Copy Number Variation Detection for the Indication of Targeted Therapy in a Lung Cancer Patients Series. Next-Generation Sequencing Panel vs Fluorescent in-Situ Hibridization.

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BACKGROUND

Copy Number Variation Detection for the Indication of Targeted Therapy in a Lung Cancer Patients Series. Next-Generation Sequencing (NGS) Panel vs Fluorescent in-Situ Hibridization (FISH).

DESIGN

Driver genes copy number variation (CNV) detection is crucial for treatment management in NSCLC. The aim of this study was to validate and compare CNVs detected by NGS panel with those obtained by a FISH assay (Figure 1).

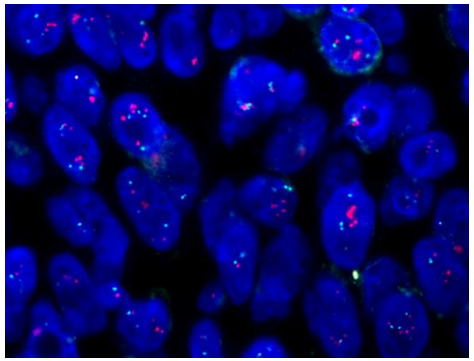

Figure 1. ERBB2 gene amplification detected by FISH assay.

GENE	PATIENTS WITH A CNV DETECTED BY NGS PANEL (%)	MEDIAN COPIES OF THE GENE BY NGS	PATIENTS WITH A CNV DETECTED BY FISH (%)	MEDIAN COPIES OF THE GENE BY FISH
NGS as the gold-standard assay				
MYC	12 (6.0%)	10.6	12 (6.0%)	15.5
FGFR1	7 (3.5%)	10.9	7 (3.5%)	15.1
CCND1	4 (2.0%)	8.3	4 (2.0%)	28.0
NF1	3 (1.5%)	15.2	-	-
EGFR	2 (1.0%)	7.5	1 (0.5%)*	10.0
CDK6	2 (1.0%)	18.6	-	-
KRAS	1 (0.5%)	5.3	-	-
FISH as the gold-standard assay				
ERBB2	2 (1.0%)	3.4	8 (4.0%)	7.4
MET	2 (1.0%)	7.6	4 (2.0%)	14.0

- FISH not performed (DNA FISH probe not available).
*One FISH analysis was not informative due to poor tissue quality.

Table 1. Summary of genes, number of patients (percentage of the global series) with a CNV detected by the NGS panel and comparison with the FISH assay.

RESULTS

This retrospective study included NSCLC patients evaluated at our institution from 2019 to 2020. All FFPE samples underwent routine ERBB2 and MET FISH amplification study and a complete morphomolecular diagnostics, CNV, fusions and gene mutations analysis using a 52 genes NGS panel. A comparison analysis based on the number of copies of each gene detected by each technique was performed (Table 1).

CONCLUSION

NGS panel increases the percentage of NSCLC patients suitable for a target therapy as it screens 52 genes in one single assay.

ERBB2 and MET FISH assay performs better than the NGS panel as it is capable to detect CNV when less than ten copies of the gene or when heterogeneity of CNVs are present in tumor cells.

NGS and FISH assay have the same accuracy in the detection of CNVs of MYC, FGFR1, CCND1 and EGFR.

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