FOUNDATION MEDICINE®

Take Note of Changes to Your Report

Tumor Mutational Burden (TMB) is now reported for both FoundationOne® and FoundationOne® Heme.
Microsatellite Instability (MSI) status is now reported for FoundationOne® only.

These measures are associated with improved outcomes for immunotherapies and can help identify patients most likely to benefit from immune checkpoint inhibitors.[6-14] The information will be displayed as follows.

THERAPEUTIC IMPLICATIONS

GENOMIC FINDINGS	FDA-APPROVED THERAPIES	FDA-APPROVED THERAPIES (In Another Tumor Type)	POTENTIAL CLINICAL TRIALS
Tumor Mutation Burden TMB-Status; XX Muts/Mb	Therapy 1	Therapy 3 Therapy 4	Yes | See section
Microsatellite Status MSI-Status	Therapy 1 Therapy 2	Therapy 3 Therapy 4	Yes | See section

TMB is a quantitative genomic biomarker associated with response to immune checkpoint inhibitors[1-7]

- For solid and hematologic malignancies, TMB-High (≥20 Mutations/Mb of genome) is on the front page of the report
- For colorectal cancer, non-small cell lung cancer, melanoma, urothelial and endometrial carcinomas, all TMB statuses (High, Intermediate, Low, or Unknown) are on the front page of the report
- In all other diseases, any TMB status other than High is in the Variants of Unknown Significance (VUS) section in the appendix

MSI is a biomarker that offers prognostic and predictive insights in colorectal and endometrial cancers[6-14]

- For solid tumors, MSI-High is on the front page of the report
- For colorectal and endometrial cancers, all MSI statuses (High, Ambiguous, Stable, or Unknown) are on the front page of the report
- In all other diseases, any MSI status other than High is reported in the Variants of Unknown Significance (VUS) section in the appendix

FOUNDATIONICE

PATIENTMATCH

0 providers have seen patients with similar tumor types and alterations.

Patients are defined as similar if they have the same or related tumor type and a similar alteration in the gene of interest. This is determined by our team of scientists and medical curators.

Similar Patients by Alteration

Please log in to foundationice.com
for detailed test results.

REVIEW COMPLETE RESULTS AT
https://foundationice.com/patient-report/TRF146301

1. Rosenberg JE, et al. Lancet. 2016;387(10031):1909-20. 2. Spigel DR, et al. J Clin Oncol. 2015;33(suppl; abstr 8009). 3. Hodi FS, et al. N Engl J Med. 2010;363(13):1290. 4. Johnson DB, et al. J Clin Oncol. 2016;34(suppl; abstr). 5. Rizvi NA, et al. Science. 2015;348(6230):124-128. 6. Lochhead P, et al. J Natl Cancer Inst. 2013. doi: 10.1093/jnci/djt173. 7. Tafe LJ, et al. Mol Diagn. 2015 Sep;17(5):472-82. 8. Kocarnik JM, et al. Gastroenterol Rep. 2015;4:269-76. 9. Salipante SJ, et al. Clin Chem. 2014;60(9):1192-9. 10. You J-F, et al. Br J Cancer. 2010;103:1840-1845. 11. Bairwa NK, et al. Methods Mol Biol. 2014;1105:497-509. 12. Goldstein J, et al. Annals of Oncology. 2014;8:1643-9. 13. Lipson EJ, et al. Clin Cancer Res. 2013;19(2):462-8. 14. Le DT, et al. N Engl J Med. 2015;372:2509-20.

FOUNDATIONONE™ Heme

Patient Name	Report Date	Tumor Type
Taneja, Sanjay	**18 April 2016**	**Thymus thymoma (NOS)**

Date of Birth	08 April 1966	**Medical Facility**	Max Healthcare	**Specimen Received**	05 April 2016
Sex	Male	**Ordering Physician**	Verma, Amit	**Specimen Site**	Mediastinum
FMI Case #	TRF146301	**Additional Recipient**	Not Given	**Date of Collection**	04 February 2016
Medical Record #	Not Given	**Medical Facility ID #**	201107	**Specimen Type**	Block
Specimen ID	NN2280 1A	**Pathologist**	Not Provided		

ABOUT THE TEST:

FoundationOne Heme™ is a next-generation sequencing (NGS) based assay that identifies genomic alterations within hundreds of cancer-related genes.

