PathGroup
Physician Centered. Patient Focused.

SmartGenomics™ Lung Profile

Oncology Services

Clinical to Genomic

Advanced Standard of Care

PathGroup SmartGenomics: Lung is designed for ***use at diagnosis*** in non-small cell lung cancer to uncover therapeutic options and aid in treatment planning to improve patient outcomes.

- **Recommended by National Comprehensive Cancer Network (NCCN) guidelines**
- Clinically actionable genomic information for 11 genes, 5 gene rearrangements/ amplifications/ fusions, and 1 immunohistochemical stain
- Full results in 7 to 10 days

Tailored Genomic Lung Profile

Next Generation Sequencing (NGS)	
AKT1	Potential resistance to EGFR TKI
BRAF	Typically non-overlapping mutation
CTNNB1	Implicated in EGFR resistance
DDR2	Novel driver of squamous cell lung cancer, response to dasatinib
EGFR	Benefit to EGFR TKI therapy; T790M included for acquired resistance to EGFR TKI therapy
ERBB2 (HER2)	Non-overlapping mutation
KRAS	Poor prognostic marker, non-overlapping mutation
NRAS	Non-overlapping mutation
PIK3CA	Acquired resistance to EGFR TKI therapy
PTEN	Associated with lack of response/acquired resistance to EGFR TKI therapy; negative prognosis, lower overall survival
TP53	Associated with lack of response/acquired resistance to EGFR TKI therapy; negative prognosis
Fluorescence In Situ Hybridization (FISH)	
ALK Rearrangement	Response to crizotinib (Xalkori-Pfizer)
ERBB2 (HER2)	Recent study (MSKCC) shows importance in therapeutic choice versus ERBB2 mutated NSCLC
MET Amplification	Poor prognostic marker, possible response to crizotinib (Xalkori-Pfizer)
RET Fusion	Co-occurs with common driver mutations, response to multiple TKIs reported
ROS1 Rearrangement	Predictive of response to crizotinib (Xalkori-Pfizer)
Immunohistochemistry (IHC)	
PDL1	Immunotherapeutic response marker

PathGroup
Physician Centered. Patient Focused.

SmartGenomics

NGS LUNG REPORT

Results from all technologies integrated into a single

Original Procedure Date: 01/06/2015, Sample Type: Lung, Block Information: 1, Original Accession number:
Tumor Percentage: 51-80%
Original Diagnosis: Invasive Adenocarcinoma

RESULTS

KRAS G13C and PIK3CA H1047R point mutations were detected by targeted next generation sequencing.

Pertinent negatives highlighted

NO EGFR or BRAF mutation was detected.

were negative for amplification or re-arrangement of ALK, ROS1, RET, and MET.

INTERPRETATIVE SUMMARY

Personalized interpretive summary provided for each patient

Review of the accompanying pathology report indicates a history of NSCLC. Microsco adenocarcinoma corresponding to the above referenced accession number. Sufficient for molecular analysis. Excellent gene coverage was achieved, which passed our inter **and PIK3CA H1047R point mutations were detected** by targeted next generation sequencing. No other mutations were detected by targeted next generation sequencing interrogating the hot-spot regions of 10 genes summarized in the NGS technical table. Please also see the NGS technical table for a summary of single nucleotide polymorphisms (SNPs). This testing is in accordance with the most recent NCCN guidelines.

Decisions regarding patient care and/or treatment should not be based on the results of this test alone or the information contained in this report, but upon the independent medical judgment of the treating physician in the context of the patient's condition and other factors in accordance with the applicable standard of care. The selection of agents identified in this report, whether none, in part, or in entirety, is at the discretion of the treating physician. Additionally, agents listed in this report, along with indicated clinical trials, are not ranked in order of potential efficacy, predicted efficacy, or level of evidence which may vary from the patient's indicated tumor type.

THERAPEUTIC ASSOCIATIONS

Potential Therapeutic Response / Drug Class	Disease Association	Gene	Alteration
Unlikely response to EGFR TKI therapy	NSCLC	KRAS and PIK3CA	Mutations
Targeted therapies (i.e. MEK/RAF/PI3K/AKT/mTOR/CDK inhibitors) may be available in an investigational context	NSCLC	KRAS and PIK3CA	Mutations

No therapeutic associations for other diseases at this time.

Prognostic and therapeutic guidance in an easy to read format

PROGNOSTIC ASSOCIATIONS

Prognostic Association	Disease Association		
Aggressive clinical course	NSCLC	KRAS and PIK3CA	Mutations

REFERENCES

1. Riely, GJ,Kris, MG,Rosenbaum, D,Marks, J,Li, A,Chitale, DA,Nafa, K,Riedel, ER,Hsu, M,Pao, W,Miller, VA,Ladanyi, M Frequency and distinctive spectrum of KRAS mutations in never smokers with lung adenocarcinoma. Clinical cancer research : an official journal of the American Association for Cancer Research. Sep, 2008;14(18)
2. Brose, MS,Volpe, P,Feldman, M,Kumar, M,Rishi, I,Gerrero, R,Einhorn, E,Herlyn, M,Minna, J,Nicholson, A,Roth, JA,Albelda, SM,Davies, H,Cox, C,Brignell, G,Stephens, P,Futreal, PA,Wooster, R,Stratton, MR,Weber, BL BRAF and RAS mutations in human lung cancer and melanoma. Cancer research. Dec, 2002;62(23)
3. Riely, GJ,Marks, J,Pao, W KRAS mutations in non-small cell lung cancer. Proceedings of the American Thoracic Society. Apr, 2009;6(2)
4. Sun, Y,Ren, Y,Fang, Z,Li, C,Fang, R,Gao, B,Han, X,Tian, W,Pao, W,Chen, H,Ji, H Lung adenocarcinoma from East Asian never-smokers is a disease largely defined by targetable oncogenic mutant kinases. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. Oct, 2010;28(30)
5. Jänne, PA,Shaw, AT,Pereira, JR,Jeannin, G,Vansteenkiste, J,Barrios, C,Franke, FA,Grinsted, L,Zazulina, V,Smith, P,Smith, I,Crinò, L Selumetinib plus docetaxel for KRAS-mutant advanced non-small-cell lung cancer: a randomised, multicentre, placebo-controlled, phase 2 study. The Lancet. Oncology. Jan, 2013;14(1)

References provided to support all findings

electronically signed on

idence of protein-modifying mutations. Please see the methodology section of this report for a comprehensive listing of the genes specific genomic coordinates will be supplied upon request. The inherited variants identified in this assay are not presently known to eported in case clinically relevant information becomes available.