BELAY DIAGNOSTICS

Date: 11/06/2025
Order ID: SumPos-Mets-1

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Summit™ 2.0 Report

Patient Information	Provisional Diagnosis	Specimen	Physician Information
Name: Jane Doe **DOB:**01/01/1990 **Sex Assigned at Birth:**Female **MRN:**11xx22xx33	**Diagnosis:**Metastatic Breast Carcinoma; Central Nervous System Neoplasm **ICD10:**C79.31	**Type:**CSF **Collected:**01/01/2025 **Received:**01/02/2025 **Specimen ID:**SumPos-Mets-1	**Institution:**Belay Diagnostics **Referring Physician:**Provider Test

RESULT SUMMARY

POSITIVE

Comments

While most chromosomal arm-level alterations are considered variants of unknown significance (VUS) on their own, a high level of chromosomal loss and gain as observed in this specimen indicates chromosomal instability, a key driver of metastasis across cancer types (PMID: 38924459).

CLINICALLY SIGNIFICANT ALTERATION DETAILS (Tier 1 or 2 per AMP/ASCO/CAP)

SNV, MNV, Indel Variants

Alteration	VAF	Actionability Summary		
		FDA/NCCN Therapies Associated	Prognostic/Diagnostic Guidelines	Clinical Trial Options
TP53 p.N239D c.715A>G	48.8%	No	Yes	Yes
TP53 p.R110L c.329G>T	1.2%	No	Yes	Yes

Copy Number Variants

Alteration	Location	Fold Change	Actionability Summary		
			FDA/NCCN Therapies Associated	Prognostic/Diagnostic Guidelines	Clinical Trial Options
EGFR Amplification	chr7	1.48	No	No	Yes
ERBB2 Amplification	chr17	18.32	Yes	No	Yes

Fusion Variants: *None*

Biomarkers

Tumor Mutation Burden (TMB)			Microsatellite Instability (MSI)	
Not Detected	**Low**	High	**Stable**	High

Aneuploidy Variants (Chromosome Arm Level Loss or Gain): *None*

VARIANTS OF UNKNOWN SIGNIFICANCE (Tier 3)

SNV/MNVs/Indels

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ABL2 N47S	*H1-2* S113A	*MDC1* A333V	*POLE* R231C	*ZFHX3* A2126T
AKT2 R467W	*HNF1A* S574_H577delinsGIQD	*MGA* R1832W	*RAD54L* R202C	*ZNF217* E349K
DOT1L A353G	*HNF1A* H577D	*MITF* M144K	*RECQL4* K626N	
E2F3 A8S	*LRP1B* G1087S	*MST1R* F433L	*ROS1* K2228_S2229delinsQC	
ERBB2 E207K	*LRP1B* T369A	*NOTCH1* D965H	*SPTA1* I1917*	
GSK3B E268K	*MDC1* R842S	*NOTCH4* G247R	*VTCN1* E204Q	

Gene Level CNVs

None

Fusions

None

Aneuploidy Variants of Unknown Significance

chr10p Gain	chr15q Loss	chr19q Gain	chr2q Loss	chr6q Loss
chr10q Gain	chr16p Gain	chr1p Gain	chr3p Loss	chr7p Gain
chr11p Loss	chr16q Gain	chr1q Gain	chr3q Gain	chr7q Gain
chr11q Loss	chr17p Loss	chr20p Gain	chr4p Loss	chr8p Loss
chr12p Gain	chr17q Gain	chr20q Gain	chr4q Gain	chr8q Gain
chr12q Gain	chr18p Loss	chr21q Loss	chr5p Gain	chr9p Loss
chr13q Loss	chr18q Loss	chr22q Loss	chr5q Gain	chr9q Gain
chr14q Loss	chr19p Loss	chr2p Gain	chr6p Loss	

ACTIONABILITY SUMMARY

FDA / NCCN Therapies for the Patient's Tumor Type (Tier 1A)

