TruSight™ Oncology 500 High-Throughput

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The HudsonAlpha CLINICAL SERVICES LAB

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STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
C1341	Malignant tumor of colon	GBW-022		Final

REPORT SUMMARY

Test Interpretation

A histopathological evaluation was performed on this specimen, consistent with a diagnosis of colon adenocarcinoma. Microdissection was performed for tumor-rich areas, and the subsequent material was submitted for genetic analysis.

A Comprehensive Genomic Profile (CGP) was performed, evaluating for DNA and RNA mutations in 500+ cancer-relevant genes. Patient medical records were not reviewed as part of this consultation.

The results of the test can help guide the management of this patient. First, a KRAS G12D mutation was identified. Patients with colorectal cancer and this mutation are not likely to benefit from cetuximab or panitumumab (or other EGFR inhibitors). Unfortunately, there are no good current FDA-approved therapies that have successfully targeted this driver mutation. New therapies targeting KRAS focus on a different variant, G12C, and have not shown effectiveness for this specific mutation. However, such drugs are currently in development (such as Mirati's MRTX1133).

Other relevant mutations were also identified in this patient, and worthy of discussion. A likely-damaging BRCA2 frameshift mutation was identified. Based on the allelic frequencies detected, it is possible this mutation is of germline origin. Although colorectal cancers are not commonly associated with BRCA2 mutations, this is possible. It is recommended that the patient be tested for germline presence of this mutation. Tumors with deficient DNA-repair pathways caused by BRCAness mutations are more sensitive to platinum-based therapies and PARP inhibitors, such as Olaparib. Although not FDA-approved in colorectal cancer, clinical trials are available, some listed in this report.

Other Biomarkers

BIOMARKER	LEVEL
TMB	Low
MSI	Stable

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Additionally, a TP53 mutation was identified in this case. Although not targetable, this mutation is frequently seen in many cancer types, and this variant has been associated with a worse prognosis in several tumor types.

Other variants were detected in this case, but should not be considered actionable, nor should they be further explored unless the patient exhausts all other available options.

Genomic Findings

IA	IB	IIC	IID
KRAS p.G12D c.35G>A	No variants reported.	***BRCA2*** p.N3110Kfs*2 c.9329dupA	No variants reported.
2 Clinical Trials		***TP53*** p.R282W c.844C>T	
		2 Clinical Trials	

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

VARIANT	CLINICAL IMPACT
KRAS p.G12D c.35G>A A NM_033360.2 VAF % 12.5 DEPTH 719	**Not likely to benefit from** — Panitumumab or Cetuximab *in Malignant tumor of colon*

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VARIANT CLINICAL IMPACT

INTERPRETATION

The KRAS protein has intrinsic GTPase activity and is an important mediator of growth factor receptor signaling resulting in the activation of the PI3K-mTOR and RAS-RAF-MEK pathways (RefSeq, Jul 2008). Cetuximab in combination with oxaliplatin is contraindicated per the EMA (Cetuximab, Revision 28) in metastatic colorectal cancer harboring a RAS mutation. Panitumumab in combination with oxaliplatin is contraindicated per the EMA (Panitumumab, Revision 31) in metastatic colorectal cancer harboring a RAS mutation. Some evidence indicates that advanced/metastatic colorectal adenocarcinoma harboring a KRAS mutation may not benefit from cetuximab in combination with oxaliplatin and uracil/ftorafur (UFT) following prior adjuvant chemotherapy, based on progression-free survival in a retrospective study of 21 participants aged more than or equal to 70 years (PMID: 23821376, 2013 (published 2014)). Some evidence indicates that locally advanced or metastatic colorectal adenocarcinoma harboring a KRAS codon 12 or 13 mutation may not benefit from erlotinib in combination with capecitabine based on time to progression in a retrospective study of 30 participants without prior systemic therapy (PMID: 28045335, 2017). Emerging evidence indicates that metastatic colorectal cancer harboring a KRAS mutation is not likely to benefit from aflibercept based on overall survival in a meta-analysis of 6790 participants with no prior anti-EGFR therapy (PMID: 32561975, 2020). Emerging evidence indicates that metastatic colorectal cancer harboring a KRAS mutation is not likely to benefit from bevacizumab based on overall survival in a meta-analysis of 6790 participants with no prior anti-EGFR therapy (PMID: 32561975, 2020). Colorectal cancer harboring a KRAS codon 12 or 13 mutation is deemed unlikely to respond to cetuximab per the FDA (Cetuximab, 125084s275lbl) and EMA (Cetuximab, Revision 28) and per NCCN (Colon Cancer, 2.2021; Rectal Cancer, 1.2021), ASCO (PMID: 28165299, 2017), and ESMO (PMID: 27380959, 2016) guidelines, either alone or in combination with other anti-cancer agents. Colorectal cancer harboring a KRAS codon 12 or 13 mutation is deemed unlikely to respond to panitumumab per the FDA (Panitumumab, 125147s207lbl) and EMA (Panitumumab, Revision 31) and per NCCN (Colon Cancer, 2.2021; Rectal Cancer, 1.2021), ASCO (PMID: 28165299, 2017), and ESMO (PMID: 27380959, 2016) guidelines, either alone or in combination with other anti-cancer agents. Emerging evidence indicates that metastatic colorectal cancer harboring a

