# Achieving Dramatic Insights Into Molecular Oncology & Precision Medicine Of NSCLC-MTB

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Delhi

# My subsequent reactions….

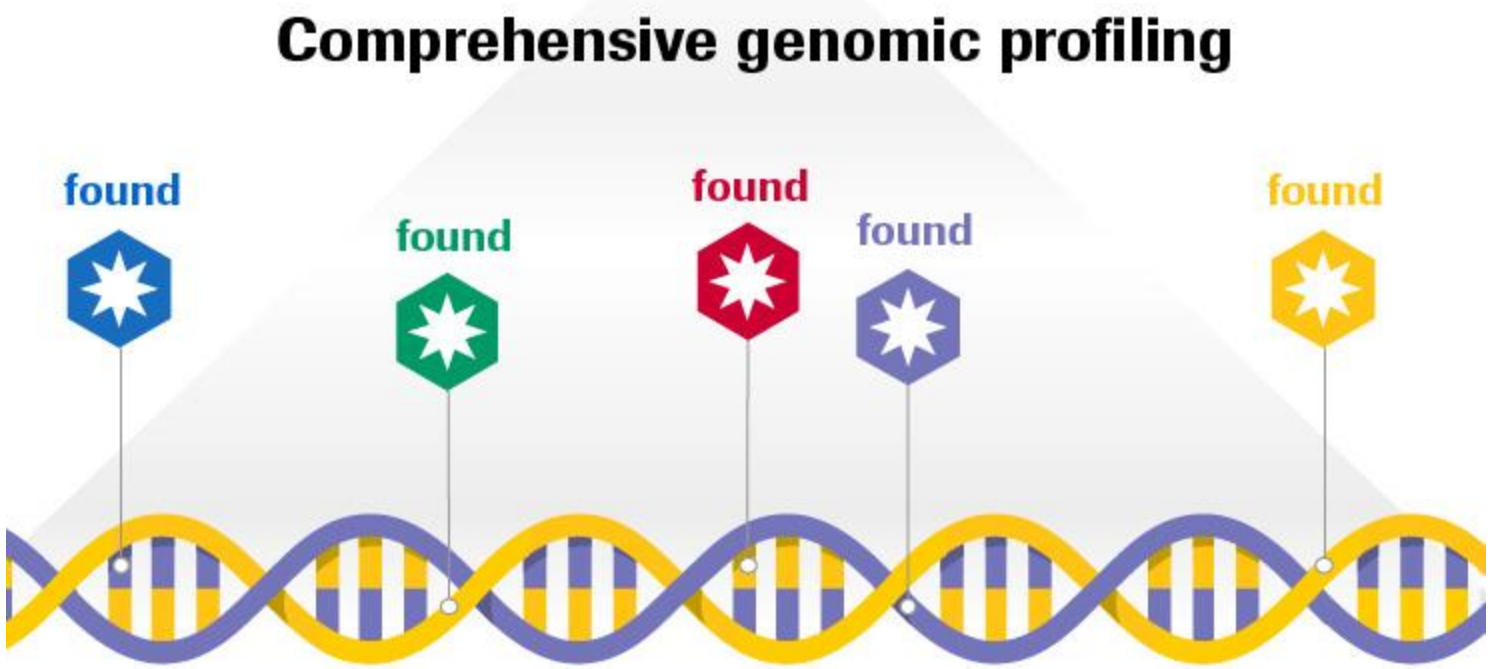
Drama!!!!


Precision medicine!!!

# Case scenario 1


- 55-year-old male, non smoker
- Stage 4 NSCLC, adenocarcinoma
- PET CT- Lung mass with multiple skeletal metastases
- MRI Brain- normal
- PDL1-80%
- How would you investigate further
  - Single gene testing
  - Short panel NGS
  - Slightly large panel NGS
  - Comprehensive Genomic Profiling( Patiala panel!!!)

# Small panel vs Large Panels: The Basics




*Kulkarni, S., & Pfeifer, J. (Eds.). (2014). Clinical genomics. Academic Press*

# A Better Nomenclature: Targeted vs large panels!!!

## The Ion AmpliSeq Cancer Hotspot Panel v2 targets
## 50 genes

| | | | | |
|---|---|---|---|---|
| *ABL1* | *EGFR* | *GNAS* | *KRAS* | *PTPN11* |
| *AKT1* | *ERBB2* | *GNAQ* | *MET* | *RB1* |
| *ALK* | *ERBB4* | *HNF1A* | *MLH1* | *RET* |
| *APC* | *EZH2* | *HRAS* | *MPL* | *SMAD4* |
| *ATM* | *FBXW7* | *IDH1* | *NOTCH1* | *SMARCB1* |
| *BRAF* | *FGFR1* | *JAK2* | *NPM1* | *SMO* |
| *CDH1* | *FGFR2* | *JAK3* | *NRAS* | *SRC* |

