FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Lung non-small cell lung carcinoma (NOS)

COUNTRY CODE
PE

REPORT DATE
01 Feb 2022

ORDERED TEST #
ORD-1288239-01

ABOUT THE TEST FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes.

PATIENT
DISEASE Lung non-small cell lung carcinoma (NOS)
DATE OF BIRTH 15 November 1962
SEX Male
MEDICAL RECORD # Not given

PHYSICIAN
MEDICAL FACILITY Arias Stella
ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID 317319
PATHOLOGIST Not Provided

SPECIMEN
SPECIMEN SITE Chest Wall
SPECIMEN ID Q21-9025-1
SPECIMEN TYPE Block
DATE OF COLLECTION 06 October 2021
SPECIMEN RECEIVED 19 January 2022

Sensitivity for the detection of copy number alterations is reduced due to sample quality.

Biomarker Findings

Microsatellite status - MS-Stable
Tumor Mutational Burden - 8 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

FGFR1 amplification
MDM2 amplification
NSD3 (WHSC1L1) amplification
STAG2 Q1190*
TP53 I232N

8 Disease relevant genes with no reportable alterations: ***ALK, BRAF, EGFR, ERBB2, KRAS, MET, RET, ROS1***

† See About the Test in appendix for details.

Report Highlights

- Evidence-matched **clinical trial options** based on this patient's genomic findings: (p. 7)

BIOMARKER FINDINGS	THERAPY AND CLINICAL TRIAL IMPLICATIONS	
Microsatellite status - MS-Stable	**No therapies or clinical trials.** see Biomarker Findings section	
Tumor Mutational Burden - 8 Muts/Mb	**No therapies or clinical trials.** see Biomarker Findings section	
GENOMIC FINDINGS	**THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)**	**THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)**
***FGFR1* -** amplification	none	none
10 Trials *see p. 7*		
***MDM2* -** amplification	none	none
1 Trial *see p. 9*		

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GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIAL OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

NOTE Genomic alterations detected may be associated with activity of certain approved therapies; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Therapies and the clinical trials listed in this report may not be complete and exhaustive. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. This report should be regarded and used as a supplementary source of information and not as the single basis for the making of a therapy decision. All treatment decisions remain the full and final responsibility of the treating physician and physicians should refer to approved prescribing information for all therapies.

Therapies contained in this report may have been approved by the US FDA.

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BIOMARKER

Microsatellite status

RESULT
MS-Stable

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence, MSS tumors are significantly less likely than MSI-H tumors to respond to anti-PD-1 immune checkpoint inhibitors[1-3], including approved therapies nivolumab and pembrolizumab[4]. In a retrospective analysis of 361 patients with solid tumors treated with pembrolizumab, 3% were MSI-H and experienced a significantly higher ORR compared with non-MSI-H cases (70% vs. 12%, p=0.001)[5].

FREQUENCY & PROGNOSIS

MSI-H is generally infrequent in NSCLC, reported in fewer than 1% of samples across several large studies[6-11], whereas data on the reported incidence of MSI-H in SCLC has been limited and conflicting[12-15]. One study reported MSI-H in lung adenocarcinoma patients with smoking history, and 3 of 4 MSI-H patients examined also had metachronous carcinomas in other organs, although this has not been investigated in large scale studies[6]. Published data investigating the prognostic implications of MSI in NSCLC are limited (PubMed, Oct 2021).

FINDING SUMMARY

Microsatellite instability (MSI) is a condition of genetic hypermutability that generates excessive amounts of short insertion/deletion mutations in the genome; it generally occurs at microsatellite DNA sequences and is caused by a deficiency in DNA mismatch repair (MMR) in the tumor[16]. Defective MMR and consequent MSI occur as a result of genetic or epigenetic inactivation of one of the MMR pathway proteins, primarily MLH1, MSH2, MSH6, or PMS2[16-18]. This sample is microsatellite-stable (MSS), equivalent to the clinical definition of an MSS tumor: one with mutations in none of the tested microsatellite markers[19-21]. MSS status indicates MMR proficiency and typically correlates with intact expression of all MMR family proteins[16,18,20-21].

BIOMARKER

Tumor Mutational Burden

RESULT
8 Muts/Mb

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence in solid tumors, increased TMB may be associated with greater sensitivity to immunotherapeutic agents, including anti-PD-L1[22-24], anti-PD-1 therapies[22-25], and combination nivolumab and ipilimumab[26-31]. Multiple clinical trials of PD-1- or PD-L1-targeting immune checkpoint inhibitors or combination of PD-1 and CTLA-4 inhibitors in NSCLC have reported that patients with tumors harboring TMB ≥10 Muts/Mb derive greater clinical benefit from these therapies than those with TMB <10 Muts/Mb (based on this assay or others); similarly, higher efficacy of anti-PD-1 or anti-PD-L1 immunotherapy for treatment of patients with NSCLC, compared with the use of chemotherapy, has been observed more significantly in cases of TMB ≥10 Muts/Mb (based on this assay or others);[22-23,26-28,32-39]. Improved OS of patients with NSCLC treated with pembrolizumab plus chemotherapy relative to chemotherapy only[40], or those treated with nivolumab plus ipilimumab also relative to chemotherapy[41], has been observed across all TMB levels.

FREQUENCY & PROGNOSIS

A large-scale genomic analysis found that unspecified lung non-small cell lung carcinoma (NSCLC), lung adenocarcinoma, and lung squamous cell carcinoma (SCC) samples harbored median TMBs between 6.3 and 9 Muts/Mb, and 12% to 17% of cases had an elevated TMB of greater than 20 Muts/Mb[42]. Lower TMB is observed more commonly in NSCLCs harboring known driver mutations (EGFR, ALK, ROS1, or MET) with the exception of BRAF or KRAS mutations, which are commonly observed in elevated TMB cases[43]. Although some studies have reported a lack of association between smoking and mutational burden in NSCLC[44-45], several other large studies did find a strong association with increased TMB[46-49]. TMB >10 muts/Mb was found to be more frequent in NSCLC metastases compared with primary tumors for both adenocarcinoma (38% vs. 25%) and SCC (41% vs. 35%) subtypes[50]. A large study of Chinese patients with lung adenocarcinoma reported a shorter median OS for tumors with a higher number of mutations in a limited gene set compared with a lower mutation number (48.4 vs. 61.0 months)[44]. Another study of patients with NSCLC correlated elevated TMB with poorer prognosis and significantly associated lower TMB in combination with PD-L1 negative status with longer median survival in patients with lung adenocarcinoma[51]. However, no significant prognostic association of TMB and/or PD-L1 status with survival has been reported in patients with lung SCC[51-52].

FINDING SUMMARY

Tumor mutation burden (TMB, also known as mutation load) is a measure of the number of somatic protein-coding base substitution and insertion/deletion mutations occurring in a tumor specimen. TMB is affected by a variety of causes, including exposure to mutagens such as ultraviolet light in melanoma[53-54] and cigarette smoke in lung cancer[32,55], treatment with temozolomide-based chemotherapy in glioma[56-57], mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes[58-62], and microsatellite instability (MSI)[58,61-62]. This sample harbors a TMB below levels that would be predicted to be associated with sensitivity to PD-1- or PD-L1-targeting immune checkpoint inhibitors, alone or in combination with other agents[22-23,26-28,32-39,63].

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GENE
FGFR1

ALTERATION
amplification

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

Alterations that activate FGFR1 may predict sensitivity to selective FGFR inhibitors including erdafitinib[64-66], pemigatinib[67], infigratinib[68-69], rogaratinib[70], Debio 1347[71-72], futibatinib[73], and derazantinib[74], or multikinase inhibitors such as pazopanib[75] and ponatinib[76-78]. The activity and efficacy of selective FGFR inhibitors for FGFR1-amplified tumors has been modest with limited responses reported in FGFR1-amplified lung squamous cell carcinoma (SCC) treated with infigratinib[79] or AZD457[80] and no responses reported among patients with FGFR1-amplified breast cancer treated with infigratinib[79]. Two case studies reported PRs in patients with FGFR1-amplified breast cancer treated with pazopanib[75].

