



Beyond Mesothelioma: Defining the Clinico-pathological Spectrum of BAP1-Mutated Lung Cancer



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INTRODUCTION

- BAP1: A tumor suppressor gene regulating homologous recombination, chromatin remodeling, cell cycle, and apoptosis
- Somatic and germline mutations occur across multiple tumors (mesothelioma, uveal melanoma, ccRCC, meningioma), including NSCLC
- Clinicopathologic and prognostic significance in lung cancer remains poorly defined

METHODS

Retrospective archival search (2019–2025) for BAP1-mutated NSCLC

All eligible cases included for analysis

BAP1 IHC performed on all cases

Collected data: demographics, smoking history, stage, treatment, histologic features

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

16 cases · median age 67.5 · male-predominant

11/16 stage III–IV

High-grade: solid/cribriform/micropapillary

BAP1 IHC loss in 100% → reliable surrogate

Co-mutations: *KRAS* (most frequent), *TP53*, *SMARCA4*, *CDKN2A/B*, *STK11*, *PIK3CA*, *EML4::ALK*; *FGFR1*/*MYC* amplification

TMB >10 in ~70%

9/16 deceased · median followup 18.8 months

Germline negative (n=2 tissue, n=1 liquid biopsy)

DISCUSSION & CONCLUSIONS

BAP1-mutant NSCLC represents a rare but distinct subset

High-grade histology and strong association with tobacco exposure

Frequent co-mutations and often elevated tumor mutation burden

Consistent loss of BAP1 by IHC supports use as a reliable surrogate marker

Typically presents at advanced stage; requires multimodal therapy

Consider germline evaluation for potential hereditary contribution

Figures

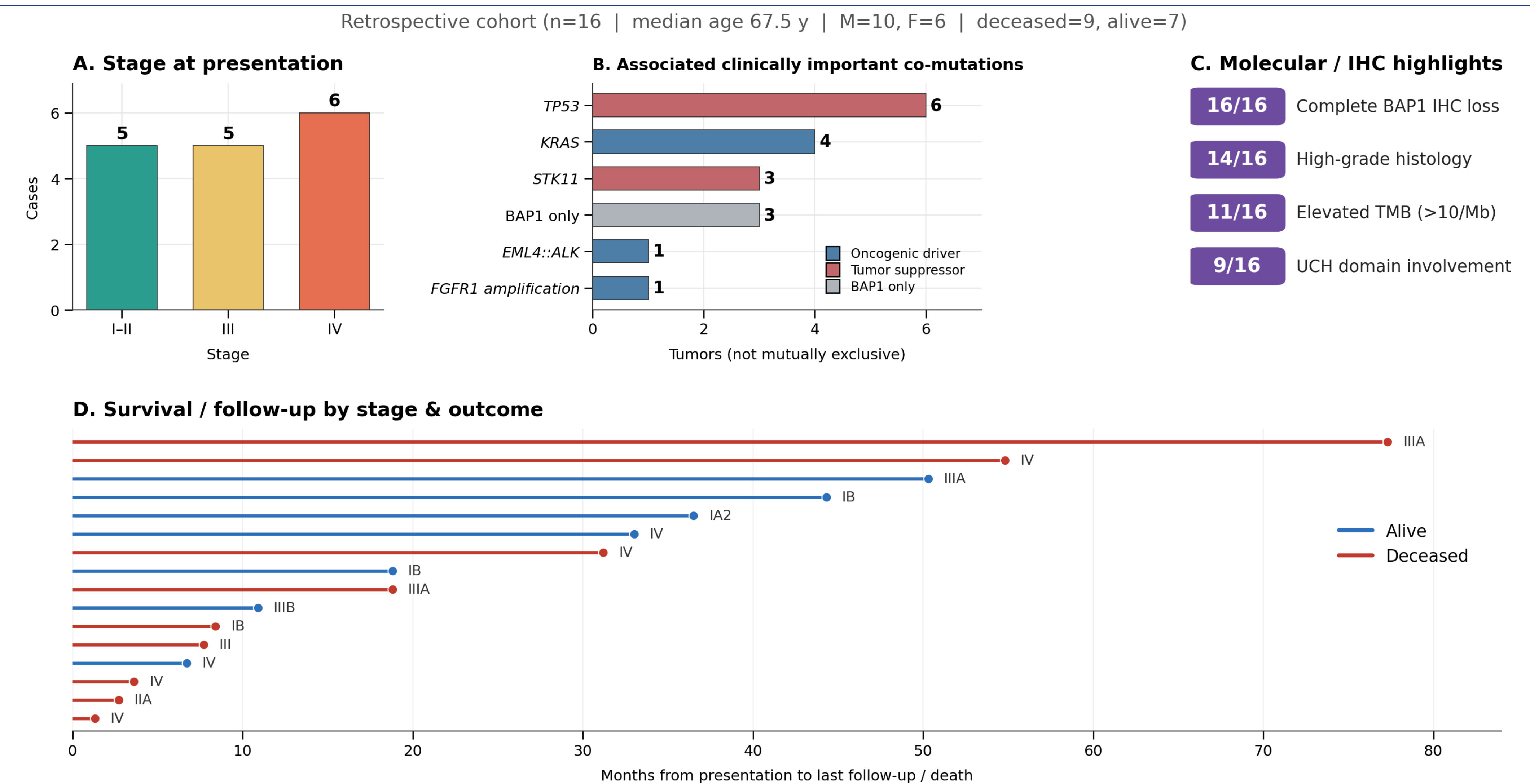


Figure 1: BAP1-Mutated NSCLC: Clinicopathologic and Molecular Summary

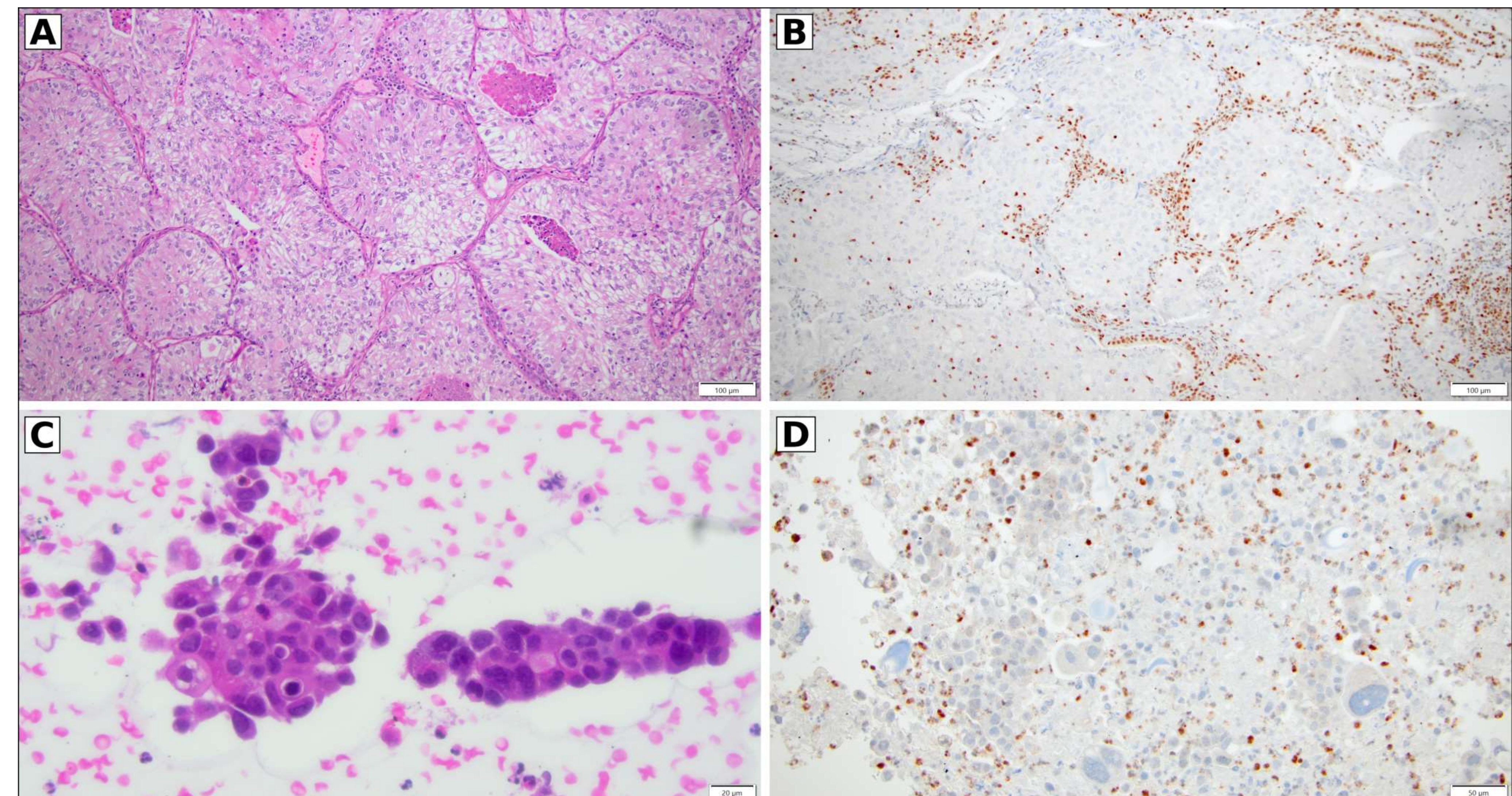


Figure 2: Representative histology and BAP1 immunohistochemistry (IHC). (A) H&E shows a poorly differentiated adenocarcinoma with solid/nested architecture. (B) BAP1 IHC demonstrates complete loss of nuclear expression in tumor cells with retained internal-control staining. (C) EBUS-FNA cytology (cell block) of adenocarcinoma. (D) Corresponding BAP1 IHC on cell block confirming loss.