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An Institutional study evaluating the benefit of blood NGS over conventional hotspot molecular genetic testing in metastatic adenocarcinoma lung

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Introduction

- Management of metastatic adenocarcinoma lung is based on detection of molecular alterations.
- Common methods of testing are single gene testing on tissue for EGFR by PCR, ALK by IHC and ROS1by FISH based methods.
- At the present time, tissue based NGS(next generation sequencing) has been widely used for the detection of aberrations in genes such as EGFR,ALK,ROS1,BRAF, NTRK and ERBB2, RET and MET.
- Though tissue based NGS testing is considered standard, blood/liquid based biopsy NGS testing is becoming valuable especially when there is lack of tissue for testing.

Objective

- To evaluate the added benefit by doing blood based NGS testing

Methods

- A Retrospective study of 182 patients of metastatic lung cancer.
- Diagnosed between Jan 2019-Nov 2021, at Manipal hospitals Bangalore aged 35-75yrs.
- Men were 134 (73.6%) and 48 (26.3%) were women. Adenocarcinoma 147 (80.7%) was the most common histology followed by 29 (15.9%) squamous cell carcinoma and others were 6(3.2%)(Fig 1.)

Fig 1. SUBTYPE

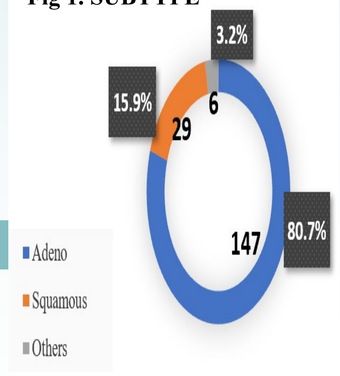
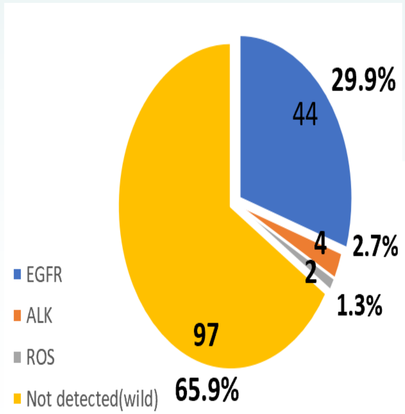


Fig 2. MOLECULAR ANALYSIS BY CONVENTIONAL HOTSPOT TESTING (TISSUE BASED)



Results

- All 147 (80.7%) adenocarcinoma patients underwent tumor tissue testing for EGFR mutation by PCR, ALK by IHC and ROS1 fusions by FISH methods.
- Tissue based molecular alterations (Fig 2.) were detected in 50 (34%) patients and 97(65.9%) patients were tested negative.
- In this study we further evaluated, 97 (65.9%) patients who had wild type alterations by conventional hotspot method to liquid/blood based NGS testing.(Fig 3.)
- Due to logistic issues only 67 (69 %) patients out of 97 underwent liquid/blood based NGS testing .

Fig 3. MOLECULAR ANALYSIS BY BLOOD NGS ON PATIENTS WITH WILD TYPE ON TISSUE BASED CONVENTIONAL TESTING

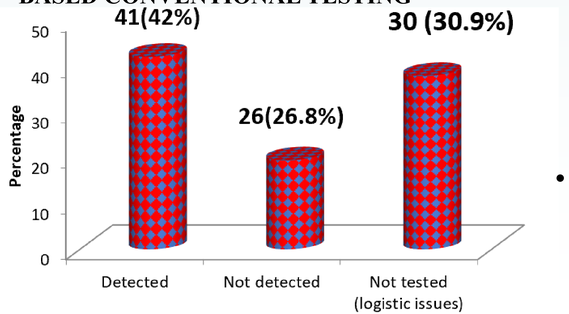


Table 1 . Molecular alterations detected on NGS BLOOD

ALTERATIONS DETECTED	PATIENTS= 41 (42%)
EGFR [14 common , 5 uncommon , 2 EGFR exon 20 insertion]	21 (21.6)
ALK	3 (3.09)
ROS1	1 (1.03)
MET exon 14 skipping	1 (1.03)
MET amplification	1 (1.03)
HER 2 neu mutation	2 (2.06)
HER 2 neu amplification	1 (1.03)
RAS mutation	5 (5.15)
TP53	3 (3.09)
RET	1 (1.03)
HER2 exon 20 insertion	2 (2.06)

Conclusion

- Patients should be evaluated with extensive NGS panel with liquid /tissue biopsy if conventional testing is wild type for molecular alterations .
- We detected additional 41 (61 %) molecular alterations in patients by doing liquid NGS testing and out of these, the added benefit was seen in 27 (40 %) patients where targetable drugs were utilized which would have missed if only conventional based testing was done.
- More validated platforms are required for doing regular liquid biopsy NGS testing in India.

REFERENCES
1.David M. DiBardino, MD, David W Rawson, MD1, Anjali Saqi, MD2,Jonas J. Heymann, MD2,Carlos A Pagan, MD2,and William A. Bulman, MD3

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