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VARIANT	CLINICAL IMPACT
	INTERPRETATION
	KRAS mutation is not likely to benefit from ramucirumab based on overall survival in a meta-analysis of 6790 participants with no prior anti-EGFR therapy (PMID: 32561975, 2020). Emerging evidence indicates that metastatic colorectal cancer harboring a KRAS mutation is not likely to benefit from regorafenib based on overall survival in a meta-analysis of 6790 participants with no prior anti-EGFR therapy (PMID: 32561975, 2020). Emerging evidence suggests that colorectal adenocarcinoma harboring a KRAS codon 12 or 13 mutation is associated with an unfavorable prognosis based on: a) overall survival in a study of 1762 participants with advanced disease following chemotherapy (PMID: 27815357, 2020); and b) disease-free survival in a prospective study of 139 participants with liver metastases following resection without targeted therapy (PMID: 31949686, 2018).

Tier II - Potential Clinical Significance

VARIANT	CLINICAL IMPACT
BRCA2 p.N3110Kfs*2 c.9329dupA C NM_000059.3 **VAF** % 39.4 **DEPTH** 777	**May benefit from** — Bevacizumab + Olaparib, Rucaparib, or Niraparib *in Malignant tumor of fallopian tube, Malignant epithelial tumor of ovary, or Primary malignant neoplasm of the peritoneum* — Cisplatin + Gemcitabine or Fluorouracil + Oxaliplatin + Irinotecan + Leucovorin *in Adenocarcinoma of pancreas* — Rucaparib *in Malignant tumor of prostate, Hormone refractory prostate cancer, Endometrioid carcinoma ovary, Primary malignant clear cell tumor of ovary, Malignant tumor of ovary, Adenocarcinoma of prostate, or Carcinosarcoma of ovary* — Olaparib *in Human epidermal growth factor 2 negative carcinoma of breast, Hormone refractory prostate cancer, Invasive micropapillary carcinoma of breast, Mixed ductal and lobular carcinoma of breast, Primary malignant clear cell tumor of ovary, Adenocarcinoma of prostate, Malignant epithelial tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of prostate, Malignant tumor of breast, Adenocarcinoma of pancreas, Infiltrating duct carcinoma of breast, Malignant tumor of fallopian tube, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Inflammatory carcinoma*

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VARIANT | CLINICAL IMPACT

of breast, Infiltrating carcinoma with ductal and lobular features, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, or Primary malignant neoplasm of the peritoneum

Unfavorable Prognosis in

— Malignant tumor of prostate, Primary malignant neoplasm of prostate, Small cell carcinoma of prostate, Adenocarcinoma of prostate, Carcinoma of prostate, or Squamous cell carcinoma of prostate

INTERPRETATION

BRCA2 is a tumor suppressor gene that is involved in DNA repair pathways and in the maintenance of genome stability (RefSeq, Dec 2008). The following associations with this genomic finding are from other tumor type contexts: Olaparib in combination with bevacizumab-awwb is NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in fallopian tube cancer harboring a BRCA2 mutation as maintenance therapy following partial or complete response to primary therapy including bevacizumab. Olaparib in combination with bevacizumab-awwb is NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in malignant epithelial ovarian cancer harboring a BRCA2 mutation as maintenance therapy in response to primary therapy with bevacizumab. Olaparib in combination with bevacizumab-awwb is NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in primary peritoneal cancer harboring a BRCA2 mutation as maintenance therapy following some response to primary therapy including bevacizumab. Olaparib in combination with bevacizumab-bvzr is NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in fallopian tube cancer harboring a BRCA2 mutation as maintenance therapy following partial or complete response to primary therapy including bevacizumab. Olaparib in combination with bevacizumab-bvzr is NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in malignant epithelial ovarian cancer harboring a BRCA2 mutation as maintenance therapy in response to primary therapy with bevacizumab. Olaparib in combination with bevacizumab-bvzr is NCCN (Ovarian Cancer Including Fallopian Tube Cancer