Biomarker	Therapies	Setting	Source(s)
ERBB2 Amplification	pertuzumab + trastuzumab +/- (paclitaxel or docetaxel)	First line	FDA (Approved), NCCN
ERBB2 Amplification	ado-trastuzumab emtansine; pertuzumab/trastuzumab/hyaluronidase; trastuzumab +/- chemotherapy; trastuzumab/hyaluronidase	Metastatic	FDA (Approved), NCCN
ERBB2 Amplification	fam-trastuzumab deruxtecan	Unresectable or metastatic	FDA (Approved), NCCN
ERBB2 Amplification	fam-trastuzumab deruxtecan	Subsequent line, and no satisfactory alternative therapy	FDA (Approved)
ERBB2 Amplification	lapatinib + capecitabine; margetuximab + chemotherapy; neratinib + capecitabine; trastuzumab + tucatinib + capecitabine	Subsequent line	FDA (Approved), NCCN
ERBB2 Amplification	lapatinib + trastuzumab	Metastatic	NCCN

FDA / NCCN Therapies with Resistance / Decreased Response (Tier 1A): *None*

Prognostic Implications per NCCN: *None*

Diagnostic Implications per WHO

Biomarker	Diseases	Note

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TP53 N239D, *TP53* R110L	Breast Neoplasm	TP53 mutations are common in breast cancer, though they occur with varying frequencies in different subtypes. In particular, TP53 mutations are most frequent in the ER-negative pathway (PMID: 23000897), including both HER2-positive and HER2-negative groups. In triple-negative breast cancer, basal-like tumors have frequent TP53 mutations (84%), with the basal-like 1 subtype showing a very high rate (92%). TP53 mutations are notably less frequent in lobular carcinoma in situ, malignant adenomyoepithelioma (AME-M), and adenoid cystic carcinoma.

CLINICAL TRIALS / INVESTIGATIONAL THERAPIES

***EGFR* Amplification + *ERBB2* Amplification**

Therapy	Clinical Trial	Location/Sponsor
MK-0472; MK-0472 + pembrolizumab; MK-0472 + MK-1084	NCT05853367 (Phase 1) Study of MK-0472 in Participants With Advanced/Metastatic Solid Tumors (MK-0472-001)	Chicago, Illinois Merck Sharp & Dohme LLC Trialsites@msd.com

***ERBB2* Amplification**

Therapy	Clinical Trial	Location/Sponsor
GLSI-100	NCT05232916 (Phase 3) Phase 3 Study to Evaluate the Efficacy and Safety of HER2/Neu Peptide GLSI-100 (GP2 + GM-CSF) in HER2/Neu Positive Subjects	Tucson, Arizona Greenwich LifeSciences, Inc. Jaye.Thompson@GreenwichLifeSciences.com
carvedilol	NCT03418961 (Phase 3) S1501 Carvedilol in Preventing Cardiac Toxicity in Patients With Metastatic HER-2-Positive Breast Cancer	Duarte, California SWOG Cancer Research Network
pertuzumab/trastuzumab /hyaluronidase + giredestrant + gonadotropin-releasing hormone analog	NCT05296798 (Phase 3) A Study to Evaluate the Efficacy and Safety of Giredestrant in Combination With Phesgo (Pertuzumab, Trastuzumab, and Hyaluronidase-zzxf) Versus Phesgo in Participants With Locally Advanced or Metastatic Breast Cancer (heredERA Breast Cancer)	Los Angeles, California Hoffmann-La Roche global-roche-genentech-trials@gene.com
trastuzumab + liposomal doxorubicin + paclitaxel	NCT00294996 (Phase 3) Trial of Myocet in Metastatic Breast Cancer	San Diego, California Sopherion Therapeutics
zanidatamab + (capecitabine or eribulin or gemcitabine or vinorelbine)	NCT06435429 (Phase 3) A Study Comparing the Efficacy and Safety of Zanidatamab to Trastuzumab, Each in Combination With Physician's Choice Chemotherapy, for the Treatment of Participants With Metastatic HER2-positive Breast Cancer	Phoenix, Arizona Jazz Pharmaceuticals ClinicalTrialDisclosure@JazzPharma.com

