NORTH WEST
LABS

Next Generation Sequencing Testing

North West Labs

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Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Hereditary Cancer Genetics (CGX)

Next Gen Sequencing

Myeloid NGS

North West Labs
(248) 301-6917 | support@nwlabs.com
29580 Northwestern Hwy, Ste 120 | Southfield, MI 48034
www.nwlabs.com

Whole Exome Sequencing (WES)

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Comprehensive Solid Tumor NGS

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Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

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Whole Exome Sequencing (WES)

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29580 Northwestern Hwy., Southfield, MI 48034
Phone: (248) 301-6917 Fax: (248) 301-6785 CLIA: 23D2126347
support@nwlabs.com www.nwlabs.com

SolidTumorCheck+ Requisition & Statement of Medical

1. PATIENT INFORMATION

Last Name | First Name

DOB (yyyy/mm/dd) | Sex ☐ F ☐ M | Medical Record Number

Street Address

City | State | Country | Zip

Preferred Contact Phone Number | Email (We will email status updates of your test)

☐ New NWL Patient ☐ Existing NWL Patient

2. SPECIMEN INFORMATION

Collection Date (yyyy/mm/dd) | Name of Person Collecting Specimen

3. ICD 10 CODE(S)

4. STAGE (REQUIRED)

Patients not eligible for systemic therapy or Stage I/II not currently accepted

☐ Advanced Cancer (Stage IIIB/IV-NSCLC, Stage III/IV-other cancer types)

Currently on Therapy? If yes, please list below ▶

5. ORDERING PHYSICIAN (or other Licensed Medical Professional)

Last Name | First Name

Email

Medical Professional Consent
My signature constitutes a Certification of Medical Necessity, and I hereby authorize and order North West Labs, Inc. to perform genetic testing and curation for this patient as indicated on this requisition. I have reviewed the medical consent on the back of this form and will provide test interpretation to the patient as appropriate. *(continued on back)*

Medical Professional Signature | Date

X

6. TEST SELECTION (MUSTchooseone)

☐ SolidTumorCheck+

7. ADDITIONAL RECIPIENT

Medical Professional Name

Phone Number | Fax Number

8. DIAGNOSIS (MUSTchooseone)

Date of Original Diagnosis (yyyy/mm/dd)

BRAIN
- ☐ Glioblastoma
- ☐ Other Primary CNS Tumor ▶

BREAST
- ☐ Breast Carcinoma

GENITOURINARY
- ☐ Bladder Carcinoma
- ☐ Prostate Adenocarcinoma
- ☐ Renal Cell Carcinoma
- ☐ Renal Pelvis Urothelial Carcinoma

GI
- ☐ Appendiceal Adenocarcinoma
- ☐ Cholangiocarcinoma
- ☐ Colorectal Adenocarcinoma
- ☐ Esophageal Squamous Cell Carcinoma
- ☐ Gastric Adenocarcinoma
- ☐ Esophageal/Gastroesophageal Junction Adenocarcinoma
- ☐ (GIST) Gastrointestinal Stromal Tumor
- ☐ Hepatocellular Carcinoma
- ☐ Pancreatic Ductal Adenocarcinoma
- ☐ Pancreatic Neuroendocrine Tumor
- ☐ Other Gastrointestinal Tumor ▶

GYNECOLOGIC
- ☐ Cervical Squamous Cell Carcinoma
- ☐ Endometrial Carcinoma
- ☐ Ovarian Carcinoma

HEAD & NECK
- ☐ Squamous Cell Carcinoma

LUNG
- ☐ Adenocarcinoma (NSCLC)
- ☐ Large Cell Carcinoma (NSCLC)
- ☐ Squamous Cell Carcinoma (NSCLC)
- ☐ Lung Carcinoid/Neuroendocrine
- ☐ Small Cell Lung Carcinoma
- ☐ Other Lung Tumor ▶

SARCOMA
- ☐ Sarcoma, please specify ▶

SKIN
- ☐ Basal Cell Carcinoma
- ☐ Squamous Cell Carcinoma
- ☐ Melanoma

THYROID
- ☐ Thyroid Carcinoma

OTHER
- ☐ Carcinoma of Unknown Primary (CUP)
- ☐ Other ▶

9. RELEVANT CLINICAL HISTORY(ALLREQUIREDformedical coverage determination)

1. The patient is seeking further treatment and is:	☐ Newly diagnosed (Stage III/IV)	☐ Not responding to therapy	
2. Has the patient received a PCHS report since their most recent progression?	☐ No	☐ Yes	
3. Is tissue-based comprehensive genomic profilling (CGP) from a recent biopsy feasible?	☐ No	☐ Yes	
4. Has tissue-based CGP from a recent biopsy been performed with a non-QNS result?	☐ No	☐ Yes	
5. Has tissue-based CGP from a recent biopsy already returned an actionable result?	☐ No	☐ Yes	