Targeted

## Oncomine Focus Assay gene list

| Detection of variants in 52 key solid tumor genes | | | | | | |
|---|---|---|---|---|---|---|
| 35 genes with hotspot mutations | | | 19 genes with copy number variations | | 23 genes with fusion drivers | |
| DNA panel, 269 amplicons | | | | | RNA panel, 271 amplicons | |
| AKT1 | FGFR2 | **MAP2K1** | ALK | **KIT** | ABL1 | FGFR2 |
| ALK | FGFR3 | MAP2K2 | AR | **KRAS** | **ALK** | FGFR3 |
| AR | **GNA11** | MET | BRAF | **MET** | AKT3 | **MET** |
| **BRAF** | GNAQ | MTOR | **CCND1** | **MYC** | AXL | NTRK1 |
| CDK4 | **HRAS** | **NRAS** | **CDK4** | MYCN | BRAF | NTRK2 |
| **CTNNB1** | IDH1 | **PDGFRA** | CDK6 | **PDGFRA** | **EGFR** | NTRK3 |
| DDR2 | IDH2 | **PIK3CA** | **EGFR** | PIK3CA | ERBB2 | PDGFRA |
| **EGFR** | JAK1 | RAF1 | ERBB2 | | ERG | PPARG |
| ERBB2 | JAK2 | RET | **FGFR1** | | ETV1 | RAF1 |
| ERBB3 | JAK3 | ROS1 | FGFR2 | | ETV4 | RET |
| ERBB4 | KIT | SMO | FGFR3 | | ETV5 | **ROS1** |
| ESR1 | **KRAS** | | FGFR4 | | FGFR1 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ABL2 | CD79A | EPHB1 | GRM8 | LIFR | MYH9 | PMS1 | SOX2 | WAS | GNAS | ATRX | TSC2 |
| ACVR2A | CD79B | EPHB4 | GUCY1A2 | LPHN3 | NCOA1 | POT1 | SSX1 | WHSC1 | HFN1A | BAP1 | WT1 |
| ADAMTS20 | CDC73 | EPHB6 | HCAR1 | LPP | NCOA2 | POU5F1 | STK36 | WRN | HRAS | CDK12 | |
| AFF1 | CDH1 | ERCC1 | HIF1A | LRP1B | NCOA4 | PPARG | SUFU | XPA | IDH1 | CDKN2A | |
| AFF3 | CDH11 | ERCC3 | HLF | LTF | NFKB1 | PPP2R1A | SYK | XPC | IDH2 | CDKN2B | |
| AKAP9 | CDH2 | ERCC4 | HOOK3 | LTK | NFKB2 | PRDM1 | SYNE1 | XPO1 | JAK2 | CEBPA | |
| APC | CDH20 | ERCC5 | HSP90AA1 | MAF | NIN | PRKAR1A | TAF1 | XRCC2 | KDR | CHEK1 | |
| ARID2 | CDH5 | ERG | HSP90AB1 | MAFB | NKX2-1 | PRKDC | TAF1L | ZNF384 | KIT | CHEK2 | |
| ARNT | CDK8 | ETS1 | ICK | MAGEA1 | NLRP1 | PSIP1 | TAL1 | ZNF521 | KRAS | CREBBP | |
| ATF1 | CDKN2C | ETV1 | IGF1R | MAGI1 | NOTCH4 | PTGS2 | TBX22 | ABL1 | MAP2K1 | DNMT3A | |
| AURKA | CIC | ETV4 | IGF2 | MALT1 | NSD1 | PTPRD | TCF12 | AKT1 | MAP2K2 | FANCA | |
| AURKB | CKS1B | EXT1 | IGF2R | MAML2 | NUMA1 | PTPRT | TCF3 | AKT2 | MAP2K4 | FANCD2 | |
| AURKC | CMPK1 | EXT2 | IKBKB | MAP3K7 | NUP214 | RALGDS | TCF7L1 | AKT3 | MAPK1 | FBXW7 | |
| BAI3 | COL1A1 | FAM123B | IKBKE | MAPK8 | NUP98 | RARA | TCF7L2 | ALK | MET | MLH1 | |
| BCL10 | CRBN | FANCC | IKZF1 | MARK1 | PAK3 | RECQL4 | TCL1A | AR | MPL | MSH2 | |
| BCL11A | CREB1 | FANCF | IL2 | MARK4 | PARP1 | REL | TET1 | AXL | MTOR | MSH6 | |
| BCL11B | CRKL | FANCG | IL21R | MBD1 | PAX3 | RHOH | TFE3 | BRAF | MYC | NBN | |
| BCL2 | CRTC1 | FANCJ | IL6ST | MCL1 | PAX5 | RNASEL | TGFBR2 | CBL | MYCN | NF1 | |
| BCL2L1 | CSMD3 | FAS | IL7R | MDM2 | PAX7 | RNF2 | TGM7 | CCND1 | NFE2L2 | NF2 | |
| BCL2L2 | CTNNA1 | FH | ING4 | MDM4 | PAX8 | RNF213 | THBS1 | CDK4 | NRAS | NOTCH1 | |
| BCL3 | CTNNB1 | FLCN | IRF4 | MEN1 | PBRM1 | RPS6KA2 | TIMP3 | CDK6 | NTRK1 | NOTCH2 | |
| BCL6 | CYLD | FLI1 | IRS2 | MITF | PBX1 | RRM1 | TLR4 | CSF1R | NTRK3 | NPM1 | |
| BCL9 | CY[illegible]C9 | FLT[illegible] | ITGA10 | [illegible] | PDE4DIP | RUNX1T1 | TLX1 | DDR2 | PAFAH1B2 | PPP2R2A | |
| BCR | CY[illegible]2D6 | FT[illegible] | ITGA9 | [illegible]R | PIK3CB | SAMD9 | TNFAIP3 | EGFR | PIK3CA | PIK3R1 | |
| BIRC2 | DAX[illegible] | FN[illegible] | ITK | [illegible]LL | PIK3CD | SBDS | TNFRSF14 | ERG | PIK3CB | PIK3R2 | |
| BIRC3 | DCC | FOXL2 | ITGB3 | MLLT10 | PGAP3 | SDHA | TNK2 | ERBB3 | PIK3CB | PTCH1 | |
| BIRC5 | DDB2 | FOXO1 | JAK1 | MMP2 | PHOX2B | SDHB | TOP1 | ERBB4 | PTPN11 | PTEN | |
| BLM | DDIT3 | FOXO3 | JAK3 | MN1 | PIK3C2B | SDHC | TPR | ERCC2 | RAF1 | RADSO | |
| BLNK | DEK | FOXP1 | JUN | MRE11A | PIK3CD | SOHD | TRIM24 | ESR1 | RET | RB1 | |
| BMPR1A | DICER1 | FOXP4 | KAT6A | MTR | PIK3CG | SEPT9 | TRIM33 | EZH2 | ROS1 | RUNX1 | |
| BRD3 | DPYD | FZR1 | KAT6B | MTRR | PIK3R2 | SGK1 | TRIP11 | FGFR1 | SF3B1 | SETD2 | |
| BTK | DST | G6PD | KDM5C | MUC1 | PIM1 | SH2D1A | TRRAP | FGFR2 | SMO | SMARCA4 | |
| BUB1B | EML4 | GATA1 | KDM6A | MUTYH | PKHD1 | SMAD2 | TSHR | FGFR3 | SRC | SMARCB1 | |
| CARD11 | EP300 | GATA2 | KEAP1 | MYB | PLAG1 | SMAD4 | UBR5 | FGFR4 | ARID1A | STK11 | |
| CASC5 | EP400 | GATA3 | KLF6 | MYCL1 | PLCG1 | SMUG1 | UGT1A1 | FLT3 | ASXL1 | TET2 | |
| CCND2 | EPHA3 | GDNF | LAMP1 | MYD88 | PLEKHG5 | SOCS1 | USP9X | GNA11 | ATM | TP53 | |
| CCNE1 | EPHA7 | GPR124 | LCK | MYH11 | PML | SOX11 | VHL | GNAQ | ATR | TSC1 | |