***TP53* N239D + *TP53* R110L**

Therapy	Clinical Trial	Location/Sponsor
ATRN-119	NCT04905914 (Phase 1/Phase 2) Study Of ATRN-119 In Patients With Advanced Solid Tumors	New Haven, Connecticut Aprea Therapeutics info@aprea.com
LP-184	NCT05933265 (Phase 1/Phase 2) Study of LP-184 in Patients with Advanced Solid Tumors	Springdale, Arkansas Lantern Pharma Inc. lyza@lanternpharma.com
anti-KRAS and anti-TP53 peripheral blood lymphocytes + aldesleukin + cyclophosphamide + fludarabine; anti-KRAS and anti-TP53 peripheral blood lymphocytes + pembrolizumab + aldesleukin + cyclophosphamide + fludarabine	NCT03412877 (Phase 2) Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Neoantigens in People With Metastatic Cancer	Bethesda, Maryland National Cancer Institute (NCI) IRC@nih.gov

TIER 1A THERAPY DETAILS

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***ERBB2* Amplification**		
Therapy	**Approval / Guideline Summary**	**Underlying Evidence**
ado-trastuzumab emtansine	FDA approved for HER2-positive, metastatic breast cancer that previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy. NCCN recommended as Category 2A.	In a Phase III trial (EMILIA) that supported FDA approval, treatment with Kadcyla (trastuzumab emtansine) improved median progression free survival (9.6 mo vs 6.4 mo) and overall survival (30.9 mo vs 25.1 mo) compared to Tykerb (lapatinib) combined with Xeloda (capecitabine) in patients with metastatic ERBB2 (HER2)-positive breast cancer (PMID: 24879797, PMID: 23020162; NCT00829166). In a Phase II (MATCH) trial, Kadcyla (trastuzumab emtansine) treatment resulted in partial response in 8.1% (3/37) and stable disease in 43% (16/37) of patients with ERBB2 (HER2) amplified non-breast, non-gastric advanced solid tumors, with a 6-month progression-free survival rate of 24.8% (J Clin Oncol 36, 2018 (suppl; abstr 100); NCT02465060).
fam-trastuzumab deruxtecan	FDA approved for adults with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy. NCCN recommended for subsequent line or first line therapy (Category 1/Preferred intervention).	The FDA approval for fam-trastuzumab deruxtecan was supported by data from the open-label, randomized, phase-III trial DESTINY-Breast03 (NCT03529110). DESTINY-Breast03 demonstrated that subsequent-line fam-trastuzumab deruxtecan, compared with ado-trastuzumab emtansine, improved median PFS (HR = 0.28, p < 0.0001; NR (n = 261) vs. 6.8 mo. (n = 263)) in patients with metastatic or unresectable, HER2+ breast carcinoma. The secondary endpoint was ORR (82.7% vs. 36.1%). The FDA approval for fam-trastuzumab deruxtecan was also supported by data from the single-arm, phase-II trial DESTINY-Breast01 (NCT03248492; PMID: 31825192). DESTINY-Breast01 demonstrated that subsequent-line fam-trastuzumab deruxtecan had an ORR of 60.3% (n = 184; CR, 4.3%; PR, 56.0%) and a median DOR of 14.8 mo. (n = 184) in patients with metastatic or unresectable, HER2+ breast carcinoma.