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VARIANT	CLINICAL IMPACT

INTERPRETATION

and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in primary peritoneal cancer harboring a BRCA2 mutation as maintenance therapy following some response to primary therapy including bevacizumab. Olaparib in combination with bevacizumab is FDA (Olaparib, 208558s019s020lbl) and EMA (Olaparib, Revision 12) approved and NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in adults with homologous recombination deficiency (HRD)-positive advanced epithelial ovarian cancer harboring a BRCA2 mutation as maintenance therapy following some response to platinum-based first-line chemotherapy. Olaparib in combination with bevacizumab is FDA (Olaparib, 208558s019s020lbl) and EMA (Olaparib, Revision 12) approved and NCCN (Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, 1.2021) guideline recommended for use in adults with homologous recombination deficiency (HRD)-positive advanced primary peritoneal cancer harboring a BRCA2 mutation as maintenance therapy following some response to platinum-based first-line chemotherapy.

TP53

p.R282W
c.844C>T

C

NM_000546.5
VAF % 25.3
DEPTH 859

Unfavorable Prognosis in

— Essential thrombocythemia, Myelodysplastic syndrome (clinical), Medulloblastoma, Acute myeloid leukemia, Acute myeloid leukemia, disease, Myelosclerosis with myeloid metaplasia, Myeloproliferative disorder, Myeloproliferative neoplasm, or Myelodysplastic syndrome

INTERPRETATION

TP53 is a tumor suppressor and regulates expression of target genes by inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism (PMID: 22294769, 2012; 20182602, 2010). Some evidence indicates that metastatic colorectal cancer harboring a TP53 mutation may benefit from panitumumab in combination with oxaliplatin and capecitabine based on objective response rate and progression-free survival in a multicenter phase II clinical trial of 62 participants without prior treatment (PMID: 29855806, 2018). The following associations with this genomic finding are from

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VARIANT	CLINICAL IMPACT
	INTERPRETATION
	other tumor type contexts: TP53 mutations are associated with an unfavorable prognosis in SHH-activated medulloblastoma per NCCN (Central Nervous System Cancers, 3.2020) guidelines.

Other Biomarkers

BIOMARKER	CLINICAL IMPACT
TMB Low 6.3 muts/Mb	**Not likely to benefit from** — Immunotherapies *in Colorectal cancer* INTERPRETATION
MSI Stable 4.0% Unstable Sites	INTERPRETATION

POTENTIAL CLINICAL TRIALS

Clinical Trials associated with this patient's genomic profile and tumor type are displayed below.

TITLE	TRIAL IDENTIFIER	PHASE	VARIANT
Study of Olaparib (MK-7339) in Combination With Pembrolizumab (MK-3475) in the Treatment of Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer (MK-7339-007/KEYLYNK-007)	**NCT04123366** https://clinicaltrials.gov/show/NCT04123366	II	***BRCA2*** p.N3110Kfs*2 c.9329dupA

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TITLE	TRIAL IDENTIFIER	PHASE	VARIANT
TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer	**NCT02693535** https://clinicaltrials.gov/show/NCT02693535	II	***BRCA2*** p.N3110Kfs*2 c.9329dupA
A Study of a Personalized Cancer Vaccine Targeting Shared Neoantigens	**NCT03953235** https://clinicaltrials.gov/show/NCT03953235	I/II	***KRAS*** p.G12D c.35G>A
Dose-Escalation/Expansion of RMC-4630 and Cobimetinib in Relapsed/Refractory Solid Tumors and RMC-4630 and Osimertinib in EGFR Positive Locally Advanced/Metastatic NSCLC	**NCT03989115** https://clinicaltrials.gov/show/NCT03989115	I/II	***KRAS*** p.G12D c.35G>A

