



EP06.11: Clinicopathological Profile and Molecular Landscape of Non-Small Cell Lung Carcinomas With *ERBB2* Alterations: An Actionable Oncogenic Driver



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INTRODUCTION

- Non-small cell lung carcinoma (NSCLC) accounts for 85% of lung cancer. They exhibit a diverse and rapidly expanding molecular landscape
- Activating *ERBB2* (Her2neu) mutations are actionable oncogenic drivers in NSCLC with approved targeted therapy available
- They occur in up to 2 to 5% of lung NSCLCs, especially those lacking *EGFR*, *ROS1* and *ALK* alterations
- They are more frequently observed in Asian population¹

METHODS

All cases of NSCLCs with *ERBB2* alterations over a period of one year were collected and analyzed for clinicopathological features, type of *ERBB2* alteration and co-occurring mutations

A total of 203 cases of NSCLCs with negative single gene testing results for *EGFR* mutation, *ALK* and *ROS1* rearrangements underwent Next Generation Sequencing (NGS) using the AmoyDx HANDLE Classic NGS Panel (40 gene DNA and RNA panel) for detection of additional clinically actionable alterations

DISCUSSION AND CONCLUSION

- ERBB2*-mutant non-small cell lung cancer represented 5.8% of NSCLCs negative for *EGFR/ALK/ROS* which is a bit higher than the prevalence reported in global studies as they took into account all NSCLCs²
- The most common *ERBB2* mutation noted in our study was HER2 Y772_A775dup / A775_G776 insYVMA which is in line with literature, and these cases were negative for Her2neu
- Her2neu amplification was noted in 1.9% of our cases and all these cases showed Her2neu immunopositivity on IHC (3+)

Region	PMID and Year of publication	Sample size	Her2neu Mutation	Her2neu Amplification
USA	4912374 (2016)	6832	3.4%	3%
USA	6900927 (2019)	43,706	2.3%	2%
Germany	33776618 (2021)	4500	2.3%, 1.5% ex 20 insertion	0.7%; Five patients both mut and amp
Greece	5783588 (2017)	502	1.8%	1%
Italy	32932213 (2020)	537	3%	1.9%
China	35151031 (2022)	21,475	3.1%	-
China	8646112 (2021)	249	6.8%	1.6%
Japan	25047676 (2014)	243	2.1 to 3.7%	-
USA, China	Xu C, Zhang Y, and Liu D, et al (2018)	490	3.5%	2.4%
India	27637917 (2016)	204	1.5%	-
Our study		203 (Single gene testing for EGFR/ALK/ROS negative)	3.9%; Two with low copy number gain amp	1.9%

Future Direction for Research

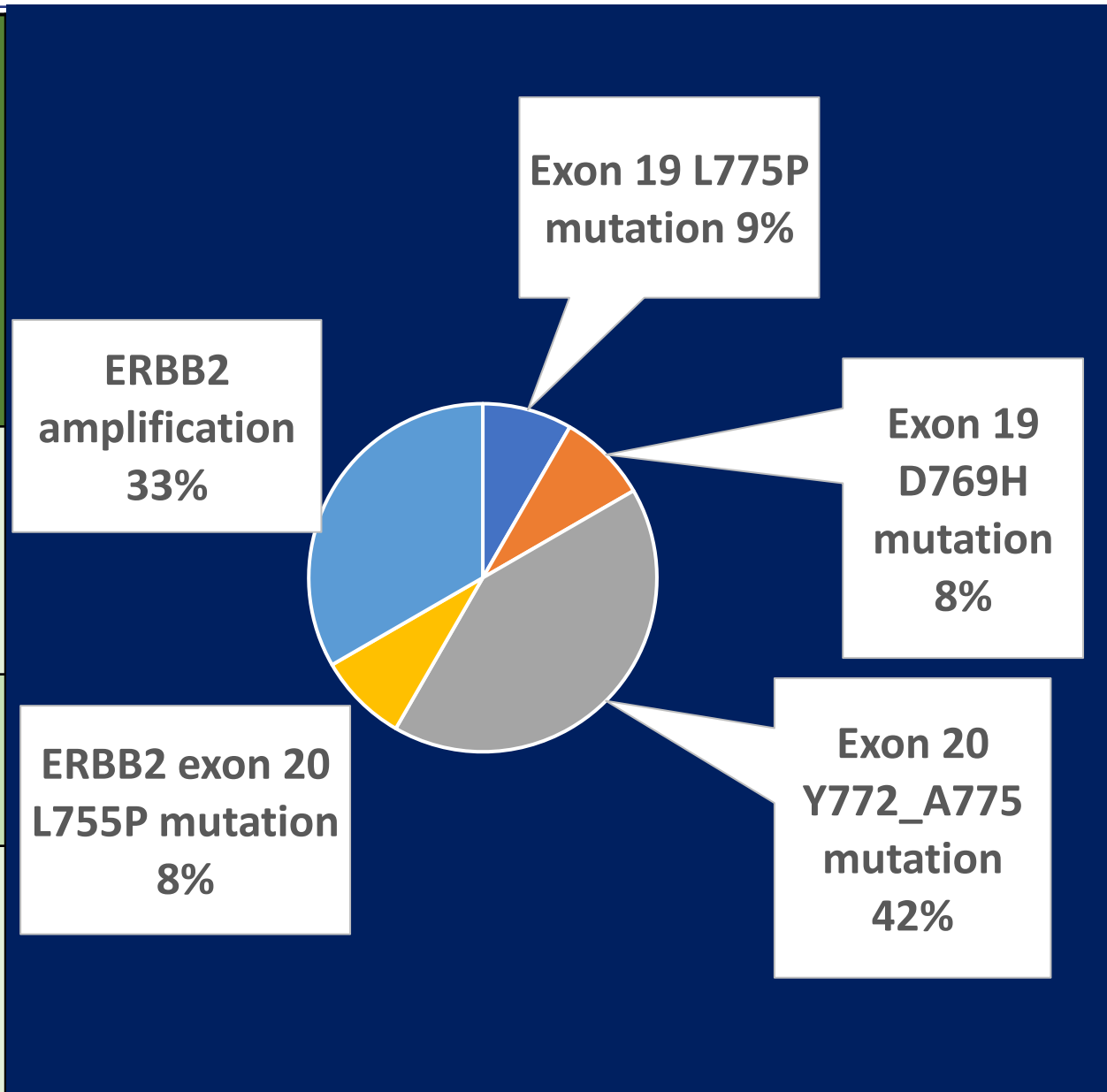
- With FDA approved targeted therapy available, understanding the heterogeneity of mutational landscape of *ERBB2* alterations in NSCLC becomes important for providing precision oncology treatment to patients and is also pivotal for further drug development

