ERBB2 alteration with or without co-existent EGFR mutation in metastatic non-small cell lung cancer

Vijendra Singh[1], Yasmine Baca[2], Seongho Kim[1], Yanis Boumber[3], Hirva Mamdani[1], Edward S. Kim[4], Ammar Sukari[1], Chul Kim[5], Gerold Bepler[1], Stephen V. Liu[5], Alexander I. Spira[6], Hossein Borghai[3], Misako Nagasaka[1].

[1]Karmanos cancer Institute, Detroit, MI; [2]Caris Life Sciences, Phoenix, AZ; [3]Fox Chase Cancer Center,Philadelphia, PA; [4]Atrium Healthcare, Levine Cancer Institute, Charlotte, NC; [5]Georgetown University, Washington, DC; [6]Virginia Cancer Specialists, Alexandria, VA.

Poster Number#5900

BACKGROUND

For epidermal growth factor (EGFR) mutated non-small cell lung carcinoma (NSCLC) multiple EGFR tyrosine kinase inhibitors (TKIs) are approved.

ERBB2 alteration (mutation and/or amplification) is associated with poor survival in NSCLS patients and is commonly reported as a resistance mechanism to EGFR TKIs.

STUDY OBJECTIVES

Investigate the prevalence of ERBB2 alteration with or without EGFR as a co-mutation in NSCLC.

Describe type of ERBB2 mutation and EGFR mutation when both are present as co-mutation.

METHODS

We obtained de-identified clinical information and next generation sequencing results for NSCLC patients from Caris Life Sciences database.

Information about ERBB2 alterations and EGFR mutations was extracted from the data-set and analyzed retrospectively.

ERBB2 alterations include ERBB2 mutations and/or ERBB2 amplification.

ERBB2 amplification was defined as DNA copy number equal to or greater than 6.

Available clinical information: Age, gender, type of lung cancer and biopsy site.

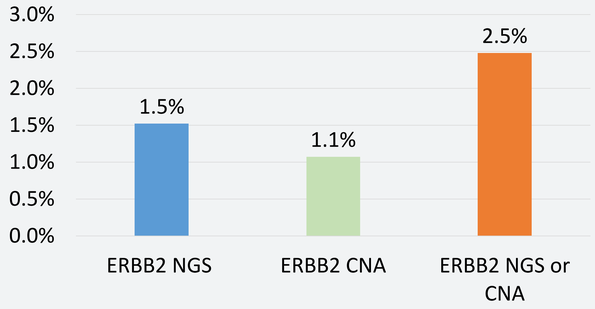
Abbreviations: NGS: next gene sequencing denotes mutation.
CNA: Copy number amplifications

Authors' Contact Information:
First Author: Vijendra Singh MD – singhv@karmanos.org
Senior Author: Misako Nagasaka MD = Nagasakm@karmanos.org

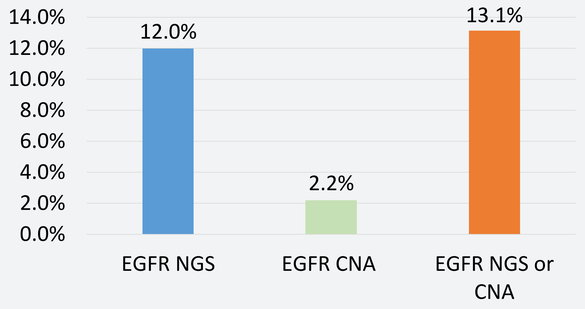
RESULTS

A total of 12946 NSCLC tumors having EGFR and/or ERBB2 NGS were available, of which 50.1% were male.

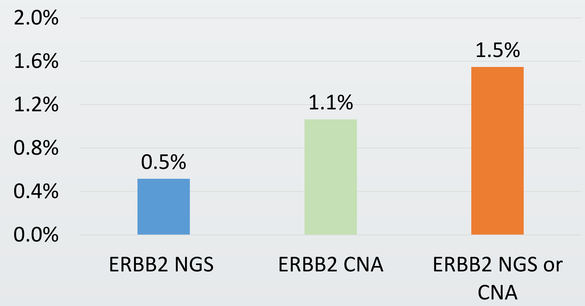
ERBB2 alteration in the complete cohort



EGFR alteration in the complete cohort



Within the EGFR-Mutated Cohort (N=1551)



Within the ERBB2-altered Cohort (N=321)

Test-Technology	Pos	Neg	Total	%
EGFR NGS	24	297	321	7.5%

Within the ERBB2-mutated Cohort (N=197)

Test-Technology	Pos	Neg	Total	%
EGFR NGS	8	189	197	4%

Within the ERBB2-amplified Cohort (N=134)

Test-Technology	Pos	Neg	Total	%
EGFR NGS	16	118	134	11.9%

Results

ERBB2 and EGFR co-mutations

Sr. N	ERBB2 mutation	EGFR mutation
1	Exon 8 (S310F)	Exon 19 (E746-A750del)
2	Exon 8 (S310F)	Exon 19 (E746-A750del)
3	Exon 8 (S310F)	Exon 19 (E746-A750del)
4	Exon 8 (S310F)	Exon 21 (L858R)
5	Exon 8 (S310F)	Exon 21 (L858R)
6	Exon 8 (S310F)	Exon 21 (L858R)
7	Exon 8 (S310Y)	Exon 21 (L858R)
8	Exon 17 (G617D)	Exon 21 (L858R)

Conclusion

- A minority of EGFR mutated NSCLC patients had ERBB2 alterations.
- In ERBB2 and EGFR co-mutated patients, exon 21 mutations for EGFR and exon 8 mutations for ERBB2 were common.
- Forty percent of patients who had exon 8 ERBB2 mutation had EGFR as a co-mutation.