fam-trastuzumab deruxtecan	FDA approved for unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.	The FDA approval for fam-trastuzumab deruxtecan was supported by data from three clinical trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831). Data from the open-label, multi-cohort, phase-II trial DESTINY-PanTumor02 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 111) conferred an ORR of 51.4% (CR = 2.7%, PR = 48.6%) and a median DoR of 19.4 mos. in patients with unresectable or metastatic HER2-positive solid tumors. Data from the open-label, two-cohort, phase-II trial DESTINY-Lung01 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 17) conferred an ORR of 52.9% (CR = 5.9%, PR = 47.1%) and a median DoR of 6.9 mos. in patients with relapsed/refractory, unresectable, or metastatic HER2-positive NSCLC. Data from the randomized, two-arm, phase-II trial DESTINY-CRC02 demonstrated that subsequent-line fam-trastuzumab deruxtecan (n = 64) conferred an ORR of 46.9% (CR = 0%, PR = 46.9%) and a median DoR of 5.5 mos. in patients with relapsed/refractory, unresectable, or metastatic HER2-positive CRC.
lapatinib + capecitabine	FDA approved for advanced or metastatic breast cancer that overexpresses HER2 and that had prior therapy including an anthracycline, a taxane, and trastuzumab. NCCN recommended as Category 2A.	The FDA approval for lapatinib + capecitabine was supported by data from the randomized, phase-III trial NCT00078572 (PMID: 17192538). NCT00078572 demonstrated that subsequent-line lapatinib + capecitabine, compared with capecitabine, improved median time to progression (HR = 0.57; p = 0.00013; 27.1 weeks vs. 18.6 weeks) in patients with locally advanced or metastatic, HER2-Positive BCa. The secondary endpoint was median OS (75.0 weeks vs. 65.9 weeks).
lapatinib + trastuzumab	NCCN recommended as subsequent line therapy for unresectable, recurrent, or metastatic HER2-positive breast cancer, without cytotoxic therapy (Category 2A).	
margetuximab + chemotherapy	FDA approved for metastatic HER2-positive breast cancer that received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. NCCN recommended as Category 2A.	In a Phase III trial (SOPHIA) that supported FDA approval, Margenza (margetuximab-cmkb) in combination with chemotherapy resulted in improved primary progression-free survival (5.8 vs 4.9 mo, HR=0.76, p=0.03) compared to Herceptin (trastuzumab) plus chemotherapy in patients with ERBB2 (HER2)-positive (IHC 3+ or FISH amplified) metastatic breast cancer whose disease progressed after two or more lines of anti-ERBB2 (HER2) therapies (PMID: 33480963; NCT02492711).
neratinib + capecitabine	FDA approved for advanced or metastatic HER2-positive breast cancer that had two or more prior anti-HER2 based regimens in the metastatic setting. NCCN recommended as Category 2A.	In a Phase III (NALA) trial that supported FDA approval, combination of Nerlynx (neratinib) and Xeloda (capecitabine) reduced risk of disease progression or death (HR=0.76, p=0.006), improved 12-month PFS (28.8%, 88 /307 vs 14.8%, 46/314) compared to lapatinib and capecitabine combination in patients with metastatic ERBB2 (HER2)-positive (amp/over exp) breast cancer who had 2 or more prior ERBB2 (HER2)-targeted therapies (J Clin Oncol 37, no. 15_suppl (May 20, 2019) 1002-1002; NCT01808573).

