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EGFR Exon20 Insertions in NSCLC: Clinicopathological Spectrum, Mutational Distribution, and Survival Implications

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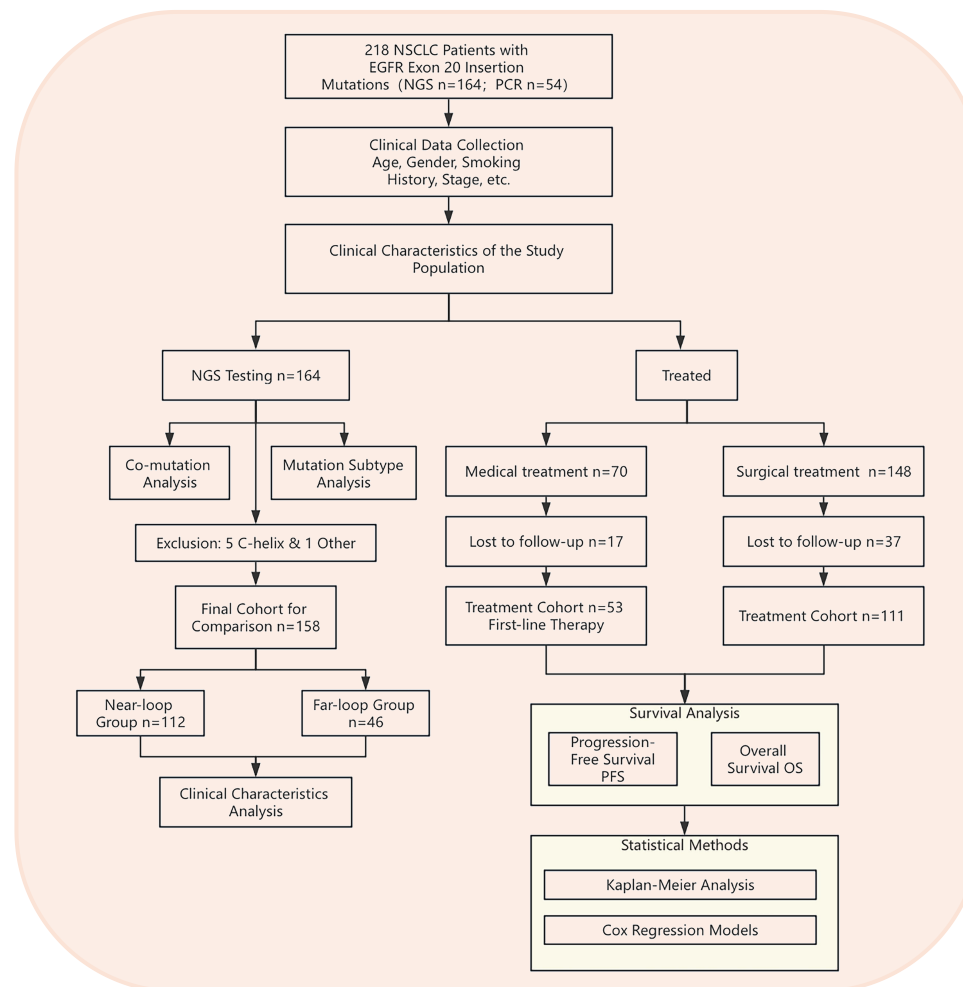
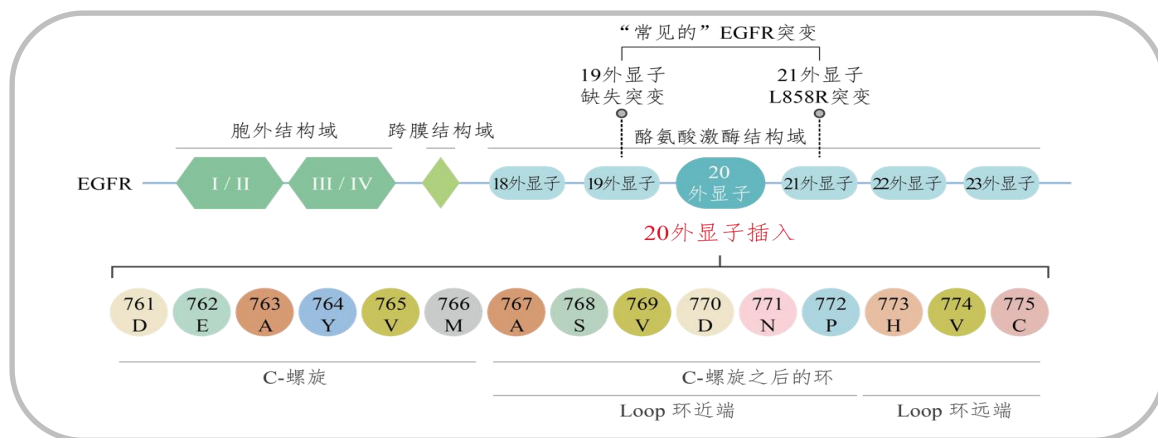
Beijing Tuberculosis and Thoracic Tumor Research Institute | Beijing Chest Hospital, Capital Medical University | Poster
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CHINA

