



P2.141 EBUS-TBNA-Derived Whole-Exome Copy-Number Burden and Immunotherapy Response in Advanced Lung Cancer Within the TRACKER Cohort



Sarah Yeo^{1,2,3,4}, Paul Wang^{4,6}, Stephen Wong⁵, Alex Ringer⁶, Will Figgett⁶, Tony Papenfuss⁶, Natalia Vukelic⁴, Farzaneh Atashrazm^{1,4}, Natasha Smallwood^{7,8}, Kate Sutherland^{4,9}, Vivek Naranbhai^{7,10}, Daniel Steinfort^{2,3}, Sagun Parakh^{1,4}, Tracy Leong^{1,3,4}

¹ Austin Health, Melbourne, Australia, ² Royal Melbourne Hospital, Melbourne, Australia, ³ The University of Melbourne, Melbourne, Australia, ⁴ TRACKER Biobank, ONJCRI, Melbourne, Australia, ⁵ Cancer Genomics Translational Research Centre, Peter MacCallum Cancer Centre, Melbourne, Australia, ⁶ Papenfuss Laboratory, WEHI, Melbourne, Australia, ⁷ Alfred Health, Melbourne, Australia, ⁸ Monash University, Melbourne, Australia, ⁹ Sutherland Laboratory, WEHI, Melbourne, Australia, ¹⁰ Laboratory of Translational Immunology, Monash University, Melbourne, Australia