— Potential Resistance —

Preclinical studies suggest that overexpression of FGFR1 may be a mechanism of acquired resistance to gefitinib; addition of an FGFR inhibitor restored gefitinib sensitivity in lung cancer cell lines[81-82].

FREQUENCY & PROGNOSIS

In the TCGA datasets, FGFR1 amplification was found in 3% of lung adenocarcinoma cases[83] and 17% of lung SCC cases[84]; FGFR1 mutation was observed in 1% of lung adenocarcinoma and lung SCC[83-84]. The prognostic significance of FGFR1 alteration in lung adenocarcinoma has not been extensively studied, however, one analysis of 345 NSCLC cases (48% adenocarcinoma, 39% SCC, 7% large cell) suggested that high level amplification of FGFR1 was predictive of shorter survival[85]. The association between FGFR1 amplification and clinical parameters in lung SCC is not clear; some studies have suggested that FGFR1 amplification is associated with poor prognosis, whereas other studies have reported no association[86-90]; one study reported significant association between FGFR1 amplification and improved OS in women (p=0.023) but not in men (p=0.423)[91].

FINDING SUMMARY

FGFR1 encodes the protein fibroblast growth factor receptor 1, which plays key roles in regulation of the cell cycle and angiogenesis and is an upstream regulator of the RAS, MAPK, and AKT signaling pathways[92]. Amplification of FGFR1 has been correlated with protein expression[87,89] and may predict pathway activation and sensitivity to therapies targeting this pathway[93-94].

GENE
MDM2

ALTERATION
amplification

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

MDM2 antagonists disrupt the MDM2-p53 interaction, thereby stabilizing p53[95]. Preclinical studies have suggested that the amplification of MDM2, in the absence of concurrent TP53 mutations, may increase sensitivity to these agents[96-97]. Preliminary Phase 1 studies of the MDM2-p53 antagonist alrizomadlin (APG-115) reported a PR in a patient with liposarcoma harboring an MDM2 amplification and wildtype for TP53 and SD in 21%–38% (6/28 and 5/13, respectively) of patients in genomically unselected solid tumors[98-99] . A Phase 2 trial of alrizomadlin in combination with pembrolizumab reported a PR in 1 of 3 patients with malignant peripheral nerve sheath tumor that had failed standard therapy, as well as PRs in patients with multiple types of solid tumors that had failed immunotherapy, including 1 out of 14 patients with non-small cell lung cancer; 1 out of 5 patients with urothelial carcinoma; and 2 out of5, 1 out of 5, and 1 out of 11 patients with mucosal, uveal, and cutaneous melanoma, respectively[100]. Phase 1b studies of the MDM2 inhibitor idasanutlin for refractory AML in combination with cytarabine or venetoclax reported anti-leukemic response rates of 33% (25/75) and 37% (11/30), respectively[101-102] ; clinical benefit (58% ORR, 7/12) with idasanutlin monotherapy has been reported for patients with polycythemia vera[103]. The dual MDM2/MDM4 inhibitor ALRN-6924 led to an ORR of 27% (4/15) for patients with TP53 wildtype peripheral T-cell lymphoma in a Phase 2 study[104]; responses have also been observed in TP53 wildtype AML, MDS, Merkel cell carcinoma, colorectal cancer, and liposarcoma[105-106] .

FREQUENCY & PROGNOSIS

In the TCGA datasets, amplification of MDM2 has been reported in 8% of lung adenocarcinoma cases[83] and 2% of lung squamous cell carcinoma cases[84]. Separate studies have reported MDM2 amplification at similar incidences of 6-7% in non-small cell lung cancer (NSCLC), mainly in patients with adenocarcinoma, but a higher incidence of 21% (24/116) has also been observed, with amplification found in various NSCLC subtypes[107-109]. The role of MDM2 expression/amplification as a prognostic marker is complex, with some studies showing a negative and others a positive effect on survival in patients with NSCLC[107,109-111].

FINDING SUMMARY

MDM2 encodes an E3 ubiquitin protein ligase, which mediates the ubiquitination and subsequent degradation of p53, Rb1, and other proteins[112-114]. MDM2 acts to prevent the activity of the tumor suppressor p53; therefore, overexpression or amplification of MDM2 may be oncogenic[115-116]. Overexpression or amplification of MDM2 is frequent in cancer[117]. Although two retrospective clinical studies suggest that MDM2 amplification may predict a short time-to-treatment failure on anti-PD-1/PD-L1 immune checkpoint inhibitors, with 4/5 patients with MDM2 amplification[118] and 2/3 patients with MDM2 or MDM4 amplification[119] experiencing tumor hyperprogression, amplification of MDM2 or MDM4 was not associated with shorter progression-free survival (PFS) in a retrospective analysis of non-small cell lung cancer (NSCLC) outcomes with immune checkpoint inhibitors (hazard ratio of 1.4, p=0.44)[36]. The latter study reported PFS of >2 months for 5/8 patients with MDM2/MDM4 amplification[36].

GENE
NSD3 (WHSC1L1)

ALTERATION
amplification

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no targeted therapies available to address genomic alterations in NSD3.

FREQUENCY & PROGNOSIS

In TCGA datasets, NSD3 amplification has been most frequently observed in lung squamous cell carcinoma (17%)[84], breast invasive carcinoma (13%)[120], bladder urothelial carcinoma (9%)[121], and head and neck squamous cell carcinoma (9%)[122] samples[123-124]. Amplification of at least one member of the NSD3-CHD8-BRD4 pathway has been associated with worse overall survival in ovarian high-grade serous carcinoma and endometrial cancer[125]. In endometrial cancers, amplification of this pathway was more frequent in endometrial serous and endometrioid serous-like carcinomas compared to low-grade endometrioid endometrial adenocarcinomas[125].

FINDING SUMMARY

NSD3, also known as WHSC1L1, encodes an enzyme that mediates histone methylation[126]. NSD3 has been shown to be amplified in various cancers[127-129].

GENE
STAG2

ALTERATION
Q1190*

TRANSCRIPT ID
NM_001042750

CODING SEQUENCE EFFECT
3568C>T

VARIANT ALLELE FREQUENCY (% VAF)
23.7%

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no therapies that directly target STAG2. However, in preclinical studies, STAG2 inactivation by mutation or knockdown resulted in increased sensitivity to PARP inhibitors[130] or oxaliplatin[131].

FREQUENCY & PROGNOSIS

STAG2 mutations have been observed most frequently in urothelial bladder carcinoma (16-35%)[121,132-135], Ewing sarcoma (13-22%)[136-137], upper urinary tract urothelial carcinoma (11%)[138], myeloid malignancies (6%)[139-140], and glioblastoma (6%)[141]. STAG2 truncation mutations are associated with loss of protein expression[132-133,135,137]. In patients with Ewing sarcoma, STAG2 and TP53 mutations often co-occur and are associated with decreased overall survival, although mutation of either STAG2 or TP53 alone was not demonstrated to affect survival[136-137]. STAG2 mutation in patients with myelodysplastic syndrome is associated with decreased overall survival and has also been associated with increased response to treatment with azacitidine or decitabine in patients with myeloid malignancies[139]. The data on the prognostic significance of STAG2 mutation or loss of STAG2 protein expression in the context of urothelial bladder carcinoma are conflicting[132-135]. In patients with pancreatic ductal adenocarcinoma, loss of STAG2 staining was significantly associated with decreased overall survival, but was also associated with survival benefit from adjuvant chemotherapy[131]. An inactivating STAG2 mutation was identified in a patient with melanoma that acquired resistance to vemurafenib and preclinical evidence suggests that loss of STAG2 expression decreases the sensitivity of BRAF V600E-positive melanoma cells to vemurafenib, dabrafenib, and trametinib[142].