Background & Study Design

A real-world retrospective cohort of EGFR Exon20 insertion-mutated NSCLC

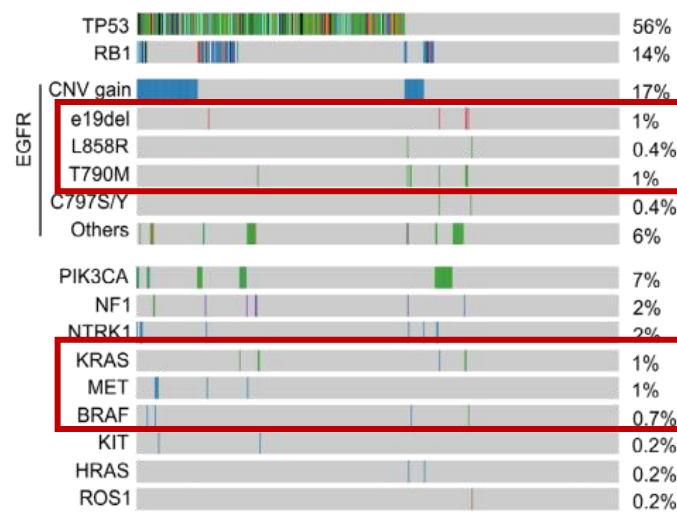
- EGFR Exon20 insertions are rare, molecularly heterogeneous, and generally insensitive to conventional EGFR-TKIs.
- We characterized clinicopathological features, insertion-site distribution, co-mutations, and survival outcomes.
- 218 consecutive patients diagnosed at Beijing Chest Hospital (Aug 2017–Aug 2024); EGFR Exon20 insertions confirmed by PCR or NGS.
- Primary endpoint: progression-free survival (PFS); secondary endpoint: overall survival (OS).



