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In a recent study published in Clinical Cancer Research, FoundationOne® successfully identified clinically relevant genomic alterations in 65% of patients with lung adenocarcinoma whose tumors previously tested negative for alterations using multiple conventional genomic tests, enabling successful targeted treatment for many of those patients.

Publication summary

47 patients with lung adenocarcinomas were identified whose tumors harbored no evidence of a genomic alteration via extensive focused non-NGS testing.

Of these patients, non-NGS testing with multiple assays resulted in tissue exhaustion in **34% (n=16/47)** of cases and a repeat biopsy was either not feasible or declined by the patient.

Testing was successfully performed on tumor from the remaining **31 cases**.

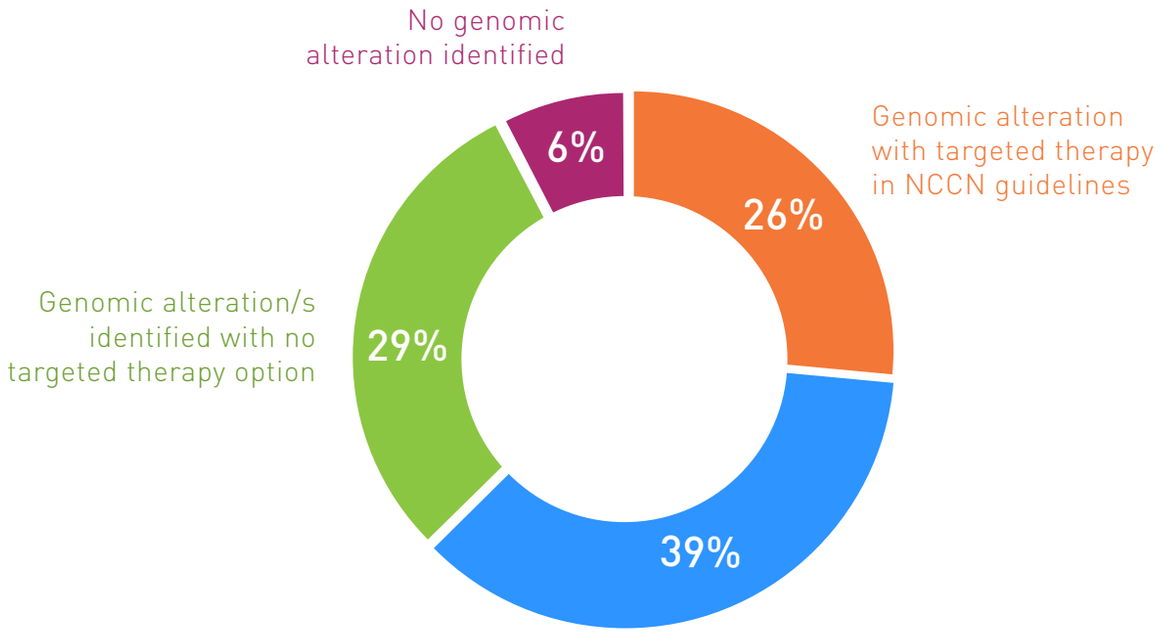
Initial Molecular Testing

Non-NGS testing comprised a number of tests for known lung cancer alterations in 11 genes (EGFR, ERBB2, KRAS, NRAS, BRAF, MAP2K1, PIK3CA, AKT1, ALK, ROS1, and RET).

- A multiplex mass-spectrometry-based system (Sequenom) was used to study 91 point mutations across 8 genes (EGFR, ERBB2, KRAS, NRAS, BRAF, MAP2K1, PIK3CA, and AKT1).
- Multiplex sizing assays tested for insertions or deletions in EGFR exons 19 and 20, and ERBB2 exon 20.
- Three FISH break apart assays were used to screen for gene rearrangements involving ALK, ROS1, and RET, respectively.

Key Findings

In **84%** of patients (n=26), ≥ 2 tumor biopsies were required to complete testing. Of these patients, **69%** (n=18/26) underwent multiple biopsies in order to complete conventional testing



An additional 39% of patients (n=12) harbored at least one potentially actionable alteration linked to a targeted therapy approved for an indication other than non-small cell lung cancer or an active clinical trial at MSKCC

To-date, two of these 12 patients have enrolled in a matched clinical trial

GENOMIC ALTERATION WITH TARGETED THERAPY IN NCCN GUIDELINES	TUMOR TESTED FROM SAME PROCEDURE AS TUMOR SUBJECTED TO NON-NGS TESTING?	TARGETED THERAPY	PATIENTS CLINICAL COURSE
EGFR G719A	YES	ERLOTINIB	RECENTLY STARTED ERLOTINIB, RESPONSE EVALUATION PENDING
BRAF V600E	YES	---	SUBSEQUENTLY PASSED AWAY
SOCS5-ALK	YES	CRIZOTINIB	DISEASE SHRINKAGE (<30%) WITH CRIZOTINIB
CLIP4-ALK	YES	CRIZOTINIB	PARTIAL RESPONSE TO CRIZOTINIB
CD74-ROS1	YES	CRIZOTINIB	RECENTLY STARTED CRIZOTINIB, RESPONSE EVALUATION PENDING
KIF5B-RET	YES	CABOZANTINIB	PARTIAL RESPONSE TO CABOZANTINIB
KIF5B-RET	NO	CABOZANTINIB	DISEASE SHRINKAGE (<30%) WITH CABOZANTINIB
CCDC6-RET	YES	CABOZANTINIB	CANDIDATE FOR CABOZANTINIB AFTER PROGRESSION ON CHEMOTHERAPY

Conclusion

Overall, these findings support the first-line use of comprehensive genomic profiling to detect the broadest range of genomic alterations in lung adenocarcinomas while preserving tissue.

Broad, hybrid capture-based next-generation sequencing identifies actionable genomic alterations in lung adenocarcinomas otherwise negative for such alterations by other genomic testing approaches. Alexander Drilon1, Lu Wang1, Maria E. Arcila1, Sohail Balasubramanian2, Joel R. Greenbowe2, Jeffrey S. Ross2, Phil Stephens2, Doron Lipson2, Vincent A. Miller2, Mark G. Kris1, Marc Ladanyi1, Naiyer A. Rizvi1, 1Memorial Sloan Kettering Cancer Center, New York, NY, 2Foundation Medicine, Inc., Cambridge, MA *Clin Cancer Res*. 2015 Jan 7. pii: clincanres. 2683. 2014. [Epub ahead of print]