BAYLOR GENETICS

ClariFind
ClariFind Comprehensive DNA Panel

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2450 Holcombe Blvd, Houston TX 77021

Patient Name:		Test Code:	20010	Physician Name:	
Date of Birth:		Date Collected:	03/27/2018	Facility:	
Sex:	F	Date Received:	04/26/2018	Location:	
Medical Record #:		Date Ordered:	04/30/2018	Phone:	
Accession #:		Date Reported:	05/14/2018	Fax:	
Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

RESULTS SUMMARY

Significant Genomic Alterations	Associated Targeted Therapies	Potential Clinical Trials
ATM Equivocal Copy Loss AMP Tier II (Potential Clinical Significance)	Niraparib FDA APPROVED OFF-LABEL Olaparib FDA APPROVED OFF-LABEL Rucaparib FDA APPROVED OFF-LABEL	☑ Trial Enrollment Available
GATA3 p.Ser438AlafsTer38 AMP Tier II (Potential Clinical Significance)	No Therapies for This Alteration	No Trials for This Alteration
RB1 Equivocal Copy Loss AMP Tier II (Potential Clinical Significance)	LY2606368 INVESTIGATIONAL *Therapies Associated with Decreased Response or Resistance: Abemaciclib, Palbociclib, Ribociclib*	☑ Trial Enrollment Available
TP53 Equivocal Copy Loss AMP Tier II (Potential Clinical Significance)	No Therapies for This Alteration	No Trials for This Alteration
ERBB2 Wild Type	*Therapies Associated with Decreased Response or Resistance: Pertuzumab, Trastuzumab, Trastuzumab Emtansine*	No Trials for This Alteration

INTERPRETATION

We were requested to perform next-generation sequencing analysis as part of the Baylor Genetics ClariFind Comprehensive DNA Panel on the tissue sample of this individual using the techniques described in the Test Methodology section of this report. Our next-generation sequencing analysis identified several clinically significant alterations as listed above for which there are associated targeted therapies and which may help satisfy eligibility criteria for clinical trials.

GATA3 is one of the most frequently mutated genes in breast cancer. Heterozygous mutations, mostly frameshifts, are seen in ~15% of estrogen receptor-positive breast cancers, the subtype in which these mutations are almost exclusively found [PMID: 29535312]. The GATA3 S438fs mutation is a frameshift mutation located in exon 6; however, this particular mutation has not been previously report to our knowledge. Most GATA3 mutations (66/99; 67%) in the TCGA dataset are heterozygous frameshift mutations in exons 5 and 6. Frameshifts in general lead to premature stop codons, which can substantially disrupt protein function. Approximately 41% (27/66) of the frameshift mutations in GATA3 are predicted to result in an early stop codon [PMID: 27251275]. Splice site and truncation mutations (found in exons 5-6) are frequently detected in luminal A tumors, and these patients are reported to have better prognosis than those with wild-type GATA3 [PMID: 29535312].

Next-generation sequencing-based copy number analysis of 39 reportable genes also detected equivocal copy number losses in ATM, RB1, and TP53. Notably, no significant copy number alteration was detected for the ERBB2 (HER2) gene. Please note, corresponding HER2 FISH analysis performed at Baylor Genetics was negative for HER2 amplification (see separate report, lab number 270891).

ATM loss in breast cancer is a well-documented event, and many groups have brought evidence of ATM loss in breast cancer and shed light on its prognostic significance, particularly as a poor prognostic indicator [PMID: 9766563; 15138484; 17366603; 17982490; 21850541; 23117476; 24285016; 25425972]. PARP inhibitor therapy has been under investigation for ATM-deficient breast cancer [PMID: 27413114; 24252502; 27613518]. However, please note that RB1 copy number loss was also detected in the patient's sample, which may be predictive of a lack of response to PARP inhibitors such as palbociclib (see below).

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RB has been reported to be aberrant in approximately 20%-35% of breast cancers [PMID: 7786597; 10516854], and aberrant RB has been associated with poor disease outcome. Additionally, loss of heterozygosity or other alterations at the RB1 locus are routinely observed in primary breast cancer specimens [PMID: 12068296; 1581913; 10193322; 16620391]. CDK4/6 inhibitors halter the phosphorylation of RB, which is dependent on an active RB protein [PMID: 28438180]. Preclinical models with palbociclib and abemaciclib showed that only RB-proficient cells responded to treatment, and cell lines with increased RB expression showed increased sensitivity [PMID: 28848657]. Loss of RB function has been demonstrated as a mechanism for palbociclib resistance [PMID: 28203301].

p53 loss results in the disruption of pathways that inhibit metastasis, and transcriptionally defective mutants are known to gain additional functions that promote metastasis [PMID: 24658082]. In ER-positive tumors, wild-type TP53 has been associated with better prognosis; in contrast, aberrant TP53 has been associated with a protective effect for ER-negative tumors [PMID: 28427202].

Of note, in-vivo studies have demonstrated that simultaneous inactivation of the p53 and RB pathways predict resistance to DNA damaging drugs [PMID: 26004085]; however, some other groups have reported that in p53-deficient settings, suppression of ATM dramatically sensitizes tumors to DNA-damaging chemotherapy [PMID: 19608766].

Further next-generation sequencing-based copy number analysis appears to show segmental losses involving chromosomes 2, 3, 5, 6, and 7, along with losses of chromosome 11 (which contains the ATM gene) and chromosome 13 (which contains the RB1 and FLT3 genes). For more detailed copy number analysis of the patient's tissue sample, chromosomal microarray analysis (180k CGH/SNP Array, test code 9505) may be considered if clinically warranted.

Additional genomic alterations of uncertain clinical significance were identified in this case, including alterations which are novel/rare or may be germline in origin. A full list of these alterations is provided with this report.

Alterations classified as benign or likely benign based on current knowledge are not reported but are available upon request.

