



P2.100: Pulmonary High-grade Neuroendocrine Carcinomas with Aberrant rhabdomyosarcomatous Differentiation: A Clinicopathologic, Genetic and Prognostic Analysis Highlighting TP53/RB1 Co-mutation and FOXO1-Negative Profile

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INTRODUCTION

Pulmonary high-grade neuroendocrine carcinomas (HG-NECs) occasionally exhibit aberrant skeletal muscle marker expression, causing diagnostic confusion with alveolar rhabdomyosarcoma (ARMS). This study clarifies this rare subtype via integrated clinicopathologic, immunohistochemical, prognostic and molecular analyses.

METHODS

Design:

- Retrospective analysis of 27 pulmonary HG-NECs expressing at least one myogenic marker (Desmin, MyoD1, or Myogenin), including 25 small cell lung carcinoma (SCLC) and 2 large cell neuroendocrine carcinoma (LCNEC) cases.
- Clinicopathological features, immunophenotypes, mutation profiles (assessed by a 41-gene panel next-generation sequencing), FOXO1 rearrangement status (evaluated by fluorescence in situ hybridization [FISH]), and clinical outcomes were analyzed.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- For small round cell tumors of the lung co-expressing neuroendocrine and myogenic markers, molecular testing for FOXO1 rearrangement and TP53/RB1 mutational status is essential to confirm HG-NEC, prevent misdiagnosis of rhabdomyosarcoma.

Future Direction for Research

- This study assists clinicians in accurate distinction between HG-NEC and rhabdomyosarcoma, improves patient tailored care, and offers directions for subsequent clinical molecular research.

REFERENCES & ACKNOWLEDGEMENTS

Reference

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RESULTS

- Our entire cohort consisted predominantly of elderly male smokers.
- Molecular profiling revealed a high frequency of concurrent TP53 (62%) and RB1 (62%) mutations, with a complete absence of FOXO1 rearrangements (0/27). This strongly supports that these tumors are TP53/RB1-deficient HG-NECs undergoing aberrant myogenic transdifferentiation, rather than ARMS.
- Survival analysis indicated that high MyoD1 expression was associated with a trend toward poorer overall survival (OS) (6 vs. 20 months, $P=0.05$), while high Myogenin expression correlated with significantly inferior OS (6.5 vs. 22 months, $P=0.04$). Desmin expression level showed no prognostic impact ($P=0.73$).

