Molecular Profiling of Patients with Non Small Cell Lung Cancer at Jefferson University Hospital

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Introduction

Companion diagnostics is the use of specific tests whose results are linked to a particular drug. It allows clinicians the ability to better target the mechanism of pathology in the patient and follow it up with a therapy specifically designed to treat the disease process at hand. This approach to medicine has particularly been championed in the field of oncology with the development of such drugs as Zelboraf for the treatment of metastatic melanoma with the BRAFV600 mutation or Xalkori for late stage lung cancer expressing an abnormal ALK protein. In the case of non-small cell lung cancer (NSCLC) Jefferson has developed an algorithm to establish if patients are positive for mutations of EGFR or alterations of ALK, ROS1, or RET genes in which case patients can be treated with drugs such as erlotinib, crizotinib, and cabozantinib.

Mutation Profile for NSCLC

- Adenocarcinomas of the lung are the least correlated with smoking and tend to be found in younger patients.
- Lung cancers unrelated to smoking have different mutational profiles.

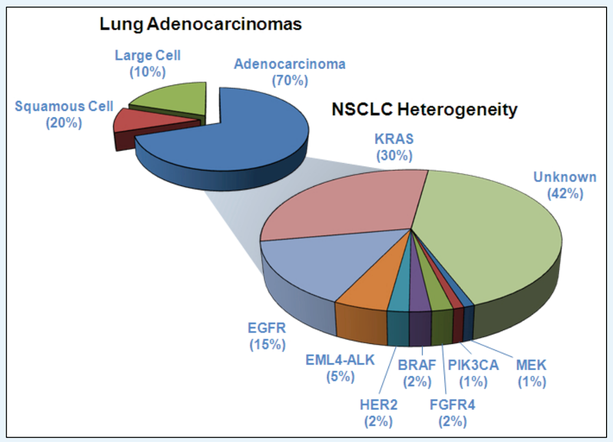

Fig. 1: Stratification of lung cancer patients by mutations and/or over-expression of various oncogenes.

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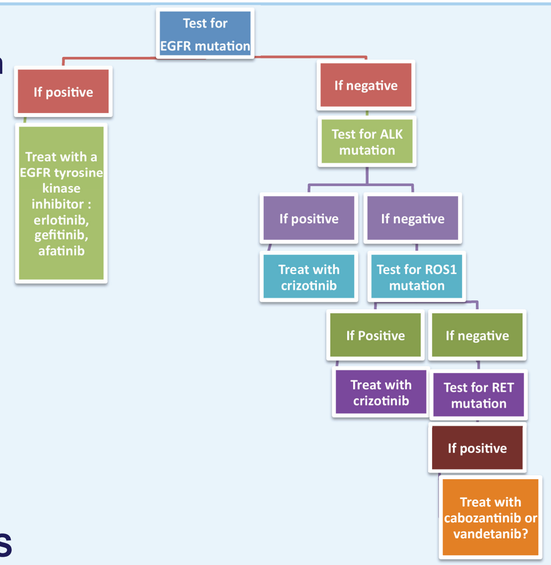
Algorithm



METHODS

- DNA sequencing is done to establish positive EGFR mutation.
- Fluorescence In Situ Hybridization (FISH) is used to establish ALK, ROS1, and RET alterations.

Data

Mutation	Prevalence	Smoking prevalence?	Most common abnormalities	Treatment	Jefferson Statistics
EGFR	Asian up to 62% Whites 10-20%	Non-smokers	Mutation in the tyrosine kinase domain (exon 18-24)	Erlotinib Gefitinib Afatinib	Total cases- 276 Total positives-43 15.5%
ALK	1%-7% no clear racial difference	Non-smokers	Inversion of 2p between 5' portion of EML4 and 3' portion of ALK	Crizotinib	Total cases-224 Total positives-5 2.2%
ROS1	1.7% Possible Asian predominance	Non-smokers	Deletion in 6q21 or translocations involving the ROS1 locus	Crizotinib	Total cases- 52 Total positives- 1 2%
RET	1%	Non smokers	Translocations involving chromosome 10q21 and 20p11.2	Vandetanib and Cabozantinib?	Total cases-28 Total positives-0 0%

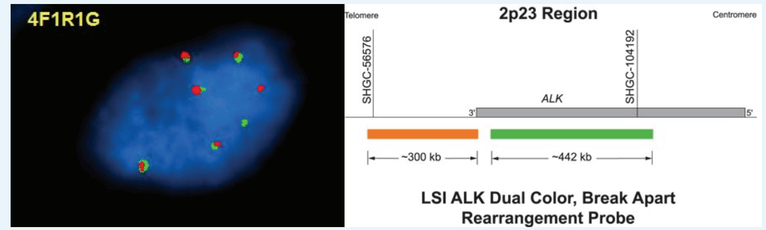


Figure 2. Biopsy staining positive for the ALK rearrangement and depiction of FDA approved rearrangement probe used.

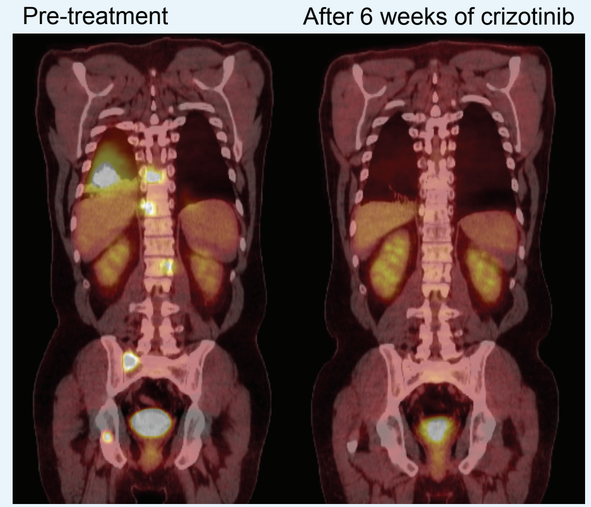


Figure 3. ALK positive NSCLC patient treated at Jefferson University Hospital with crizotonib.

References

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