PATIENT RESULTS

0 genomic alterations

0 therapies associated with potential clinical benefit

0 therapies associated with lack of response

0 clinical trials

TUMOR TYPE: THYMUS THYMOMA (NOS)

Genomic Alterations Identified†

No Reportable genomic alterations were detected

† For a complete list of the genes assayed and performance specifications, please refer to the Appendix

For more comprehensive information please log on to the Interactive Cancer Explorer™
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APPENDIX

VARIANTS OF UNKNOWN SIGNIFICANCE

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 make their significance unclear. We choose to include them here in the event that they become clinically meaningful in the future.

ARID1A
A162_A165>A

ATM
D841A

BARD1
P358_S364del

BRCA2
C3253Y

ELP2
C231Y

GPR124
A1169T

HDAC4
A446L

IKZF3
Y401C

MED12
Q2120_Q2121>HQ
QQQQ

MLL3
F320fs*12

PCLO
V3204D

SETD2
T1866A

WDR90
P609T

XBP1
M1L

ZNF703
H402_D403>PTHLG
GSSCSTCSAHD

APPENDIX

GENES ASSAYED IN FOUNDATIONONE HEME

FoundationOne Heme is designed to include all genes known to be somatically altered in human hematologic malignancies, sarcomas, and pediatric cancers 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 utilizes DNA sequencing to interrogate 405 genes as well as selected introns of 31 genes involved in rearrangements, in addition to RNA sequencing of 265 genes. 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	*ACTB*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*AMER1*	*APC*	*APH1A*	*AR*	*ARAF*	*APFRP1*	*ARHGAP26*
ARID1A	*ARID2*	*ASMTL*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*	*AURKB*	*AXIN1*	*AXL*	*B2M*	*BAP1*
BARD1	*BCL10*	*BCL11B*	*BCL2*	*BCL2L2*	*BCL6*	*BCL7A*	*BCOR*	*BCORL1*	*BIRC3*	*BLM*	*BRAF*	*BRCA1*
BRCA2	*BRD4*	*BRIP1*	*BRSK1*	*BTG2*	*BTK*	*BTLA*	*C11orf30*	*CAD*	*CARD11*	*CBFB*	*CBL*	*CCND1*
CCND2	*CCND3*	*CCNE1*	*CCT6B*	*CD22*	*CD274*	*CD36*	*CD58*	*CD70*	*CD79A*	*CD79B*	*CDC73*	*CDH1*
CDK12	*CDK4*	*CDK6*	*CDK8*	*CDKN1B*	*CDKN2A*	*CDKN2B*	*CDKN2C*	*CEBPA*	*CHD2*	*CHEK1*	*CHEK2*	*CIC*
CIITA	*CKS1B*	*CPS1*	*CREBBP*	*CRKL*	*CRLF2*	*CSF1R*	*CSF3R*	*CTCF*	*CTNNA1*	*CTNNB1*	*CUX1*	*CXCR4*
DAXX	*DDR2*	*DDX3X*	*DNM2*	*DNMT3A*	*DOT1L*	*DTX1*	*DUSP2*	*DUSP9*	*EBF1*	*ECT2L*	*EED*	*EGFR*
ELP2	*EP300*	*EPHA3*	*EPHA5*	*EPHA7*	*EPHB1*	*ERBB2*	*ERBB3*	*ERBB4*	*ERG*	*ESR1*	*ETS1*	*ETV6*