Molecular Heterogeneity

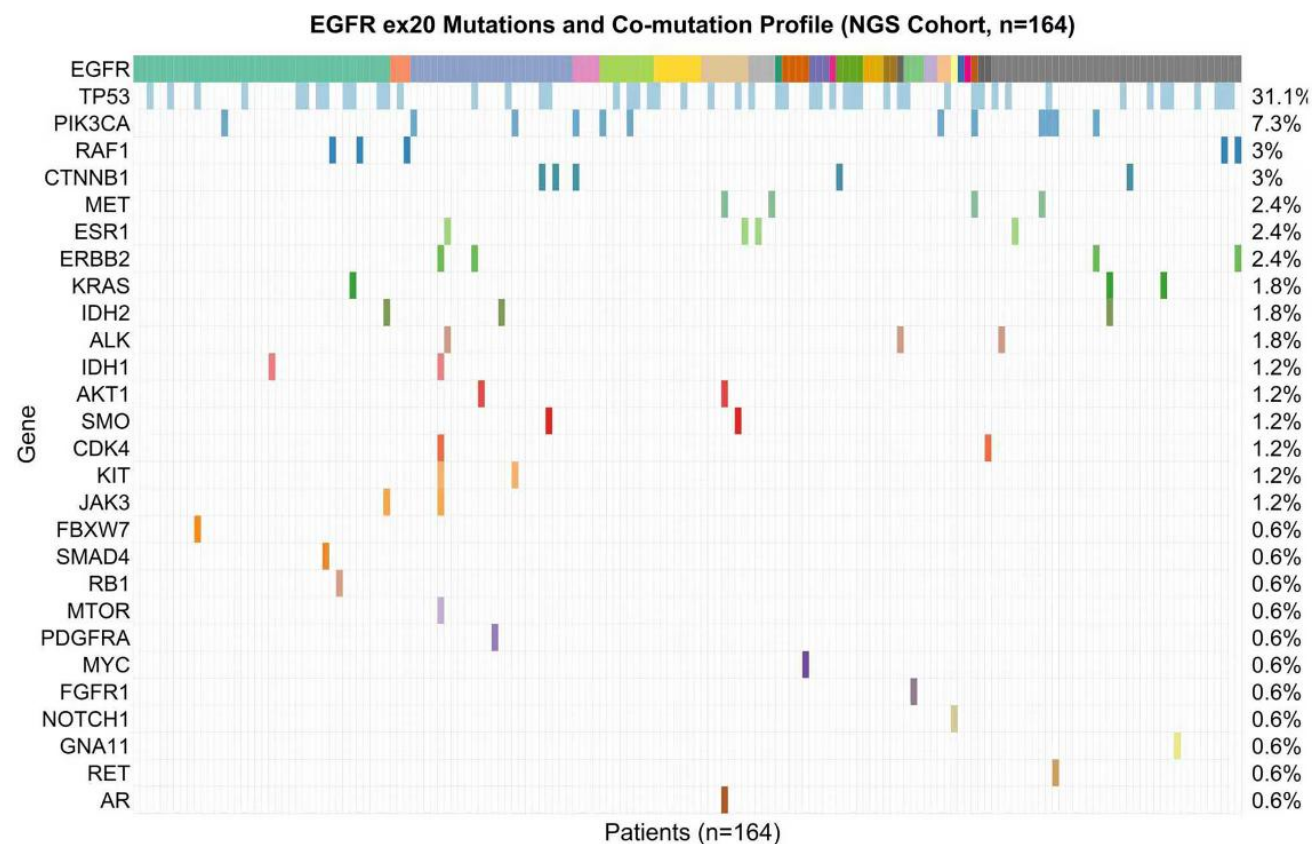
Near-loop mutations predominated, with diverse co-mutation patterns

- Among NGS-profiled patients, near-loop mutations were more common than far-loop mutations (112 vs 46 in the comparative cohort).
- Far-loop mutations were associated with a higher proportion of stage III–IV disease ($p = 0.0037$).
- TP53 was the most frequent co-mutated gene; common Exon20ins subtypes included A767_V769dup and S768_D770dup.



The proportion of combined classic mutations is very low.

The proportion of cases with co-occurrence of other common targeted driver genes is very low.