FINDING SUMMARY

STAG2 encodes a subunit of the cohesin complex, which maintains sister chromatid cohesion. The cohesin complex includes four subunits: SMC1A, SMC3, RAD21, and either STAG1 or STAG2[143]. Cohesin is also involved in transcriptional regulation, DNA replication and DNA repair[143]. STAG2 mutations, which are mostly truncating, or loss of STAG2 protein expression have been reported in multiple cancer types[143-144]. STAG2 deletion has been shown to promote tumorigenesis in preclinical studies[131], and STAG2 inactivation has been proposed to promote tumorigenesis via a mechanism that involves increased aneuploidy[132,134,141] or altered transcriptional regulation[133,135,139-140].

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GENE
TP53

ALTERATION
I232N

TRANSCRIPT ID
NM_000546

CODING SEQUENCE EFFECT
695T>A

VARIANT ALLELE FREQUENCY (% VAF)
27.2%

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no approved therapies to address TP53 mutation or loss. However, tumors with TP53 loss of function alterations may be sensitive to the WEE1 inhibitor adavosertib[145-148], or p53 gene therapy and immunotherapeutics such as SGT-53[149-153] and ALT-801[154]. In a Phase 1 study, adavosertib in combination with gemcitabine, cisplatin, or carboplatin elicited PRs in 9.7% and SDs in 53% of patients with solid tumors; the response rate was 21% (4/19) for patients with TP53 mutations versus 12% (4/33) for patients who were TP53 wildtype[155]. A Phase 2 trial of adavosertib in combination with chemotherapy (gemcitabine, carboplatin, paclitaxel, or doxorubicin) reported a 32% (30/94, 3 CR) ORR and a 73% (69/94) DCR for patients with platinum-refractory TP53-mutated ovarian, Fallopian tube, or peritoneal cancer[156]. A smaller Phase 2 trial of adavosertib in combination with carboplatin achieved a 43% (9/21, 1 CR) ORR and a 76% (16/21) DCR for patients with platinum-refractory TP53-mutated ovarian cancer[157]. The combination of adavosertib with paclitaxel and carboplatin for patients with TP53-mutated ovarian cancer also significantly increased PFS compared with paclitaxel and carboplatin alone[158]. In the Phase 2 VIKTORY trial, patients with TP53-mutated metastatic and/or recurrent gastric cancer experienced a 24% (6/25) ORR with adavosertib combined with paclitaxel[159]. A Phase 1 trial of neoadjuvant adavosertib in combination with cisplatin and docetaxel for head and neck squamous cell carcinoma (HNSCC) elicited a 71% (5/7) response rate for patients with TP53 alterations[160]. The Phase 2 FOCUS4-C trial for patients with TP53- and RAS-mutated colorectal cancer reported improvement in PFS (3.61 vs. 1.87 months, HR=0.35, p=0.0022), but not OS (14.0 vs 12.8 months, p=0.93), following adavosertib treatment compared with active monitoring[161]. In a Phase 1b clinical trial of SGT-53 in combination with docetaxel for patients with solid tumors, 75% (9/12) of evaluable patients experienced clinical benefit, including 2 confirmed and 1 unconfirmed PRs and 2 instances of SD with significant tumor shrinkage[153]. Missense mutations leading to TP53 inactivation may also be sensitive to therapies that reactivate mutated p53 such as APR-246[162-164]. In a Phase 1b trial for patients with p53-positive high-grade serous ovarian cancer, APR-246 combined with carboplatin and pegylated liposomal doxorubicin achieved a 52% (11/21) response rate and 100% DCR[165]. ATR inhibitor treatment of chronic lymphocytic leukemia (CLL) cells with biallelic inactivation of TP53 suppressed cell viability, promoted DNA damage, and attenuated xenograft growth in preclinical studies[166-167]; however, ATR inhibitors as monotherapy had little effect on these parameters in solid tumor models in other preclinical studies[168-169]. Therefore, it is unclear whether TP53 inactivation predicts sensitivity to ATR inhibition.

FREQUENCY & PROGNOSIS

TP53 is one of the most commonly mutated genes in lung cancer; mutations have been reported in 43-80% of non-small cell lung cancers (NSCLCs)[83-84,170-175], including 42-52% of lung adenocarcinomas and 58-83% of lung squamous cell carcinomas (cBioPortal, COSMIC, Feb 2021)[48-49,83-84]. TP53 homozygous deletion has been observed in 1.4% of lung adenocarcinoma and <1% of lung squamous cell carcinoma cases (cBioPortal, Feb 2021)[123-124]. In one study of 55 patients with lung adenocarcinoma, TP53 alterations correlated with immunogenic features including PD-L1 expression, tumor mutation burden and neoantigen presentation; likely as a consequence of this association TP53 mutations correlated with improved clinical outcomes to PD-1 inhibitors pembrolizumab and nivolumab in this study[176]. Mutations in TP53 have been associated with lymph node metastasis in patients with lung adenocarcinoma[177].

FINDING SUMMARY

Functional loss of the tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers[115]. Alterations such as seen here may disrupt TP53 function or expression[178-182].

POTENTIAL GERMLINE IMPLICATIONS

Germline mutations in TP53 are associated with the very rare autosomal dominant disorder Li-Fraumeni syndrome and the early onset of many cancers[183-185], including sarcomas[186-187]. Estimates for the prevalence of germline TP53 mutations in the general population range from 1:5,000[188] to 1:20,000[187]. For pathogenic TP53 mutations identified during tumor sequencing, the rate of germline mutations was 1% in the overall population and 6% in tumors arising before age 30[189]. In the appropriate clinical context, germline testing of TP53 is recommended.

POTENTIAL CLONAL HEMATOPOIESIS IMPLICATIONS

Variants seen in this gene have been reported to occur in clonal hematopoiesis (CH), an age-related process in which hematopoietic stem cells acquire somatic mutations that allow for clonal expansion[190-195]. CH in this gene has been associated with increased mortality, risk of coronary heart disease, risk of ischemic stroke, and risk of secondary hematologic malignancy[190-191]. Clinical management of patients with CH in this gene may include monitoring for hematologic changes and reduction of controllable risk factors for cardiovascular disease[196]. Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH[194,197-198]. Patient-matched peripheral blood mononuclear cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH.

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NOTE Clinical trials are ordered by gene and prioritized by: age range inclusion criteria for pediatric patients, proximity to ordering medical facility, later trial phase, and verification of trial information within the last two months. While every effort is made to ensure the accuracy of the information contained below, the information available in the public domain is continually updated and should be investigated by the physician or research staff. This is not a comprehensive list of all available clinical trials. Foundation Medicine displays a subset of trial options and ranks them in this order of descending priority: Qualification for pediatric trial → Geographical proximity → Later trial phase. Clinical trials listed here may have additional enrollment criteria that may require medical screening to determine final eligibility. For additional information about listed clinical trials or to conduct a search for additional trials, please see clinicaltrials.gov. Or visit https://www.foundationmedicine.com/genomic-testing#support-services.

GENE
FGFR1

ALTERATION
amplification

RATIONALE
FGFR inhibitors may be relevant in tumors with alterations that activate FGFR1.

