

Extensive molecular profiling of lung cancer using new genetic platforms: A single institution's experience

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Relevant Financial Relationships:

- Research Grant Pfizer
- Advisory Board Diaceutics, BMS
- Honoraria Pfizer, BMS, MSD, Angelini, Roche

Relevant Nonfinancial Relationships:

- Serves as reviewer for several peer-reviewed journals

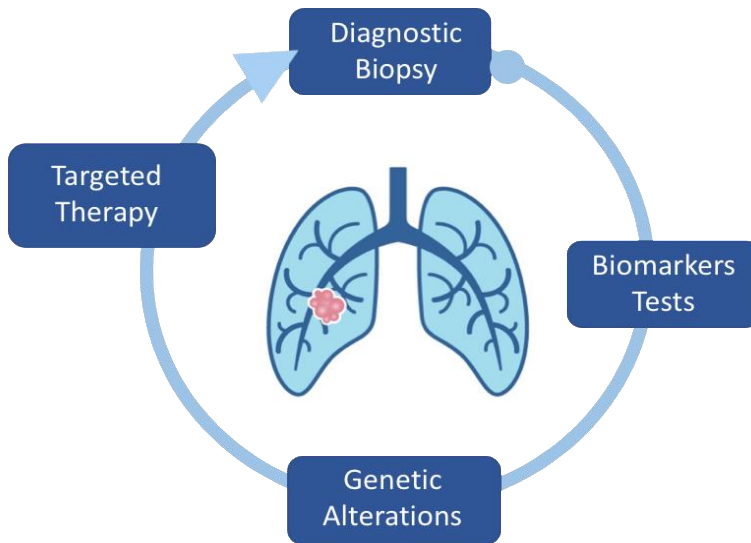
 COLLEGE of AMERICAN PATHOLOGISTS

 IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

 AMP
ASSOCIATION FOR MOLECULAR PATHOLOGY

Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment with Targeted Tyrosine Kinase Inhibitors

Guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and the Association for Molecular Pathology



2018

NSCLC Recommendations IASLC/AMP/CAP Guidelines

1 'Must-test'

EGFR

ALK

ROS1

2 'Optional-test'

BRAF

KRAS

RET

MET

HER2

Lindeman N, et al. Arch Pathol Lab Med 2018

N=335 NSCLC EIV from 2016 to 2018

NGS Oncomine Solid Tumour - DNA

22 genes - 92 Amplicons

EGFR, ERBB2, ERBB4, MET, FGFR1, FGFR2, FGFR3, DDR2, ALK, KRAS, NRAS, PIK3CA, BRAF, PTEN, MAP2K1, AKT1, TP53, STK11, CTNNB1, SMAD4, FBXW7, NOTCH1



IonTorrent
PGM

nCounter Elements - RNA

Customized Panel- 72 Probes

Fusion genes: *ALK, ROS1, RET, NTRK1*

Splicing: *MET Δ ex14*

Immune genes: *CD4, CD8, GZMM, PD1, PD-L1, IFNG, FOXP3*



nCounter
FLEX

N=305

N=150

3%
3%
14%

Adenocarcinoma

Squamous Cell Carcinoma

LCNEC

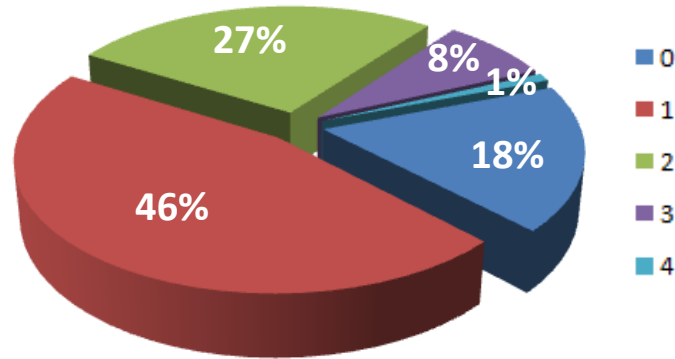
NOS

LCNEC: Large Cell Neuroendocrine Carcinom; NOS; Not Otherwise Specified

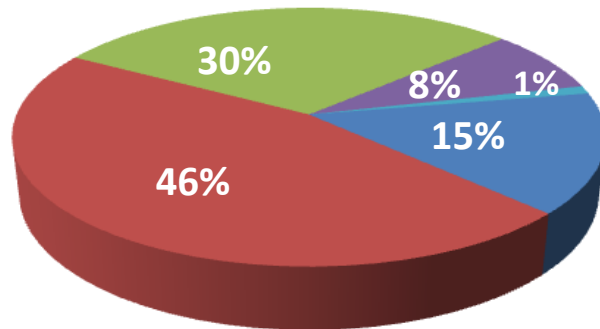
80% of NSCLC tumors are carriers of a mutation