Annotated for gain-of-function mutations

Annotated for loss-of-function mutations

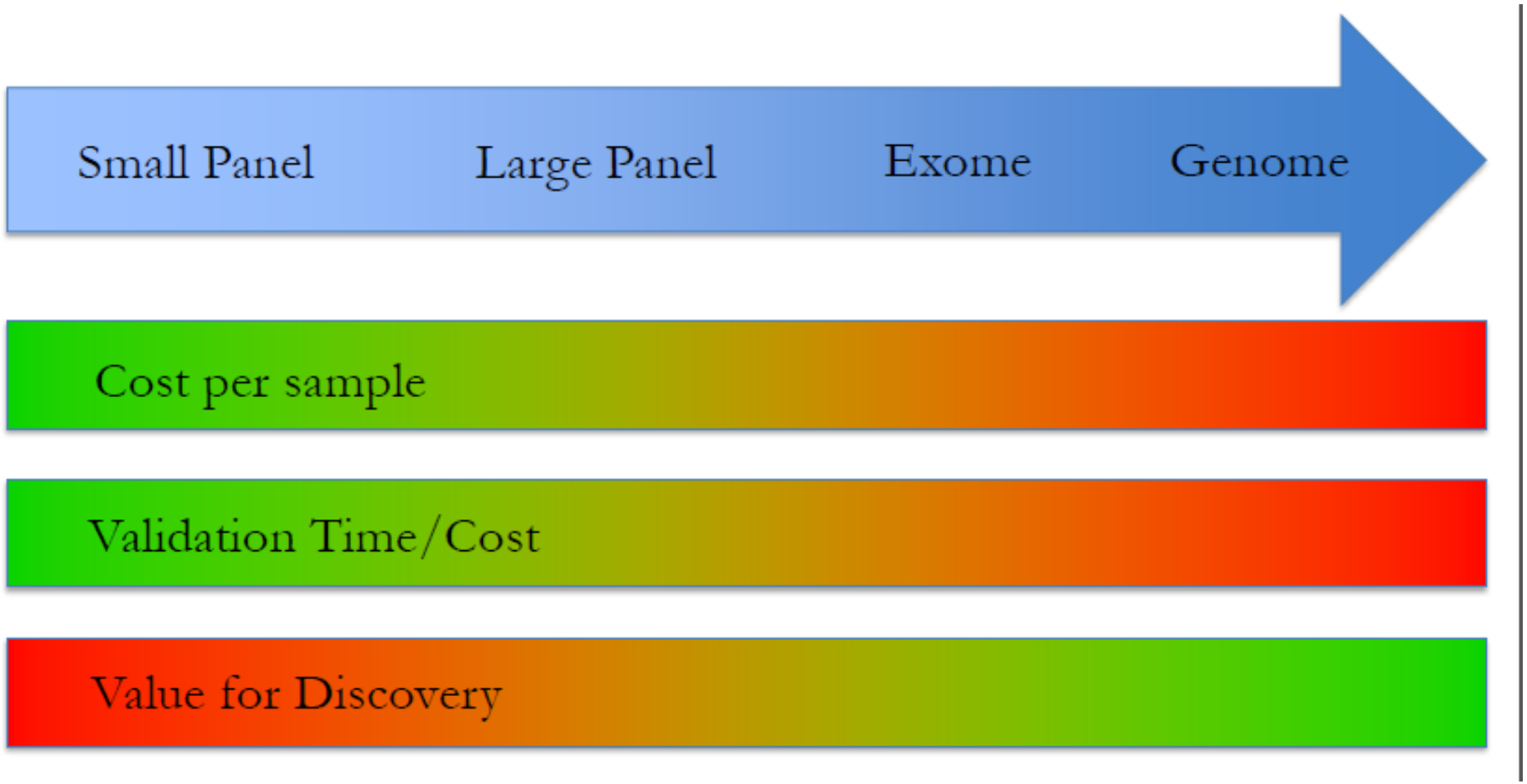
# How to choose

**Small: looking for expected things**

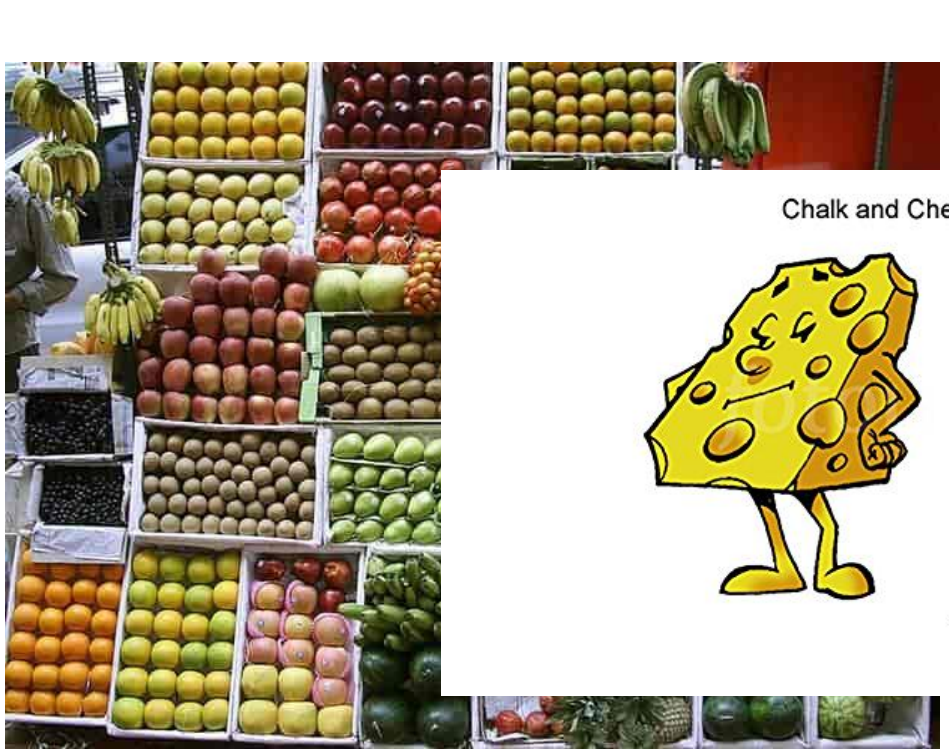
- Diagnostic use in tumors with known actionable biomarkers
- Cost constraints
- Tissue constraints
- Require faster results

**Large: when you don’t know what to look for**

- Diagnostic use in tumors which are molecularly heterogeneous with not many actionable targets
- Tissue not an issue
- Results may not deter ongoing treatment line
- Cost also not an issue
- Research intent


Small Panel
Large Panel
Exome
Genome
Cost per sample
Validation Time/Cost
Value for Discovery

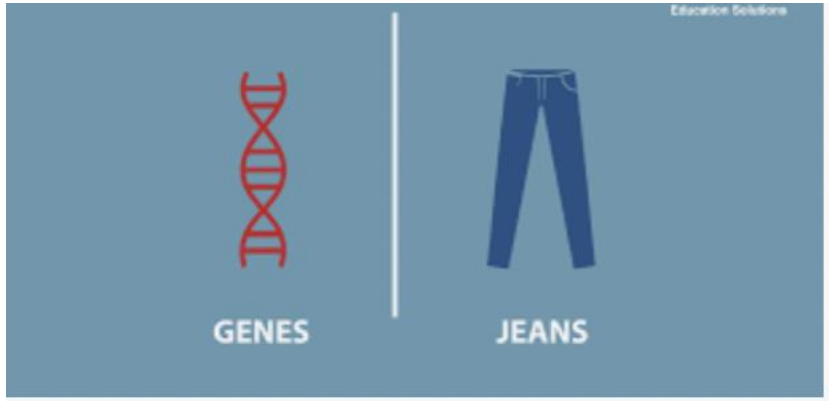
# Status of NGS reports/ companies offering NGS in India…






# Lets discuss the common terminologies/ medical jargon used in the NGS report

- VAF
- Depth
- Coverage
- Cellularity
- DNA/RNA
- VUS….




Making Sense

Rajiv Gandhi Cancer Institute and Research Centre
A Unit of Indraprastha Cancer Society
Registered under "Societies Registration Act 1860"

Rajiv Gandhi Cancer Institute and Research Center
Sector-5, Rohini,
New Delhi-110085
http://www.rgcirc.org/

[redacted] Date: 25Apr 2022 1 of 7

**Patient Information**

[redacted]

**Age/Sex:** 55Y/Female
**Referred Doctor:** Dr. ULLAS BATRA/ MANSI SH
**Sample Type:** Tumor Tissue (FFPE block)- B/2795/2022(3-

Diagnosis: Important to correlate with alterations detected