10. BILLING INFORMATION Please attach a copy of the front and back of the patient's insurance card and/or the patient face sheet

Patient Status (Medicare only) ☐ Hospital Inpatient ☐ Hospital Outpatient ☐ Non-Hospital Patient

☐ Insurance (please fill in below) ☐ Medicare - Part B ☐ Medicaid ☐ Hospital/Institution ☐ Self-Pay (Please contact Client Services for billing information)

Primary Insurance	Insured Name	Policy #	Group #
Patient Relationship to Insured ☐ Self ☐ Spouse ☐ Child ☐ Other	Insured DOB		

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Test Requisition & Statement of Medical Necessity *continued*

5. Medical Professional Consent *(continued from front)*

As may be required by applicable state laws and regulations, I have supplied information to the patient regarding somatic genomic testing, and the patient has givenconsent for this testing to be performed by North West Labs, Inc. (NWL) and for the results to be reported back to me. I understand that NWL is relying only on the diagnosis or diagnosis code that I provide on the test requisition form in providing information about potential therapeutic options and clinical trials associated with the reported genomic testing results, and that an incorrect diagnosis or diagnosis code would adversely affect the relevance of the information provided by PCHS. I understand that I remain free in my medical decisions on how to use the results of SolidTumorCheckK+ test in my management of this patient. I have obtained in writing the patient's data privacy consent to transmit the health data on this requisition form for the purpose of processing this order and performing the SolidTumorCheckK+ test. I authorize NWL to select the most appropriate test.

I hereby authorize PCHS to release test results and relevant medical information to the patient's third-party payer, when necessary, as part of the reimbursement process. I have obtained the patient's consent for NWL to submit claims and, if necessary, to appeal claims on the patient's behalf to pursue reimbursement, as well as for NWL to receive payment directly from the patient's insurance carrier. Medicare will only pay for tests that meet the Medicare coverage criteria and are reasonable and necessary to treat or diagnose an individual patient. With respect to tests reimbursed by Medicare, Medicaid or other third-party payers, I attest that NWL testing is medically necessary, and the results will be used in the management of the patient's condition. I agree to provide a copy of relevant clinical history and medical records in order to support a request from a health plan, at no cost to PCHS. I acknowledge that patients who are United States residents may be enrolled in NWL Access, NWL Financial Assistance Program only if they sign the assignment of benefits form.

For Medicare Beneficiaries Only

If SolidTumorCheckK+ test is ordered: a Medicare Advance Beneficiary Notice (ABN) must be submitted for any Medicare patient for whom has previously had a SolidTumorCheck+ test and has not progressed since the previous test was performed. If SolidTumorCheckK+ is ordered: a Medicare Advance Beneficiary Notice (ABN) must be submitted for any Medicare patient for whom the questions in Section 9 on the previous page are marked in the following manner: NSCLC patients, an ABN is required if (1) question 2 is marked "Yes" or (2) if question 5 is marked "Yes" or (3) if tissue-based CGP from a recent biopsy was feasible but not performed; non-CNS solid tumor patients other than NSCLC, an ABN is required if any question is marked "Yes"; all CNS patients require an ABN. ABN forms that have been pre-populated with NWL tests/prices can be obtained from PCHS ABN forms can be sent to NWL with the kit/sample, via emailed to: appointment@nwlabs.com

Patient Assignment of Benefits Form (required)

ASSIGNMENT OF BENEFITS

I hereby assign and convey all applicable health insurance benefits and/or insurance reimbursement, as well as all rights and obligations that I have under my health plan, to NWL. for services performed by NWL. I appoint NWL. as my authorized representative to

- File medical claims with my health plan;
- File appeals and grievances with my health plan;
- File appeals or grievances with an external review committee at a state insurance board, independent review organization, Office of Personnel Management, Department of Labor or equivalent agency;
- File a complaint, regarding inaccurate claims processing, appeal processing or pricing to CMS or their agent regarding my Medicare Part C plan
- Release medical and insurance information necessary to process claims or appeals;
- Obtain medical records related to services provided by NWL when it is required to process a claim or appeal;
- Collect payment of any and all medical benefits and insurance proceeds directly from my health plan (including Medicare and Medicaid);
- Resolve any insurance related matter regarding a service provided by NWL directly with my health plan

I acknowledge and agree that I remain responsible for applicable co-payments, deductibles and co-insurance as required by my medical and/or other healthcare benefits plans. If I receive payment of medical and/or other health benefits on account of services provided by PCHS I shall pay PCHS. the full amount of that payment.