Nº of mutations per sample

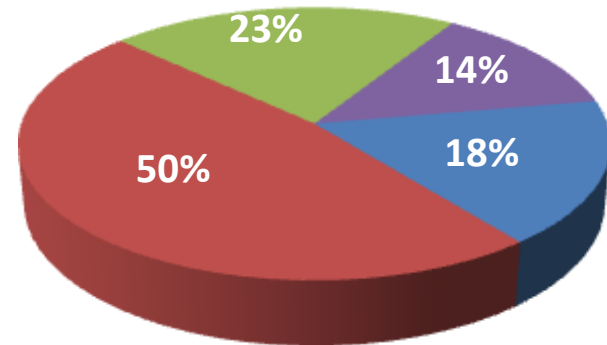
N= 200 mut/249



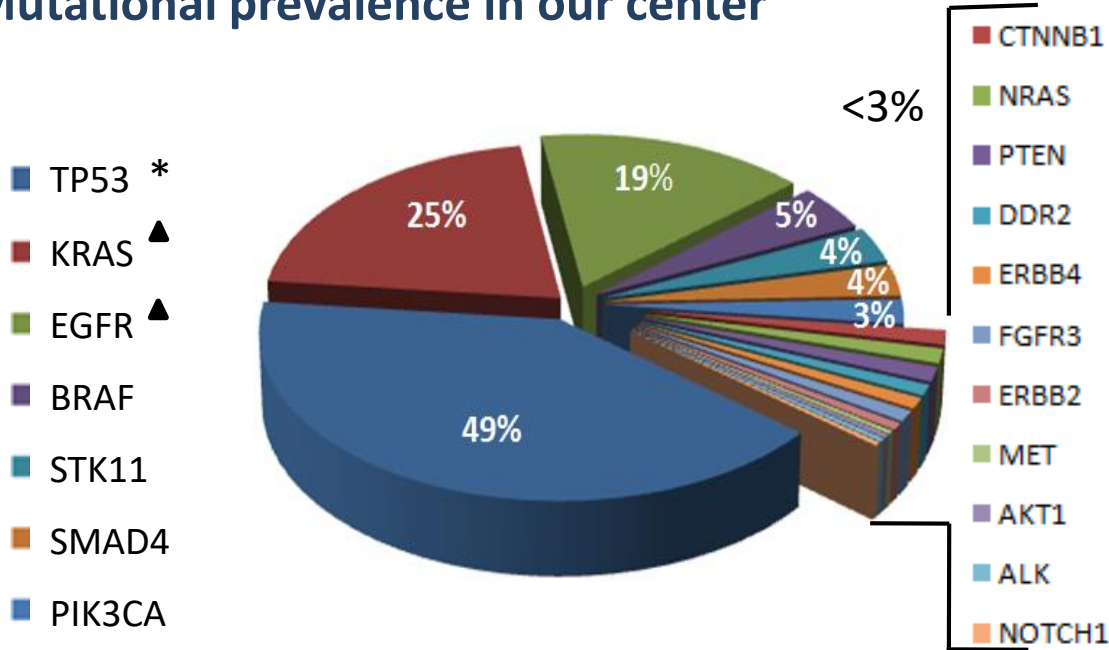
Adenocarcinoma



Squamous Cell Carcinoma

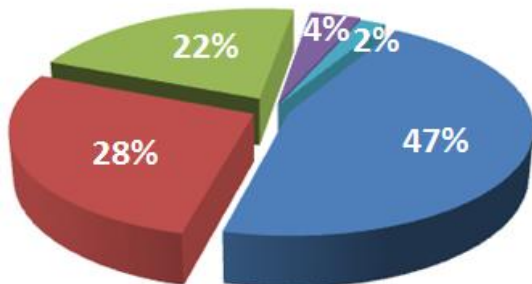


Mutational prevalence in our center

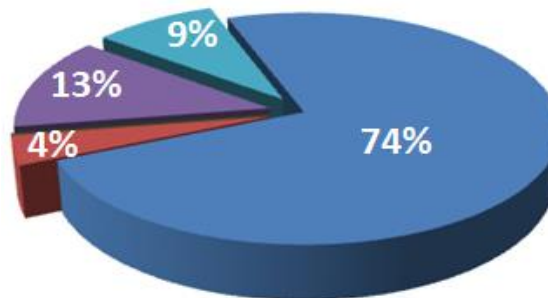


N=249
80% mut
(200/249)