**DIAGNOSIS: NON SMALL CELL LUNG CARCINOMA**

**Tumor Fraction in the submitted section:90%**

Tumor % in the block when compared to normal tissue: In order to interpret the VAF of the variants detected

Report Highlight: Alterations detected

- ***KRAS*** **p.(G12S) (Missense)**
- ***TP53*** **p.(H179R) (Missense)**
- ***BAG4-FGFR1*** **(Fusion)**

Report Highlights: Gives an overview of the alterations detected

- **REPORT:**
- 55 year old female
- NSCLC-Adenocarcinoma on tissue biopsy, TTF1 positive,
- EGFR by RTPCR, ALK IHC: negative

- **NGS : Custom Smart Lung panel done**

Type of mutation: for eg this is KRAS non G12C

Denotes mutation burden relative to the wildtype counterpart

## DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Locus | Variant Allele Frequency | Transcript | Variant Effect | Clinical Significance |
|---|---|---|---|---|---|---|---|
| *KRAS* | p.(G12S) | c.34G>A | chr12:25398285 | 33.07% | NM_033360.4 | Missense | Strong Clinical Significance |
| *TP53* | p.(H179R) | c.536A>G | chr17:7578394 | 60.25% | NM_000546.6 | Missense | Variant of Clinical Significance |

## Gene Fusions (RNA)

| Genes | Variant ID | Locus |
|---|---|---|
| BAG4-FGFR1 | BAG4-FGFR1.B1F2 | chr8:38034657 - chr8:38315052 |

Type of fusion: the partners, and the exons (eg this is imp especially in ALK)

Clinical significance as per AMP guidelines and evidence available in literature

## NGS SMART Lung Panel

# Assay Information and Methodology

Test Description. – This customized panel is a multi-biomarker next generation sequencing assay that interrogates the under n
nucleotide Variants (SNVs) and Fusion Rearrangements as mentioned below.

