Regional reporting of the incidence of Anaplastic Lymphoma Kinase mutation in 379 non-small-cell lung cancer patients from Kolkata: Using immunohistochemistry as the diagnostic modality in a significant subset

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Abstract

Context: Regional epidemiology of anaplastic lymphoma kinase (ALK) mutation in non-small-cell lung cancer (NSCLC) is an unmet need in India, and so is the knowledge of its incidence based on immunohistochemistry (IHC). **Aims:** Reporting the incidence of ALK mutation in NSCLC from Kolkata, incorporating IHC as the diagnostic modality in a considerable subset of patients. **Subjects and Methods:** It is a retrospective observational study done on NSCLC patients with adenocarcinoma histology, unselected by epidermal growth factor receptor, whose samples were tested for ALK mutation status between March 1, 2013, and March 15, 2017. The study involved all cancer facilities in Kolkata, except Tata Medical Centre. Up to June 2015, the tests were done by fluorescence *in situ* hybridization (FISH) and from July 2015 to the end, tests were done using IHC, as per the standard testing guidelines existing during the respective time periods. Results were documented in a de-identified manner to analyze the incidence of ALK mutations. **Results:** A total of 379 patients was tested for ALK mutations. March 2013 to June 2015, 200 (52.77%) patients were tested by FISH, 17 (8.5%) samples were unreportable and 4 patients [(2.19%) 4/183] tested positive for ALK mutations. From July 2015 to March 2017, 179 (47.22%) patients were tested by IHC, 9 (5.02%) samples were unreportable, and 10 patients [(5.88%) 10/170] tested positive for ALK mutations. Overall, 26 (6.8%) samples were unreportable and 14 [(3.9%) 14/353] patients tested positive for ALK mutations. **Conclusions:** The overall incidence of ALK mutation positive NSCLC in Kolkata is 3.9%. The incidence by IHC is 5.88% and by FISH is 2.19%, in the subset of patients tested by these two modalities respectively.

Key words: Anaplastic lymphoma kinase gene rearrangement, anaplastic lymphoma kinase mutation by immunohistochemistry, anaplastic lymphoma kinase mutation in lung adenocarcinoma unselected by epidermal growth factor receptor, anaplastic lymphoma kinase mutation in nonsmall cell lung cancer, incidence of anaplastic lymphoma kinase mutation from Kolkata

Introduction

Regional epidemiology of anaplastic lymphoma kinase (ALK) gene rearrangement (ALK mutation) in non-small-cell lung cancer (NSCLC) is an unmet need in India, and so is the knowledge of its incidence when immunohistochemistry (IHC) is used as the detection tool. This study from Kolkata was envisaged primarily to report the incidence of ALK mutation from the eastern part of the country and at the same time, to generate the first report of its incidence based on IHC, from India.

Subjects and Methods

It is a retrospective observational study, done in Kolkata, on a cohort of NSCLC patients with adenocarcinoma histology, unselected by epidermal growth factor receptor mutation status, whose formalin-fixed, paraffin embedded samples were tested for ALK mutation status between March 1, 2013, and March 15, 2017. The study involved all cancer facilities in Kolkata, except Tata Medical Centre (All patients tested in-house), and all the tests were done free as a part of Patients Assistance Programme of Pfizer Limited. From March 1, 2013, to June 30, 2015, the ALK mutation tests were done by fluorescence *in situ* hybridization (FISH) using FDA approved Abbot Vysis ALK Break Apart FISH Probe Kit (Abbott Molecular, Abbott Park, IL, USA). And, from July 1, 2015, to March 15, 2017, ALK mutation tests were done by IHC using FDA approved Ventana (Roche) ALK assay with D5F3 rabbit monoclonal antibody, following the standard testing guidelines existing during the respective time periods. The test results were documented in a de-identified manner to analyze the incidence of ALK mutation.

Results

A total of 379 samples were tested over the entire study period, out of which 26 (6.8%) samples were found to be inadequate for reporting. The main reasons were identified to be, lack of tissue; extensive necrosis; inappropriate fixation; and inappropriate storage. Those "un-interpretable by FISH" were also considered as inadequate for reporting. Finally, out of the 353 reportable samples, 14 [(3.9%] 14/353] tested positive for ALK mutations.

From March 1, 2013, to June 30, 2015, 200 (52.77%) patients were tested by FISH, 17 (8.5%) samples were inadequate for reporting (including uninterpretable by FISH in 7 patients), and 4 patients [(2.19%] 4/183] tested positive for ALK mutations. From July 1, 2015, to March 15, 2017, 179 (47.22%) patients were tested by IHC, 9 (5.02%) samples were inadequate for reporting and 10 patients [(5.88%] 10/170] tested positive for ALK mutations.

Discussion

The global incidence of ALK mutation in NSCLC is 3%–7%[1] as compared to 2.7%–3% in India.[2,3] However, most of these reported incidences were based on RT-PCR or FISH as the method of detection, which for justified reasons, has evolved over a period of time to make way for IHC as the testing modality.[4,5] IHC is now the current standard, since its approval in June 2015 by FDA.[6]

This study, which spans over 4 years from March 2013 to March 2017, covered both the detection methods of ALK mutation in their respective time frames. Therefore, allowing

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a considerable subset of patients (47.22%) to be tested by the current standard for ALK detection. Both, the overall incidence (3.9%) and the incidence in the subset of patients using FISH (2.19%), as found in our study, is at par with any published literature. However, the 5.88% incidence of ALK mutation as detected by IHC is lower than the IHC-based incidences reported worldwide (6.24%–10.66%).[7-10]

Conclusion

This is the first regional reporting of the incidence of ALK positive NSCLC from the eastern India, and, also one of the earliest reporting based on IHC in a substantial subset of patients. The overall incidence of ALK mutation positive NSCLC in Kolkata is 3.9%. The incidence by IHC is 5.88% and by FISH is 2.19%, in the subset of patients tested by these two modalities respectively. This study was not planned to identify any concordance or statistical differences between the two detection methods, and therefore not reported. The study, though, is limited by its retrospective nature and the lack of demographic, clinical and survival data.

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Conflicts of interest

There are no conflicts of interest.

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