AUTHORIZATION RELEASE

I hereby authorize Precheck Health Services, Inc. to

- Release any information necessary to my health benefit plan (or its administrator) regarding my illness and treatments;
- Process and submit insurance claims generated in the course of examination or treatment; and
- Allow a photocopy of my signature to be used to process insurance claims, payment, grievances or appeals. This authorization will remain in effect until revoked by me in writing.

OUT-OF-NETWORK DISCLOSURE AND PATIENT CONSENT

I understand that NWL may be designated as an out-of-network service by some insurance plans. As a result, there may be costs associated with these services that are not covered by my insurance plan. I hereby consent for out-of-network services to be provided by NWL.

NWL will provide upon request, the estimated amount that NWL expects to bill for services associated with out-of-network plans.

ERISA AUTHORIZATION

I hereby designate, authorize, and convey to NWL, to the full extent permissible under law and under any applicable insurance policy and/or employee health care benefit plan, the following:

- The right and ability to act as my Authorized Representative in connection with any claim, right, or cause of action against my health plan that I may have under such insurance policy and/or benefit plan; and
- The right and ability to act as my Authorized Representative to pursue such claim, right, or cause of action in connection with said insurance policy and/or benefit plan (including, but not limited to, the right and ability to act as my Authorized Representative with respect to a benefit plan governed by the provisions of ERISA as provided in 29 C.F.R. §2560.5031(b)(4)) with respect to any healthcare expense incurred as a result of the services I received from Provider and, to the extent permissible under the law, to claim on my behalf, such benefits, claims, or reimbursement, and any other applicable remedy, including fines. I understand I can revoke this authorization in writing at any time.

A photocopy of this Authorization shall be as effective and valid as the original.
This form is not an Advanced Beneficiary Notification (ABN).
If you have any questions, please do not hesitate to contact us at 1.305.203.4711 or appointment@nwlabs.com

X	PRINT NAME OF PATIENT	DATE
SIGNATURE OF PATIENT	EMAIL	

North West Labs
29580 Northwestern Hwy
Southfield, MI 48034
Tel (248) 301-6917
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Sample Name:
Sample Type:
Primary Tumor Site:
Sample Collected:

Sample Cancer Type: Ovarian Cancer

Relevant Ovarian Cancer Findings

Gene	Finding
BRCA1	***BRCA1 Q1756Pfs*74***
BRCA2	None detected

HRD Status: ***HR Deficient (HRD+)***

Genomic Alteration	Finding
Microsatellite Status	***Microsatellite stable***
Tumor Mutational Burden	***2.86 Mut/Mb measured (Low)***
Genomic Instability	***GIM 30 (High)***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Clinical Trials
IA	*BRCA1 Q1756Pfs*74* Allele Frequency: 69.95%	**bevacizumab + olaparib** [1, 2] **olaparib** [1, 2] **rucaparib** [1] niraparib	38
IA	*Genomic Instability* GIM 30 (High)	**bevacizumab + olaparib** [1, 2] niraparib	12
IIC	*TP53 R248Q* Allele Frequency: 43.15%	None	11

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Locus	Allele Frequency	Coverage	Transcript	Variant Effect	Oncomine Variant Class
TP53	p.(R248Q)	c.743G>A	chr17:7577538	43.15%	2000	NM_000546.6	missense	Hotspot
BRCA1	p.(Q1756Pfs*74)	c.5266_5267insC	chr17:41209079	69.95%	1990	NM_007294.4	frameshift Insertion	Truncating

Biomarker Descriptions

BRCA1 (BRCA1 DNA repair associated)

Background: The breast cancer early onset gene 1 (BRCA1) encodes one of two BRCA proteins (BRCA1 and BRCA2) initially discovered as major hereditary breast cancer genes. Although structurally unrelated, both BRCA1 and BRCA2 exhibit tumor suppressor function and are integrally involved in the homologous recombination repair (HRR) pathway, a pathway critical in the repair of damaged DNA[1,2]. Specifically, BRCA1/2 are required for the repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity[1,2]. Inherited pathogenic mutations in BRCA1/2 are known to confer increased risk in women for breast and ovarian cancer and in men for breast and prostate cancer[3,4,5]. For individuals diagnosed with inherited pathogenic or likely pathogenic BRCA1/2 variants, estimated lifetime risks range from 41% to 90% for developing breast cancer and 8 to 62% for developing ovarian cancer[6].