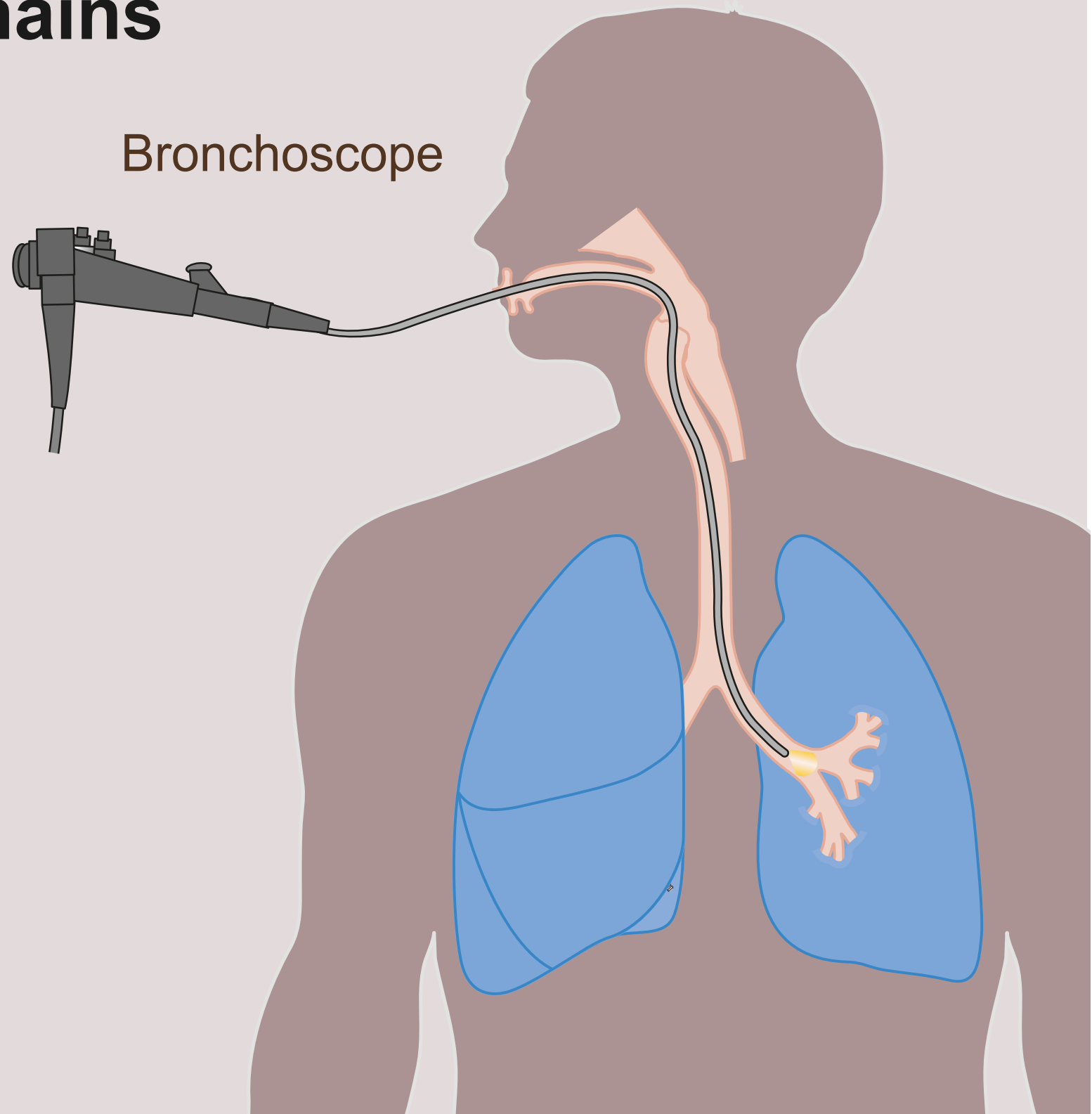
Correspondence: sarah.yeo@austin.org.au

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INTRODUCTION

Immunotherapy (IO) resistance remains common in advanced lung cancer and is incompletely explained by existing biomarkers

EBUS-TBNA provides tumour tissue for whole-exome sequencing in clinically relevant stage IV disease (1). Within the Australian TRACKER biobank (3), we evaluated whether tumour copy-number variation burden, previously associated with immune evasion, differs according to immunotherapy response. This study focuses on a real-world cohort treated with immunotherapy (IO).



METHODS

Experimental Design

Prospective translational cohort substudy within the national Australian TRACKER Biobank.

Participants and samples Patients with stage IV lung cancer undergoing diagnostic linear EBUS-TBNA (2021–2025). Mediastinal and hilar nodal samples underwent DNA extraction and whole-exome sequencing.

Outcome Immunotherapy response was defined by radiological improvement at 6 months; others were classified as non-responders.

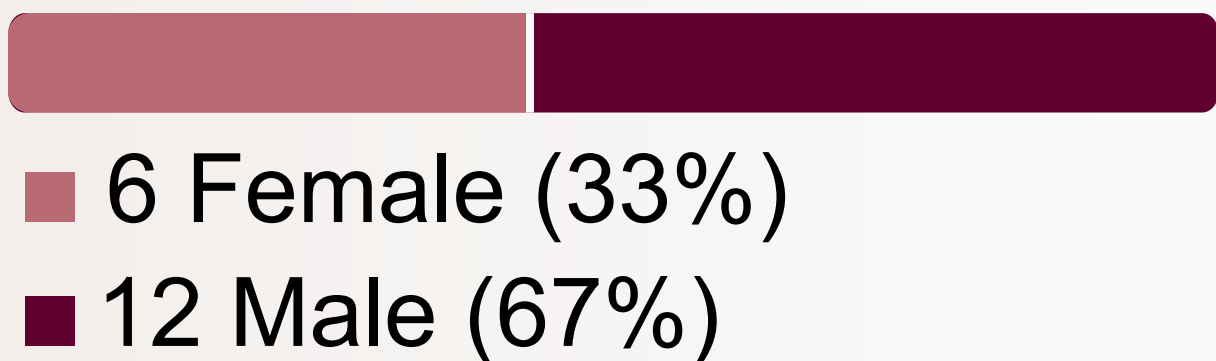
Genomic analysis Somatic variants, tumour mutational burden and genome-wide copy-number variations were called and annotated (2). FACETS estimated global CNV burden and the genomic fraction affected by copy-number gains, losses and copy-neutral loss of heterozygosity.

Primary analysis Global CNV burden and subclass distributions were compared between IO responders and non-responders.