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pertuzumab + trastuzumab +/- (paclitaxel or docetaxel)	FDA approved with paclitaxel for HER2-positive metastatic breast cancer that has not received prior anti-HER2 therapy or chemotherapy for metastatic disease. NCCN recommended as a Preferred intervention (Category 1 for docetaxel, Category 2A for paclitaxel). Per NCCN, may also be considered if previously treated with trastuzumab plus chemotherapy in the absence of pertuzumab.	The FDA approval for pertuzumab + trastuzumab +/- (docetaxel or paclitaxel) was supported by data from the double-blind, placebo-controlled, phase-III trial CLEOPATRA (NCT00567190; PMID: 22149875). CLEOPATRA demonstrated that first-line pertuzumab + trastuzumab + docetaxel, compared with placebo + trastuzumab + docetaxel, improved median PFS (HR = 0.62; p < 0.0001; 18.5 mo. vs. 12.4 mo.; no. of events, 47.5% (191/402) vs. 59.6% (242/406)) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were OS (HR = 0.68), ORR (80.2% (275/343) vs. 69.3% (233/336)) and median DOR (20.2 mo. vs. 12.5 mo.).
pertuzumab/trastuzumab /hyaluronidase	FDA approved with paclitaxel for HER2-positive metastatic breast cancer that has not received prior anti-HER2 therapy or chemotherapy for metastatic disease. Per NCCN, pertuzumab/trastuzumab/hyaluronidase injection for subcutaneous use may be substituted anywhere that the combination of intravenous pertuzumab and intravenous trastuzumab are given as part of systemic therapy.	In a Phase III trial (FeDeriCa) that supported FDA approval, Phesgo (pertuzumab/trastuzumab/hyaluronidase-zzxf) demonstrated pharmacokinetics, safety, and efficacy comparable to i.v. pertuzumab and trastuzumab (H+P) (Cancer Res 2020;80(4 Suppl):Abstract nr PD4-07; NCT03493854), warranted the extrapolation of data from a Phase III trial supporting the approval of H+P plus docetaxel in Erbb2 (Her2)-positive metastatic breast cancer (PMID: 23602601; NCT00567190) for approval of Phesgo (FDA.gov).
trastuzumab + tucatinib + capecitabine	FDA approved for advanced unresectable or metastatic HER2-positive breast cancer, including brain metastases, that had one or more prior anti-HER2-based regimens in the metastatic setting. NCCN recommended as Category 1 /Preferred intervention.	In a Phase II trial (HER2CLIMB) that supported FDA approval, addition of Tukysa (tucatinib) to Herceptin (trastuzumab) and Xeloda (capecitabine) significantly improved progression-free survival at 1 year (PFS1) compared to placebo (33.1% vs 12.3%, HR=0.54, p<0.001) in patients with metastatic ERBB2 (HER2)-positive breast cancer who received prior HER2-targeted therapy, PFS1 was significantly improved (24.9% vs 0%, HR=0.48, p<0.001) in patients with brain metastasis (PMID: 31825569; NCT02614794).
trastuzumab +/- chemotherapy	FDA approved for HER2-overexpressing metastatic breast cancer, with paclitaxel as first-line treatment, and as a single agent after one or more chemotherapy regimens. NCCN recommended with various chemotherapy options as Category 2A.	The FDA approval for trastuzumab +/- chemotherapy was supported by two trials: Study 5 (PMID:11248153) and Study 6. Data from the open-label, randomized, phase-III trial Study 5 demonstrated that first-line trastuzumab + chemotherapy, compared with chemotherapy, improved median time to progression (p < 0.0001; 7.2 mo. vs. 4.5 mo.) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were ORR (45% vs. 29%), median DOR (8.3 mo. vs 5.8. mo.), and median OS (25.1 mo. vs. 20.3 mo.). Data from the open-label, single-arm, phase-II trial Study 6 demonstrated that subsequent-line trastuzumab conferred an ORR of 14 % (CR, 2%; PR, 12%) in patients with metastatic, HER2-Positive BCa.
trastuzumab/hyaluronidase	FDA approved for HER2-overexpressing metastatic breast cancer, with paclitaxel as first-line treatment, and as a single agent after one or more chemotherapy regimens. Per NCCN, trastuzumab/hyaluronidase injection for subcutaneous use may be substituted for trastuzumab in any regimen.	The FDA approval for trastuzumab/hyaluronidase +/- chemotherapy was supported by two trials: H0648g (PMID: 11248153) and H0649g. Data from the open-label, randomized, phase-III trial H0648g demonstrated that first-line trastuzumab + chemotherapy, compared with chemotherapy, improved median time to progression (p < 0.0001; 7.2 mo. vs. 4.5 mo.) in patients with metastatic, HER2-Positive BCa. Secondary endpoints were ORR (45% vs. 29%), median DOR (8.3 mo. vs 5.8. mo.), and median OS (25.1 mo. vs. 20.3 mo.). Data from the open-label, single arm phase-II trial H0649g demonstrated that subsequent-line trastuzumab conferred an ORR of 14 % (CR, 2%; PR, 12%) in patients with metastatic, HER2-Positive BCa.