NCT03976375

PHASE 3

Efficacy and Safety of Pembrolizumab (MK-3475) With Lenvatinib (E7080/MK-7902) vs. Docetaxel in Participants With Metastatic Non-Small Cell Lung Cancer (NSCLC) and Progressive Disease (PD) After Platinum Doublet Chemotherapy and Immunotherapy (MK-7902-008/E7080-G000-316/LEAP-008)

TARGETS
FGFRs, RET, PDGFRA, VEGFRs, KIT, PD-1

LOCATIONS: Cali (Colombia), Bogota (Colombia), Medellin (Colombia), Monteria (Colombia), Valledupar (Colombia), Barranquilla (Colombia), Rosario (Argentina), Caba (Argentina), Buenos Aires (Argentina), Ponce (Puerto Rico)

NCT02549937

PHASE 1/2

A Multi-Center, Open-Label Study of Sulfatinib(HMPL-012) in Patients With Advanced Solid Tumors

TARGETS
FGFR1, CSF1R, VEGFRs

LOCATIONS: Florida, Texas, Tennessee, Virginia, New York, Wisconsin, Colorado, California, Milano (Italy)

NCT04042116

PHASE 1/2

A Study to Evaluate Lucitanib in Combination With Nivolumab in Patients With a Solid Tumor

TARGETS
FGFRs, VEGFRs, PD-1

LOCATIONS: Florida, North Carolina, Tennessee, Oklahoma, Ohio, Pennsylvania, New York, Massachusetts, Colorado, California

NCT03377023

PHASE 1/2

Phase I/II Study of Nivolumab and Ipilimumab Combined With Nintedanib in Non Small Cell Lung Cancer

TARGETS
FGFR1, LCK, SRC, VEGFRs, FGFR2, FGFR3, FLT3, LYN, PD-1, CTLA-4

LOCATIONS: Florida

NCT04565275

PHASE 1/2

A Study of ICP-192 in Patients With Advanced Solid Tumors

TARGETS
FGFR2, FGFR1, FGFR3, FGFR4

LOCATIONS: Florida, Arizona, Colorado, Minnesota

NCT03516981

PHASE 2

A Study of Biomarker-Directed, Pembrolizumab (MK-3475) Based Combination Therapy for Advanced Non-Small Cell Lung Cancer (MK-3475-495/KEYNOTE-495)

TARGETS
CTLA-4, LAG-3, PD-1, FGFRs, RET, PDGFRA, VEGFRs, KIT

LOCATIONS: Florida, Texas, Virginia, Maryland, Pennsylvania, New York, New Jersey, Connecticut, Toronto (Canada)

NCT04716933

PHASE 3

Safety and Efficacy Study of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (MK-7902/E7080) as First-line Intervention in Adults With Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-7902-006/E7080-G000-315/LEAP-006)-China Extension Study

TARGETS
PD-1, KIT, VEGFRs, FGFRs, PDGFRA, RET

LOCATIONS: Harbin (China), Changchun (China), Urumuqi (China), Beijing (China), Tianjin (China), Shanghai (China), Zhengzhou (China), Hangzhou (China), Wen Zhou (China), Wuhan (China)

NCT04676412

PHASE 3

Efficacy and Safety Study of Pembrolizumab (MK-3475) With or Without Lenvatinib (MK-7902/E7080) in Adults With Programmed Cell Death-Ligand 1 (PD-L1)-Positive Treatment-naïve Non-small Cell Lung Cancer (NSCLC) [MK-7902-007/E7080-G000-314/LEAP-007] - China Extension Study

TARGETS
PD-1, KIT, VEGFRs, FGFRs, PDGFRA, RET

LOCATIONS: Chang chun (China), Beijing (China), Shanghai (China), Nanjing (China), Hangzhou (China), Hefei (China), Changsha (China)

NCT02272998

PHASE 2

Ponatinib for Patients Whose Advanced Solid Tumor Cancer Has Activating Mutations Involving the Following Genes: FGFR1, FGFR2, FGFR3, FGFR4, RET, KIT.

TARGETS
FGFRs, VEGFRs, ABL, RET, FLT3, KIT

LOCATIONS: Ohio

NCT04729348

PHASE 2

Pembrolizumab And Lenvatinib In Leptomeningeal Metastases

TARGETS
PD-1, KIT, VEGFRs, FGFRs, PDGFRA, RET

LOCATIONS: Massachusetts

GENE
MDM2

ALTERATION
amplification

RATIONALE
Inhibitors of the MDM2-p53 interaction are being tested in clinical trials. Overexpression or amplification of MDM2 may increase sensitivity to these agents, but more data are required.

NCT03611868

PHASE 1/2

A Study of APG-115 in Combination With Pembrolizumab in Patients With Metastatic Melanomas or Advanced Solid Tumors

TARGETS
MDM2, PD-1

LOCATIONS: Florida, Texas, Tennessee, Arkansas, Virginia, District of Columbia, Pennsylvania, Missouri

Electronically signed by Erik Williams, M.D. | 01 February 2022
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NOTE One or more variants of unknown significance (VUS) were detected in this patient's tumor. These variants may not have been adequately characterized in the scientific literature at the time this report was issued, and/or the genomic context of these alterations makes their significance unclear. We choose to include them here in the event that they become clinically meaningful in the future.

KMT2A (MLL)	***MKNK1***	***NBN***	***PARP3***
A53V	L189V	E81K	T244R

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FoundationOne CDx is designed to include genes known to be somatically altered in human solid tumors that are validated targets for therapy, either approved or in clinical trials, and/or that are unambiguous drivers of oncogenesis based on current knowledge. The current assay interrogates 324 genes as well as introns of 36 genes involved in rearrangements. The assay will be updated periodically to reflect new knowledge about cancer biology.

DNA GENE LIST: ENTIRE CODING SEQUENCE FOR THE DETECTION OF BASE SUBSTITUTIONS, INSERTION/DELETIONS, AND COPY NUMBER ALTERATIONS

ABL1	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*ALOX12B*	*AMER1 (FAM123B)*	*APC*
AR	*ARAF*	*ARFRP1*	*ARID1A*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*
AURKB	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*	*BCL2L2*	*BCL6*
BCOR	*BCORL1*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*BRIP1*	*BTG1*	*BTG2*
BTK	*C11orf30 (EMSY)*	*C17orf39 (GID4)*	*CALR*	*CARD11*	*CASP8*	*CBFB*	*CBL*	*CCND1*
CCND2	*CCND3*	*CCNE1*	*CD22*	*CD274 (PD-L1)*	*CD70*	*CD79A*	*CD79B*	*CDC73*
CDH1	*CDK12*	*CDK4*	*CDK6*	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*
CDKN2C	*CEBPA*	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CSF1R*	*CSF3R*
CTCF	*CTNNA1*	*CTNNB1*	*CUL3*	*CUL4A*	*CXCR4*	*CYP17A1*	*DAXX*	*DDR1*
DDR2	*DIS3*	*DNMT3A*	*DOT1L*	*EED*	*EGFR*	*EP300*	*EPHA3*	*EPHB1*
EPHB4	*ERBB2*	*ERBB3*	*ERBB4*	*ERCC4*	*ERG*	*ERRFI1*	*ESR1*	*EZH2*
FAM46C	*FANCA*	*FANCC*	*FANCG*	*FANCL*	*FAS*	*FBXW7*	*FGF10*	*FGF12*
FGF14	*FGF19*	*FGF23*	*FGF3*	*FGF4*	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*
FGFR4	*FH*	*FLCN*	*FLT1*	*FLT3*	*FOXL2*	*FUBP1*	*GABRA6*	*GATA3*
GATA4	*GATA6*	*GNA11*	*GNA13*	*GNAQ*	*GNAS*	*GRM3*	*GSK3B*	*H3F3A*
HDAC1	*HGF*	*HNF1A*	*HRAS*	*HSD3B1*	*ID3*	*IDH1*	*IDH2*	*IGF1R*
IKBKE	*IKZF1*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*	*JAK2*	*JAK3*
JUN	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*	*KIT*	*KLHL6*
KMT2A (MLL)	*KMT2D (MLL2)*	*KRAS*	*LTK*	*LYN*	*MAF*	*MAP2K1 (MEK1)*	*MAP2K2 (MEK2)*	*MAP2K4*
MAP3K1	*MAP3K13*	*MAPK1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*	*MEN1*
MERTK	*MET*	*MITF*	*MKNK1*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH3*
MSH6	*MST1R*	*MTAP*	*MTOR*	*MUTYH*	*MYC*	*MYCL (MYCL1)*	*MYCN*	*MYD88*
NBN	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOTCH1*	*NOTCH2*	*NOTCH3*
NPM1	*NRAS*	*NSD3 (WHSC1L1)*	*NT5C2*	*NTRK1*	*NTRK2*	*NTRK3*	*P2RY8*	*PALB2*
PARK2	*PARP1*	*PARP2*	*PARP3*	*PAX5*	*PBRM1*	*PDCD1 (PD-1)*	*PDCD1LG2 (PD-L2)*	*PDGFRA*
PDGFRB	*PDK1*	*PIK3C2B*	*PIK3C2G*	*PIK3CA*	*PIK3CB*	*PIK3R1*	*PIM1*	*PMS2*
POLD1	*POLE*	*PPARG*	*PPP2R1A*	*PPP2R2A*	*PRDM1*	*PRKAR1A*	*PRKCI*	*PTCH1*
PTEN	*PTPN11*	*PTPRO*	*QKI*	*RAC1*	*RAD21*	*RAD51*	*RAD51B*	*RAD51C*
RAD51D	*RAD52*	*RAD54L*	*RAF1*	*RARA*	*RB1*	*RBM10*	*REL*	*RET*
RICTOR	*RNF43*	*ROS1*	*RPTOR*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*
SF3B1	*SGK1*	*SMAD2*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*
SOX2	*SOX9*	*SPEN*	*SPOP*	*SRC*	*STAG2*	*STAT3*	*STK11*	*SUFU*
SYK	*TBX3*	*TEK*	*TET2*	*TGFBR2*	*TIPARP*	*TNFAIP3*	*TNFRSF14*	*TP53*
TSC1	*TSC2*	*TYRO3*	*U2AF1*	*VEGFA*	*VHL*	*WHSC1*	*WT1*	*XPO1*
XRCC2	*ZNF217*	*ZNF703*						

DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*CD74*	*EGFR*	*ETV4*
ETV5	*ETV6*	*EWSR1*	*EZR*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*KMT2A (MLL)*
MSH2	*MYB*	*MYC*	*NOTCH2*	*NTRK1*	*NTRK2*	*NUTM1*	*PDGFRA*	*RAF1*
RARA	*RET*	*ROS1*	*RSPO2*	*SDC4*	*SLC34A2*	*TERC**	*TERT***	*TMPRSS2*

*TERC is an NCRNA

**Promoter region of TERT is interrogated

ADDITIONAL ASSAYS: FOR THE DETECTION OF SELECT CANCER BIOMARKERS

Loss of Heterozygosity (LOH) score
Microsatellite (MS) status
Tumor Mutational Burden (TMB)

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FoundationOne CDx fulfills the requirements of the European Directive 98/79 EC for in vitro diagnostic medical devices and is registered as a CE-IVD product by Foundation Medicine's EU Authorized Representative, Qarad b.v.b.a, Cipalstraat 3, 2440 Geel, Belgium. CE

ABOUT FOUNDATIONONE CDX

FoundationOne CDx was developed and its performance characteristics determined by Foundation Medicine, Inc. (Foundation Medicine). FoundationOne CDx may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratories are qualified to perform high-complexity clinical testing.

Please refer to technical information for performance specification details: www.rochefoundationmedicine.com/f1cdxtech.

INTENDED USE

FoundationOne®CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI), tumor mutational burden (TMB), and for selected forms of ovarian cancer, loss of heterozygosity (LOH) score, using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with therapies in accordance with approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

TEST PRINCIPLES

FoundationOne CDx will be performed exclusively as a laboratory service using DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor samples. The proposed assay will employ a single DNA extraction method from routine FFPE biopsy or surgical resection specimens, 50-1000 ng of which will undergo whole-genome shotgun library construction and hybridization-based capture of all coding exons from 309 cancer-related genes, one promoter region, one non-coding (ncRNA), and select intronic regions from 34 commonly rearranged genes, 21 of which also include the coding exons. The assay therefore includes detection of alterations in a total of 324 genes. Using an Illumina® HiSeq platform, hybrid capture–selected libraries will be sequenced to high uniform depth (targeting >500X median coverage with >99% of exons at coverage >100X). Sequence data will be processed using a customized analysis pipeline designed to accurately detect all classes of genomic alterations, including base substitutions, indels, focal copy number amplifications, homozygous gene deletions, and selected genomic rearrangements (e.g.,gene fusions). Additionally, genomic signatures including loss of heterozygosity (LOH), microsatellite instability (MSI) and tumor mutational burden (TMB) will be reported.

THE REPORT

Incorporates analyses of peer-reviewed studies and other publicly available information identified by Foundation Medicine; these analyses and information may include associations between a molecular alteration (or lack of alteration) and one or more drugs with potential clinical benefit (or potential lack of clinical benefit), including drug candidates that are being studied in clinical research. The F1CDx report may be used as an aid to inform molecular eligibility for clinical trials. Note: A finding of biomarker alteration does not necessarily indicate pharmacologic effectiveness (or lack thereof) of any drug or treatment regimen; a finding of no biomarker alteration does not necessarily indicate lack of pharmacologic effectiveness (or effectiveness) of any drug or treatment regimen.

Diagnostic Significance

FoundationOne CDx identifies alterations to select cancer-associated genes or portions of genes (biomarkers). In some cases, the Report also highlights selected negative test results regarding biomarkers of clinical significance.

Qualified Alteration Calls (Equivocal and Subclonal)

An alteration denoted as "amplification – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence that the copy number of a gene exceeds the threshold for identifying copy number amplification. The threshold used in FoundationOne CDx for identifying a copy number amplification is four (4) for ERBB2 and six (6) for all other genes. Conversely, an alteration denoted as "loss – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence for homozygous deletion of the gene in question. An alteration denoted as "subclonal" is one that the FoundationOne CDx analytical methodology has identified as being present in <10% of the assayed tumor DNA.

Ranking of Therapies and Clinical Trials

Ranking of Therapies in Summary Table

Therapies are ranked based on the following criteria: Therapies with clinical benefit (ranked alphabetically within each evidence category), followed by therapies associated with resistance (when applicable).

Ranking of Clinical Trials

Pediatric trial qualification → Geographical proximity → Later trial phase.

NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) CATEGORIZATION

Biomarker and genomic findings detected may be associated with certain entries within the NCCN Drugs & Biologics Compendium® (NCCN Compendium®) (www.nccn.org). The NCCN Categories of Evidence and Consensus indicated reflect the highest possible category for a given therapy in association with each biomarker or genomic finding. Please note, however, that the accuracy and applicability of these NCCN categories within a report may be impacted by the patient's clinical history, additional biomarker information, age, and/or co-occurring alterations. For additional information on the NCCN categories, please refer to the NCCN Compendium®. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Limitations

1. In the fractional-based MSI algorithm, a tumor specimen will be categorized as MSI-H, MSS, or MS-Equivocal according to the fraction of microsatellite loci determined to be altered or unstable (i.e., the fraction unstable loci score). In the F1CDx assay, MSI is evaluated based on a genome-wide analysis across >2000 microsatellite loci. For a given microsatellite locus, non-somatic alleles are discarded, and the microsatellite is categorized as unstable if remaining alleles differ from the reference genome. The final fraction unstable loci score is calculated as the number of unstable microsatellite loci divided by the number of evaluable microsatellite loci. The MSI-H and MSS cut-off thresholds were determined by analytical concordance to a PCR comparator assay using a pan-tumor FFPE tissue sample set. Patients with results categorized as "MS-

Stable" with median exon coverage <300X, "MS-Equivocal," or "Cannot Be Determined" should receive confirmatory testing using a validated orthogonal (alternative) method.