EXOSC6	*EZH2*	*FAF1*	*FAM46C*	*FANCA*	*FANCC*	*FANCD2*	*FANCE*	*FANCF*	*FANCG*	*FANCL*	*FAS*	*FBXO11*
FBXO31	*FBXW7*	*FGF10*	*FGF14*	*FGF19*	*FGF23*	*FGF3*	*FGF4*	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*	*FGFR4*
FHIT	*FLCN*	*FLT1*	*FLT3*	*FLT4*	*FLYWCH1*	*FOXL2*	*FOXO1*	*FOXO3*	*FOXP1*	*FRS2*	*GADD45B*	*GATA1*
GATA2	*GATA3*	*GID4*	*GNA11*	*GNA12*	*GNA13*	*GNAQ*	*GNAS*	*GPR124*	*GRIN2A*	*GSK3B*	*GTSE1*	*HDAC1*
HDAC4	*HDAC7*	*HGF*	*HIST1H1C*	*HIST1H1D*	*HIST1H1E*	*HIST1H2AC*	*HIST1H2AG*	*HIST1H2AL*	*HIST1H2AM*	*HIST1H2BC*	*HIST1H2BJ*	*HIST1H2BK*
HIST1H2BO	*HIST1H3B*	*HNF1A*	*HRAS*	*HSP90AA1*	*ICK*	*ID3*	*IDH1*	*IDH2*	*IGF1R*	*IKBKE*	*IKZF1*	*IKZF2*
IKZF3	*IL7R*	*INHBA*	*INPP4B*	*INPP5D*	*IRF1*	*IRF4*	*IRF8*	*IRS2*	*JAK1*	*JAK2*	*JAK3*	*JARID2*
JUN	*KAT6A*	*KDM2B*	*KDM4C*	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KIT*	*KLHL6*	*KMT2A*	*KMT2B*
KMT2C	*KRAS*	*LEF1*	*LRP1B*	*LRRK2*	*MAF*	*MAFB*	*MAGED1*	*MALT1*	*MAP2K1*	*MAP2K2*	*MAP2K4*	*MAP3K1*
MAP3K14	*MAP3K6*	*MAP3K7*	*MAPK1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*	*MEF2C*	*MEN1*	*MET*	*MIB1*
MITF	*MKI67*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH3*	*MSH6*	*MTOR*	*MUTYH*	*MYC*	*MYCL*	*MYCN*
MYD88	*MYO18A*	*NCOR2*	*NCSTN*	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOD1*	*NOTCH1*	*NOTCH2*	*NPM1*
NRAS	*NT5C2*	*NTRK1*	*NTRK2*	*NTRK3*	*NUP93*	*NUP98*	*P2RY8*	*PAG1*	*PAK3*	*PALB2*	*PASK*	*PAX5*
PBRM1	*PC*	*PCBP1*	*PCLO*	*PDCD1*	*PDCD11*	*PDCD1LG2*	*PDGFRA*	*PDGFRB*	*PDK1*	*PHF6*	*PIK3CA*	*PIK3CG*
PIK3R1	*PIK3R2*	*PIM1*	*PLCG2*	*POT1*	*PPP2R1A*	*PRDM1*	*PRKAR1A*	*PRKDC*	*PRSS8*	*PTCH1*	*PTEN*	*PTPN11*
PTPN2	*PTPN6*	*PTPRO*	*RAD21*	*RAD50*	*RAD51*	*RAF1*	*RARA*	*RASGEF1A*	*RB1*	*RELN*	*RET*	*RHOA*
RICTOR	*RNF43*	*ROS1*	*RPTOR*	*RUNX1*	*S1PR2*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SERP2*	*SETBP1*	*SETD2*
SF3B1	*SGK1*	*SMAD2*	*SMAD4*	*SMARCA1*	*SMARCA4*	*SMARCB1*	*SMC1A*	*SMC3*	*SMO*	*SOCS1*	*SOCS2*	*SOCS3*
SOX10	*SOX2*	*SPEN*	*SPOP*	*SRC*	*SRSF2*	*STAG2*	*STAT3*	*STAT4*	*STAT5A*	*STAT5B*	*STAT6*	*STK11*
SUFU	*SUZ12*	*TAF1*	*TBL1XR1*	*TCF3*	*TCL1A*	*TET2*	*TGFBR2*	*TLL2*	*TMEM30A*	*TMSB4XP8*	*TNFAIP3*	*TNFRSF11A*
TNFRSF14	*TNFRSF17*	*TOP1*	*TP53*	*TP63*	*TRAF2*	*TRAF3*	*TRAF5*	*TSC1*	*TSC2*	*TSHR*	*TUSC3*	*TYK2*
U2AF1	*U2AF2*	*VHL*	*WDR90*	*WHSC1*	*WISP3*	*WT1*	*XBP1*	*XPO1*	*YY1AP1*	*ZMYM3*	*ZNF217*	*ZNF24*
ZNF703	*ZRSR2*											