Genes Analyzed for SNVs *AKT1, ALK, BRAF, EGFR, ERBB2, KRAS, KEAP1, MET, NRAS, NTRK1, PTEN, PIK3CA, RB1, ROS1, TP53, STK11.*

Genes Analyzed for Rearrangements - *ABL1, AKT3, ALK, AXL, BRAF, EGFR, ERBB2, ERG, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, MET, NTRK1, NTRK2, NTRK3, PDGFRA, PPARG, RAF1, RET, ROS1, SMO.*

Quality Metrics: PASSED - For the DNA based assay, the panel and the va .3
Software using the following quality metrics (MEDQCOV greater than 1000. he
RNA based assay greater than 5000 mapped reads were used as cutoffs.

Sample Input and Analytical sensitivity - The assay utilizes a minimum of 20ng DNA and 20ng RNA at 500X coverage and provides an analytical sensitivity of more than equal to 5 percent for DNA based genetic alterations.

Note:- This information in this report does not constitute a treatment recommendation or not to use any specific therapeutic agent, and should not be interpreted as treatment advice. Decisions concerning patient care and treatment rest solely within the discretion of the patient's treating physician.

Genes covered in the panel: Imp to match the gene to the clinical context

Coverage for tissue somatic panel: min median coverage of 500-1000x warranted

Analytical sensitivity: 5%: lowest VAF detected in this assay

Fusion QC: 5000 reads cut off as per NCI MATCH

# Case 1

- 65 year old male, smoker
- Diagnosed as stage IV NSCLC, sq cell ca, p40 positive, TTF 1 negative
- PDL1- 60%
- PET CT- lung mass with pl effusion with multiple skeletal metastases
- Options of treatment
  - Pembrolizumab and Chemotherapy- KN 407
  - Pembrolizumab alone- KN24/42
  - CM 9LA- Nivo Ipi + 2 x pacli carbo
  - Chemotherapy followed by 2nd line IO( on progression)-CM017
  - Any other

- Patient was started on KN 407 regimen
- PET CT after 4 cycles- partial response to treatment
- Continued on Pembrolizumab maintenance
- PET CT after 8 cycles- progressive disease with increase in effusion and new lymphadenopathy and bony lesions
- What to do now??

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Sector-5, Rohini,
New Delhi-110085
http://www.rgcirc.org/

[redacted]



**Patient Information**

**Name:** M[redacted]
**CR No.:**
**Age/Sex:** 71Y/Male
**Referred Doctor:** Dr. Ullas Batra
**Sample Type:** Tumor Tissue (FFPE block)- **B-10363-2022**

DIAGNOSIS: Non-Small Cell Lung Cancer-Squamous Cell Carcinoma
Tumor Fraction in the submitted section:60%

## Report Highlight: Alterations detected

- ***MET* exon 14 skipping Tier IA**
- ***MET* p.(D1020N)(VUS) Tier III**

## Variant Details:

### RNA variant

| Gene | Variant ID | Locus |
|---|---|---|
| *MET-MET** | MET-MET.M13M15 | chr7:116411708-chr7:116414935 |

*The above variant has been confirmed orthogonally using Gel Electrophoresis.

### DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Locus | Variant Allele Frequency | Transcript | Variant Effect | Clinical Significance |
|---|---|---|---|---|---|---|---|
| *MET* | p.? | c.3082+1G>A | chr7:116412044 | 8.79% | NM_001127500.3 | Splice site | Oncogenic **(Tier IA)** |
| *MET* | p.(D1020N) | c.3058G>A | chr7:116412019 | 10.23% | NM_001127500.3 | missense | Variant of Uncertain Significance **(Tier III)** |

National Comprehensive Cancer Network®

# NCCN Guidelines Version 5.2022
# Non-Small Cell Lung Cancer

NCCN Guidelines Index
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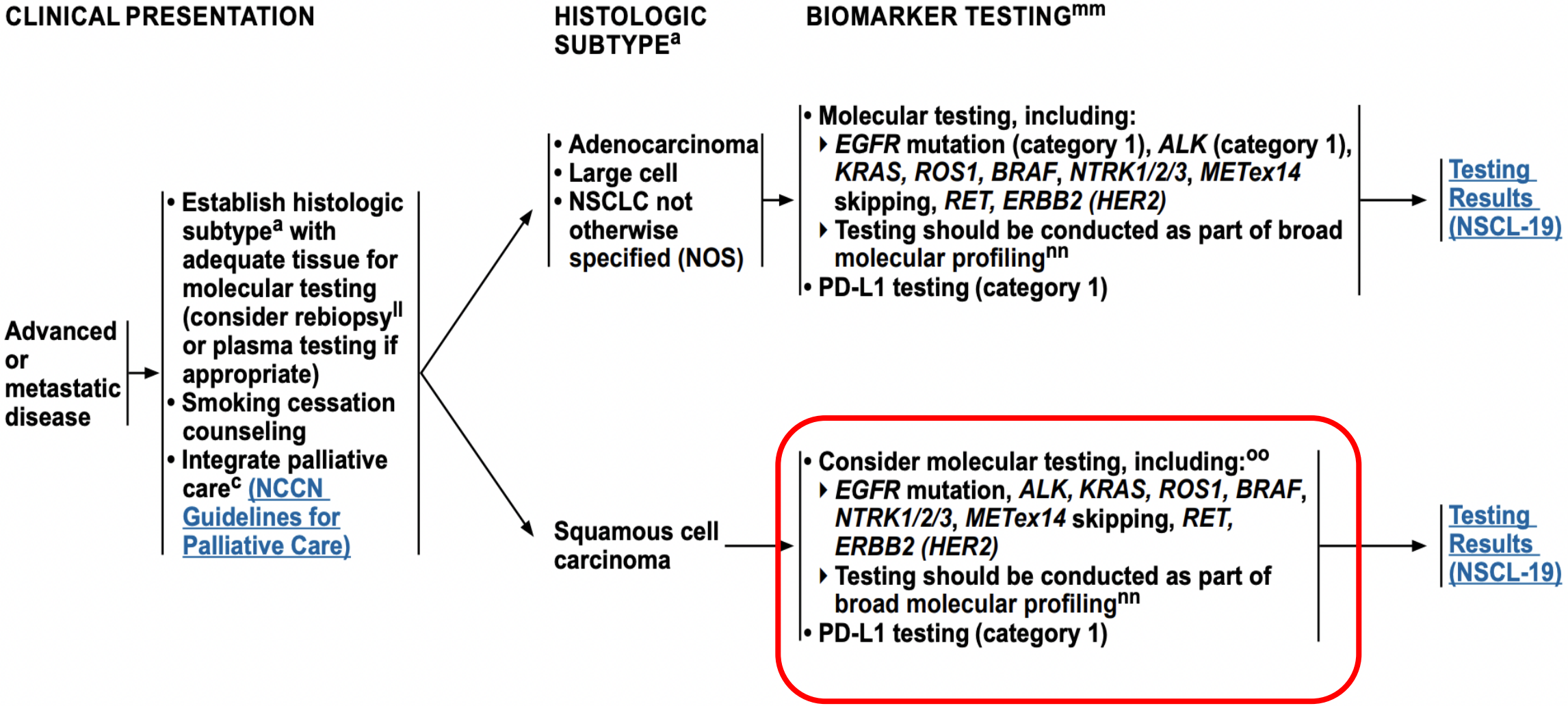
Discussion