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SIGNIFICANT GENOMIC ALTERATIONS

Alterations	Interpretation
ATM Equivocal Copy Loss	**AMP Tier:** II (Potential Clinical Significance) **Type of Evidence:** Therapeutic; Prognostic **Evidence-Based Variant Categorization:** Level C: FDA-approved therapies for different tumor types or investigational therapies; multiple small published studies with some consensus ATM serine/threonine kinase (ATM) is a gene that encodes a protein that is a member of the PI3/PI4-kinase family. The protein functions as a cell cycle checkpoint kinase and regulates multiple downstream effectors. Missense mutations, nonsense mutations, silent mutations, whole gene deletions, frameshift deletions and insertions, and in-frame deletions and insertions are observed in cancers such as endometrial cancer, intestinal cancer, and stomach cancer. ATM loss in breast cancer is a well-documented event, and many groups have brought evidence of ATM loss in malignant breast cancer and shed light on its prognostic significance, particularly as a poor prognostic indicator [PMID: 9766563; 15138484; 17366603; 17982490; 21850541; 23117476; 24285016; 25425972]. Targeted Treatment: PARP inhibitor therapy has been under investigation for ATM-deficient breast cancer [PMID: 27413114; 24252502; 27613518].

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Alterations	Interpretation
GATA3 **p.Ser438AlafsTer38**	**AMP Tier:** II (Potential Clinical Significance) **Type of Evidence:** Prognostic **Evidence-Based Variant Categorization:** Level C: FDA-approved therapies for different tumor types or investigational therapies; multiple small published studies with some consensus GATA binding protein 3 (GATA3) is a gene that encodes a transcription factor protein that contains two zinc fingers. The protein functions in immune regulation by regulating T-cell development. Missense mutations, nonsense mutations, silent mutations, frameshift insertions and deletions, and in-frame insertions and deletions are observed in cancers such as biliary tract cancer, breast cancer, and intestinal cancer. GATA3 is one of the most frequently mutated genes in breast cancer. Heterozygous mutations, mostly frameshifts, are seen in ~15% of estrogen receptor-positive breast cancers, the subtype in which these mutations are almost exclusively found. Human patient data have shown that high GATA3 expression, a feature of luminal subtype breast cancers, is associated with a better prognosis [PMID: 29262572]. The expression level of GATA3 is strongly associated with estrogen receptor alpha (ERa), and loss of GATA3 expression is associated with poor prognosis [PMID: 29535312]. The GATA3 S438fs mutation is a frameshift mutation located in exon 6; however, this particular mutation has not been previously reported to our knowledge. Most GATA3 mutations (66/99; 67%) in the TCGA dataset are heterozygous frameshift mutations in exons 5 and 6. Frameshifts in general lead to premature stop codons, which can substantially disrupt protein function. Approximately 41% (27/66) of the frameshift mutations in GATA3 are predicted to result in an early stop codon [PMID: 27251275]. Splice site and truncation mutations (found in exons 5-6) are frequently detected in luminal A tumors, and these patients are reported to have better prognosis than those with wild-type GATA3 [PMID: 29535312].

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Alterations	Interpretation
RB1 Equivocal Copy Loss	**AMP Tier:** II (Potential Clinical Significance) **Type of Evidence:** Therapeutic; Prognostic **Evidence-Based Variant Categorization:** Level C: FDA-approved therapies for different tumor types or investigational therapies; multiple small published studies with some consensus Retinoblastoma 1 (RB1) is a gene that encodes a protein that is a negative regulator of the cell cycle as well as a tumor suppressor. Missense mutations, nonsense mutations, silent mutations, frameshift deletions and insertions, and in-frame deletions are observed in cancers such as cancers of the fallopian tubes, cancers of the eye, and intestinal cancer. The retinoblastoma tumor suppressor (RB) protein is functionally inactivated in the majority of human cancers and is aberrant in one-third of all breast cancers. RB regulates G(1)/S-phase cell-cycle progression and is a critical mediator of antiproliferative signaling [PMID: 17160137]. RB has been reported to be aberrant in approximately 20%-35% of breast cancers [PMID: 7786597; 10516854], and aberrant RB has been associated with poor disease outcome. Additionally, loss of heterozygosity or other alterations at the RB1 locus are routinely observed in primary breast cancer specimens [PMID: 12068296; 1581913; 10193322; 16620391]. Targeted Treatment: CDK4/6 inhibitors halter the phosphorylation of RB, which is dependent on an active RB protein [PMID: 28438180]. Preclinical models with palbociclib and abemaciclib showed that only RB-proficient cells responded to treatment, and cell lines with increased RB expression showed increased sensitivity [PMID: 28848657]. Loss of RB function has been demonstrated as a mechanism for palbociclib resistance [PMID: 28203301].

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Alterations	Interpretation
TP53 Equivocal Copy Loss	**AMP Tier:** II (Potential Clinical Significance) **Type of Evidence:** Prognostic **Evidence-Based Variant Categorization:** Level C: FDA-approved therapies for different tumor types or investigational therapies; multiple small published studies with some consensus Tumor protein p53 (TP53) is a gene that codes for a tumor suppressor protein. The protein regulates expression of genes involved in cell cycle arrest, apoptosis, senescence, DNA repair, and changes in metabolism [https://www.ncbi.nlm.nih.gov/gene/7157]. In cancer, its normal roles are not fulfilled, leading to cell survival, DNA damage, and cell proliferation. TP53 is the most frequently mutated gene in cancer; it is mutated in about half of all cancers [https://ghr.nlm.nih.gov/gene/TP53]. TP53 is most frequently mutated in ovarian, colon, and esophageal cancers, although it is significantly mutated in many other cancer types [http://cancer.sanger.ac.uk/cosmic/gene/analysis?ln=TP53]. p53 loss not only prevents incipient tumor cells from undergoing oncogene-induced senescence and apoptosis, but it also perturbs cell-cycle check points. This enables p53-deficient tumor cells with DNA damage to continue cycling, creating a permissive environment for the acquisition of additional mutations. Theoretically, this could contribute to the evolution of a cancer genome that is conducive to metastasis. Importantly, p53 loss also results in the disruption of pathways that inhibit metastasis, and transcriptionally defective mutants are known to gain additional functions that promote metastasis [PMID: 24658082]. In ER-positive tumors, wild-type TP53 has been associated with better prognosis; in contrast, aberrant TP53 has been associated with a protective effect for ER-negative tumors [PMID: 28427202].