TIER III - VARIANTS OF UNCERTAIN SIGNIFICANCE

BIRC3 p.N130T NM_001165.4 c.389A>C VAF 52.3 %	***BMPR1A*** p.R228* NM_004329.2 c.682C>T VAF 10 %	***BMPR1A*** p.H360Q NM_004329.2 c.1080T>A VAF 23.4 %	***BRD4*** NM_058243.2 c.2158+481G>T VAF 42.4 %	***CBL*** p.R787H NM_005188.3 c.2360G>A VAF 49 %	***CSF3R*** p.(=) NM_156039.3 c.2199G>A VAF 12.9 %	***EPHA3*** p.K207T NM_005233.5 c.620A>C VAF 6.2 %
KDR p.S265L NM_002253.2 c.794C>T VAF 17.7 %	***MGA*** p.D2317N NM_001164273.1 c.6949G>A VAF 26.9 %	***PIK3CA*** p.V105_N107del NM_006218.2 c.312_320del9 VAF 4.9 %	***PIK3R1*** p.E451D NM_181523.2 c.1353A>C VAF 44.9 %	***PLCG2*** p.S162T NM_002661.3 c.485G>C VAF 44.5 %	***PREX2*** p.R155Q NM_024870.2 c.464G>A VAF 6.5 %	
RANBP2 p.A994T NM_006267.4 c.2980G>A VAF 43.3 %	***ZFHX3*** p.E3423D NM_006885.3 c.10269A>C VAF 8.4 %					

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CLASSIFICATION AND LEVELS OF EVIDENCE

The variant classification system used in this report is based on joint consensus recommendations of the Association for Molecular Pathology, American Society of Clinical Oncology, and the College of American Pathologists (J Mol Diagn 2017, 19:4-23). Tiers IA, IB, IIC, IID, III and IV describe variant categories of descending clinical significance in the patient. Variants in Tier IV are not reported in accordance with the consensus recommendations.

IA	IB	IIC	IID
Variant of strong clinical significance, Level A evidence (FDA approved therapy or practice guideline in patient's tumor type)	Variant of strong clinical significance, Level B Evidence (consensus in the field based on well-powered studies in patient's tumor type)	Variant of potential clinical significance, Level C evidence (FDA approved therapy or practice guideline in other tumor type(s), evidence from multiple small published studies, or based on availability of investigational therapies)	Variant of potential clinical significance, Level D evidence (case reports or preclinical studies)

III	Variant of uncertain clinical significance
IV	Benign or likely benign variant

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TEST DETAILS

REPORTED GENES

A total of 523 genes were subjected to targeted next generation sequencing analysis. Details available upon request.

CGW VERSION

CGW_v6.14

DATABASE DETAILS

The versions, releases, builds, dates of the following databases were used to generate this report.

- Genomic Build: GRCh37.p13
- Genomic Annotation Sources: NCBI RefSeq v105
- ExAC: v1.0
- gnomAD: r2.1
- dbSNP: 149
- dbNSFP: 3.5c
- NHLBI ESP: v.0.0.30
- COSMIC: v92
- ClinVar: 20190603

CODING EXON COVERAGE METRICS

Level 2: 100x coverage for > 50% of positions was not achieved for the targeted exon regions listed below:

Gene	Transcript ID (Exon/Intron('))			
TCEB1	***ANKRD26***	***SETD2***	***DNMT1***	***INSR***
NM_005648.3 (2)	NM_014915.2 (19)	NM_014159.6 (13)	NM_001130823.1 (5)	NM_000208.2 (1)
TGFBR1	***PTPRS***	***HGF***	***PTPRT***	***MRE11A***
NM_004612.2 (1)	NM_002850.3 (15)	NM_000601.4 (12)	NM_007050.5 (1)	NM_005591.3 (20)

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KDM6A NM_021140.2 (9)	***KIF5B*** NM_004521.2 (5)	***KMT2B*** NM_014727.1 (1)	***BBC3*** NM_014417.4 (2)	***XIAP*** NM_001167.3 (4)
XIAP NM_001167.3 (5)	***RB1*** NM_000321.2 (15)	***XPO1*** NM_003400.3 (6)	***PIK3R2*** NM_005027.3 (6)	***MAGI2*** NM_012301.3 (22)
MALT1 NM_006785.3 (1)	***MALT1*** NM_006785.3 (8)	***NOTCH3*** NM_000435.2 (24)	***NOTCH3*** NM_000435.2 (1)	

PERTINENT NEGATIVES

Pertinent negatives were not reported for this case.