TEST DETAILS

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PANEL CONTENT AND REPORTING TRANSCRIPTS

ABL1 NM_005157.4^
ABL2 NM_007314.3
ACVR1 NM_001105.4
ACVR1B NM_020328.3
AKT1 NM_001014432.1
AKT2 NM_001626.4+
AKT3 NM_005465.4
ALK NM_004304.4^+
ANKRD11 NM_001256182.1
ANKRD26 NM_014915.2
APC NM_000038.5
AR NM_000044.3+
ARAF NM_001654.4
ARFRP1 NM_003224.4
ARID1A NM_006015.4
DNAJB1 NM_006145.1
DNMT1 NM_001130823.1
DNMT3A NM_022552.4
DNMT3B NM_006892.3
DOT1L NM_032482.2
E2F3 NM_001949.4
EED NM_003797.3
EGFL7 NM_016215.4
EGFR NM_005228.3^+
EIF1AX NM_001412.3
EIF4A2 NM_001967.3
EIF4E NM_001130679.1
EML4 NM_019063.3
EP300 NM_001429.3
EPCAM NM_002354.2
EPHA3 NM_005233.5
H2BC5 NM_021063.3
H3C1 NM_003529.2
H3C2 NM_003537.3
H3C3 NM_003531.2
H3C4 NM_003530.4
H3C6 NM_003532.2
H3C7 NM_021018.2
H3C8 NM_003534.2
H3C10 NM_003536.2
H3C11 NM_003533.2
H3C12 NM_003535.2
H3C15 NM_001005464.2
H3C14 NM_021059.2
H3C13 NM_001123375.2
H3-4 NM_003493.2
HLA-A NM_002116.7
HLA-B NM_005514.6
MYC NM_002467.4+
MYCL NM_001033082.2+
MYCN NM_005378.4+
MYD88 NM_002468.4
MYOD1 NM_002478.4
NAB2 NM_005967.3^
NBN NM_002485.4
NCOA3 NM_181659.2
NCOR1 NM_006311.3
NEGR1 NM_173808.2
NF1 NM_001042492.2
NF2 NM_000268.3
NFE2L2 NM_006164.4
NFKBIA NM_020529.2
NKX2-1 NM_001079668.2
COP1 NM_022457.5
RHEB NM_005614.3
RHOA NM_001664.2
RICTOR NM_152756.3+
RIT1 NM_006912.5
RNF43 NM_017763.4
ROS1 NM_002944.2^
RPS6KA4 NM_003942.2
RPS6KB1 NM_003161.3+
RPS6KB2 NM_003952.2
RPTOR NM_020761.2
RUNX1 NM_001754.4
RUNX1T1 NM_175635.2
RYBP NM_012234.5
SDHA NM_004168.2
SDHAF2 NM_017841.2

