Developing a quality assurance program on the detection of anaplastic lymphoma kinase (ALK) gene rearrangement in non-small cell lung cancer (NSCLC)

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Introduction

Anaplastic lymphoma kinase (ALK) gene rearrangement status in non-small cell lung cancer (NSCLC) is a critical biomarker to predict sensitivity to tyrosine kinase inhibitors (TKIs) such as crizotinib. In 2015, the RCPAQAP Molecular Genetics discipline developed a pilot external quality assurance (EQA) program for the detection of ALK translocation in NSCLC. The purpose of the EQA is to promote and maintain high quality testing by assessing the ability of laboratories to detect the ALK gene rearrangement. Prior to this pilot program, a sample exchange for ALK translocation in NSCLC was maintained from 2012 to 2014. Due to increased demand, the sample exchange program was transitioned into a pilot EQA study in 2015. In 2016, a total of fifteen laboratories from Australia, Hong Kong and Taiwan participated in this pilot program. Each participating laboratory was provided with patient-derived specimens for detection of the ALK gene rearrangement. Participants were assessed for their accuracy to detect and clinically interpret the ALK gene rearrangement. This report highlights the findings of the pilot EQA from 2015 to 2016.

Participation

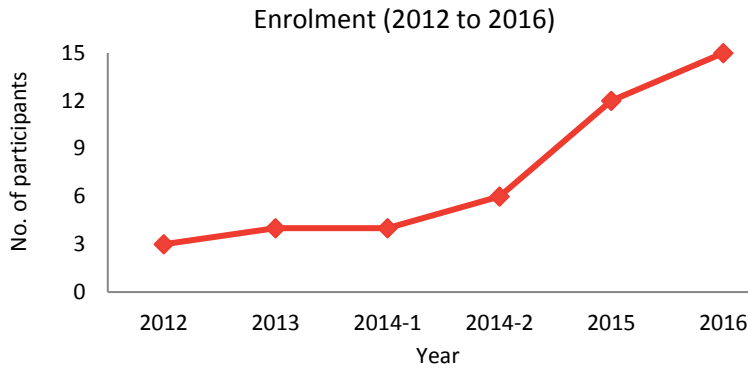
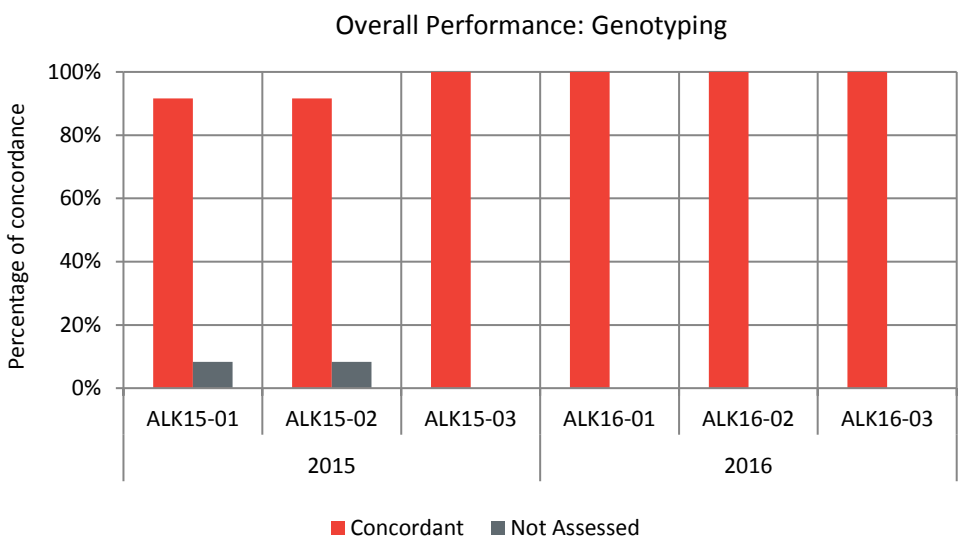


Figure 1. Participation in the ALK Translocation in NSCLC quality assurance program from 2012 to 2016.