METHODOLOGY

Pathology Assessment: Pathologist reviews on H&E stained section of the tissue block or stained cytology slide were considered to assess adequacy and, as needed, guide enrichment of tumor for sequencing analysis. The in-house validation ensured that the samples passed all established laboratory QC metrics. This excludes exons, within the specified transcripts of the genes and listed in the Coding Exon Coverage Metrics section above, for which variants may not have been reliably detected.

Assay Methods: The test was performed using the Illumina TruSight™ Oncology 500 (TSO500) targeted hybrid-capture based next generation sequencing assay. It employs Unique molecular identifiers (UMI) to enable detection of variants, present in formalin-fixed paraffin-embedded (FFPE) tumor samples, at low VAFs with a high degree of sensitivity and specificity. TSO500 is designed to detect multiple classes of mutations including single-nucleotide variants (SNVs), multi-nucleotide variants (<3bp), small Insertions (1-18bp)/Deletions (1-27bp) and Copy Number Variants (CNVs). The assay also detects, quantitatively, microsatellite instability (MSI) and tumor mutational burden (TMB). Fusions and splice variants are detected in RNA. DNA and RNA are extracted from the same FFPE tissue using the Allprep DNA/RNA FFPE Kit (Qiagen, Inc.). RNA is then reverse transcribed to cDNA. The genomic DNA and cDNA are sheared to prepare sequencing libraries. The regions of interest are hybridized to biotinylated probes, magnetically pulled down with streptavidin-coated beads, and eluted to enrich the library pool. Finally, libraries are normalized using a simple bead-based protocol, then pooled and sequenced on an Illumina NovaSeq 6000 instrument.

Secondary Analysis Methods: The DNA and RNA data is analyzed using the Illumina Software TSO500 v2.2 Local App and a customized analysis pipeline within the Clinical Genomics Workspace software platform from PierianDx.

Variant Calling: Variants are reported according to HGVS nomenclature (www.hgvs.org/mutnomen) and classified as per the AMP classification system into tiers IA, IB, IIC, IID, III and IV. These tiers are stratified by clinical utility ('actionability' for clinical decision-making as to diagnosis, prognosis, treatment options, and carrier status) and previously reported data in

the medical literature. Variations found in gnomAD (https://gnomad.broadinstitute.org/) that have ≥1% minor allele frequency (except those that are also in ClinVar denoted as clinically relevant, used in a clinical diagnostic assay, or reported as a mutation in a publication) are classified as known polymorphisms.
Exons from some transcripts included in the RefSeq annotation release v105 found in genes reported in certain gene subsets of this test are not targeted by the assay. The untargeted exons are disclaimed and are identified as follows: *HIST2H3A* NM_001005464.2 exon 1, *HIST2H3C* NM_021059.2 exon 1, *MYB* NM_001130173.1 exon 1, *PAX8* NM_003466.3 exon 8, *PDPK1* NM_002613.4 exon 3, *PDPK1* NM_002613.4 exon 8, *PDPK1* NM_002613.4 exon 1, *PDPK1* NM_002613.4 exon 6, *PDPK1* NM_002613.4 exon 4, *PDPK1* NM_002613.4 exon 5, *PDPK1* NM_002613.4 exon 9, *PDPK1* NM_002613.4 exon 10, *RANBP2* NM_006267.4 exon 13, *RANBP2* NM_006267.4 exon 8, *REL* NM_002908.2 exon 9, *SUZ12* NM_015355.2 exon 3, *FGF8* NM_033164.3 exon 1, *RECQL4* NM_004260.3 exon 1, *ICOSLG* NM_015259.4 exon 1, *NOTCH1* NM_017617.3 exon 1.
Additionally, all small variant calls in the *HLA-A*, *KMT2B*, *KMT2C*, and *KMT2D* genes are filtered out due to potential mis-mapping as a result of sequence homology with other genomic regions.

Notes:

- This assay does not detect complex structural alterations or indels, with the exception of a subset of clinically relevant complex EGFR exon 19 indels that are specifically targeted. Variants located outside of targeted regions too will not be detected.
- It is possible that pathogenic variants may not be reported by one or more of the tools because of the parameters used. However, tool parameters were optimized to maximize specificity and sensitivity.

DISCLAIMER

This Report was generated using the materials and methods described above, which required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and/or other items may compromise the quality or accuracy of the Report.

