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ALK Positivity Rate is Highly Dependent on Patient Age

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Background

The anaplastic lymphoma kinase (ALK) gene codes for a transmembrane receptor tyrosine kinase (RTK) in the insulin receptor superfamily. It has been identified as the fusion partner and driver oncogene in non-small cell lung cancer as well as a number of different malignancies. The reported frequency of ALK translocations in NSCLC ranges from 2-7%. Crizotinib was approved for the treatment of ALK positive NSCLC patients as determined by the presence of an ALK gene rearrangement based on a companion diagnostic FISH assay. We assessed a large series of patients to determine the positivity rate of this assay in a US based population.

Design

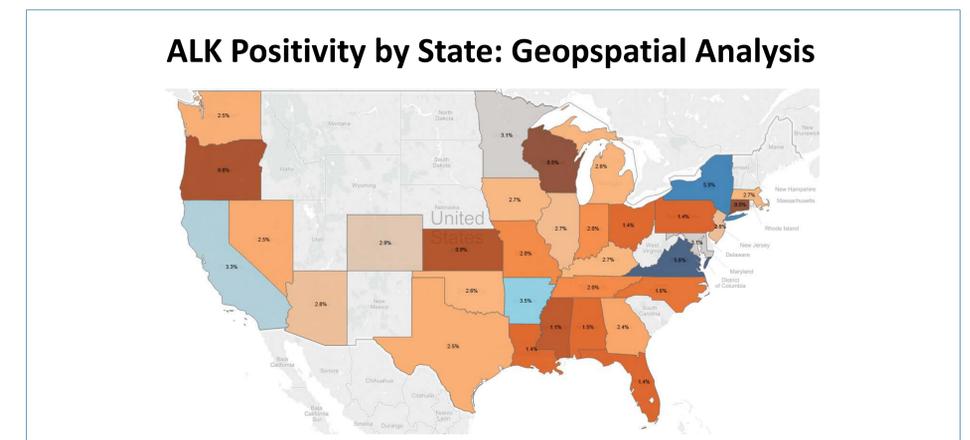
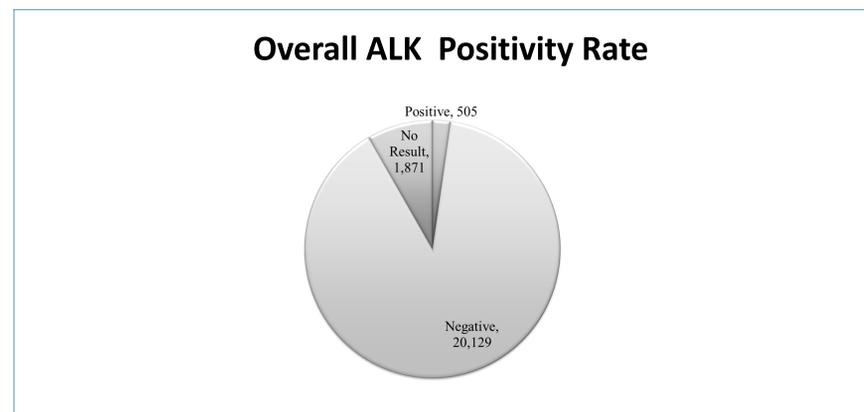
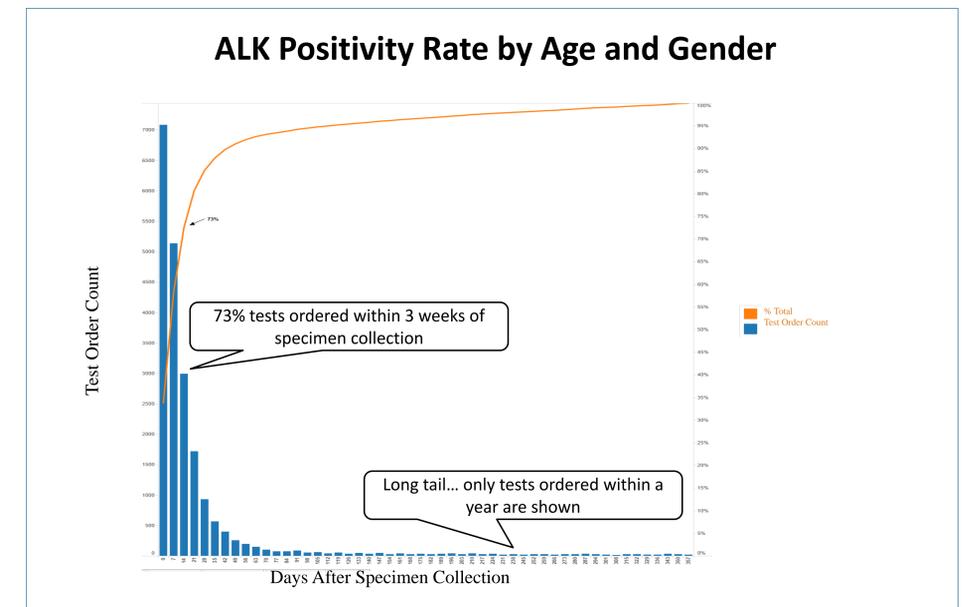
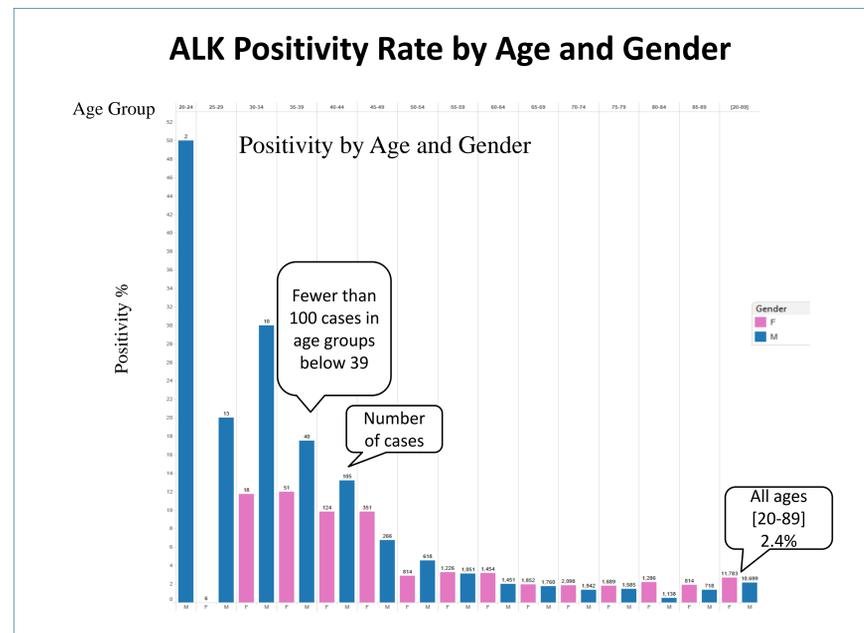
20810 consecutive formalin fixed paraffin embedded non-small cell lung cancer samples sent to our laboratory for determination of ALK rearrangement status were assessed using the Abbott LSI ALK break apart rearrangement FISH probe. Fifty tumor cells were enumerated for the presence of a break apart signal which was considered as present when at least one set of orange and green signals were 2 or more signal diameters apart or when a single orange signal without a corresponding green signal was observed in more than 15% of the tumor cells.

Results

Of the 22505 samples tested, 1871 did not contain sufficient tumor content to conduct testing or demonstrated suboptimal hybridization. 505 (2.44%) samples demonstrated an ALK rearrangement. The positivity rate was highly variable by age, ranging from 15.9% in patients less than 40 to 3.72% in patients between 40 and 65 to 1.73% in patients older than 65.

Conclusions

The frequency of ALK rearrangements was 2.44% in our series of NSCLC patients. This number is in line with the expected rates based on previous studies and helps define the positivity rate in a US based population. Interestingly, the rate of positivity was highly dependent on the age of the patient with younger patients demonstrating a much higher rate of ALK rearrangements.



Age of Patients	% ALK rearrangement detected
< 40 Years	15.9%
40-65 Years	3.72%
> 65 Years	1.73%

Conclusions

- The literature range of ALK rearrangements in adenocarcinoma of the lung between 2-7%
- We noticed significant geospatial variation in ALK positivity rates
- All ALK testing was performed in a single lab and analyzed by the same pathologists
- Younger patients (<40) demonstrated ALK rearrangements by FISH in 15.9% of cases while older patients (>65) demonstrated rearrangements in 1.73% of cases