# The Indian data….

# Case 2…

- 55 year old male
- Diagnosed as stage 4 NSCLC
- PET CT- Right lung mass with adrenal and bony mets
- ALK positive by IHC
- NGS- not done
- What is the role of variant detection in the front line management of ALK rearranged NSCLC?

# The case continues….

- Started o Alectinib 600 mg bd
- Tolerability well
- PET CT- after 6 months- partial response to treatment
- PET CT –after 15 months- progressive disease in the form of new lung nodules and supraclavicular lymphadenopathy
- MRI Brain- normal
- What will you do now?
  - Change to Lorlatinib
  - Biopsy and NGS- “to get dramatic insights and personalized medicine”
  - Any other??

- Un
- Bio
- NG

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New Delhi-110085
http://www.rgcirc.org/

[redacted]

Date: 23Apr2022 

**Patient Information**

[redacted]

**Referred Doctor:** Dr. Ullas Batra/Mansi Sharma/Amrith
**Sample Type:** Tumor Tissue (FFPE block)- **B/3357/22(2-2)**

**DIAGNOSIS: Non-Small Cell Lung Cancer**
**Tumor Fraction in the submitted section:80%**

## Report Highlight: Alterations detected

- ***EML4-ALK* (Fusion)**
- ***ALK* p.(Ile1171Asn) (Missense)**

## Variant Details

### Gene Fusions (RNA)

| Genes | Variant ID | Locus |
|---|---|---|
| *EML4-ALK* | *EML4-ALK*.E6aA20.AB374361 | chr2:42491871 - chr2:29446394 |

### DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Locus | Variant Allele Frequency | Transcript | Variant Effect | Clinical Significance |
|---|---|---|---|---|---|---|---|
| *ALK* | p.(Ile1171Asn) | c.3512_3513delTCins AT | chr2:29445212 | 15.03% | NM_004304.5 | Missense | Strong clinical significance |

**Clinical Significance:**

The *ALK* gene encodes the *ALK* receptor tyrosine kinase (RTK) with sequence similarity to the insulin receptor subfamily of kinases. *ALK* is the target of recurrent alterations in cancer, the most common being chromosomal rearrangements that generate fusion genes containing the intact *ALK* tyrosine kinase domain combined with multiple partner genes. ALK fusion kinases are constitutively activated and drive oncogenic transformation via activation of downstream *STAT3, PI3K/AKT/MTOR*, and *RAS/RAF/MEK/ERK* pathways. About 5% of non-small cell lung cancer (NSCLC) cases generate recurrent *ALK* fusions with *EML4*, *KIF5B*, and *HIP1*[**PMID: 20979469, 27386342, 23198868**]

*ALK* (Ile1171Asn) mutation has been identified in *ALK* fusion positive NSCLC following disease progression on *ALK* inhibitor Alectinib. [Level of evidence: R2][**www.oncokb.org**]

# Lets talk to dr google……


Case Reports > Lung Cancer. 2015 May;88(2):231-4. doi: 10.1016/j.lungcan.2015.02.005.
Epub 2015 Feb 12.

## I1171 missense mutation (particularly I1171N) is a common resistance mutation in ALK-positive NSCLC patients who have progressive disease while on alectinib and is sensitive to ceritinib

Sai-Hong Ignatius Ou [1], Joel Greenbowe [2], Ziad U Khan [3], Michele C Azada [3], Jeffrey S Ross [4], Phil J Stevens [2], Siraj M Ali [2], Vincent A Miller [2], Barbara Gitlitz [5]

Affiliations + expand

PMID: 25736571 DOI: 10.1016/j.lungcan.2015.02.005

# The options of treatment now….

- Change over to ceretinib
- Change over to Lorlatinib
- Continue chemotherapy
- ABCP regimen
- Any other

# Case 3

- 87 year old male
- Underwent surgery for CA Lung at the age of 82
- Received 4 cycles of chemo
- Now has recurrent disease
- PET CT- lung mass with bilateral lung nodules with bony lesions
- Biopsy- NSCLC NOS
- Sample sent for NGS

# The story con

- NGS report….