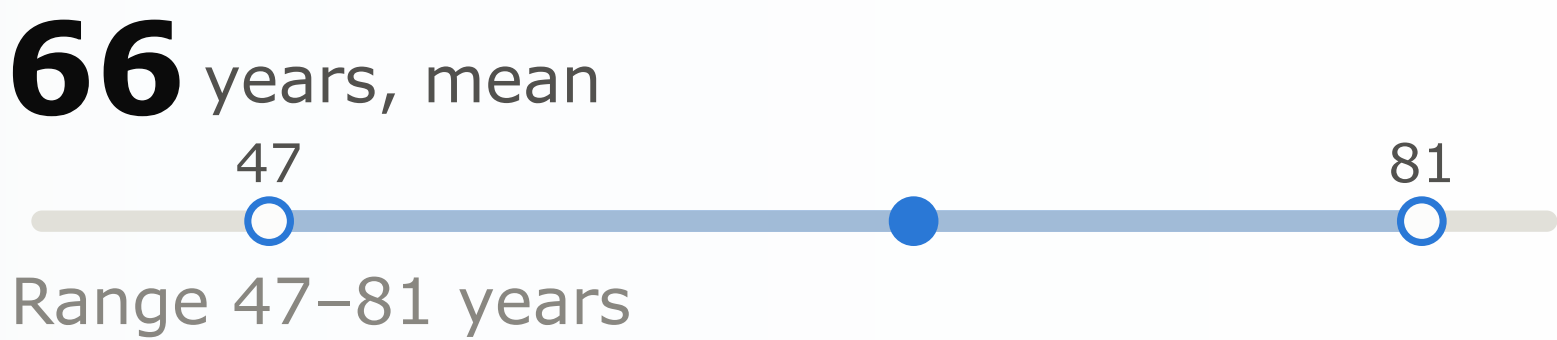
DEMOGRAPHICS

18 patients with stage IV non-small cell lung cancer.