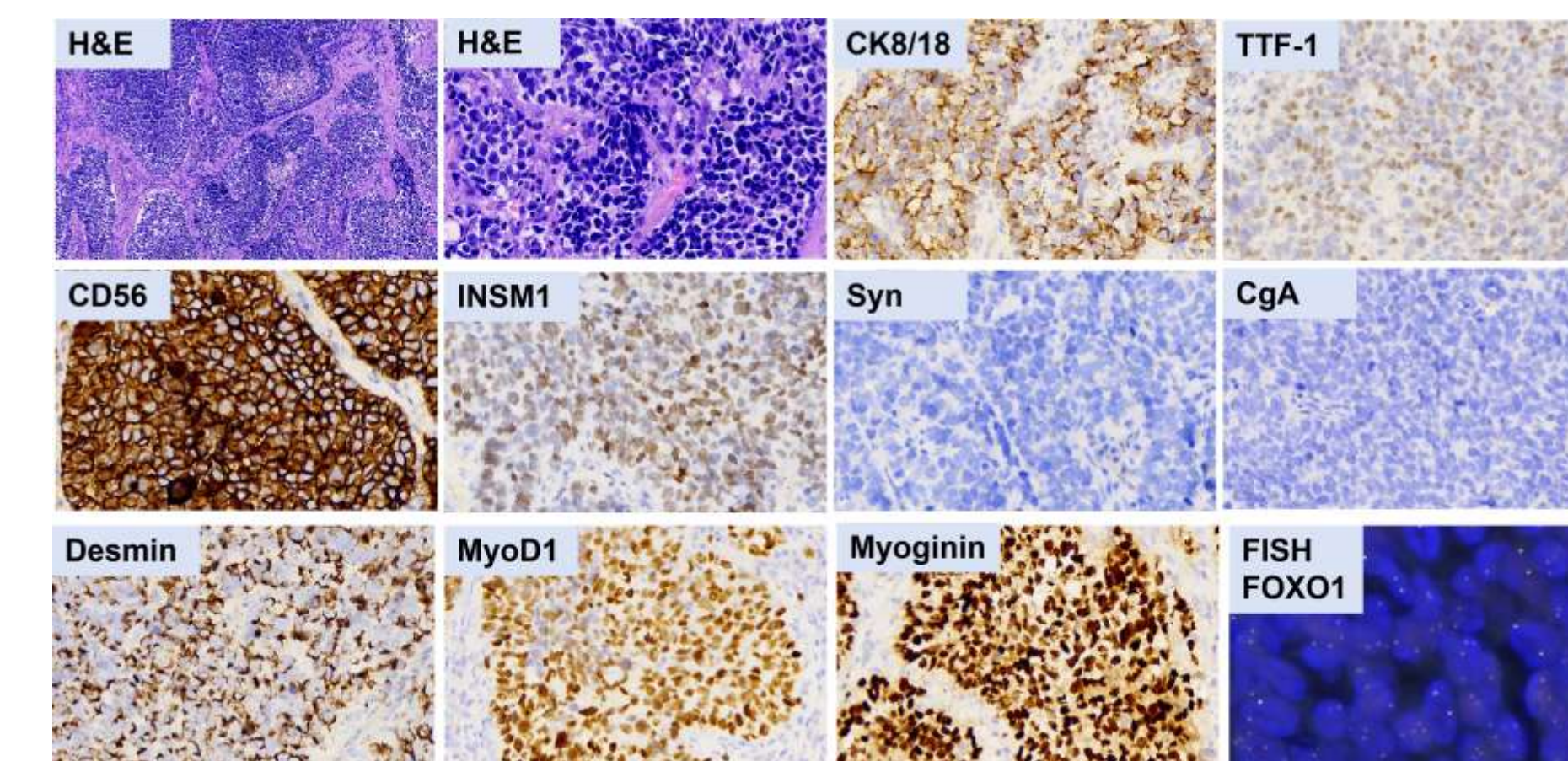


Figure 1. Histology, immunohistochemistry and FISH findings of SCLC with aberrant myogenic marker expression.