FOUNDATIONONE®CDx

PATIENT Mehra, Subhash
TUMOR TYPE Lung adenocarcinoma
COUNTRY CODE IN
REPORT DATE 22 Sep 2020
ORDERED TEST # ORD-0902067-01

**ABOUT THE TEST** FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes.

**PATIENT**

DISEASE Lung adenocarcinoma

[redacted]

SEX Male
MEDICAL RECORD # Not given

**PHYSICIAN**

[redacted]

ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID 201107
PATHOLOGIST Provided, Not

**SPECIMEN**

SPECIMEN SITE Lung
SPECIMEN ID S-3986/14 (H1948/14) E
SPECIMEN TYPE Block
DATE OF COLLECTION 27 February 2014
SPECIMEN RECEIVED 16 September 2020

**Sensitivity for the detection of copy number alterations is reduced due to sample quality.**

## Biomarker Findings

**Microsatellite status** - MS-Stable
**Tumor Mutational Burden** - 3 Muts/Mb

## Genomic Findings

*For a complete list of the genes assayed, please refer to the Appendix.*

***BRAF*** V600_K601>E
***EED*** splice site 966+1G>T
***NFE2L2*** W24R
***SETD2*** E2477fs*10

**7 Disease relevant genes with no reportable alterations: *ALK, EGFR, ERBB2, KRAS, MET, RET, ROS1***

**6** Therapies with Clinical Benefit
**0** Therapies with Lack of Response
**10** Clinical Trials

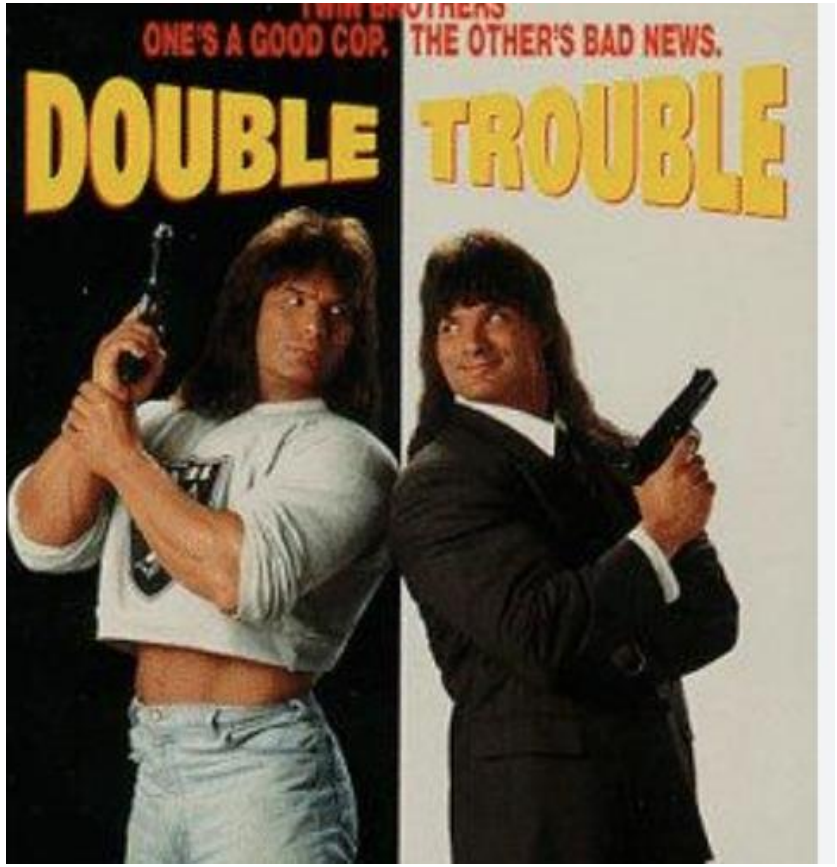
| BIOMARKER FINDINGS | ACTIONABILITY |
|---|---|
| Microsatellite status - MS-Stable | **No therapies or clinical trials.** see Biomarker Findings section |
| Tumor Mutational Burden - 3 Muts/Mb | **No therapies or clinical trials.** see Biomarker Findings section |

| GENOMIC FINDINGS | THERAPIES WITH CLINICAL BENEFIT (IN PATIENT'S TUMOR TYPE) | THERAPIES WITH CLINICAL BENE (IN OTHER TUMOR TYPE) |
|---|---|---|
| *BRAF* - V600_K601>E | Trametinib | Binimetinib |
| | | Cobimetinib |
| | | Regorafenib |
| | | Selumetinib |
| | | Sorafenib |