SEX



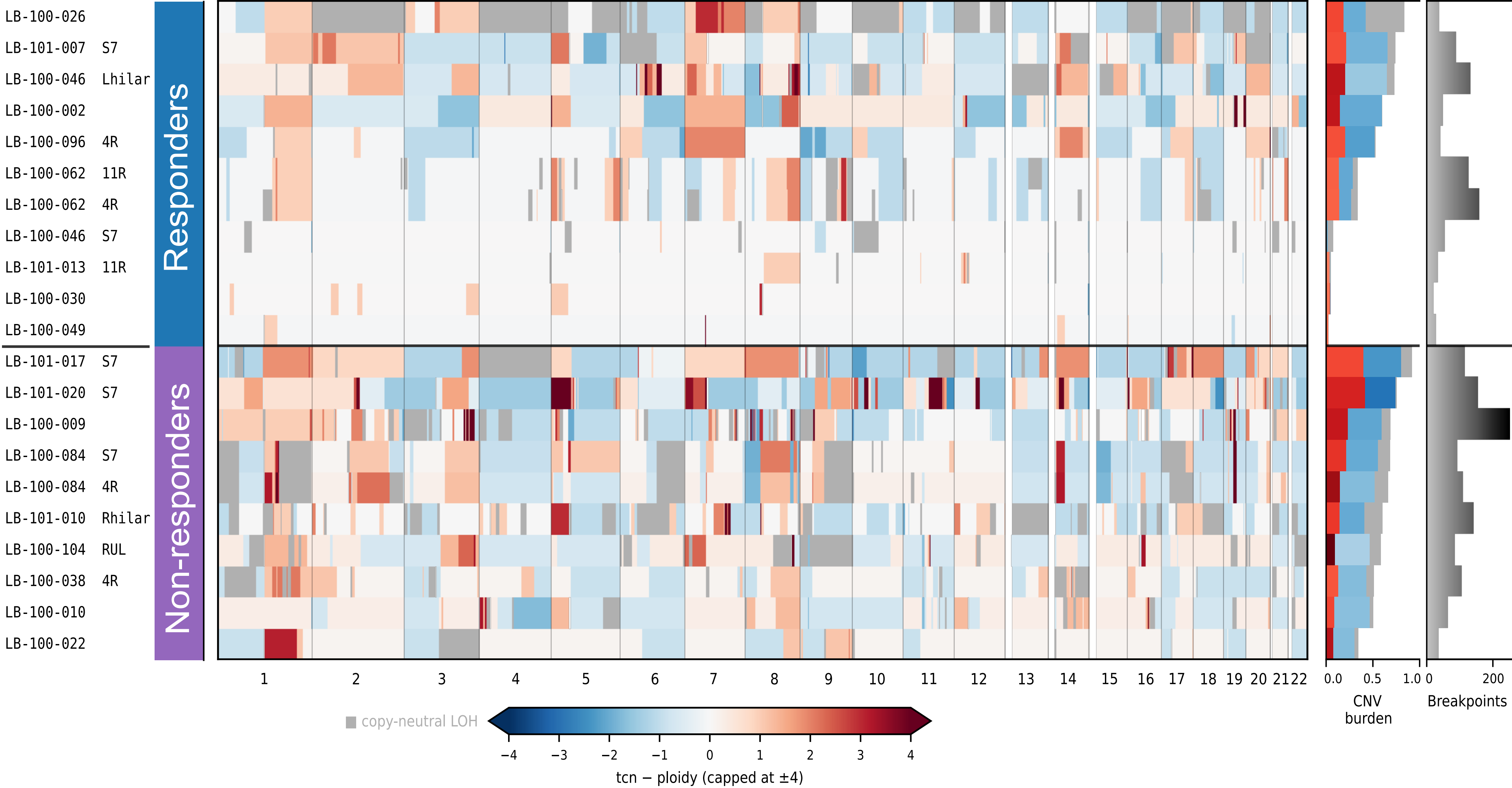
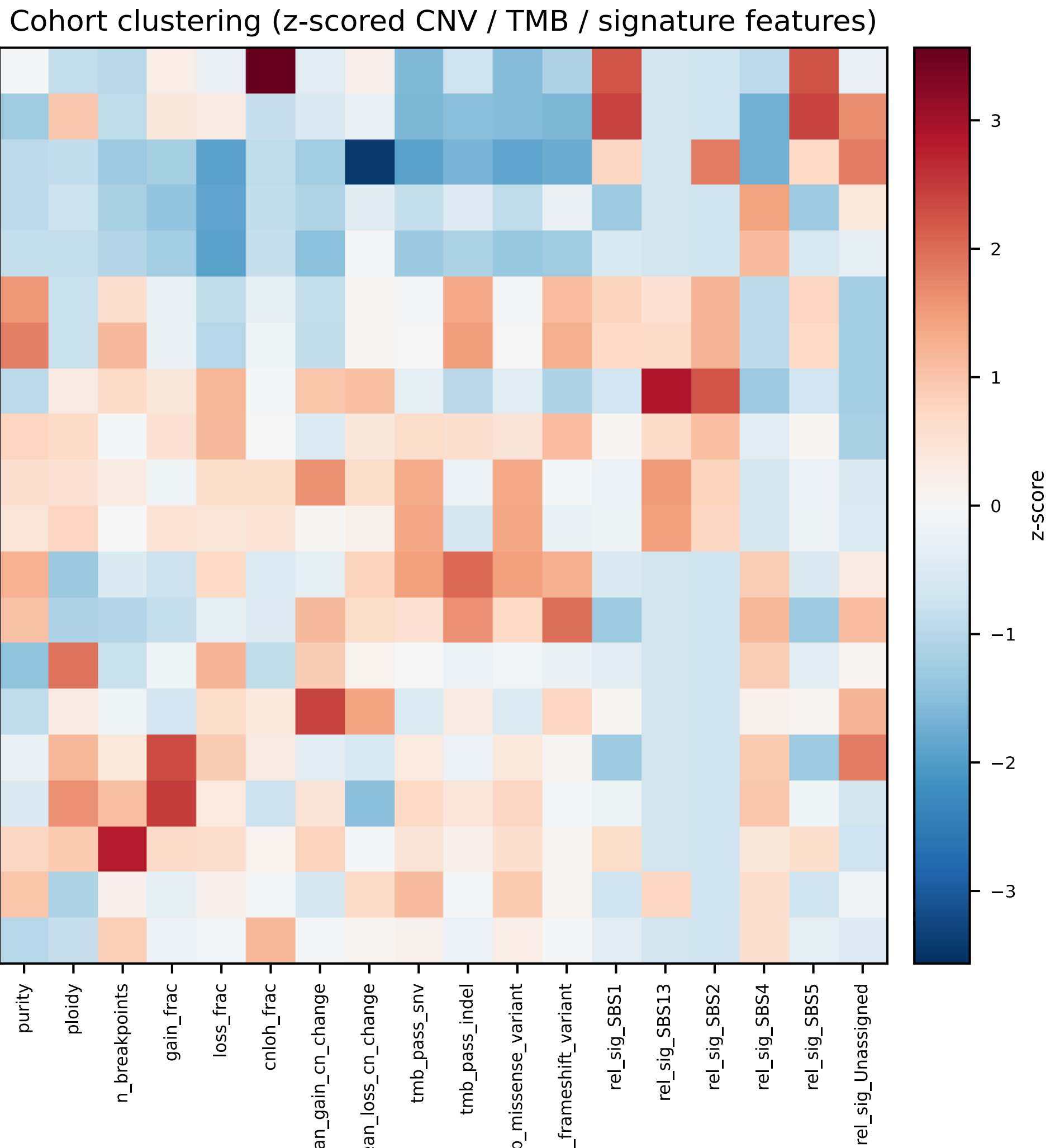
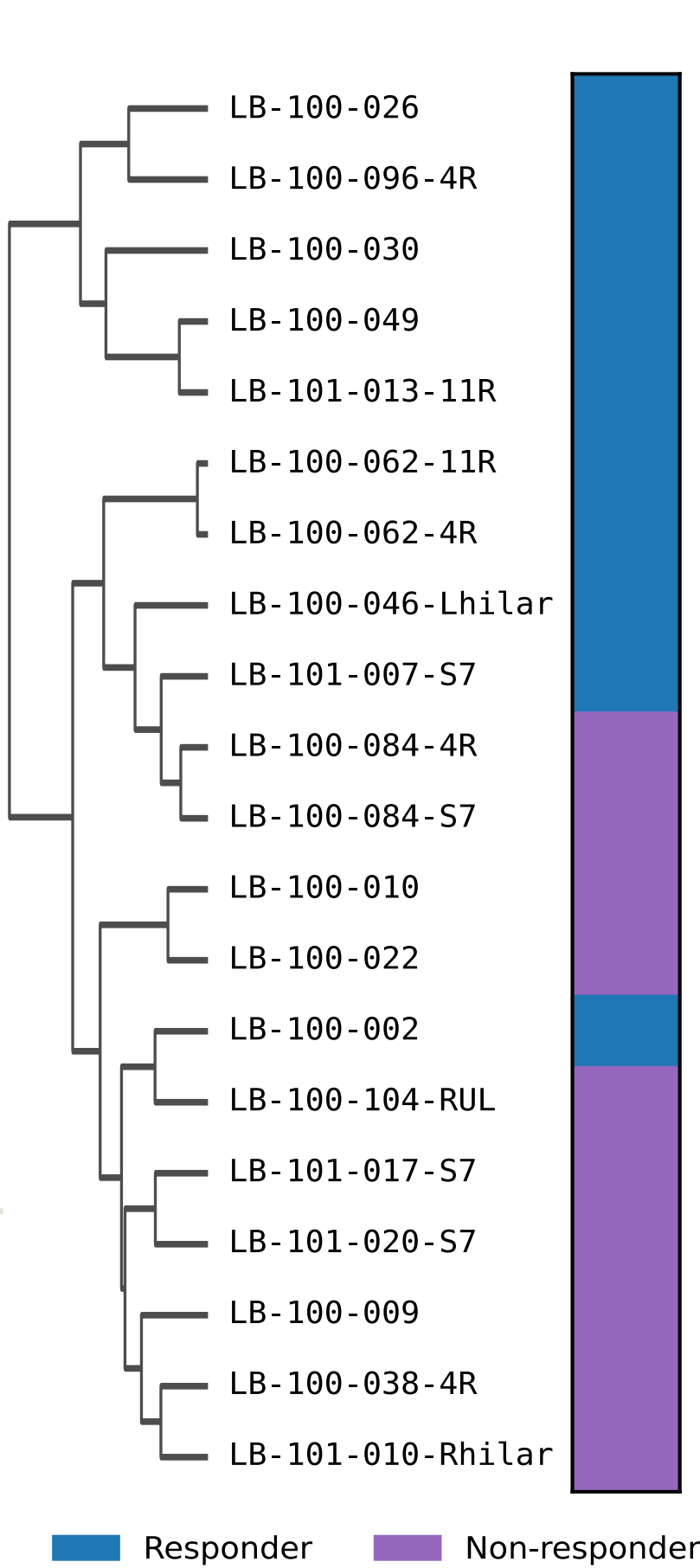
BASELINE AGE