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ASSOCIATED TARGETED THERAPIES

Drug	Summary
Niraparib *Zejula* For ATM Equivocal Copy Loss	**Evidence-Based Therapeutic Categorization in This Patient:** FDA Approved; Off-Label Use **Description:** Niraparib is an orally active PARP inhibitor developed by Tesaro to treat ovarian cancer. FDA approval on March 2017. **Indication:** Niraparib is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy. **Mechanism of Action:** Niraparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, PARP-1 and PARP-2, which play a role in DNA repair. In vitro studies have shown that niraparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis and cell death. Increased niraparib-induced cytotoxicity was observed in tumor cell lines with or without deficiencies in BRCA1/2. Niraparib decreased tumor growth in mouse xenograft models of human cancer cell lines with deficiencies in BRCA1/2 and in human patient-derived xenograft tumor models with homologous recombination deficiency that had either mutated or wild type BRCA1/2. **Targets:** Poly ADP-ribose polymerase 1, Poly ADP-ribose polymerase 2
Olaparib *Lynparza* For ATM Equivocal Copy Loss	**Evidence-Based Therapeutic Categorization in This Patient:** FDA Approved; Off-Label Use **Description:** Lynparza is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair. Olaparib has been shown to inhibit growth of select tumor cell lines in vitro and decrease tumor growth in mouse xenograft models of human cancer both as monotherapy or following platinum-based chemotherapy. Increased cytotoxicity and anti-tumor activity following treatment with olaparib were noted in cell lines and mouse tumor models with deficiencies in BRCA. In vitro studies have shown that olaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complex, resulting in disruption of cellular homeostasis and cell death. **Indication:** Olaparib is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated as monotherapy in patients with deleterious or suspected deleterious germline BRCA mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. **Mechanism of Action:** Olaparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair. Olaparib has been shown to inhibit growth of select tumor cell lines in vitro and decrease tumor growth in mouse xenograft models of human cancer both as monotherapy or following platinum-based chemotherapy. Increased cytotoxicity and anti-tumor activity following treatment with olaparib were noted in cell lines and mouse tumor models with deficiencies in BRCA. In vitro studies have shown that olaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complex, resulting in disruption of cellular homeostasis and cell death. **Targets:** Poly ADP-ribose polymerase 1, Poly ADP-ribose polymerase 2, Poly ADP-ribose polymerase 3

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Drug	Summary
Rucaparib *Rubraca* For ATM Equivocal Copy Loss	**Evidence-Based Therapeutic Categorization in This Patient:** FDA Approved; Off-Label Use **Description:** Rucaparib is a poly (ADP-ribose) polymerase (PARP) inhibitor approved (accelerated) in December 2016 for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. **Indication:** Treatment of ovarian cancer, specifically those with alterations in BRCA1 and BRCA2 genes in the tumor tissue of ovarian cancer. **Mechanism of Action:** Rucaparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3, which play a role in DNA repair. In vitro studies have shown that rucaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. Increased rucaparib-induced cytotoxicity was observed in tumor cell lines with deficiencies in BRCA1/2 and other DNA repair genes. Rucaparib has been shown to decrease tumor growth in mouse xenograft models of human cancer with or without deficiencies in BRCA. Rucaparib sensitizes cancer cells to X-radiation or (131)I-meta-iodobenzylguanidine treatment. It is likely that the mechanism of radiosensitization entails the accumulation of unrepaired radiation-induced DNA damage. The administration of PARP-1 inhibitors and (131)I-meta-iodobenzylguanidine to high risk neuroblastoma patients may be beneficial. **Targets:** Poly ADP-ribose polymerase 1, Poly ADP-ribose polymerase 2, Poly ADP-ribose polymerase 3
LY2606368 For RB1 Equivocal Copy Loss	**Evidence-Based Therapeutic Categorization in This Patient:** Investigational New Drug **Description:** An inhibitor of checkpoint kinase 1 (chk1) with potential antineoplastic activity [https://www.cancer.gov/publications/dictionaries/cancer-drug/def/prexasertib]. **Indication:** Prexasertib (LY2606368) has been used in trials studying the treatment and basic science of prostate cancer, leukemia, breast cancer, and ovarian cancer, among others. **Mechanism of Action:** Upon administration, prexasertib selectively binds to chk1, thereby preventing activity of chk1 and abrogating the repair of damaged DNA. This may lead to an accumulation of damaged DNA and may promote genomic instability and apoptosis. Prexasertib may potentiate the cytotoxicity of DNA-damaging agents and reverse tumor cell resistance to chemotherapeutic agents. Chk1, a serine/threonine kinase, mediates cell cycle checkpoint control and is essential for DNA repair and plays a key role in resistance to chemotherapeutic agents [https://www.cancer.gov/publications/dictionaries/cancer-drug/def/prexasertib]. **Targets:** Checkpoint kinase 1 (chk1)

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THERAPIES ASSOCIATED WITH DECREASED RESPONSE OR RESISTANCE

Drug	Brand Name	Matching Alteration(s)	Notes
Abemaciclib	Verzenio	RB1 Equivocal Copy Loss	See Interpretation section
Palbociclib	Ibrance	RB1 Equivocal Copy Loss	See Interpretation section
Pertuzumab	Perjeta, Perjeta-herceptin	ERBB2 Wild Type	
Ribociclib	Kisqali Femara Co-pack, Kisqali	RB1 Equivocal Copy Loss	See Interpretation section
Trastuzumab	Herceptin, Perjeta-herceptin	ERBB2 Wild Type	
Trastuzumab Emtansine	Kadcyla	ERBB2 Wild Type	

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POTENTIAL CLINICAL TRIALS

Trial Name	Phase	Matching Alteration(s)	Intervention(s)	NCT ID	Nearest Location	Miles Away
A Study to Determine the Safety of BTP-114 for Treatment in Patients With Advanced Solid Tumors With BRCA Mutations	Phase 1	ATM Equivocal Copy Loss	BTP-114	NCT02950064	Placon Therapeutics Clinical Trial Site, Houston, Texas, United States	187
My Pathway: A Study Evaluating Herceptin/Perjeta, Tarceva, Zelboraf/Cotellic, Erivedge, Alecensa, and Tecentriq Treatment Targeted Against Certain Molecular Alterations in Participants With Advanced Solid Tumors	Phase 2	ATM Equivocal Copy Loss	Trastuzumab, Pertuzumab, Erlotinib, Vemurafenib, Cobimetinib, Vismodegib, Alectinib, Atezolizumab	NCT02091141	MD Anderson, Houston, Texas, United States	187
Study of the PARP Inhibitor BMN 673 in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)	Phase 2	ATM Equivocal Copy Loss	Talazoparib Tosylate	NCT02286687	University of Texas MD Anderson Cancer Center, Houston, Texas, United States	187
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	Phase 2	ATM Equivocal Copy Loss	Erlotinib, Axitinib, Bosutinib, Crizotinib, Palbociclib, Sunitinib, Temsirolimus, Trastuzumab and Pertuzumab, Vemurafenib and Cobimetinib, Vismodegib, Cetuximab, Dasatinib, Regorafenib, Olaparib, Pembrolizumab, Nivolumab and Ipilimumab	NCT02693535	The University of Texas MD Anderson Cancer Center, Houston, Texas, United States	187
OLAParib COmbinations	Phase 2	ATM Equivocal Copy Loss	AZD2014, AZD2281, AZD5363, AZD1775	NCT02576444	Vanderbilt University, Nashville, TN, United States	823
The Safety, Pharmacokinetics and Antitumor Activity of BGB-A317 in Combination With BGB-290 in Subjects With Advanced Solid Tumors	Phase 1	ATM Equivocal Copy Loss	BGB-A317, BGB-290	NCT02660034	Vanderbilt University, Nashville, TN, United States	823