**10 Trials** *see p. 10*

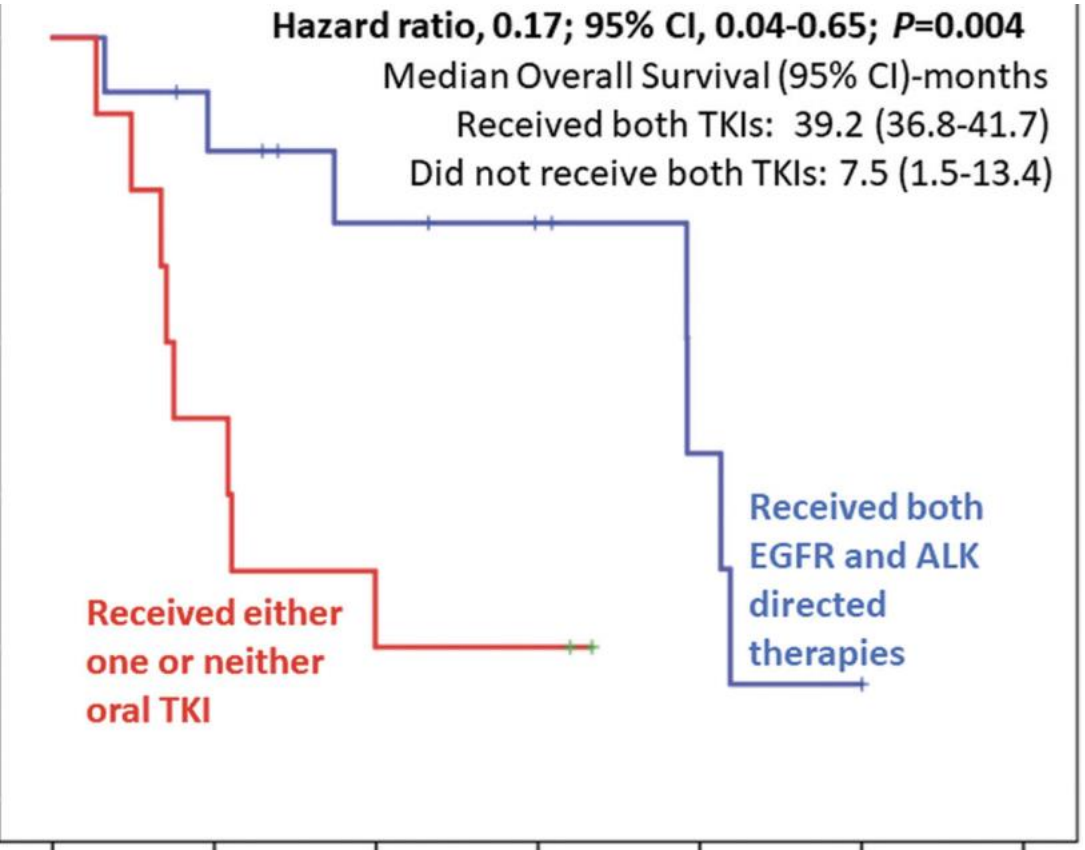
# Case scenario 4

- 45 year old female
- Stage 4 NSCLC
- Bx- adenocarcinoma
- Sent for single gene testing- EGFR mutant, ALK positive by IHC
- Confirmed By NGS
- What now?
  - Start with EGFR TKIs
  - Start with ALK TKIs
  - Concurrent EGFR and ALK TKI
  - Chemotherapy
  - Kuch aur!!!!



# Lung cancer with dual *EGFR* and *ALK* driver alterations at baseline: a retrospective observational cohort study

Vanita Noronha, Anuradha Chougule, Pratik Chandrani, Rajiv Kumar Kaushal, Vijay Maruti Patil, Nandini Menon, Akhil Kapoor, Sunil Chopade, Ajaykumar Singh, Omshree Shetty, Amit Dutt, Shripad Banavali & Kumar Prabhash




In conclusion, the dominant driver in NSCLC with dual *EGFR/ALK* alterations is *ALK*; targeting both molecular drivers concurrently is an attractive therapeutic option.

# Case scenario….

MICROSCOPIC EXAMINATION:

001. FNAC & FNAB : 4R :

SMEARS & CELL BLOCK : POSITIVE FOR MALIGNANT CELLS

METASTATIC POORLY DIFFERENTIATED CARCINOMA

nild pl

002. FNAC & FNAB : 11L :

SMEARS SHOW OCCASIONAL ATYPICAL CELL CLUSTER ALONG WITH FEW LYMPHOID CELLS AND BRONCHIAL EPITHELIAL CELLS IN A HEMORRHAGIC BACKGROUND.

CELL BLOCK - METASTATIC POORLY DIFFERENTIATED CARCINOMA

ADVICE : IHC FOR FURTHER CHARACTERIZATION

# IHC reports….

ON IHC, TUMOR CELLS ARE POSITIVE FOR CK (HETEROGENOUS PATTERN), TTF1, CD56(FOCAL) WHILE ARE NEGATIVE FOR P40, SYNAPTOPHYSIN, CHROMOGRANIN & INSM1.

P53 IS STRONG AND DIFFUSE- MUTANT TYPE P53.

P16 IS POSITIVE (SHOWS STRONG AND DIFFUSE EXPRESSION).

.

Ki67 ~ 55-60%.

OPINION: METASTATIC POORLY DIFFERENTIATED CARCINOMA,
FAVOUR SMALL CELL CARCINOMA.

ADVICE: S.CHROMOGRANIN/ PRO GRP LEVELS.

# The case continues…

- Since the pt was non smoker, EGFR by Cobas was sent on Blood- del 19 mutant
- Tissue insuff for further molecular testing
- Repeat bx- insufficient tissue
- What to do now??

# Clinical History

- 67 year old male
- Ex smoker
- NSCLC-Adenocarcinoma
- Tissue: single gene assay: negative
- Tissue inadequate for NGS.
- Liquid NGS done: no actionable mutation
- Given Pembro pem carb
- PD after 6 cycles
- Started on weekly paclitaxel
- Sent a Liquid biopsy- against wishes of treating unit

- Liquid NG


Summary of Detecte t Options

KEY Approved in ind

| Detected Alteration(s)/ Biomarker(s) | NA or fication |
| --- | --- |
| *MET* Exon 14 Skipping S | |

# The case continues….

- Patient was started on capmatinib
- Responded well
- After 10 months, had disease PD
- NGS- liquid bx sent
- Change over to type 2 met inhibitc

**REPORTING**

| | |
|---|---|
| Report Date: | NOV-07-2022 |
| Receipt Date: | OCT-28-2022 |
| Collection Date: | OCT-26-2022 |
| Specimen: | Blood |
| Status: | FINAL |

**PHYSICIAN**

**Ullas Batra**

Account: M/S Medleader Laboratories PVT. LTD.

Address: 57/42, First Fl, Panchayat Main Rd, Seevaram Perungudi, Chennai, 600096, India

Ph: 919655290919 | Fax: N/A

Additional Recipient: N/A

*Complete Tumor Response Map on page 2*

**Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options**

KEY ✓ Approved in indication ~ Approved in other indication ✗ Lack of response

| Detected Alteration(s) / Biomarker(s) | Associated FDA-approved therapies | Clinical trial availability (see page 3) | % cfDNA or Amplification |
|---|---|---|---|
| *MET* D1228H | ✗ Crizotinib, Savolitinib | Yes | 0.2% |
| *MET* Exon 14 Skipping SNV | ✓ Capmatinib, Tepotinib | Yes | 2.3% |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