2. TMB by F1CDx is determined by counting all synonymous and non-synonymous variants present at 5% allele frequency or greater (after filtering) and the total number is reported as mutations per megabase (mut/Mb) unit. Observed TMB is dependent on characteristics of the specific tumor focus tested for a patient (e.g., primary vs. metastatic, tumor content) and the testing platform used for the detection; therefore, observed TMB results may vary between different specimens for the same patient and between detection methodologies employed on the same sample. The TMB calculation may differ from TMB calculations used by other assays depending on variables such as the amount of genome interrogated, percentage of tumor, assay limit of detection (LoD), filtering of alterations included in the score, and the read depth and other bioinformatic test specifications. Refer to the SSED for a detailed description of these variables in FMI's TMB calculation https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019B.pdf. The clinical validity of TMB defined by this panel has been established for TMB as a qualitative output for a cut-off of 10 mutations per megabase but has not been established for TMB as a quantitative score.
3. The LOH score is determined by analyzing SNPs spaced at 1Mb intervals across the genome on the FoundationOne CDx test and extrapolating an LOH profile, excluding arm- and chromosome-wide LOH segments. Detection of LOH has been verified only for ovarian cancer patients, and the LOH score result may be reported for epithelial ovarian, peritoneal, or Fallopian tube carcinomas. The LOH score will be reported as "Cannot Be Determined" if the sample is not of sufficient quality to confidently determine LOH. Performance of the LOH classification has not been established for samples below 35% tumor content. There may be potential interference of ethanol with LOH detection. The interfering effects of xylene, hemoglobin, and triglycerides on the LOH score have not been demonstrated.
4. Alterations reported may include somatic (not inherited) or germline (inherited) alterations; however, the test does not distinguish between germline and somatic alterations. The test does not provide information about susceptibility.
5. Biopsy may pose a risk to the patient when archival tissue is not available for use with the assay. The patient's physician should determine whether the patient is a candidate for biopsy.
6. Reflex testing to an alternative FDA approved companion diagnostic should be performed for patients who have an *ERBB2* amplification result detected with copy number equal to 4 (baseline ploidy of tumor +2) for confirmatory testing. While this result is considered negative by FoundationOne®CDx (F1CDx), in a clinical concordance study with an FDA approved FISH test, 70% (7 out of 10 samples) were positive, and 30% (3 out of 10 samples) were negative by the FISH test with an average ratio of 2.3. The frequency of *ERBB2* copy number 4 in breast cancer is estimated to be approximately 2%. Multiple references listed in https://www.mycancergenome.org/content/disease/breast-cancer/ERBB2/238/ report the frequency of HER2 overexpression as 20% in breast cancer. Based on the F1CDx HER2 CDx concordance study, approximately 10% of HER2 amplified samples had copy number 4. Thus, total frequency is conservatively estimated to be approximately 2%.

REPORT HIGHLIGHTS

The Report Highlights includes select genomic and therapeutic information with potential impact on patient care and treatment that is specific to the genomics and tumor type of the sample analyzed. This section may highlight information including targeted therapies with potential sensitivity or resistance; evidence-matched clinical trials; and variants with potential diagnostic, prognostic, nontargeted treatment, germline, or clonal hematopoiesis implications. Information included in the Report Highlights is expected to evolve with advances in scientific and clinical research. Findings included in the Report Highlights should be considered in the context of all other information in this report and other relevant patient information. Decisions on patient care and treatment are the responsibility of the treating physician.

VARIANT ALLELE FREQUENCY

Variant Allele Frequency (VAF) represents the fraction of sequencing reads in which the variant is observed. This attribute is not taken into account for therapy inclusion, clinical trial matching, or interpretive content. Caution is recommended in interpreting VAF to indicate the potential germline or somatic origin of an alteration, recognizing that tumor fraction and tumor ploidy of samples may vary.

Precision of VAF for base substitutions and indels

BASE SUBSTITUTIONS	%CV*
Repeatability	5.11 - 10.40
Reproducibility	5.95 - 12.31
INDELS	**%CV***
Repeatability	6.29 - 10.00
Reproducibility	7.33 - 11.71

**Interquartile Range = 1st Quartile to 3rd Quartile*

VARIANTS TO CONSIDER FOR FOLLOW-UP GERMLINE TESTING

The variants indicated for consideration of follow-up germline testing are 1) limited to reportable short variants with a protein effect listed in the ClinVar genomic database (Landrum et al., 2018; 29165669) as Pathogenic, Pathogenic/Likely Pathogenic, or Likely Pathogenic (by an expert panel or multiple submitters), 2) associated with hereditary cancer-predisposing disorder(s), 3) detected at an allele frequency of >10%, and 4) in select genes reported by the ESMO Precision Medicine Working Group (Mandelker et al., 2019; 31050713) to have a greater than 10% probability of germline origin if identified during tumor sequencing. The selected genes are *ATM, BAP1, BRCA1, BRCA2, BRIP1, CHEK2, FH, FLCN, MLH1, MSH2, MSH6, MUTYH, PALB2, PMS2, POLE, RAD51C, RAD51D, RET, SDHA, SDHB, SDHC, SDHD, TSC2,* and *VHL*, and are not inclusive of all cancer susceptibility genes. The content in this report should not substitute for genetic counseling or follow-up germline testing, which is needed to distinguish whether a finding in this patient's tumor sequencing is germline or somatic. Interpretation should be based on clinical context.

VARIANTS THAT MAY REPRESENT CLONAL HEMATOPOIESIS

Variants that may represent clonal hematopoiesis (CH) are limited to select reportable short variants in defined genes identified in solid tumors only. Variant selection was determined based on gene tumor-suppressor or oncogene status, known role in solid tumors versus hematological malignancies, and literature prevalence. The defined genes are *ASXL1, CBL, DNMT3A, IDH2, JAK2, KMT2D (MLL2), MPL, MYD88, SF3B1, TET2,* and *U2AF1* and are not inclusive of all CH genes. The content in this report should not substitute for dedicated hematological workup. Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH. Patient-matched peripheral blood mononuclear

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cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH. Interpretation should be based on clinical context.

LEVEL OF EVIDENCE NOT PROVIDED

Drugs with potential clinical benefit (or potential lack of clinical benefit) are not evaluated for source or level of published evidence.

NO GUARANTEE OF CLINICAL BENEFIT

This Report makes no promises or guarantees that a particular drug will be effective in the treatment of disease in any patient. This Report also makes no promises or guarantees that a drug with potential lack of clinical benefit will in fact provide no clinical benefit.

NO GUARANTEE OF REIMBURSEMENT

Foundation Medicine makes no promises or guarantees that a healthcare provider, insurer or other third party payor, whether private or governmental, will reimburse a patient for the cost of FoundationOne CDx.

TREATMENT DECISIONS ARE RESPONSIBILITY OF PHYSICIAN

Drugs referenced in this Report may not be suitable for a particular patient. The selection of any, all or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) resides entirely within the discretion of the treating physician. Indeed, the information in this Report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care in a given community. A treating physician's decisions should not be based on a single test, such as this Test, or the information contained in this Report. Certain sample or variant characteristics may result in reduced sensitivity. FoundationOne CDx is performed using DNA derived from tumor, and as such germline events may not be reported.