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Trial Name	Phase	Matching Alteration(s)	Intervention(s)	NCT ID	Nearest Location	Miles Away
Nivolumab and Veliparib in Treating Patients With Recurrent or Refractory Stage IV Solid Tumors That Cannot Be Removed by Surgery or Lymphoma With or Without Alterations in DNA Repair Genes	Phase 1	ATM Equivocal Copy Loss	Nivolumab, Veliparib	NCT03061188	Northwestern University, Chicago, Illinois, United States	1053
Rucaparib and Irinotecan in Cancers With Mutations in DNA Repair	Phase 1	ATM Equivocal Copy Loss	Rucaparib, Irinotecan	NCT03318445	University of California San Francisco, San Francisco, California, United States	1488
A Study of LY2606368 (Prexasertib) in Patients With Solid Tumors With Replicative Stress or Homologous Repair Deficiency	Phase 2	RB1 Equivocal Copy Loss	LY2606368	NCT02873975	Dana Farber Cancer Institute, Boston, Massachusetts, United States	1763

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Date of Birth:
Sex: F
Medical Record #:
Accession #:
Lab Number: 856458
Family Number:
Zip Code: 78212
Indication: Metastatic breast carcinoma

Test Code: 20010
Date Collected: 03/27/2018
Date Received: 04/26/2018
Date Ordered: 04/30/2018
Date Reported: 05/14/2018
Addt'l Report Date:
Sample Type: FFPE-SLIDES
Collection Site: Skin, right breast
Estimated Tumor Cellularity: 70%

Physician Name:
Facility:
Location:
Phone:
Fax:

REPORTED ALTERATIONS BY NEXT-GENERATION SEQUENCING

BASE SUBSTITUTIONS, INSERTIONS, DELETIONS

AMP Tier	Gene	Protein Syntax	Coding Syntax	Genomic Change (GRCh37/hg19)	UMI Variant Reads/Total	Variant Allele Fraction (%)	COSMIC / dbSNP	Notes
II	GATA3	NP_001002295.1:p.Ser438AlafsTer38	NM_001002295.1:c.1311delC	NC_000010.10:g.8115962delC	539 / 1470	36.7		
III	BAP1	NP_004647.1:p.Glu406Lys	NM_004656.3:c.1216G>A	NC_000003.11:g.52438503C>T	228 / 1072	21.3	rs748928044	
III	ERBB3	NP_001973.2:p.Leu1177Ile	NM_001982.3:c.3529C>A	NC_000012.11:g.56495339C>A	452 / 892	50.7	rs55699040	
III	EXO1	NP_569082.2:p.Gly759Glu	NM_130398.3:c.2276G>A	NC_000001.10:g.242048680G>A	676 / 1249	54.1	rs4150001	
III	FGFR3	NP_000133.1:p.Phe384Leu	NM_000142.4:c.1150T>C	NC_000004.11:g.1806131T>C	1062 / 1063	99.9	COSM724 rs17881656	
III	FLT4		NM_002020.4:c.2407-5C>T	NC_000005.9:g.180047313G>A	392 / 791	49.6	rs377603682	Splice region variant
III	GEN1	NP_872431.3:p.Arg302His	NM_182625.3:c.905G>A	NC_000002.11:g.17954003G>A	414 / 849	48.8	rs148607792	
III	KMT2A	NP_001184033.1:p.Ser2819ProfsTer14	NM_001197104.1:c.8454delC	NC_000011.9:g.118375061delC	477 / 858	55.6		
III	ROS1	NP_002935.2:p.Arg1948His	NM_002944.2:c.5843G>A	NC_000006.11:g.117641128C>T	590 / 806	73.2	rs140237260	

Estimated Tumor Mutational Burden (variants listed above / MB of genome targeted (0.84)) = 10.71

COPY NUMBER ALTERATIONS

AMP Tier	Gene	Chromosome	Start (GRCh37/hg19)	End (GRCh37/hg19)	Log2 Ratio	Estimated Copies	Change	Notes
II	ATM	11	108093558	108239826	-0.607	1.31	Equivocal Copy Loss	
II	RB1	13	48877882	49056026	-0.6747	1.25	Equivocal Copy Loss	
II	TP53	17	7571719	7590868	-0.4565	1.46	Equivocal Copy Loss	
III	FLT3	13	28577410	28674729	-0.6869	1.24	Equivocal Copy Loss	

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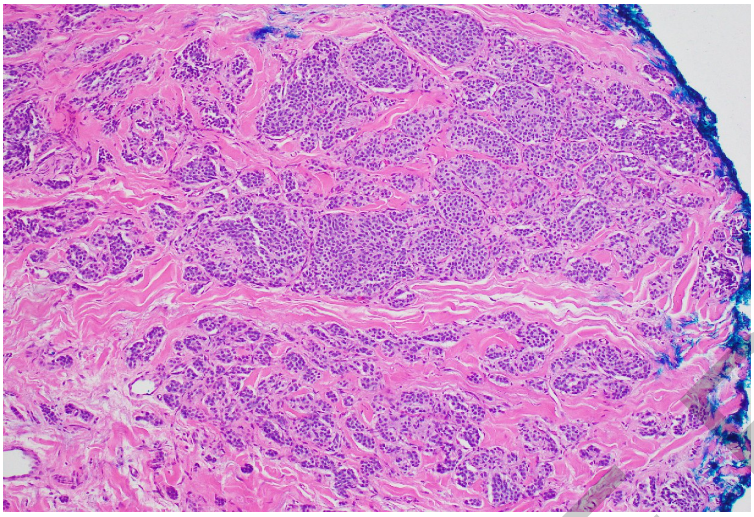
Patient Name:		Test Code:	20010	Physician Name:	
Date of Birth:		Date Collected:	03/27/2018	Facility:	
Sex:	F	Date Received:	04/26/2018	Location:	
Medical Record #:		Date Ordered:	04/30/2018	Phone:	
Accession #:		Date Reported:	05/14/2018	Fax:	
Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

SPECIMEN DETAILS



H&E-stained tissue section at 100x magnification.