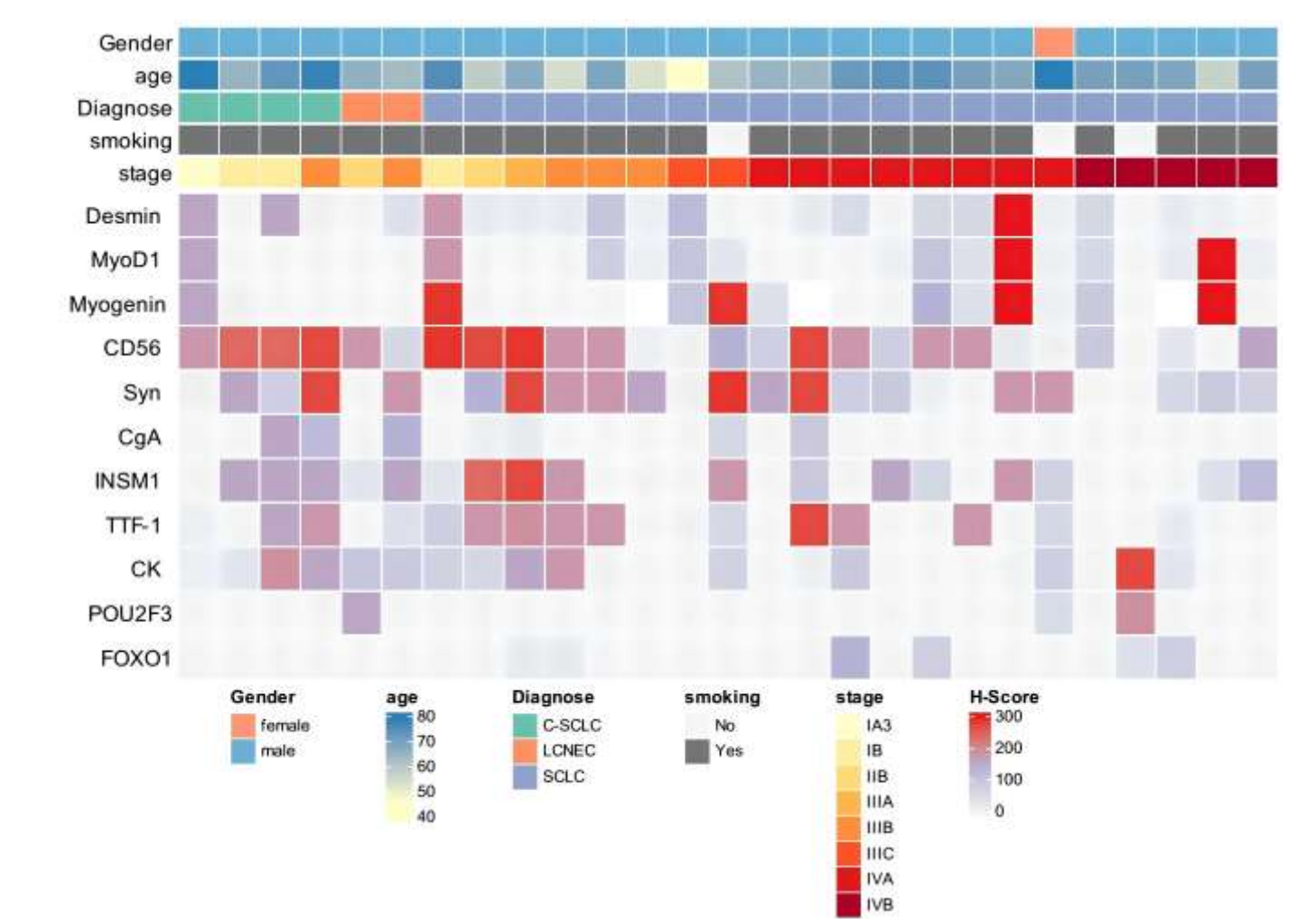


Figure 2. Clinicopathological and Immunophenotypic Characteristics for the 27-patient cohort.

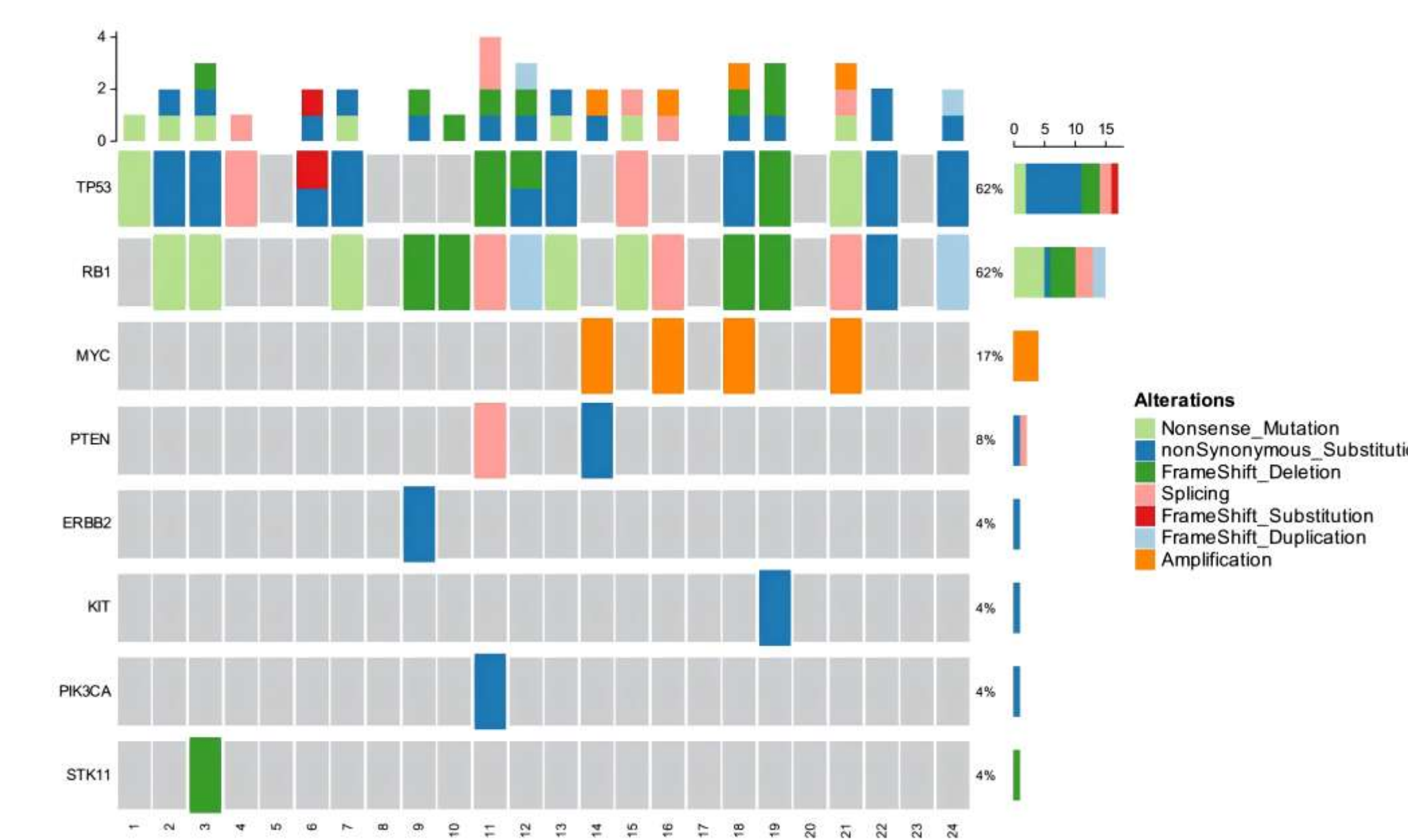


Figure 3. Oncoprint of genetic alterations in 24 HG-NECs.

