

Introduction

- Breast Cancer genes (BRCA1 and BRCA2) play a critical role in the homologous recombination repair (HRR) pathway.

- While BRCA mutations are well described in breast, ovarian, pancreatic, and prostatic cancers, their prevalence and clinical significance in lung cancer remain poorly characterized, especially from low- and middle- income countries.

Methodology

-Retrospective study from a tertiary care cancer centre in South India

-April 2022 – March 2026

-All lung cancer patients undergoing next-generation sequencing (NGS) were screened; those with BRCA1/2 mutations were included.

-Clinical characteristics, co-mutation patterns, treatment details, and survival outcomes were captured

-Primary endpoint: Prevalence of BRCA1/2 mutations among NGS-tested lung cancer patients

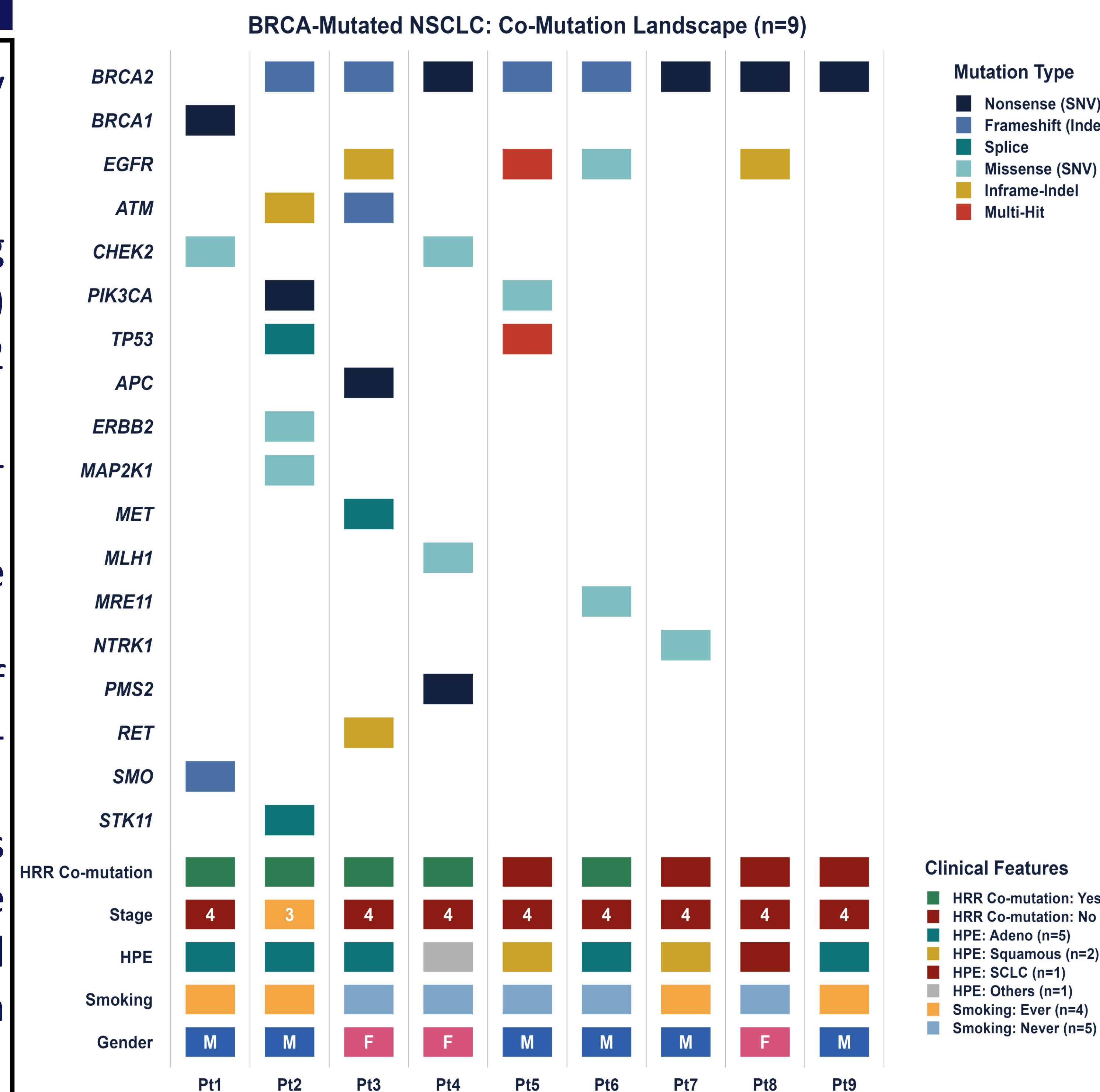
-Secondary endpoints: To assess the co-mutation profile, the progression-free survival (PFS), and overall survival (OS) of patients with BRCA1/2 mutated lung cancer