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Patient Name:		Test Code:	20010	Physician Name:	
Date of Birth:		Date Collected:	03/27/2018	Facility:	
Sex:	F	Date Received:	04/26/2018	Location:	
Medical Record #:		Date Ordered:	04/30/2018	Phone:	
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Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

TEST DESCRIPTION

The ClariFind Comprehensive DNA Panel is a next-generation sequencing assay covering all coding regions (+/- 5-10bp flanking intronic sequences and including the TERT promoter region) of 277 key cancer genes for both solid tumors and hematologic malignancies and is designed for the detection of somatic base substitutions, insertions, deletions, and copy number alterations in a patient's tumor sample. Copy number alterations are reported for 39 key cancer genes (designated by * below).

ABL1 NM_005157.4	ACVR1B NM_020328.3	AKT1 NM_001014432.1	AKT2* NM_001626.4	AKT3 NM_005465.4	ALK* NM_004304.4	AMER1 NM_152424.3	APC NM_000038.5	AR* NM_000044.3	ARAF NM_001654.4	ARID1A NM_006015.4	ARID1B NM_020732.3	ARID2 NM_152641.2	ASXL1 NM_015338.5
ATM* NM_000051.3	ATR NM_001184.3	ATRX NM_000489.3	AURKA NM_198433.1	AURKB NM_004217.3	AURKC NM_003160.2	AXIN1 NM_003502.3	AXIN2 NM_004655.3	B2M NM_004048.2	BAP1 NM_004656.3	BCL2 NM_000633.2	BCL2L1 NM_138578.1	BCL6 NM_001706.4	BCOR NM_017745.5
BCORL1 NM_021946.4	BCR NM_004327.3	BIRC3 NM_001165.4	BLM NM_000057.2	BRAF* NM_004333.4	BRCA1 NM_007294.3	BRCA2 NM_000059.3	BRIP1 NM_032043.2	BTK NM_000061.2	CALR NM_004343.3	CARD11 NM_032415.4	CBL NM_005188.3	CBLB NM_170662.3	CBLC NM_012116.3
CCND1* NM_053056.2	CCND3 NM_001760.3	CCNE1* NM_001238.2	CD274 NM_014143.3	CD79A NM_001783.3	CD79B NM_000626.2	CDC73 NM_024529.4	CDH1 NM_004360.3	CDK12 NM_016507.2	CDK4* NM_000075.3	CDK6* NM_001259.6	CDKN2A* NM_000077.4	CDKN2B NM_004936.3	CDKN2C NM_001262.2
CEBPA NM_004364.3	CHEK1 NM_001114122.2	CHEK2 NM_007194.3	CIC NM_015125.3	CREBBP NM_004380.2	CRLF2 NM_022148.3	CSF1R NM_005211.3	CSF3R NM_156039.3	CTCF NM_006565.3	CTNNA1 NM_001903.2	CTNNB1 NM_001904.3	CUX1 NM_181552.3	CXCR4 NM_001008540.1	CYLD NM_015247.2
DAXX NM_001350.4	DDR1 NM_001954.4	DDR2 NM_001014796.1	DICER1 NM_177438.2	DNM2 NM_001005360.2	DNMT3A NM_022552.4	DOT1L NM_032482.2	EED NM_003797.3	EGFR* NM_005228.3	EGLN1 NM_022051.2	EP300 NM_001429.3	EPAS1 NM_001430.4	EPHA3 NM_005233.5	EPHA5 NM_004439.5
ERBB2* NM_004448.2	ERBB3* NM_001982.3	ERBB4 NM_005235.2	ERG NM_004449.4	ESR1* NM_001122742.1	ETNK1 NM_018638.4	ETV6 NM_001987.4	EXO1 NM_130398.3	EZH2 NM_004456.4	FAM175A NM_139076.2	FAM46C NM_017709.3	FANCA NM_000135.2	FANCC NM_000136.2	FANCD2 NM_033084.3
FANCE NM_021922.2	FANCF NM_022725.3	FANCG NM_004629.1	FAS NM_000043.4	FBXW7 NM_033632.3	FGF4 NM_002007.2	FGF6 NM_020996.1	FGFR1* NM_023110.2	FGFR2* NM_000141.4	FGFR3* NM_000142.4	FGFR4* NM_213647.1	FH NM_000143.3	FLCN NM_144997.5	FLT3* NM_004119.2
FLT4 NM_002020.4	FOXL2 NM_023067.3	FUBP1 NM_003902.3	GALNT12 NM_024642.4	GATA1 NM_002049.3	GATA2 NM_032638.4	GATA3 NM_001002295.1	GEN1 NM_182625.3	GNA11 NM_002067.2	GNAQ NM_002072.3	GNAS NM_000516.4	GREM1 NM_013372.6	GRIN2A NM_000833.3	H3F3A NM_002107.4
HGF NM_000601.4	HIST1H3B NM_003537.3	HNF1A NM_000545.5	HOXB13 NM_006361.5	HRAS NM_005343.2	HSP90AA1 NM_001017963.2	ID3 NM_002167.4	IDH1 NM_005896.2	IDH2 NM_002168.2	IGF1R* NM_000875.3	IKZF1 NM_006060.5	IKZF3 NM_012481.4	IL7R NM_002185.3	INHBA NM_002192.2
IRF4 NM_002460.3	JAK1 NM_002227.2	JAK2* NM_004972.3	JAK3 NM_000215.3	KAT6A NM_001099412.1	KDM5C NM_004187.3	KDM6A NM_021140.2	KDR NM_002253.2	KEAP1 NM_012289.3	KIT* NM_000222.2	KMT2A NM_001197104.1	KMT2B NM_014727.1	KMT2C NM_170606.2	KMT2D NM_003482.3
KRAS* NM_004985.3	LRP1B NM_018557.2	MAP2K1 NM_002755.3	MAP2K2 NM_030662.3	MAP2K4 NM_003010.3	MAP3K1 NM_005921.1	MAP3K14 NM_003954.3	MAPK1 NM_002745.4	MCL1 NM_021960.4	MDM2* NM_002392.5	MDM4* NM_002393.4	MED12 NM_005120.2	MEF2B NM_001145785.1	MEN1 NM_130799.2
MET* NM_001127500.1	MITF NM_000248.3	MLH1 NM_000249.3	MPL NM_005373.2	MRE11A NM_005590.3	MSH2 NM_000251.2	MSH6 NM_000179.2	MTOR NM_004958.3	MUTYH NM_012222.2	MYC* NM_002467.4	MYCL* NM_001033082.2	MYCN* NM_005378.4	MYD88 NM_002468.4	NF1* NM_001042492.2
NF2 NM_000268.3	NFE2L2 NM_006164.4	NFKBIA NM_020529.2	NKX2-1 NM_003317.3	NOTCH1 NM_017617.3	NOTCH2 NM_024408.3	NOTCH3 NM_000435.2	NPM1 NM_002520.6	NRAS* NM_002524.4	NSD1 NM_022455.4	NTRK1 NM_002529.3	NTRK2 NM_006180.3	NTRK3 NM_002530.3	PAK3 NM_002578.3
PALB2 NM_024675.3	PAX5 NM_016734.2	PBRM1 NM_181042.4	PDGFRA* NM_006206.4	PDGFRB* NM_002609.3	PHF6 NM_032458.2	PIK3CA* NM_006218.2	PIK3R1 NM_181523.2	PIK3R2 NM_005027.3	PIM1 NM_002648.3	PLCG1 NM_002660.2	PMS1 NM_000534.4	PMS2 NM_000535.5	POLD1 NM_001256849.1
POLE NM_006231.2	PPM1D NM_003620.3	PPP2R1A NM_014225.5	PRDM1 NM_001198.3	PRKAR1A NM_212472.2	PRKDC NM_006904.6	PRSS1 NM_002769.4	PTCH1 NM_000264.3	PTEN* NM_000314.4	PTPN11 NM_002834.3	RAC1 NM_006908.4	RAD21 NM_006265.2	RAD50 NM_005732.3	RAD51 NM_002875.4
RAF1 NM_002880.3	RB1* NM_000321.2	RET* NM_020975.4	RHEB NM_005614.3	RHOA NM_001664.2	RIT1 NM_006912.5	RNF43 NM_017763.4	ROS1 NM_002944.2	RUNX1 NM_001754.4	SDHB NM_003000.2	SETBP1 NM_015559.2	SETD2 NM_014159.6	SF3B1 NM_012433.2	SMAD2 NM_005901.5
SMAD4 NM_005359.5	SMARCA4 NM_001128844.1	SMARCB1 NM_003073.3	SMC1A NM_006306.3	SMC3 NM_005445.3	SMO NM_005631.4	SOCS1 NM_003745.1	SOX2 NM_003106.3	SOX9 NM_000346.3	SPOP NM_001007226.1	SRC NM_005417.4	SRSF2 NM_003016.4	STAG2 NM_001042751.1	STAT3 NM_139276.2
STK11* NM_000455.4	SUFU NM_016169.3	SUZ12 NM_015355.2	TAL1 NM_003189.2	TCF3 NM_003200.3	TERT NM_198253.2	TET2 NM_001127208.2	TGFBR2 NM_003242.5	TNFAIP3 NM_006290.3	TNFRSF14 NM_003820.2	TP53* NM_000546.5	TRAF3 NM_145725.2	TSC1 NM_000368.4	TSC2 NM_000548.3
TSHR NM_000369.2	U2AF1 NM_006758.2	U2AF2 NM_007279.2	VHL NM_000551.3	WHSC1 NM_001042424.2	WT1 NM_024426.4	XPO1 NM_003400.3	XRCC2 NM_005431.1	XRCC3 NM_001100119.1	ZNF217 NM_006526.2	ZRSR2 NM_005089.3			