Adenocarcinoma

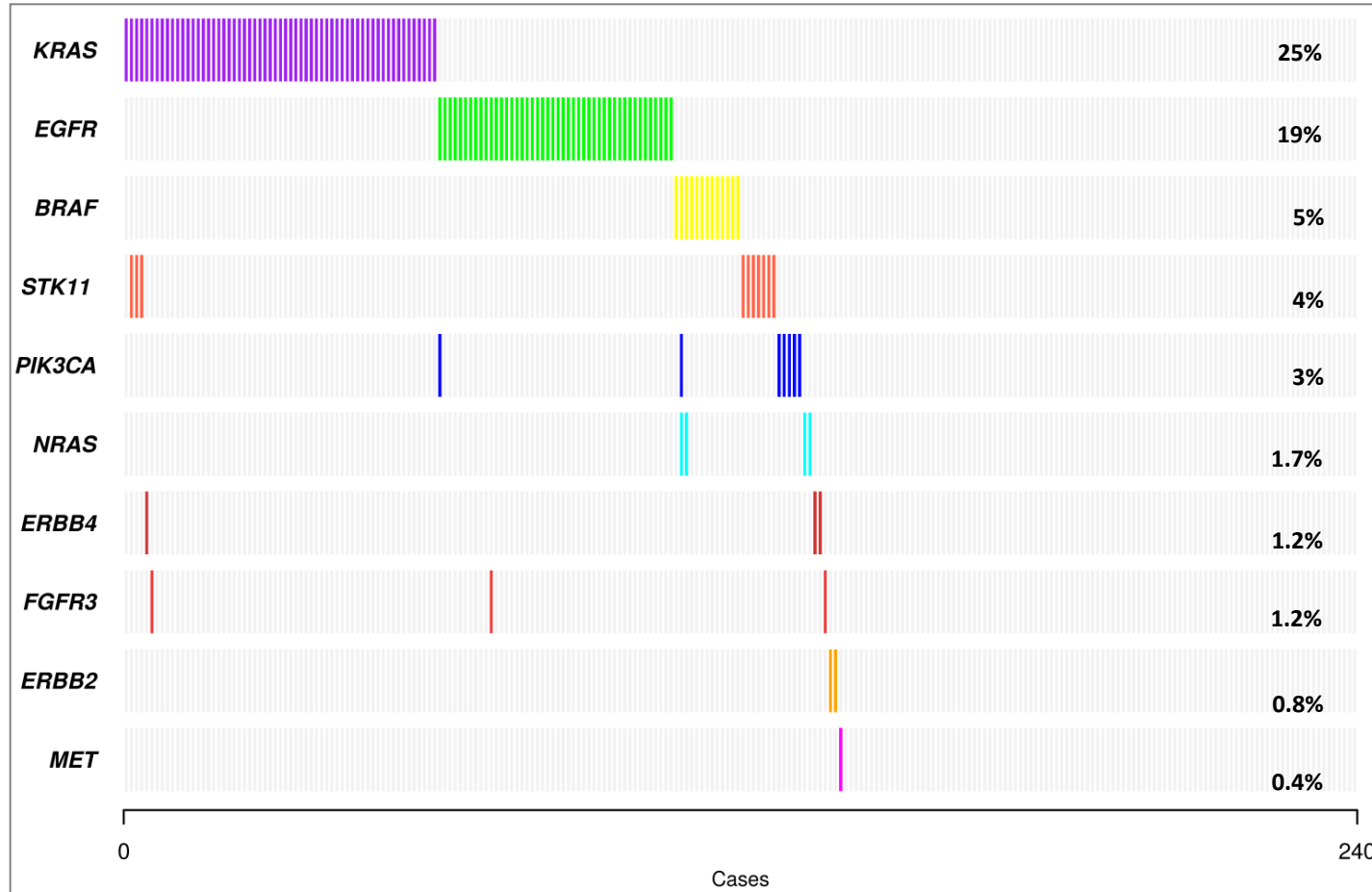


Squamous Cell Carcinoma

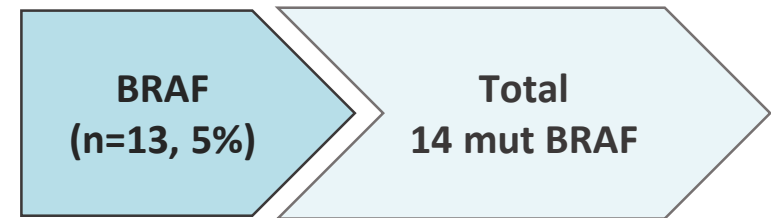
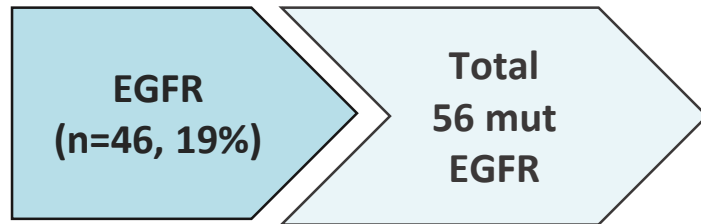


* p=0.05
▲ p=0.01