REFERENCES

- Nath N, Ali Osama M, Nambirajan A, et al. (2026) Molecular Alterations in Lung Cancer – Beyond EGFR, ALK and ROS1. New Advancements in Lung Cancer
- Ning Yi Yap et al; Prevalence and treatment of human epidermal growth factor receptor altered non-small cell lung cancer: a retrospective analysis and systematic literature review

RESULTS

Case no.	Age	Sex	Smoking history	Histology	Site of metastasis	Multiplex testing	Co-existing mutation	Her2neu IHC	Treatment	Follow up from the date of diagnosis
1	64	M	Yes	NSCLC-NOS with SMARCA4 deficiency	Anterior abdominal wall	<i>ERBB2</i> exon 19 D769H mutation	TP53	NA	Chemotherapy 5 cycles	Alive
2	35	M	Yes	Adenocarcinoma, NOS	Cervical LN	<i>ERBB2</i> exon 20 Y772_A775 mutation	TP53	NA	Chemotherapy 2 cycles	Expired in 3 months
3	47	M	No	Adenocarcinoma, NOS	Non-metastatic	<i>ERBB2</i> exon 20 L755P mutation	None	NA	NA	NA
4	46	F	No	Adenocarcinoma, NOS	Cervical LN	<i>ERBB2</i> exon 20 Y772_A775 mutation; <i>ERBB2</i> low copy number amplification	TP53, RB1	NA	Chemotherapy	Alive
5	64	F	No	Adenocarcinoma, NOS	Cervical LN	<i>ERBB2</i> exon 20 Y772_A775 mutation	None	Negative (0)	Patient denied chemotherapy	Alive
6	47	M	No	Adenocarcinoma, NOS	Brain, LN	<i>ERBB2</i> exon 20 Y772_A775 mutation	None	NA	Chemotherapy 3 cycles	Expired after 5 months
7	65	M	Yes	Adenocarcinoma, NOS	NA	<i>ERBB2</i> exon 20 Y772_A775 mutation	TP53	NA	Chemotherapy 12 cycles	Expired after 4 months
8	63	F	No	Adenocarcinoma, NOS	Liver, Cervical LN	<i>ERBB2</i> exon 20 Y772_A775 mutation <i>ERBB2</i> amplification; low copy number	RB1	Negative (0)	Chemotherapy 1 cycle	Expired in 3 months
9	65	M	Yes	NSCLC favouring SCC	NA	<i>ERBB2</i> amplification; high copy number	TP53	Positive (3+)	NA	NA
10	70	M	Yes	NSCLC-NOS	Brain, vertebrae	<i>ERBB2</i> amplification; high copy number	TP53	Positive (3+)	Chemotherapy 4 cycles plus Pembrolizumab	Alive
11	79	M	Yes	Adenocarcinoma, NOS	NA	<i>ERBB2</i> amplification; high copy number	TP53, KEAP1	Positive (3+)	NA	NA
12	52	M	Yes	NSCLC with adenocarcinoma and squamous differentiation	Non-metatstatic	<i>ERBB2</i> amplification; high copy number	None	Positive (3+)	Chemotherapy and Radiotherapy	Alive



Case 11: *ERBB2* amplification; high copy number with negative *EGFR/ALK/ROS*