TEST METHODOLOGY

The ClariFind Comprehensive DNA Panel is performed on genomic DNA extracted from the patient's specimen. For formalin-fixed paraffin-embedded (FFPE) tissue samples, a histopathologic review is performed to determine tissue adequacy, identify the appropriate area with tumor for DNA extraction, and estimate the tumor cellularity in that area. Manual microdissection is then performed to isolate the designated area with tumor for DNA extraction. For all other sample types, tumor enrichment is not performed. Sequencing libraries are constructed incorporating unique molecular identifiers (UMIs) for each original DNA molecule. Target enrichment is performed using multiplex PCR with region-specific and universal primers. Next-generation sequencing is performed on the Illumina HiSeq platform. Base substitutions, insertions, deletions, and copy number alterations are identified using a Baylor Genetics proprietary pipeline that includes the QIAGEN Biomedical Genomics Workbench (API version 10.1.1), Pindel (0.2.5b8), and other custom tools, then annotated against the GRCh37 (hg19) reference human genome. Genomic alterations identified according to internal recommendations are curated and categorized by clinical significance according to the Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer [PMID: 27993330], supported by the Association for Molecular Pathology (AMP). Benign or likely benign variants (AMP Tier IV) are not reported. Whenever pertinent, the absence of an alteration (i.e. wild type) may also be reported. Variant nomenclature is based on the convention recommended by the Human Genome Variation Society (http://varnomen.hgvs.org/). Confirmation of genomic alterations is

Patient Name:		Test Code:	20010	Physician Name:	
Date of Birth:		Date Collected:	03/27/2018	Facility:	
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Accession #:		Date Reported:	05/14/2018	Fax:	
Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

performed according to internal recommendations by Sanger sequencing, orthogonal next-generation sequencing, or other methods. The information provided in the report (including the interpretation, genomic alteration details, targeted therapies, therapies associated with decreased response or resistance, and potential clinical trials) is generated from proprietary tools and analyses of relevant peer-reviewed publications, public and proprietary databases, society guidelines, and other publicly available information identified by Baylor Genetics.