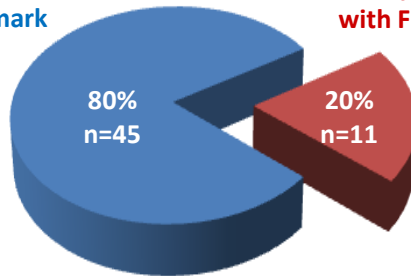
The main driver oncogenes are mutually exclusive



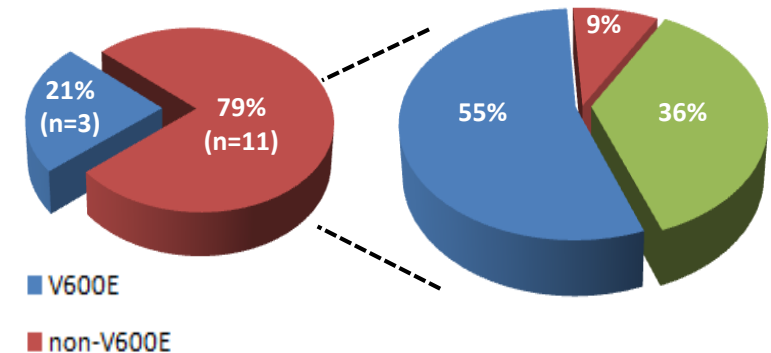
Impact on the molecular test selected (EGFR / BRAF)