DNA Gene List: For the Detection Select Rearrangements

ALK	*BCL2*	*BCL6*	*BCR*	*BRAF*	*CCND1*	*CRLF2*	*EGFR*	*EPOR*	*ETV1*	*ETV4*	*ETV5*	*ETV6*
EWSR1	*FGFR2*	*IGH*	*IGK*	*IGL*	*JAK1*	*JAK2*	*KMT2A*	*MYC*	*NTRK1*	*PDGFRA*	*PDGFRB*	*RAF1*
RARA	*RET*	*ROS1*	*TMPRSS2*	*TRG*								

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RNA Gene List: For the Detection of Select Gene Fusions

ABI1	*ABL1*	*ABL2*	*ACSL6*	*AFF1*	*AFF4*	*ALK*	*ARHGAP26*	*ARHGEF12*	*ARID1A*	*ARNT*	*ASXL1*
ATF1	*ATG5*	*ATIC*	*BCL10*	*BCL11A*	*BCL11B*	*BCL2*	*BCL3*	*BCL6*	*BCL7A*	*BCL9*	*BCOR*
BCR	*BIRC3*	*BRAF*	*BTG1*	*CAMTA1*	*CARS*	*CBFA2T3*	*CBFB*	*CBL*	*CCND1*	*CCND2*	*CCND3*
CD274	*CDK6*	*CDX2*	*CHIC2*	*CHN1*	*CIC*	*CIITA*	*CLP1*	*CLTC*	*CLTCL1*	*CNTRL*	*COL1A1*
CREB3L1	*CREB3L2*	*CREBBP*	*CRLF2*	*CSF1*	*CTNNB1*	*DDIT3*	*DDX10*	*DDX6*	*DEK*	*DUSP22*	*EGFR*
EIF4A2	*ELF4*	*ELL*	*ELN*	*EML4*	*EP300*	*EPOR*	*EPS15*	*ERBB2*	*ERG*	*ETS1*	*ETV1*
ETV4	*ETV5*	*ETV6*	*EWSR1*	*FCGR2B*	*FCRL4*	*FEV*	*FGFR1*	*FGFR1OP*	*FGFR2*	*FGFR3*	*FLI1*
FNBP1	*FOXO1*	*FOXO3*	*FOXO4*	*FOXP1*	*FSTL3*	*FUS*	*GAS7*	*GLI1*	*GMPS*	*GPHN*	*HERPUD1*
HEY1	*HIP1*	*HIST1H4I*	*HLF*	*HMGA1*	*HMGA2*	*HOXA11*	*HOXA13*	*HOXA3*	*HOXA9*	*HOXC11*	*HOXC13*
HOXD11	*HOXD13*	*HSP90AA1*	*HSP90AB1*	*IGH*	*IGK*	*IGL*	*IKZF1*	*IL21R*	*IL3*	*IRF4*	*ITK*
JAK1	*JAK2*	*JAK3*	*JAZF1*	*KAT6A*	*KDSR*	*KIF5B*	*KMT2A*	*LASP1*	*LCP1*	*LMO1*	*LMO2*
LPP	*LYL1*	*MAF*	*MAFB*	*MALT1*	*MDS2*	*MECOM*	*MKL1*	*MLF1*	*MLLT1*	*MLLT10*	*MLLT3*
MLLT4	*MLLT6*	*MN1*	*MNX1*	*MSI2*	*MSN*	*MUC1*	*MYB*	*MYC*	*MYH11*	*MYH9*	*NACA*
NBEAP1	*NCOA2*	*NDRG1*	*NF1*	*NF2*	*NFKB2*	*NIN*	*NOTCH1*	*NPM1*	*NR4A3*	*NSD1*	*NTRK1*
NTRK2	*NTRK3*	*NUMA1*	*NUP214*	*NUP98*	*NUTM2A*	*OMD*	*P2RY8*	*PAFAH1B2*	*PAX3*	*PAX5*	*PAX7*
PBX1	*PCM1*	*PCSK7*	*PDCD1LG2*	*PDE4DIP*	*PDGFB*	*PDGFRA*	*PDGFRB*	*PER1*	*PHF1*	*PICALM*	*PIM1*
PLAG1	*PML*	*POU2AF1*	*PPP1CB*	*PRDM1*	*PRDM16*	*PRRX1*	*PSIP1*	*PTCH1*	*PTK7*	*RABEP1*	*RAF1*
RALGDS	*RAP1GDS1*	*RARA*	*RBM15*	*RET*	*RHOH*	*RNF213*	*ROS1*	*RPL22*	*RPN1*	*RUNX1*	*RUNX1T1*
RUNX2	*SEC31A*	*SEPT5*	*SEPT6*	*SEPT9*	*SET*	*SH3GL1*	*SLC1A2*	*SNX29*	*SRSF3*	*SS18*	*SSX1*
SSX2	*SSX4*	*STAT6*	*STL*	*SYK*	*TAF15*	*TAL1*	*TAL2*	*TBL1XR1*	*TCF3*	*TCL1A*	*TEC*
TET1	*TFE3*	*TFG*	*TFPT*	*TFRC*	*TLX1*	*TLX3*	*TMPRSS2*	*TNFRSF11A*	*TOP1*	*TP63*	*TPM3*
TPM4	*TRIM24*	*TRIP11*	*TTL*	*TYK2*	*USP6*	*WHSC1*	*WHSC1L1*	*YPEL5*	*ZBTB16*	*ZMYM2*	*ZNF384*
ZNF521											