TECHNICAL PERFORMANCE

ACCURACY	**Tumor Cellularity**	**Variant Allele Fraction**	**Performance**
Sensitivity: Base Substitutions	>=20%	2%	97.4% (PPV = 94.6%)
	>=20%	>=5%	>99.9% (PPV = 97.5%)
Sensitivity: Insertions/Deletions (1-52 bp)	>=20%	5-15%	96%
	>=20%	>15%	>99%
Sensitivity: Copy Number Alterations (amplifications with copy number >=6 or homozygous deletions)	>=30%	-	>99%
Specificity: All Variant Types	-	-	>99%
Average Unique Molecular Identifier Coverage Across All Targets	>1500X		
REPRODUCIBILITY			
Intra-Batch Precision	100%		
Inter-Batch Precision	99.8%		

The following are regions in the panel with generally less than 100X median unique molecular identifier (UMI) coverage at 95% of base positions, which may result in decreased sensitivity:

AKT3 Exon 5, ARID1B Exon 14, ATR Exon 37, AURKB Exon 2, AURKC Exon 6, AXIN1 Exon 11, BCR Exon 18, BRCA2 Exon 18, CBL Exon 5, CD79A Exon 2, CSF3R Exon 12, EED Exon 6, EGFR Exon 6, EP300 Exon 13, EPAS1 Exon 16, FANCG Exon 1, FBXW7 Exon 1, FGFR1 Exon 16, IRF4 Exon 2, JAK1 Exon 9, JAK1 Exon 23, KMT2B Exon 1, KMT2C Exon 41, MCL1 Exon 3, MED12 Exon 42, MEN1 Exon 1, MSH2 Exon 14, NF2 Exon 4, NOTCH1 Exon 18, NOTCH2 Exon 33, NTRK1 Exon 3, PIK3CA Exon 14, PMS2 Exon 1, PMS2 Exon 2, PMS2 Exon 4, POLD1 Exon 17, PPP2R1A Exon 4, RAD50 Exon 16, SF3B1 Exon 21, TP53 Exon 10, U2AF2 Exon 8.

COVERAGE LIMITATIONS FOR THIS SAMPLE

The following are variants recorded in the COSMIC database (v81) which showed less than 100X unique molecular identifier (UMI) coverage in this patient's sample:

AKT3 c.928C>G (p.Pro310Ala), AKT3 c.929C>G (p.Pro310Arg), ASXL1 c.24G>A (p.Lys8=), ATRX c.2763C>T (p.Val921=), AURKC c.630C>A (p.His210Gln), BCR c.3075C>T (p.Ile1025=), BCR c.3106A>G (p.Arg1036Gly), CD79A c.190G>A (p.Val64Ile), CD79A c.205G>A (p.Val69Ile), EED c.587T>A (p.Leu196Gln), EED c.619C>T (p.Leu207=), EGFR c.630G>T (p.Leu210=), EPAS1 c.2565G>A (p.Thr855=), FANCG c.1766T>C (p.Leu589Pro), FGFR1 c.109C>T (p.Pro37Ser), MAP3K1 c.3674A>C (p.Glu1225Ala), NF2 c.424G>A (p.Ala142Thr), NF2 c.425C>T (p.Ala142Val), NF2 c.431dupA (p.Tyr144Ter), NF2 c.432C>A (p.Tyr144Ter), NF2 c.436G>A (p.Val146Ile), NF2 c.447+1G>A (p.?), NF2 c.447+2T>C (p.?), NOTCH2 c.112G>A (p.Glu38Lys), NOTCH2 c.137A>G (p.Asn46Ser), NTRK1 c.311G>A (p.Arg104His), NTRK1 c.320C>T (p.Ala107Val), PMS2 c.2007-4G>A (p.?), PMS2 c.2013G>A (p.Thr671=), PMS2 c.2466T>C (p.Leu822=), PMS2 c.2570G>C (p.Gly857Ala), POLD1 c.102C>T (p.Phe34=), RAD50 c.2566C>T (p.Gln856Ter), SF3B1 c.423A>G (p.Lys141=), SF3B1 c.494A>T (p.Glu165Val), TP53 c.11C>T (p.Pro4Leu), TP53 c.13C>T (p.Gln5Ter), TP53 c.28G>A (p.Val10Ile), TP53 c.30C>T (p.Val10=), TP53 c.31G>A (p.Glu11Lys), TP53 c.31G>C (p.Glu11Gln), TP53 c.8A>G (p.Glu3Gly), U2AF2 c.757G>A (p.Val253Met), U2AF2 c.789C>T (p.Ile263=), U2AF2 c.805T>C (p.Tyr269His)

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Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

GLOSSARY

Amplification: Estimated copy number >=6 in diploid tumors or high-level copy number gain in aneuploid tumors (relative to the estimated tumor cellularity, if known, and quality of data), as determined by our algorithm.

AMP Tier: Genomic alterations are categorized by clinical significance according to the Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer [PMID: **27993330**], supported by the Association for Molecular Pathology (AMP), as follows:

- **AMP Tier I:** Strong clinical significance
- **AMP Tier II:** Potential clinical significance
- **AMP Tier III:** Unknown clinical significance
- **AMP Tier IV:** Benign or likely benign variants (not reported)

Estimated Tumor Mutational Burden: Calculated as the total number of base substitutions, insertions, and deletions classified as AMP Tier I-III (excluding benign or likely benign variants), as listed in the Reported Alterations by Next-Generation Sequencing table, divided by the megabases of genome targeted in our panel (0.84). For further information, please see [PMID: **28420421**].

Equivocal Copy Gain: There is evidence, which may not be unambiguous, that the genomic alteration meets criteria for a copy number gain but does not meet the threshold for amplification (relative to the estimated tumor cellularity, if known, and quality of data), as determined by our algorithm.

Equivocal Copy Loss: There is evidence, which may not be unambiguous, that the genomic alteration meets criteria for a copy number loss but does not meet the threshold for a homozygous deletion (relative to the estimated tumor cellularity, if known, and quality of data), as determined by our algorithm.

Evidence-Based Variant Categorization: Genomic alterations are subcategorized by levels of evidence according to the Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer [PMID: **27993330**], supported by the Association for Molecular Pathology (AMP), as follows:

- **Level A:** FDA-approved therapy; included in professional guidelines
- **Level B:** Well-powered studies with consensus from experts in the field
- **Level C:** FDA-approved therapies for different tumor types or investigational therapies; multiple small published studies with some consensus
- **Level D:** Preclinical trials or a few case reports without consensus

FDA Approved: Drug is approved by the United States Food and Drug Administration (FDA) for clinical use for the patient's cancer type.

Homozygous Deletion: Estimated copy number at or near 0 (relative to the estimated tumor cellularity, if known, and quality of data), as determined by our algorithm.

Investigational New Drug: Drug is not currently FDA approved for clinical use and is still under investigation.