Clinicopathological Profile

The cohort was enriched for women, never-smokers, and adenocarcinoma

n = 218

Median age: 59 years

59.2%

Female

70.2%

Never-smokers

98.2%

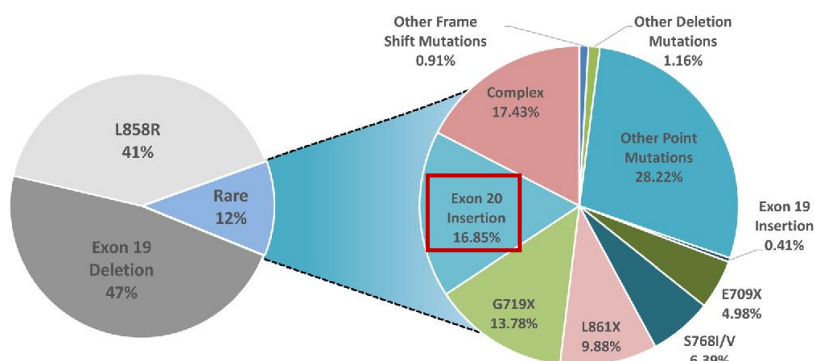
Adenocarcinoma

67.9%

Stage I–II at diagnosis

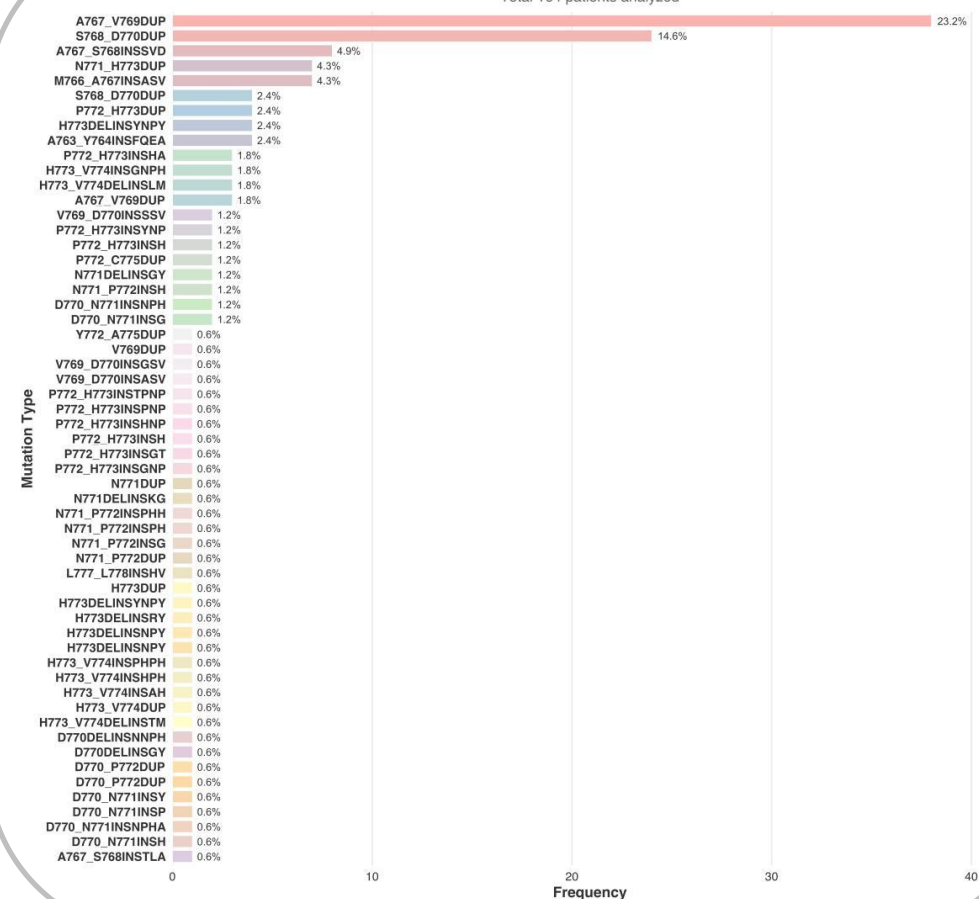
63.8%

PD-L1 <1% among
tested patients



Distribution of EGFR 20 Insertion Mutation Types

Total 164 patients analyzed



Survival Outcomes & Prognostic Factors

Advanced-stage patients with complete follow-up: n = 53

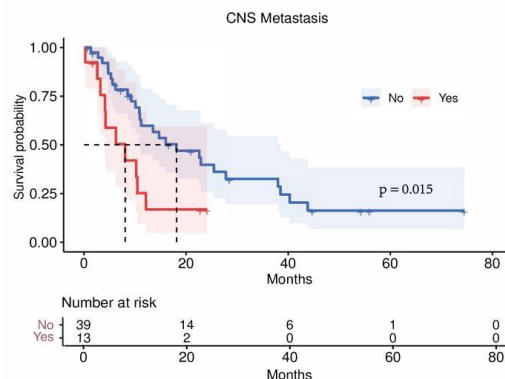
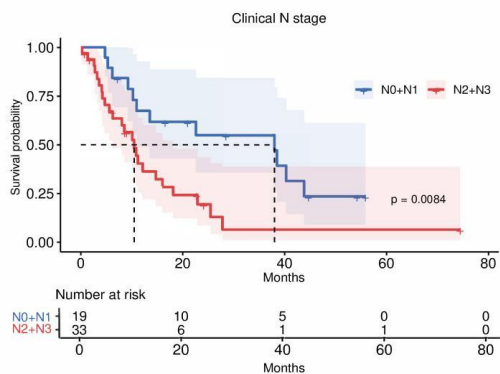
10.4 months