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APPENDIX

FOUNDATIONONE HEME PERFORMANCE SPECIFICATIONS

SENSITIVITY	Base Substitutions at ≥5% Minor Allele Frequency	>99%
	Insertions/Deletions (1-40 base pairs) at ≥10% Minor Allele Frequency	98%
	Focal Copy Number Alterations (homozygous deletions or amplifications ≥8 copies)	>95%
	Known Gene Fusions	>95%
SPECIFICITY	Positive Predictive Value (PPV) for Base Substitutions, Insertions/Deletions, and Focal Copy Number Alterations	>99%
	Positive Predictive Value (PPV) for Known Gene Fusions	>95%
REPRODUCIBILITY	Concordance between replicates inter-batch	97%
	Concordance between replicates intra-batch	97%

Assay specifications were determined for typical median exon coverage of approximately 500X. For additional information regarding the validation of FoundationOne, please refer to the article, Frampton, GM. et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing, Nat Biotechnol (2013 Oct. 20).

For additional information specific to the performance of this specimen, please contact Foundation Medicine, Inc. at 1-888-988-3639.

APPENDIX

ABOUT FOUNDATIONONE HEME™

FoundationOne Heme™: FoundationOne Heme (the Test) was developed and its performance characteristics determined by Foundation Medicine, Inc. (Foundation Medicine). The Test has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The Test may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing.

Diagnostic Significance: FoundationOne Heme identifies alterations to select cancer-associated genes or portions of genes (biomarkers). In some cases, the Test 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 FoundationOne Heme 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 Heme for identifying a copy number amplification is five (5) for ERBB2 and six (6) for all other genes. Conversely, an alteration denoted as "loss – equivocal" implies that FoundationOne Heme data provide some, but not unambiguous, evidence for homozygous deletion of the gene in question. An alteration denoted as "subclonal" is one that FoundationOne Heme analytical methodology has identified as being present in <10% of the assayed tumor DNA.

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.

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.

Alterations and Drugs Not Presented in Ranked Order: In this Report, neither any biomarker alteration, nor any drug associated with potential clinical benefit (or potential lack of clinical benefit), are ranked in order of potential or predicted efficacy.

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 the Test.

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. These include: subclonal alterations in heterogeneous samples, low sample quality or with homozygous losses of <3 exons; and deletions and insertions >40bp, or in repetitive/high homology sequences. FoundationOne Heme is performed using DNA and RNA derived from tumor, and as such germline events may not be reported. The following targets typically have low coverage resulting in a reduction in sensitivity: *SDHD* exon 4, *TNFRSF11A* exon1, and *TP53* exon 1.

FoundationOne Heme complies with all European Union (EU) requirements of the IVD Directive 98/79EC. As such, the FoundationOne Heme Assay has been registered for CE mark by our EU Authorized Representative, Qarad b.v.b.a, Cipalstraat 3, 2440 Geel, Belgium. CE

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