Mutations detected by qPCR assays with FDA/CE-IVD mark

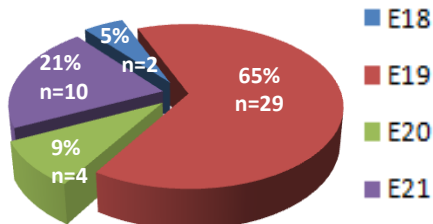


Mutations NOT detected by qPCR assays with FDA/CE-IVD mark

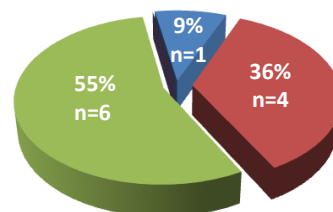


Exonic distribution of mutations

FDA/CE-IVD kits



NGS

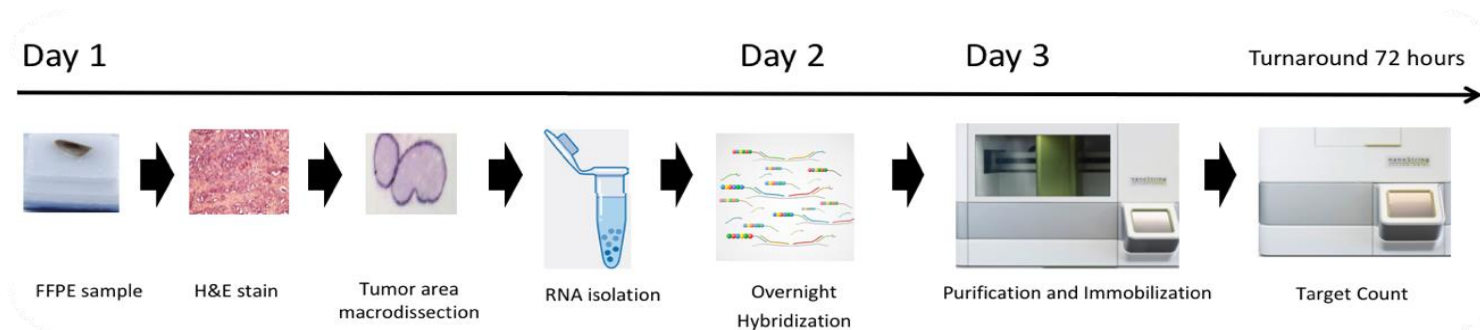


BRAF kinase activity

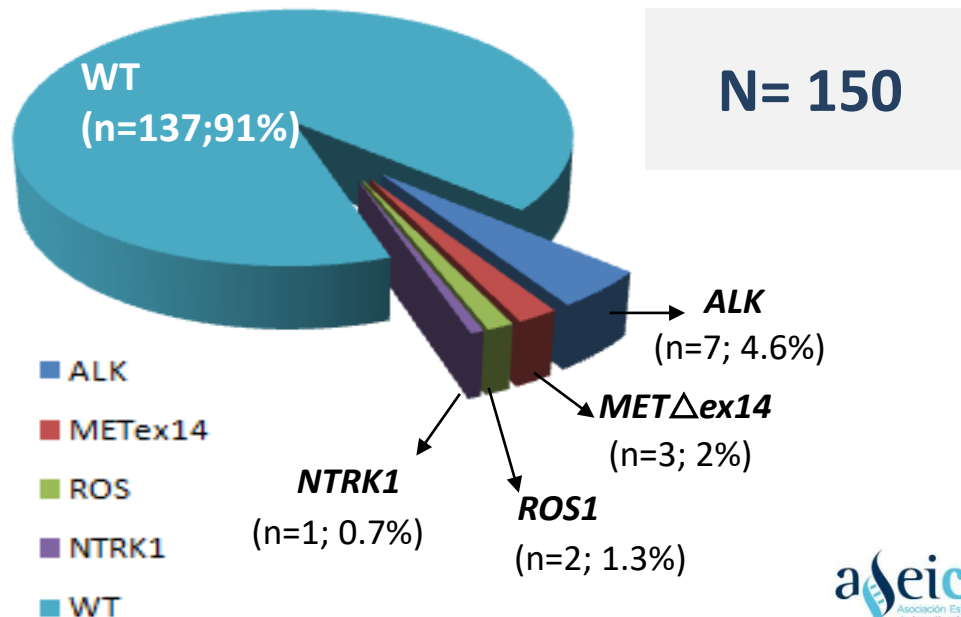
Activating	Inactivating	Unknown
p.Gly469Ala (n=4)	p.Gly466Val (n=1)	p.Arg444Leu (n=1)
p.Gly469Val (n=1)		p.Gly464Ala (n=1)
p.Gly464Val (n=1)		p.Lys601Asn (n=1)
		p.Trp604Cys (n=1)