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ARID1B NM_020732.3
ARID2 NM_152641.2
ARID5B NM_032199.2
ASXL1 NM_015338.5
ASXL2 NM_018263.4
ATM NM_000051.3+
ATR NM_001184.3
ATRX NM_000489.3
AURKA NM_198433.1
AURKB NM_004217.3
AXIN1 NM_003502.3
AXIN2 NM_004655.3
AXL NM_021913.4
B2M NM_004048.2
BAP1 NM_004656.3
BARD1 NM_000465.2
BBC3 NM_001127240.2
BCL10 NM_003921.4
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BCL2L1 NM_138578.1
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BCL2L2 NM_001199839.1
BCL6 NM_001706.4
BCOR NM_001123385.1
BCORL1 NM_021946.4
BCR NM_004327.3^
BIRC3 NM_001165.4
BLM NM_000057.2
BMPR1A NM_004329.2
BRAF NM_004333.4^+
BRCA1 NM_007294.3+
BRCA2 NM_000059.3+
BRD4 NM_058243.2
BRIP1 NM_032043.2
BTG1 NM_001731.2
BTK NM_000061.2
EMSY NM_020193.3
CALR NM_004343.3
CARD11 NM_032415.4
CASP8 NM_001228.4
CBFB NM_001755.2
CBL NM_005188.3
CCND1 NM_053056.2+
CCND2 NM_001759.3
CCND3 NM_001760.3+
CCNE1 NM_001238.2+
CD274 NM_014143.3
CD276 NM_001024736.1
CD74 NM_001025159.2^
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+
CDK8 NM_001260.1
CDKN1A NM_000389.4
CDKN1B NM_004064.3
CDKN2A NM_000077.4
CDKN2B NM_004936.3
CDKN2C NM_001262.2
CEBPA NM_004364.3
EPHA5 NM_004439.5
EPHA7 NM_004440.3
EPHB1 NM_004441.4
ERBB2 NM_004448.2+
ERBB3 NM_001982.3+
ERBB4 NM_005235.2
ERCC1 NM_001983.3+
ERCC2 NM_000400.3+
ERCC3 NM_000122.1
ERCC4 NM_005236.2
ERCC5 NM_000123.3
ERG NM_001136154.1
ERRFI1 NM_018948.3
ESR1 NM_001122742.1+
ETS1 NM_001143820.1
ETV1 NM_004956.4^
ETV4 NM_001079675.2^
ETV5 NM_004454.2
ETV6 NM_001987.4^
EWSR1 NM_013986.3^
EZH2 NM_004456.4
AMER1 NM_152424.3
ABRAXAS1 NM_139076.2
TENT5C 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
FANCI NM_001113378.1
FANCL NM_001114636.1
FAS NM_000043.4
FAT1 NM_005245.3
FBXW7 NM_033632.3
FGF1 NM_001144934.1+
FGF10 NM_004465.1+
FGF14 NM_175929.2+
FGF19 NM_005117.2+
FGF2 NM_002006.4+
FGF23 NM_020638.2+
FGF3 NM_005247.2+
FGF4 NM_002007.2+
FGF5 NM_004464.3+
FGF6 NM_020996.1+
FGF7 NM_002009.3+
FGF8 NM_033163.3+
FGF9 NM_002010.2+
FGFR1 NM_023110.2+
FGFR2 NM_000141.4^+
FGFR3 NM_000142.4^+
FGFR4 NM_213647.1+
FH NM_000143.3
FLCN NM_144997.5
FLI1 NM_002017.4
FLT1 NM_002019.4
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TSC1 NM_000368.4
TSC2 NM_000548.3

BELAY DIAGNOSTICS

Date: 11/06/2025
Order ID: SumPos-Mets-1

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Summit™ 2.0 Report

CENPA NM_001809.3
CHD2 NM_001271.3
CHD4 NM_001273.2
CHEK1 NM_001114122.2+
CHEK2 NM_007194.3+
CIC NM_015125.3
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ZFHX3 NM_006885.3
ZNF217 NM_006526.2
ZNF703 NM_025069.1
ZRSR2 NM_005089.3
MTAP NM_002451.3+*

^Summit™ also reports fusion events for this gene
+Summit™ also reports copy number alterations for this gene
*Summit™ only reports copy number alterations for this gene

Aneuploidy (chromosome arm level loss and gain)									
chr1p	chr3p	chr5p	chr7p	chr9p	chr11p	chr13q	chr16q	chr18q	chr20q
chr1q	chr3q	chr5q	chr7q	chr9q	chr11q	chr14q	chr17p	chr19p	chr21q
chr2p	chr4p	chr6p	chr8p	chr10p	chr12p	chr15q	chr17q	chr19q	chr22q
chr2q	chr4q	chr6q	chr8q	chr10q	chr12q	chr16p	chr18p	chr20p	