SELECT ABBREVIATIONS

ABBREVIATION	DEFINITION
CR	Complete response
DCR	Disease control rate
DNMT	DNA methyltransferase
HR	Hazard ratio
ITD	Internal tandem duplication
MMR	Mismatch repair
muts/Mb	Mutations per megabase
NOS	Not otherwise specified
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
SD	Stable disease
TKI	Tyrosine kinase inhibitor

MR Suite Version 5.2.0

The median exon coverage for this sample is 1,070x

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1. Gatalica Z, et al. Cancer Epidemiol. Biomarkers Prev. (2014) pmid: 25392179
2. Kroemer G, et al. Oncoimmunology (2015) pmid: 26140250
3. Lal N, et al. Oncoimmunology (2015) pmid: 25949894
4. Le DT, et al. N. Engl. J. Med. (2015) pmid: 26028255
5. Ayers et al., 2016; ASCO-SITC Abstract P60
6. Warth A, et al. Virchows Arch. (2016) pmid: 26637197
7. Ninomiya H, et al. Br. J. Cancer (2006) pmid: 16641899
8. Vanderwalde A, et al. Cancer Med (2018) pmid: 29436178
9. Zang YS, et al. Cancer Med (2019) pmid: 31270941
10. Dudley JC, et al. Clin. Cancer Res. (2016) pmid: 26880610
11. Takamochi K, et al. Lung Cancer (2017) pmid: 28676214
12. Pylkkänen L, et al. Environ. Mol. Mutagen. (1997) pmid: 9329646
13. Gonzalez R, et al. Ann. Oncol. (2000) pmid: 11061602
14. Chen XQ, et al. Nat. Med. (1996) pmid: 8782463
15. Merlo A, et al. Cancer Res. (1994) pmid: 8174113
16. Kocarnik JM, et al. Gastroenterol Rep (Oxf) (2015) pmid: 26337942
17. You JF, et al. Br. J. Cancer (2010) pmid: 21081928
18. Bairwa NK, et al. Methods Mol. Biol. (2014) pmid: 24623249
19. Boland CR, et al. Cancer Res. (1998) pmid: 9823339
20. Pawlik TM, et al. Dis. Markers (2004) pmid: 15528785
21. Boland CR, et al. Gastroenterology (2010) pmid: 20420947
22. Samstein RM, et al. Nat. Genet. (2019) pmid: 30643254
23. Goodman AM, et al. Mol. Cancer Ther. (2017) pmid: 28835386
24. Goodman AM, et al. Cancer Immunol Res (2019) pmid: 31405947
25. Cristescu R, et al. Science (2018) pmid: 30309915
26. Ready N, et al. J. Clin. Oncol. (2019) pmid: 30785829
27. Hellmann MD, et al. N. Engl. J. Med. (2018) pmid: 29658845
28. Hellmann MD, et al. Cancer Cell (2018) pmid: 29657128
29. Hellmann MD, et al. Cancer Cell (2018) pmid: 29731394
30. Rozeman EA, et al. Nat Med (2021) pmid: 33558721
31. Sharma P, et al. Cancer Cell (2020) pmid: 32916128
32. Rizvi NA, et al. Science (2015) pmid: 25765070
33. Colli LM, et al. Cancer Res. (2016) pmid: 27197178
34. Wang VE, et al. J Immunother Cancer (2017) pmid: 28923100
35. Carbone DP, et al. N. Engl. J. Med. (2017) pmid: 28636851
36. Rizvi H, et al. J. Clin. Oncol. (2018) pmid: 29337640
37. Forde PM, et al. N. Engl. J. Med. (2018) pmid: 29658848
38. Miao D, et al. Nat. Genet. (2018) pmid: 30150660
39. Chae YK, et al. Clin Lung Cancer (2019) pmid: 30425022
40. Paz-Ares et al., 2019; ESMO Abstract LBA80
41. Hellmann MD, et al. N. Engl. J. Med. (2019) pmid: 31562796
42. Chalmers ZR, et al. Genome Med (2017) pmid: 28420421
43. Spigel et al., 2016; ASCO Abstract 9017
44. Xiao D, et al. Oncotarget (2016) pmid: 27009843
45. Shim HS, et al. J Thorac Oncol (2015) pmid: 26200269
46. Govindan R, et al. Cell (2012) pmid: 22980976
47. Ding L, et al. Nature (2008) pmid: 18948947
48. Imielinski M, et al. Cell (2012) pmid: 22980975
49. Kim Y, et al. J. Clin. Oncol. (2014) pmid: 24323028
50. Stein et al., 2019; DOI: 10.1200/PO.18.00376
51. Chen Y, et al. J. Exp. Clin. Cancer Res. (2019) pmid: 31088500
52. Yu H, et al. J Thorac Oncol (2019) pmid: 30253973
53. Pfeifer GP, et al. Mutat. Res. (2005) pmid: 15748635
54. Hill VK, et al. Annu Rev Genomics Hum Genet (2013) pmid: 23875803
55. Pfeifer GP, et al. Oncogene (2002) pmid: 12379884
56. Johnson BE, et al. Science (2014) pmid: 24336570
57. Choi S, et al. Neuro-oncology (2018) pmid: 29452419
58. Cancer Genome Atlas Research Network, et al. Nature (2013) pmid: 23636398
59. Briggs S, et al. J. Pathol. (2013) pmid: 23447401
60. Heitzer E, et al. Curr. Opin. Genet. Dev. (2014) pmid: 24583393
61. Nature (2012) pmid: 22810696
62. Roberts SA, et al. Nat. Rev. Cancer (2014) pmid: 25568919
63. Marabelle A, et al. Lancet Oncol. (2020) pmid: 32919526
64. Loriot Y, et al. N. Engl. J. Med. (2019) pmid: 31340094
65. Tabernero J, et al. J. Clin. Oncol. (2015) pmid: 26324363
66. Karkera JD, et al. Mol. Cancer Ther. (2017) pmid: 28416604
67. Necchi et al., 2018; ESMO Abstract 900P
68. Pal SK, et al. Cancer Discov (2018) pmid: 29848605
69. Pal SK, et al. Cancer (2020) pmid: 32208524
70. Schuler M, et al. Lancet Oncol. (2019) pmid: 31405822
71. Farouk Sait S, et al. JCO Precis Oncol (2021) pmid: 34250399
72. Voss MH, et al. Clin. Cancer Res. (2019) pmid: 30745300
73. Bahleda R, et al. Ann Oncol (2020) pmid: 32622884
74. Papadopoulos KP, et al. Br. J. Cancer (2017) pmid: 28972963
75. Cheng FT, et al. J Natl Compr Canc Netw (2017) pmid: 29223982
76. Khodadoust MS, et al. Leukemia (2016) pmid: 26055304
77. Tanasi I, et al. Blood (2019) pmid: 31434701
78. Strati P, et al. Leuk. Lymphoma (2018) pmid: 29119847
79. Nogova L, et al. J. Clin. Oncol. (2017) pmid: 27870574
80. Aggarwal C, et al. J Thorac Oncol (2019) pmid: 31195180
81. Ware KE, et al. Oncogenesis (2013) pmid: 23552882
82. Terai H, et al. Mol. Cancer Res. (2013) pmid: 23536707
83. Nature (2014) pmid: 25079552
84. Nature (2012) pmid: 22960745
85. Gadgeel SM, et al. PLoS ONE (2013) pmid: 24255716
86. Cote et al., 2012; ASCO Abstract 7063
87. Kim HR, et al. J. Clin. Oncol. (2013) pmid: 23182986
88. Heist RS, et al. J Thorac Oncol (2012) pmid: 23154548
89. Kohler LH, et al. Virchows Arch. (2012) pmid: 22648708
90. Craddock KJ, et al. J Thorac Oncol (2013) pmid: 24077455
91. Flockerzi FA, et al. Virchows Arch. (2018) pmid: 29270870
92. Turner N, et al. Nat. Rev. Cancer (2010) pmid: 20094046
93. André F, et al. Lancet Oncol. (2014) pmid: 24508104
94. Dienstmann R, et al. Ann. Oncol. (2014) pmid: 24265351
95. Cheok CF, et al. Nat Rev Clin Oncol (2011) pmid: 20975744
96. Ohnstad HO, et al. Cancer (2013) pmid: 23165797
97. Gamble LD, et al. Oncogene (2012) pmid: 21725357
98. Zhang et al., 2019; ASCO Abstract 3124
99. Rasco et al., 2019; ASCO Abstract 3126
100. Tolcher et al., 2021; ASCO Abstract 2506
101. Martinelli et al., 2016; EHA21 Abstract S504
102. Daver et al., 2018; ASH Abstract 767
103. Mascarenhas et al., 2019; ASH Abstract 134
104. Shustov et al., 2018; ASH Abstract 1623
105. Sallman et al., 2018; ASH Abstract 4066
106. Meric-Bernstam et al., 2017; ASCO Abstract 2505
107. Higashiyama M, et al. Br. J. Cancer (1997) pmid: 9155050
108. Marchetti A, et al. Diagn. Mol. Pathol. (1995) pmid: 7551299
109. Dworakowska D, et al. Lung Cancer (2004) pmid: 15165086
110. Onel K, et al. Mol. Cancer Res. (2004) pmid: 14757840
111. Ren YW, et al. Asian Pac. J. Cancer Prev. (2013) pmid: 24175836
112. Sdek P, et al. Mol. Cell (2005) pmid: 16337594
113. Brady M, et al. Mol. Cell. Biol. (2005) pmid: 15632057
114. Li M, et al. Mol. Cell (2004) pmid: 15053880
115. Brown CJ, et al. Nat. Rev. Cancer (2009) pmid: 19935675
116. Cordon-Cardo C, et al. Cancer Res. (1994) pmid: 8306343
117. Beroukhim R, et al. Nature (2010) pmid: 20164920
118. Kato S, et al. Clin. Cancer Res. (2017) pmid: 28351930
119. Singavi et al., 2017; ESMO Abstract 1140PD
120. Ciriello G, et al. Cell (2015) pmid: 26451490
121. Nature (2014) pmid: 24476821
122. Nature (2015) pmid: 25631445
123. Cerami E, et al. Cancer Discov (2012) pmid: 22588877
124. Gao J, et al. Sci Signal (2013) pmid: 23550210
125. Jones DH, et al. Mol Clin Oncol (2017) pmid: 28781807
126. Kim SM, et al. Biochem. Biophys. Res. Commun. (2006) pmid: 16682010
127. Kang D, et al. Genes Chromosomes Cancer (2013) pmid: 23011637
128. Chen Y, et al. PLoS ONE (2014) pmid: 24874471
129. Morishita M, et al. Biochim. Biophys. Acta (2011) pmid: 21664949
130. Bailey ML, et al. Mol. Cancer Ther. (2014) pmid: 24356817
131. Evers L, et al. Genome Med (2014) pmid: 24484537
132. Solomon DA, et al. Nat. Genet. (2013) pmid: 24121789
133. Balbás-Martínez C, et al. Nat. Genet. (2013) pmid: 24121791
134. Guo G, et al. Nat. Genet. (2013) pmid: 24121792
135. Taylor CF, et al. Hum. Mol. Genet. (2014) pmid: 24270882
136. Tirode F, et al. Cancer Discov (2014) pmid: 25223734
137. Brohl AS, et al. PLoS Genet. (2014) pmid: 25010205
138. Hoang ML, et al. Sci Transl Med (2013) pmid: 23926200
139. Thota S, et al. Blood (2014) pmid: 25006131
140. Kon A, et al. Nat. Genet. (2013) pmid: 23955599
141. Solomon DA, et al. Science (2011) pmid: 21852505
142. Shen CH, et al. Nat. Med. (2016) pmid: 27500726
143. Solomon DA, et al. BMB Rep (2014) pmid: 24856830
144. Kandoth C, et al. Nature (2013) pmid: 24132290
145. Hirai H, et al. Cancer Biol. Ther. (2010) pmid: 20107315
146. Bridges KA, et al. Clin. Cancer Res. (2011) pmid: 21799033
147. Rajeshkumar NV, et al. Clin. Cancer Res. (2011) pmid: 21389100
148. Osman AA, et al. Mol. Cancer Ther. (2015) pmid: 25504633
149. Xu L, et al. Mol. Cancer Ther. (2002) pmid: 12489850
150. Xu L, et al. Mol. Med. (2001) pmid: 11713371
151. Camp ER, et al. Cancer Gene Ther. (2013) pmid: 23470564
152. Kim SS, et al. Nanomedicine (2015) pmid: 25240597
153. Pirollo KF, et al. Mol. Ther. (2016) pmid: 27357628