Molecular alterations detected by nCounter

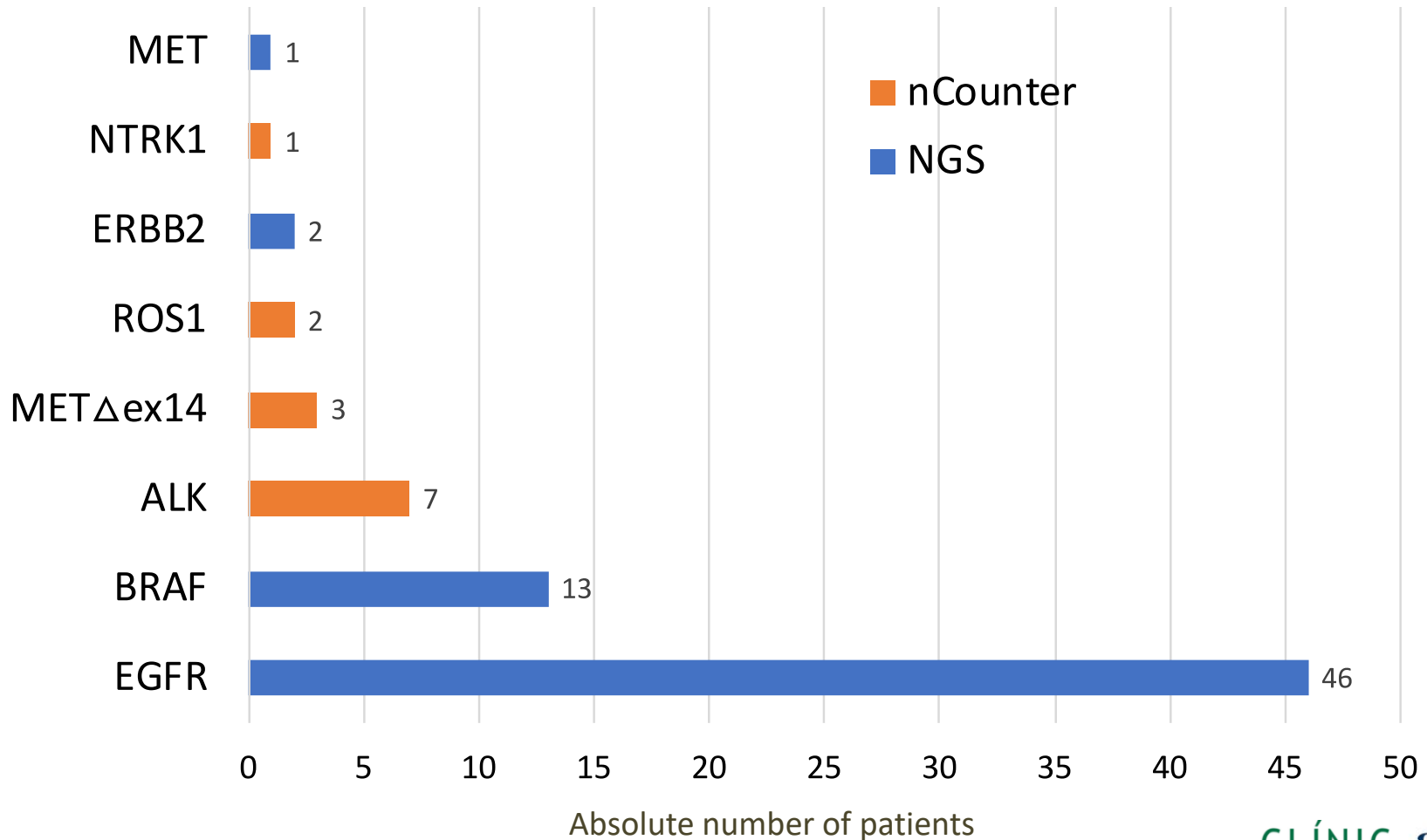
nCounter Workflow



Mutation	Cases	%
<i>ALK</i>	7	4.6
<i>MET</i> Δ <i>ex14</i>	3	2
<i>ROS1</i>	2	1.3
<i>NTRK</i>	1	0.7
WT	137	91



34% of patients have an actionable genomic alteration



Conclusions

- The adoption of new technologies is feasible in routine clinical practice
- Our results support the efficiency of NGS technology, identifying 80% of lung tumors harboring any genetic alteration, results similar to those reported in the literature (Lung Cancer Mutation Consortium)
- NGS allows a higher gene coverage allowing the identification of mutations non-captured by traditional diagnostic testing technologies (20% EGFR, 79% BRAF non-V600)
- In our series, 1 out of 3 patients (34%) carried an 'actionable' alteration with potential for target-inhibition

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