326 lung cancer patients with NGS reports
9 positive for BRCA mutation – 2.8%

Baseline Characteristics

Mean Age (SD), y	56.2 (±13.2)	Histopathology	
Male	6 (66.7%)	- Adenocarcinoma	5 (55.6%)
Female	3 (33.3%)	- Squamous cell ca	2 (22.2%)
Never-smoker	5 (55.6%)	- Small cell ca.	1 (11.1%)
Ever-smoker	4 (44.4%)	- Others	1 (11.1%)
Stage-III	1 (11.1%)	Driver alteration	
Stage-IV	8 (88.9%)	- Positive	5 (55.6%)
		- Negative	4 (44.4%)

No Family history of malignancy in any patient
Germline BRCA positive in 2/2 patients; cascade testing negative 1/1



Results

BRCA2 – 8 patients (88.9%)
BRCA1 – 1 patient (11.1%)

Non-sense mutation – 5 (55.6%)
Frameshift indel – 4 (44.4%)

BRCA – Loss of function – all patients

AMP/ASCO/CAP classification
Tier 2 – 8 (88.9%) | Tier 1 – 1 (11.1%)

Median Variant Allelic Frequency
15 (range 4 – 94)
VAF ≥ 50% in 4 patients

Median Follow-up
11.1 months

Median PFS
7.4 months
(95% CI 4.8 – 10.0)

Median OS
14.4 months
(95% CI 4.1 – 24.8)

Additional mutation in HRR genes seen in 5 patients (55.6%)