Results



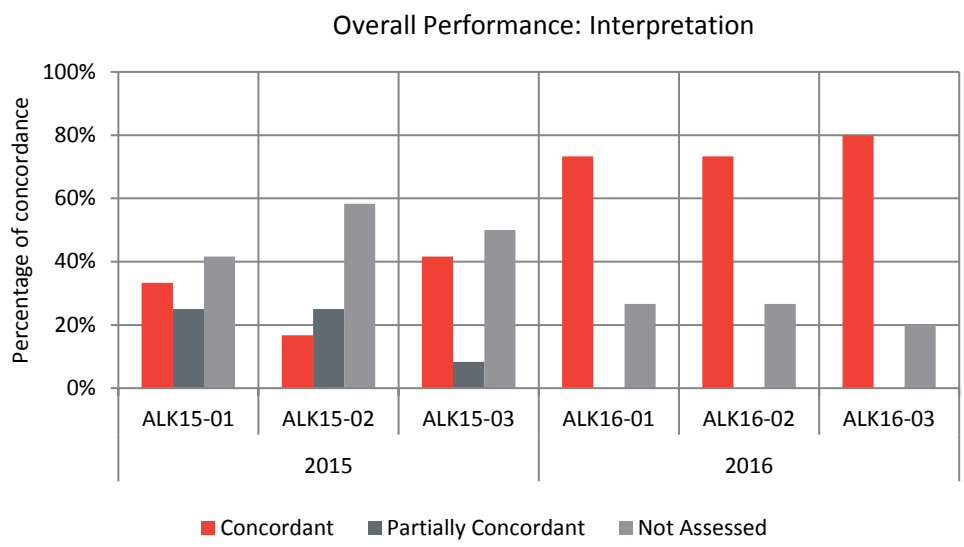
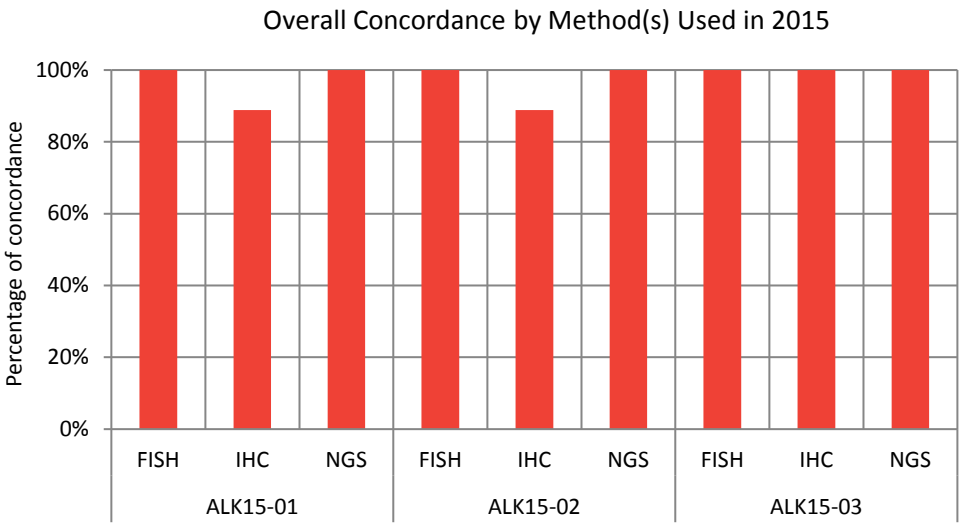


Figure 2. Overall performance of participants in the 2015 and 2016 ALK Translocation in NSCLC pilot programs. Concordant or Partially Concordant = in agreement or partial agreement with expected/consensus result, respectively; Not Assessed = result not provided.



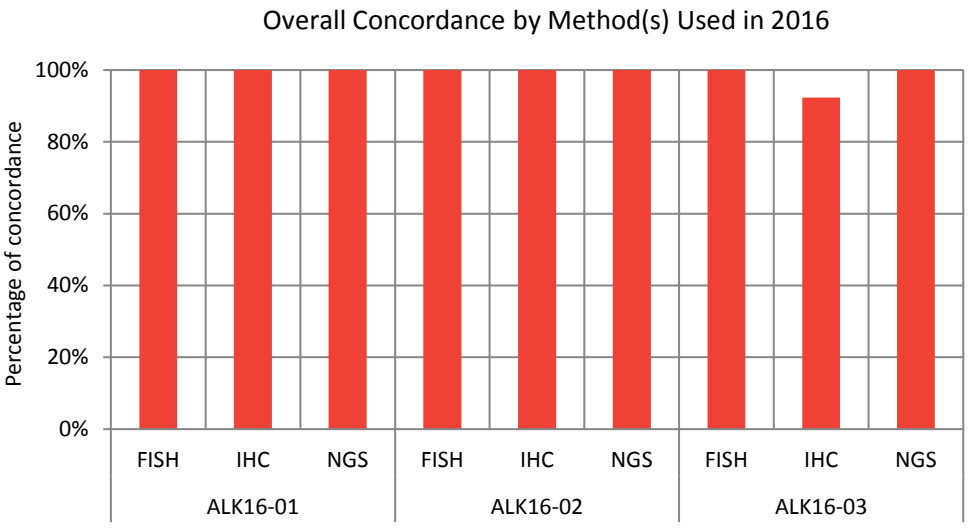


Figure 3. Overall performance of participants in the 2015 and 2016 ALK Translocation in NSCLC pilot programs, based on technique used. FISH = fluorescence in situ hybridisation, IHC = immunohistochemistry, NGS = Next Generation Sequencing.

Discussion & Conclusion

- Overall performance in the 2015 and 2016 ALK Translocation in NSCLC pilot programs were satisfactory (Figure 2). Two participants failed to provide a result in the 2015 program and were not assessed.
- In 2015, the majority of participants were either partially concordant in their clinical interpretation by not fully stating the clinical significance of the ALK results reported, or were not assessed if clinical interpretation was not provided. Improvement in the interpretation of ALK results was observed in 2016, despite several participants failing to provide a clinical interpretation of their results.
- It is important that laboratories state the clinical significance of the absence or presence of an ALK translocation in NSCLC in their reports.
- Most participants achieved concordant results using either the FISH or NGS approach in detection of the ALK gene rearrangement. However, a small number of participants failed to detect the ALK gene rearrangement using IHC (Figure 3).
- Most participants used a combination of FISH and IHC for ALK testing in the 2015 and 2016 pilot programs. However, one participant, using NGS analysis, detected the EML4-ALK fusion in the ALK16-03 sample, which is in line with results obtained when using the traditional FISH and/or IHC approach for this case.
- NGS is not commonly used for ALK testing. NGS is however widely used for screening other NSCLC-related gene variants such as EGFR and KRAS mutations[1]. Given that there are more than twenty known EML4-ALK breakpoints variants in NSCLC[1], it is important to note that some cases may not be detected when using the FISH and/or IHC techniques[3,4], leading to the possibility that patients may not be selected for beneficial treatment.
- Vysis ALK Break Apart FISH probe kit was used by all participants utilising the FISH technique in detection of ALK gene rearrangement.
- Ventana Optiview DAB was the most commonly (>85%) used detection system in IHC analysis of ALK gene rearrangement.
- The International System for Human Cytogenetic Nomenclature (ISCN) should be used to describe genomic rearrangement identified by FISH.

References

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