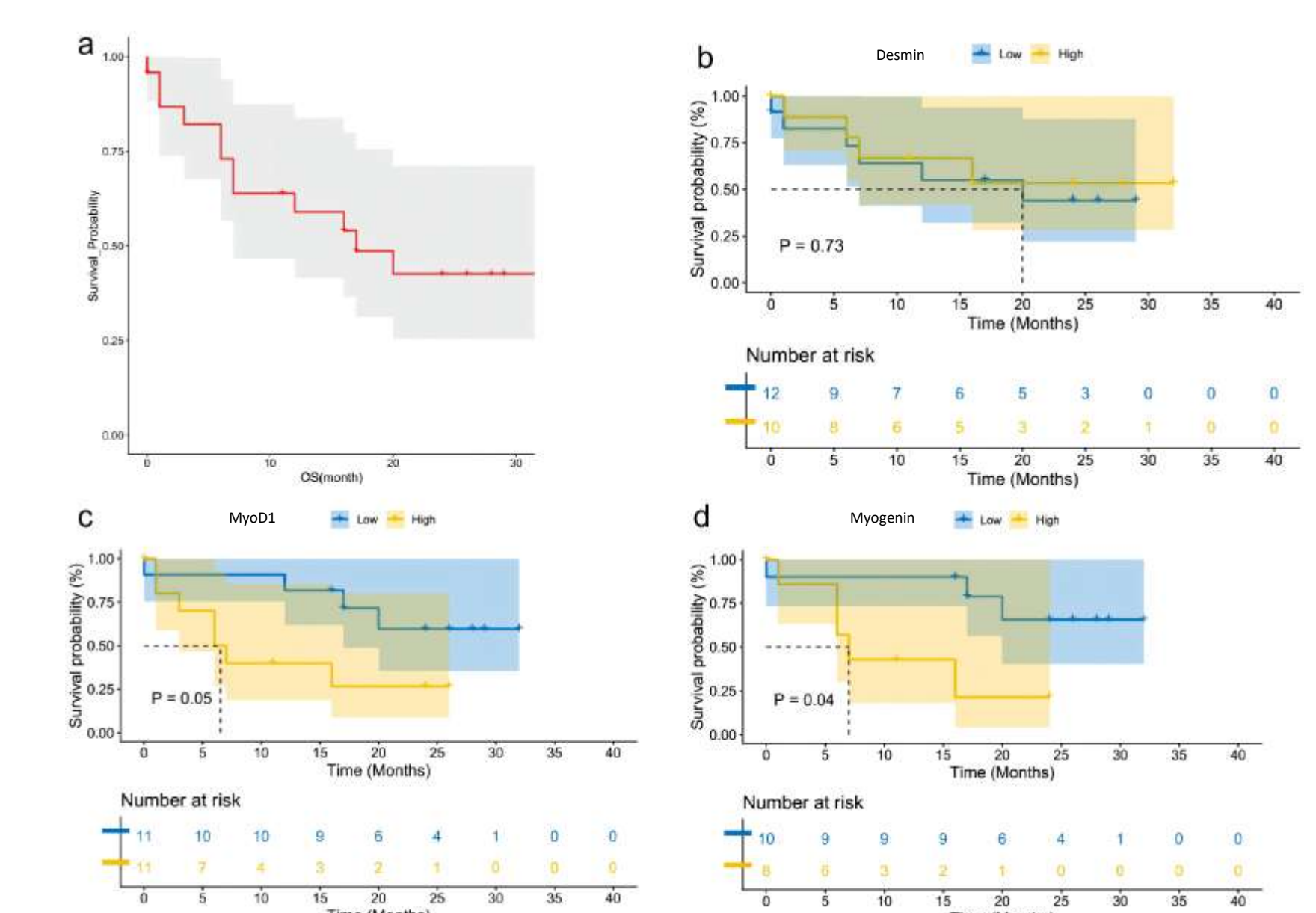


Figure 4. Kaplan-Meier overall survival (OS) curves for HG-NECs.