High-throughput diagnostic profiling of clinically actionable gene fusions in lung cancer.

Abstract:
Molecular profiling of non-small cell lung cancers (NSCLC) has a strong impact on clinical decision making and current oncological therapies. Besides detection of activating mutations in EGFR, analysis of ALK and ROS1 gene rearrangements has come into focus for targeted therapies. Targeted massive parallel sequencing (MPS) has been established for routine diagnostic profiling of the most prevalent oncogenic mutations in NSCLC, but not for the detection of gene rearrangements yet. Here, we present and evaluate an MPS-based panel sequencing approach which simultaneously detects ALK, ROS1, and RET fusions as well as somatic mutations in a single multiplex assay using formalin-fixed paraffin-embedded (FFPE) tissue. To this end, we first evaluated sensitivity and specificity of the fusion assay retrospectively by employing it to a set of 50 NSCLC with known gene fusions (n = 35) and with no gene fusions (n = 15). The sensitivity and specificity of the MPS assay for the detection of known fusions was 100%. In a second prospective phase, we implemented the approach of parallel mutation and gene fusion detection in our routine diagnostic workflow to assess performance of the test in a diagnostic outreach setting. Our prospective screening of 109 NSCLC samples revealed four gene fusions all of which were confirmed by FISH. In conclusion, our approach facilitates
simultaneous high-throughput detection of gene fusions and somatic mutations in NSCLC samples and is able to replace conventional methods. © 2015 Wiley Periodicals, Inc.