Median PFS

20.9 months

Median OS

- Advanced N stage was associated with shorter PFS: 10.5 vs 38.0 months ($p = 0.0084$).
- Baseline CNS metastasis was associated with shorter PFS: 8.1 vs 18.1 months ($p = 0.015$).
- No clinical factor was independently prognostic after multivariable analysis; OS associations were not significant.



Characteristic	Groups	Pvalue	Hazard Ratio	
Ages (years)	≤65 vs >65	0.118	1.793(0.86–3.733)	
Gender	Male vs Female	0.696	0.877(0.454–1.694)	
Smoking history	Smoker vs Never	0.456	1.293(0.658–2.538)	
Clinical T stage	T1+T2 vs T3+T4	0.802	1.089(0.560–2.118)	
Clinical N stage	N0+N1 vs N2+N3	0.011	0.386(0.186–0.800)	
Clinical stage	IA–IIB vs IIIA–IVB	0.084	0.352(0.108–1.150)	
ECOG score	0–1 vs ≥2	0.764	1.129(0.512–2.487)	
CNS Metastasis	Yes vs No	0.018	2.522(1.169–5.436)	
PD-L1	< 1% vs 1%–50%	0.913	0.948(0.363–2.474)	
PD-L1	< 1% vs ≥50%	0.902	0.927(0.277–3.103)	
Co-mutation	Yes vs No	0.451	1.381(0.596–3.207)	
Treatment modality	Chemotherapy vs Chemoimmunotherapy	0.794	0.867(0.297–2.530)	
Treatment modality	Chemotherapy vs Targeted Therapy	0.153	0.327(0.071–1.517)	
Treatment modality	Chemotherapy vs Sensitive Targeted Therapy	0.442	0.599(0.163–2.209)	
With or without sensitive targeted therapy	Yes vs No	0.556	1.373(0.477–3.949)	
With or without immunotherapy	Yes vs No	0.142	0.409(0.124–1.350)	
Mutation site	Near-loop Mutation vs Far-loop Mutation	0.312	0.648(0.279–1.503)	
Liver metastasis	Yes vs No	0.014	6.501(1.45–29.129)	
Presence of TP53 co-mutation	Yes vs No	0.713	1.134(0.579–2.222)	

Conclusions

Clinical implications of EGFR Exon20 insertion heterogeneity

1 | Distinct Clinical Profile

Predominantly observed in women, never-smokers, and patients with adenocarcinoma.

2 | Substantial Molecular Heterogeneity

Near-loop mutations predominated, and TP53 was the most frequent co-mutated gene.

3 | Near-loop vs Far-loop

Far-loop mutations presented at more advanced stage, but survival outcomes were broadly comparable.

4 | Prognostic Implications

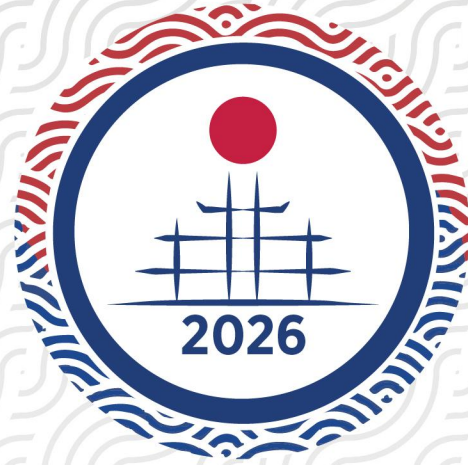
Advanced nodal disease and baseline CNS metastasis were associated with shorter PFS.

TAKE-HOME MESSAGE

EGFR Exon20 insertion-mutated NSCLC is clinically and molecularly heterogeneous, and baseline disease burden - particularly nodal and CNS involvement - may help identify patients at higher risk of early progression.

Limitations

Larger, multicenter prospective studies are needed to validate subtype-specific biological and prognostic differences.



Thank You.