of **1,655 patients** were analyzed, including **1,189 SCLC** and **466 EPSCC** cases.
- SCLC demonstrated a higher mutational burden than EPSCC (**median mutation count 9 vs. 6; p < 0.005**).
- Clinical characteristics differed significantly: SCLC had a higher proportion of females (**53.9%**), whereas EPSCC was more common in males (**61.0%**) (**p < 0.005**). SCLC patients were also slightly older (**66.5 vs. 66 years; p = 0.01**).
- White patients were more frequently represented in SCLC (**72.3% vs. 59.9%; p = 0.005**).
- SCLC was enriched for **TP53 (74.8% vs. 50.3%)** and **RB1 (61.5% vs. 41.4%)** alterations (*both p < 0.001*), as well as **EGFR**, **KIT**, **KMT2B**, **FGFR3**, **PIK3CG**, **PDGFRB**, and **KEAP1** (*all p < 0.01*).
- EPSCC showed higher frequencies of **SETDB1 (8.4% vs. 1.4%)**, **SMARCA4 (8.6% vs. 4.6%)**, **CDKN1A (3.5% vs. 0.9%)**, and **FANCC (2.0% vs. 0.4%)** (*all p < 0.01*).
- These findings support distinct clinical and molecular profiles for SCLC and EPSCC.

|                       | SCLC<br>(n=1,189) | EPSCC<br>(n=466) | P value |
|-----------------------|-------------------|------------------|---------|
| Median mutation count | 9                 | 6                | <0.005  |
| Median age (years)    | 66.5              | 66.0             | 0.01    |
| Female (%)            | 53.9              | 39.0             | <0.005  |
| Male (%)              | 46.1              | 61.0             | <0.005  |
| White race (%)        | 72.3              | 59.9             | 0.005   |

| Gene Alteration | SCLC (%) | EPSCC (%) | Enriched In | P value |
|-----------------|----------|-----------|-------------|---------|
| TP53            | 74.8     | 50.3      | SCLC        | <0.001  |
| RB1             | 61.5     | 41.4      | SCLC        | <0.001  |
| EGFR            | 7.7      | 1.6       | SCLC        | <0.001  |
| KIT             | 5.0      | 1.0       | SCLC        | <0.001  |
| KMT2B           | 8.7      | 3.7       | SCLC        | <0.01   |
| FGFR3           | 4.1      | 1.2       | SCLC        | <0.01   |
| PIK3CG          | 5.3      | 2.0       | SCLC        | <0.01   |
| PDGFRB          | 4.0      | 1.5       | SCLC        | <0.01   |
| KEAP1           | 4.1      | 1.5       | SCLC        | <0.01   |
| CDKN1A          | 0.9      | 3.5       | EPSCC       | <0.001  |
| SETDB1          | 1.4      | 8.4       | EPSCC       | <0.01   |
| FANCC           | 0.4      | 2.0       | EPSCC       | <0.01   |
| SMARCA4         | 4.6      | 8.6       | EPSCC       | <0.01   |