Methods and Limitations

The Summit™ 2.0 comprehensive genomic profiling next-generation sequencing (NGS) test investigates tumor derived nucleic acid extracted from cerebrospinal fluid (CSF) for clinically relevant single/multi nucleotide variants (SNVs, MNVs), insertions and deletions (indels), gene level copy number variants (CNVs), chromosomal arm level loss/gain (aneuploidy), and other biomarkers such as tumor mutational burden (TMB) and microsatellite instability (MSI). Methodology involves evaluation of 520 genes for SNVs, MNVs, Indels, 62 genes for CNVs, 27 genes for fusions, as well as TMB, MSI and low pass whole genome sequencing (>0.1x) for the detection of chromosomal aneuploidy (PMID: 37014860). Libraries are sequenced on the Illumina NovaSeq XPlus. The LOD (limit of detection) for SNVs, MNVs and Indels was determined to be 0.3% variant allelic frequency (VAF), for CNVs was determined to be >=2-fold change for amplifications and < 0.5-fold change for deletions, for fusions was determined to be >=2 supporting reads, and for aneuploidy was determined to be log2(*r*) of 0.09. Reporting on TMB and MSI requires >=15ng total nucleic acid yield, for TMB low <10 Mut/Mb, >=10 Mut/Mb for TMB high and MSI high when total unstable sites is >=5%. Variants (mutations and aneuploidy) are called against the human genome build reference hg19 using Summit™Omics pipeline version 1.0.0, developed at Belay Diagnostics.

Tertiary analysis is performed using the precision oncology workbench (GenomOncology) based on the joint AMP/ASCO/CAP consensus guidelines for interpretation of sequence variants in cancer (PMID: 27993330). Please reach out to contact@belaydiagnostics.com for additional information or queries.

Disclaimers

This test was developed, and its performance characteristics determined by Belay Diagnostics Laboratory (CLIA# 14D2302605), which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This test has not been cleared or

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Summit™ 2.0 Report

approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes. However, the results of this test do not establish a diagnosis and should not be used alone for diagnosis or patient care decisions or otherwise replace the judgment of a treating physician and must always be interpreted in the context of all relevant clinical and pathological data.

This test is performed only to evaluate for somatic (i.e., tumor-specific) variants within the genes listed and cannot distinguish between germline and somatic alterations with absolute certainty. This test therefore does not report on incidental findings as defined by the American College for Medical Genetics and Genomics (ACMG) (PMID: 37347242). If a germline variant is suspected, follow-up germline testing using non-neoplastic (normal) tissue should be performed by a laboratory permitted to perform germline genetic testing along with genetic counseling. It is possible for a genomic variant to be present yet go undetected by our assay either due to the heterogeneous nature of the specimen or the limits of detection of our assay. Therefore, to the extent a particular genomic variant is not reported, Belay Diagnostics LLC does not guarantee that the variant does not exist in the specimen provided. Likely benign, and benign variants are not reported. For any reported variant of uncertain significance (VUS), if the classification changes, there is no obligation to send out a new report updating this information.

The information presented in the clinical trials and therapeutic sections of this report is compiled from public sources which are continuously updated. While we strive to ensure this information is accurate and complete, we cannot guarantee the accuracy or completeness of this information. This public sourced information is not ranked in order of potential or predicted efficacy and may not be complete. Specific eligibility criteria should be reviewed as applicable. This information may include associations between a genomic variant (or lack of a variant) and one or more therapeutic agents with potential clinical benefit (or lack of clinical benefit), including agents that are being studied in clinical research. The finding of a genomic variant does not necessarily indicate or demonstrate pharmacologic effectiveness (or lack thereof) of any agent or treatment regimen found in public source information. Similarly, the finding of "no clinically significant variant" does not necessarily indicate or demonstrate lack of pharmacologic effectiveness (or lack of effectiveness) of any agent or treatment regimen found in public source information. Belay Diagnostics expressly disclaims, and makes no representation of or warranty of, the accuracy or completeness with respect to the publicly available information included herein or reviewed or collected during creation of this report.

ACTIONABILITY REFERENCES

FDA: U.S. Food & Drug Administration (fda.gov)

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WHO: World Health Organization Classification of Tumours online (tumourclassification.iarc.who.int)

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