NCCN Category: Drug is categorized by the National Comprehensive Cancer Network (NCCN) Categories of Evidence and Consensus [**https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx**] for the patient's cancer type according to the following:

- **Level 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Level 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Level 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- **Level 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Off-Label Use: Drug is FDA approved for clinical use but not for the patient's cancer type.

PMID: PubMed identification number; unique identifier for an article in PubMed.

Trial Enrollment Available Nearby: Potential clinical trial may be available for patient enrollment within 100 miles of the provided zip code.

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Sex:	F	Date Received:	04/26/2018	Location:	
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Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

DISCLAIMER

The Report: The ClariFind Comprehensive DNA Panel report incorporates analyses of relevant peer-reviewed publications, public and proprietary databases, society guidelines, and other publicly available information identified by Baylor Genetics. These may include associations between genomic alterations (or lack of genomic alterations), targeted therapies or therapies associated with decreased response or resistance, and potential clinical trials. Genomic alterations, targeted therapies or therapies associated with decreased response or resistance, and potential clinical trials are not ranked in order of potential or predicted efficacy for the patient. Baylor Genetics makes every effort to ensure that the information provided is up-to-date at the time the report is generated; however, information may be continuously updated in the public domain and should also be investigated by the physician and medical staff.

Incidental Findings: Unless otherwise specified, this test is performed on a patient's tumor sample without a paired germline sample. The ClariFind Comprehensive DNA Panel report may include genomic alterations which may be of germline origin, including those which may be clinical significant for the patient and/or the patient's family; however, this test is designed and validated for the detection and reporting of somatic genomic alterations and is not meant for the detection and reporting of germline genomic alterations or to diagnose any germline condition. When clinically warranted, genetic counseling and appropriate germline testing performed on a germline sample from the patient should be considered for further evaluation.

Variants with Low-Level Variant Allele Fractions: The ClariFind Comprehensive DNA Panel report may include variants of strong or potential clinical significance with low-level variant allele fractions between 2-5%. Certain COSMIC hotspot mutations, or variants previously identified in the same patient, may also be reported with variant allele fractions between 1-2%, at the discretion of the laboratory director. Variants with allele fractions less than 1% are not reported. The report may also include variants of unknown clinical significance when the detected variant allele fractions are >=5%. Variants of unknown clinical significance with variant allele fractions <5% will not be routinely reported.

Large Insertions or Deletions: The detection of large (>52 bp) insertions or deletions may be limited by this next-generation sequencing assay; however, if detected, clinically significant large insertions or deletions will still be reported. FLT3 internal tandem duplications will also be reported when detected. However, separate FLT3 mutation analysis (test code 9045) is recommended for all patients with newly diagnosed acute myeloid leukemia, especially for expedited consideration of FLT3-inhibitor therapy (see NCCN Guidelines for Acute Myeloid Leukemia at https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf).

Copy Number Alterations: The ClariFind Comprehensive DNA Panel report may include copy number alterations identified by next-generation sequencing. Variations in sample quality, sample input, and estimated tumor cellularity (if known), or the presence of pseudogenes or other homologous sequences may result in a signal-to-noise ratio that precludes analysis of some regions or the entire sample. In addition, copy number changes are reported at the gene level, unless otherwise specified. Thus, next-generation sequencing analysis may not detect all copy number changes. A normal next-generation sequencing copy number result does not exclude the possibility of copy number changes of a gene or a portion of a gene. For more detailed copy number evaluation, other testing may be considered such as chromosomal microarray studies (test codes 9505 or 9515) or FISH analysis.

Laboratory Errors: The chance that rare laboratory errors may occur cannot be completely excluded. Possible sources of laboratory errors include, but are not limited to, sample mix-ups, cross-contamination, and sequencing errors. Sequencing errors can result from poor quality and/or low-input samples, from contamination issues, from genetic variants or difficult sequences (such as repetitive or homologous regions) which interfere with assay performance and/or analysis, from subclonal alterations at levels below standard detection, and from other sources.

No Guarantee of Clinical Benefit: The ClariFind Comprehensive DNA Panel report makes no promises or guarantees that any targeted therapies will provide clinical benefit for the patient and that any therapies associated with decreased response or resistance will result in decreased or lack of clinical benefit for the patient. The therapies listed in the report may include FDA-approved drugs (for the patient's cancer type or for off-label use) or investigational new drugs.

No Guarantee of Clinical Trial Enrollment: The ClariFind Comprehensive DNA Panel report makes no promises or guarantees that any potential clinical trials listed will be open and available for enrollment or that the patient will qualify for enrollment in any clinical trials. The potential clinical trials listed in the report are not meant to be a complete list of all available trials, and Baylor Genetics does not promise or guarantee that other clinical trials are not also available for the patient. Not all locations for the clinical trials are listed; when a United States ZIP code is provided, Baylor Genetics will attempt to provide the nearest location for the clinical trial, if this information is available. For additional information regarding a specific clinical trial, please go to clinicaltrials.gov and type in the NCT ID into the search field.

No Guarantee of Reimbursement: Baylor Genetics makes no promises or guarantees of reimbursement for the cost of testing from any healthcare provider, insurer, or other third-party payor, whether private or governmental.

Treatment Decisions are the Responsibility of the Patient's Physician: The ClariFind Comprehensive DNA Panel report must be interpreted by the patient's physician within the appropriate clinical context and in conjunction with all other relevant information. Treatment decisions should not be solely

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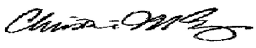
Patient Name:		Test Code:	20010	Physician Name:	
Date of Birth:		Date Collected:	03/27/2018	Facility:	
Sex:	F	Date Received:	04/26/2018	Location:	
Medical Record #:		Date Ordered:	04/30/2018	Phone:	
Accession #:		Date Reported:	05/14/2018	Fax:	
Lab Number:	856458	Addt'l Report Date:			
Family Number:		Sample Type:	FFPE-SLIDES		
Zip Code:	78212	Collection Site:	Skin, right breast		
Indication:	Metastatic breast carcinoma	Estimated Tumor Cellularity: 70%			

based on the results of this test or the information provided in this report. All responsibility and liability regarding treatment decisions arising from this test and report reside with the patient's physician and not Baylor Genetics.



Christine M. Eng, M.D.
Medical Director

Brian Y. Merritt, M.D.

This test was developed and its performance characteristics determined by Baylor Genetics. It has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as purely investigational or for research only. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high-complexity clinical laboratory testing (CAP# 2109314 / CLIA# 45D0660090; Lab Director: Christine M. Eng, MD).