The Report has been created based on, or incorporates references to, various scientific manuscripts, references, and other sources of information, including without limitation manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. PierianDx makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information provided by or contained in such manuscripts, references, and other sources of information. If any of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the Report may be adversely impacted. PierianDx is not obligated to notify you of any impact that future scientific or medical research findings may have on the Report.

The Report must always be interpreted and considered within the clinical context, and a physician should always consider the Report along with all other pertinent information and data that a physician would prudently consider prior to providing a diagnosis to a patient or developing and implementing a plan of care for a patient. The Report should never be considered or relied upon alone in making any diagnosis or prognosis. The manifestation of many diseases are caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene

variants may not have been considered in the Report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environmental factors, and other variables that are not addressed by the Report (or that are otherwise unknown). This Report is based on a next generation sequencing assay which does not distinguish between somatic and germline variants. If a germline variant is in question, further testing may be recommended. As such, the relevance of the Report should be interpreted in the context of a patient's clinical manifestations. The Report provided by PierianDx is provided on an "AS IS" basis. PierianDx makes no representation or warranty of any kind, expressed or implied, regarding the Report. In no event shall PierianDx be liable for any actual damages, indirect damages, and/or special or consequential damages arising out of or in any way connected with the Report, your use of the Report, your reliance on the Report, or any defect or inaccurate information included within the Report.

Medical knowledge annotation is constantly updated and reflects the current knowledge at the time.

The test performance characteristics were determined by the PierianDx Molecular Laboratory. The Report was generated by the PierianDx Molecular Laboratory as required by the CLIA 1988 regulations. The Report, and the tests used to generate the Report, have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The test results have been shown to be clinically useful. This laboratory is CLIA certified to perform high complexity testing.

REFERENCES

PMID **22294769**: (Naccarati A, *et al.*; Mutations and polymorphisms in TP53 gene--an overview on the role in colorectal cancer.; Mutagenesis; 2012 Mar;27(2):211-8)

PMID **23821376**: (Di Bartolomeo M, *et al.*; Lack of KRAS, NRAS, BRAF and TP53 mutations improves outcome of elderly metastatic colorectal cancer patients treated with cetuximab, oxaliplatin and UFT.; Target Oncol; 2014 Jun;9(2):155-62)

PMID **27380959**: (Van Cutsem E, *et al.*; ESMO consensus guidelines for the management of patients with metastatic colorectal cancer.; Ann Oncol; 2016 Aug;27(8):1386-422)

PMID **27815357**: (Summers MG, *et al.*; *BRAF* and *NRAS* Locus-Specific Variants Have Different Outcomes on Survival to Colorectal Cancer.; Clin Cancer Res; 2017 Jun 1;23(11):2742-2749)

PMID **28045335**: (Vincent MD, *et al.*; Phase II trial of capecitabine plus erlotinib versus capecitabine alone in patients with advanced colorectal cancer.; Future Oncol; 2017 Apr;13(9):777-786)

PMID **28165299**: (Sepulveda AR, *et al.*; Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline From the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology.; J Clin Oncol; 2017 May 1;35(13):1453-1486)

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PMID **29855806**: (Papaxoinis G, *et al.*; Phase II study of panitumumab combined with capecitabine and oxaliplatin as first-line treatment in metastatic colorectal cancer patients: clinical results including extended tumor genotyping.; Med Oncol; 2018 May 31;35(7):101)

PMID **31949686**: (Lin Q, *et al.*; Prognostic impact of *KRAS* and *BRAF* mutations in patients who underwent simultaneous resection for initially resectable colorectal liver metastases.; Int J Clin Exp Pathol; 2018;11(12): 5981-5991)

PMID **32561975**: (Stahler A, *et al.*; Current treatment options in RAS mutant metastatic colorectal cancer patients: a meta-analysis of 14 randomized phase III trials.; J Cancer Res Clin Oncol; 2020 Aug;146(8):2077-2087)

PATIENT AND ORDER DETAILS

PATIENT

SEX

ETHNICITY

SPECIMEN

EXT. SPECIMEN ID

SPECIMEN TYPE

Formalin-fixed paraffin-embedded tissue specimen

DATE COLLECTED

05/01/2021

DATE RECEIVED

05/01/2021

CASE

ACCESSION NUMBER

GBW-022_C1341-KW-D0268-R0244

DATE ACCESSIONED

05/01/2021 08:00

DATE REPORTED

REVIEW STATUS

Final