IO RESPONSE



NUMBER OF LN STATIONS SAMPLED



DISCUSSION AND CONCLUSION

Actionable Take Away Message

Preliminary analyses suggest that higher CNV burden, particularly a greater burden of genomic deletions, may be associated with non-response to immunotherapy.

Future direction for research

Larger, independent cohorts will define the value of CNV burden as an orthogonal genomic layer for integrated multi-omic prediction of immunotherapy response.

The TRACKER biobank provides a platform for integrated multiomics analyses combining copy-number architecture with somatic mutations, tumour mutational burden, transcriptomic profiling and longitudinal clinical outcomes. Such work may clarify the biological links between genomic instability, immune evasion and immunotherapy resistance.

References

Fielding, D., et al. (2024). "Evaluation of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA) Samples from Advanced Non-Small Cell Lung Cancer for Whole Genome, Whole Exome and Comprehensive Panel Sequencing." *Cancers (Basel)* 16(4).

Guille, A., et al. (2025). "A benchmarking study of individual somatic variant callers and voting-based ensembles for whole-exome sequencing." *Briefings in Bioinformatics* 26(1).

Yeo, S., et al. (2025). "Lung cancer biobanking in Australia: challenges and future directions." *Med J Aust* 223(4): 180-184.

Acknowledgement

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