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154. Hajdenberg et al., 2012; ASCO Abstract e15010
155. Leijen S, et al. J. Clin. Oncol. (2016) pmid: 27601554
156. Moore et al., 2019; ASCO Abstract 5513
157. Leijen S, et al. J. Clin. Oncol. (2016) pmid: 27998224
158. Oza et al., 2015; ASCO Abstract 5506
159. Lee J, et al. Cancer Discov (2019) pmid: 31315834
160. Méndez E, et al. Clin. Cancer Res. (2018) pmid: 29535125
161. Seligmann JF, et al. J Clin Oncol (2021) pmid: 34538072
162. Lehmann S, et al. J. Clin. Oncol. (2012) pmid: 22965953
163. Mohell N, et al. Cell Death Dis (2015) pmid: 26086967
164. Fransson Å, et al. J Ovarian Res (2016) pmid: 27179933
165. Gourley et al., 2016; ASCO Abstract 5571
166. Kwok M, et al. Blood (2016) pmid: 26563132
167. Boudny M, et al. Haematologica (2019) pmid: 30975914
168. Dillon MT, et al. Mol. Cancer Ther. (2017) pmid: 28062704
169. Middleton FK, et al. Cancers (Basel) (2018) pmid: 30127241
170. Mogi A, et al. J. Biomed. Biotechnol. (2011) pmid: 21331359
171. Tekpli X, et al. Int. J. Cancer (2013) pmid: 23011884
172. Vignot S, et al. J. Clin. Oncol. (2013) pmid: 23630207
173. Maeng CH, et al. Anticancer Res. (2013) pmid: 24222160
174. Cortot AB, et al. Clin Lung Cancer (2014) pmid: 24169260
175. Itakura M, et al. Br. J. Cancer (2013) pmid: 23922113
176. Dong ZY, et al. Clin. Cancer Res. (2017) pmid: 28039262
177. Seo JS, et al. Genome Res. (2012) pmid: 22975805
178. Joerger AC, et al. Annu. Rev. Biochem. (2008) pmid: 18410249
179. Kato S, et al. Proc. Natl. Acad. Sci. U.S.A. (2003) pmid: 12826609
180. Kamada R, et al. J. Biol. Chem. (2011) pmid: 20978130
181. Zerdoumi Y, et al. Hum. Mol. Genet. (2017) pmid: 28472496
182. Yamada H, et al. Carcinogenesis (2007) pmid: 17690113
183. Bougeard G, et al. J. Clin. Oncol. (2015) pmid: 26014290
184. Sorrell AD, et al. Mol Diagn Ther (2013) pmid: 23355100
185. Nichols KE, et al. Cancer Epidemiol. Biomarkers Prev. (2001) pmid: 11219776
186. Kleihues P, et al. Am. J. Pathol. (1997) pmid: 9006316
187. Gonzalez KD, et al. J. Clin. Oncol. (2009) pmid: 19204208
188. Lalloo F, et al. Lancet (2003) pmid: 12672316
189. Mandelker D, et al. Ann. Oncol. (2019) pmid: 31050713
190. Jaiswal S, et al. N. Engl. J. Med. (2014) pmid: 25426837
191. Genovese G, et al. N. Engl. J. Med. (2014) pmid: 25426838
192. Xie M, et al. Nat. Med. (2014) pmid: 25326804
193. Acuna-Hidalgo R, et al. Am. J. Hum. Genet. (2017) pmid: 28669404
194. Severson EA, et al. Blood (2018) pmid: 29678827
195. Fuster JJ, et al. Circ. Res. (2018) pmid: 29420212
196. Hematology Am Soc Hematol Educ Program (2018) pmid: 30504320
197. Chabon JJ, et al. Nature (2020) pmid: 32269342
198. Razavi P, et al. Nat. Med. (2019) pmid: 31768066

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