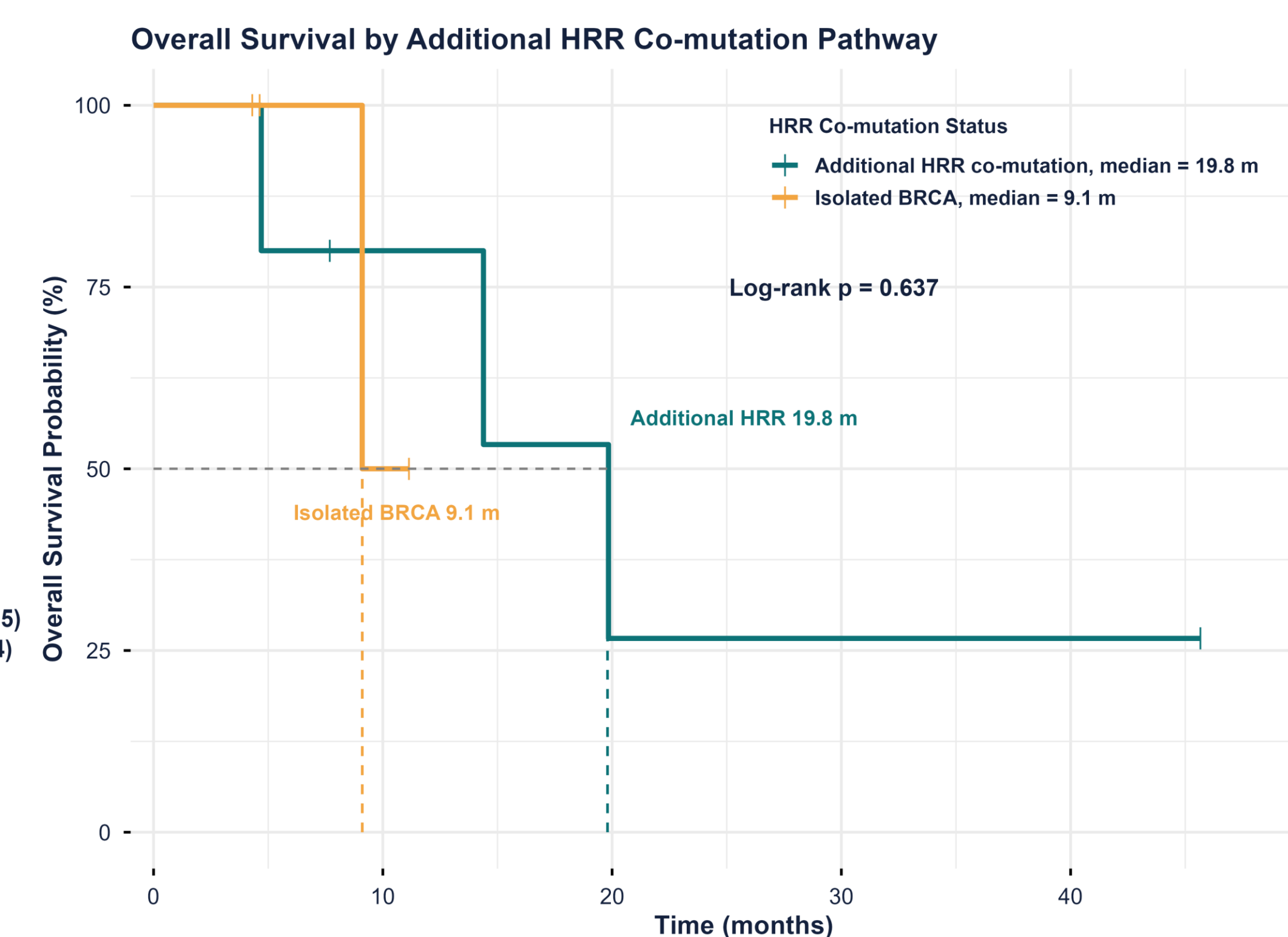
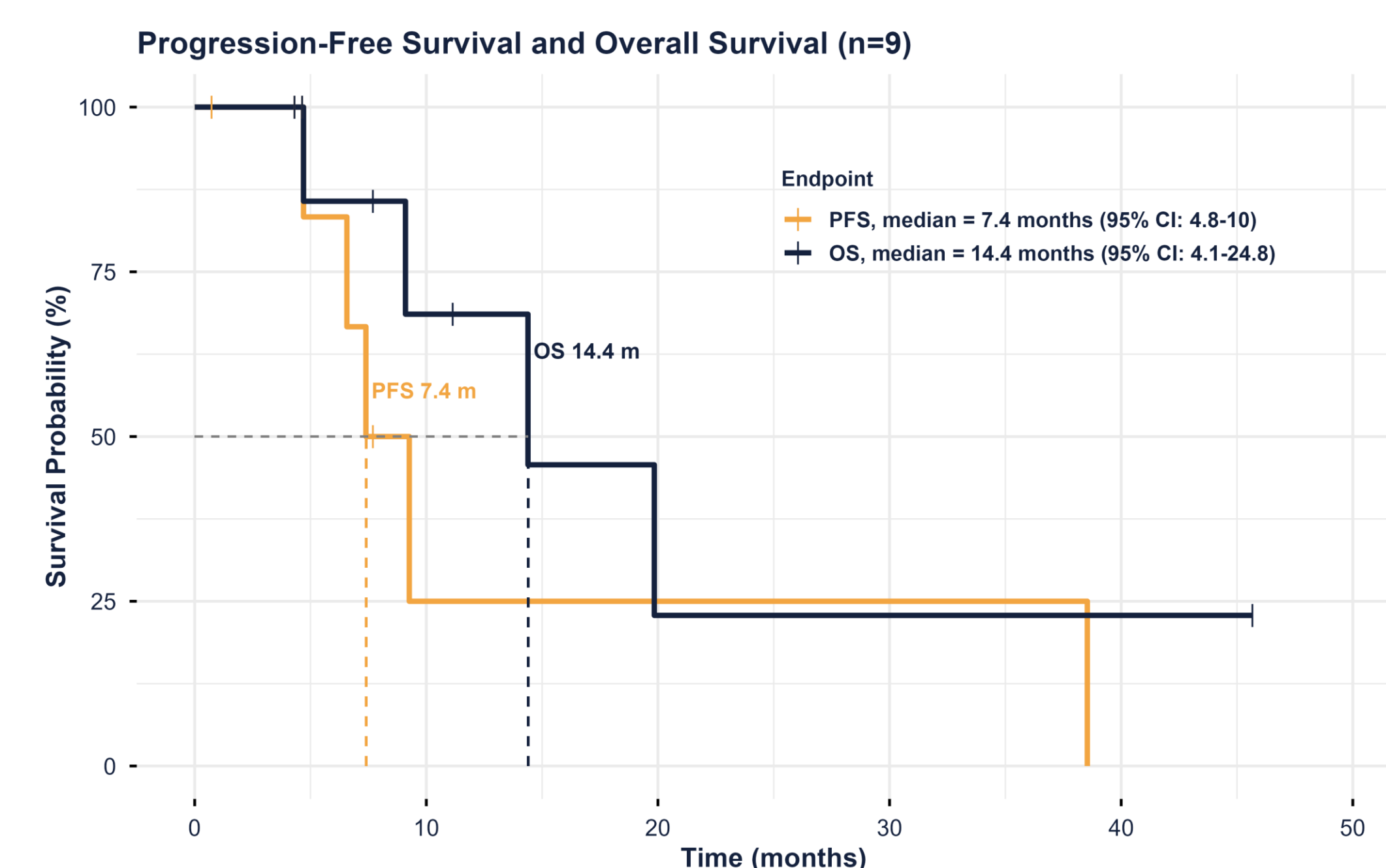
Commonest co-mutations
EGFR (n=4), TP53 (n=2),
PIK3CA, ATM and CHEK2 (n=2)

1st line treatment given

Palliative chemotherapy + TKI (4, 44.5%)
Palliative chemotherapy (3, 33.3%)
Concurrent Chemoradiation (1, 11.1%)
Immunotherapy (1, 11.1%)

Objective Response Rate (ORR) among
7 response-assessed patients
5/7 – 71.4%

PARP-inhibitors given in 1 patient in
the refractory setting – response could
not be assessed due to advanced
disease and early death



Conclusion

- BRCA gene mutations were uncommon in patients with lung cancer in this South Indian cohort, with a predominance of BRCA2 and loss-of-function alterations
- Co-mutations are common, particularly involving HRR pathway genes, and targetable drivers like EGFR
- A signal toward improved survival in patients with concurrent HRR alterations suggests a potential role of enhanced homologous recombination deficiency, warranting further investigation.