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer, 5-10% of breast cancer, and 1-4% of prostate cancer[7,8,9,10,11,12,13,14]. Somatic alterations in BRCA1 are observed in 5-10% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, and cervical squamous cell carcinoma, 3-4% of lung squamous cell carcinoma, lung adenocarcinoma, stomach adenocarcinoma, ovarian serous cystadenocarcinoma, colorectal adenocarcinoma, and breast invasive carcinoma, and 2% of head and neck squamous cell carcinoma and glioblastoma multiforme[15,16].

Potential relevance: Individuals possessing BRCA1/2 pathogenic germline or somatic mutations are shown to exhibit sensitivity to platinum based chemotherapy as well as treatment with poly (ADP-ribose) polymerase inhibitors (PARPi)[17]. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells[18,19]. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib[20] (2014) was the first PARPi to be approved by the FDA for BRCA1/2 aberrations. Originally approved for the treatment of germline variants, olaparib is now indicated (2018) for the maintenance treatment of both germline BRCA1/2-mutated (gBRCAm) and somatic BRCA1/2-mutated (sBRCAm) epithelial ovarian, fallopian tube, or primary peritoneal cancers that are responsive to platinum-based chemotherapy. Olaparib is also indicated for the treatment of patients with gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib[20] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA1. Rucaparib[21] is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC. Talazoparib[22] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Niraparib[23] (2017) is another PARPi approved for the treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancers with a deleterious or suspected deleterious BRCA mutation. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[24]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[25]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA mutations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[26], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers. Like PARPi, pidnarulex promotes synthetic lethality but through an alternative mechanism which involves stabilization of G-quadruplexes at the replication fork leading to DNA breaks and genomic instability.

TP53 (tumor protein p53)

Background: The TP53 gene encodes the p53 tumor suppressor protein that binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis. Alterations in TP53 is required for oncogenesis as they result in loss of protein function and gain of transforming potential[27]. Germline mutations in TP53 are the

Biomarker Descriptions (continued)

underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[28,29].

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)[15,16,30,31,32,33]. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common including substitutions at codons R158, R175, Y220, R248, R273, and R282[15,16]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[34,35,36,37].

Potential relevance: The small molecule p53 reactivator, PC14586, received a fast track designation (2020) by the FDA for advanced tumors harboring a TP53 Y220C mutation[38]. The FDA has granted fast track designation (2019) to the p53 reactivator, eprenetapopt,[39] and breakthrough designation[40] (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation[41,42]. TP53 mutations confer poor prognosis in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL)[43,44,45,46,47]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[48]. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occuring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system[49].

HR Deficient

Background: Homologous recombination repair (HRR) is a DNA repair mechanism that targets double stranded breaks (DSBs) and interstrand cross-links (ICL) in DNA[50]. Homologous recombination deficiency (HRD) is characterized by the cell's inability to repair these DSBs[50,51]. HRD is caused by genetic or epigenetic alterations in the HRR pathway genes, most notably BRCA1 and BRCA2 along with other genes such as ATM and PALB2[52,53,54,55]. A consequence of HRD due to the failure to repair DSBs is genomic instability[56,57]. Genomic instability is an increased tendency towards acquiring genomic alterations during cell division[58,59,60,61,62,63]. These alterations include small structural variations (i.e., single nucleotide variants (SNVs), insertions, and deletions) as well as significant structural variations (i.e., loss or gain of large chromosome fragments)[59,64,65]. Variations of genomic instability include chromosomal instability, intrachromosomal instability, microsatellite instability, and epigenetic instability[58]. Importantly, while the impact of frame-shift mutations in specific HRR genes can be mitigated by secondary mutations that restore the correct reading frame and thereby alleviate HRD, the effects of genomic instability are permanent and not reversible[66,67,68]. For this reason, the alterations characteristic of genomic instability are referred to as genomic scars[69,70]. Some of the genomic scar signatures that are characteristic of the HRD phenotype include loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale transition (LST)[50,71]. Current methods for HRD detection are heterogeneous and the definition for HRD positive tumors varies depending on the cancer type[50]. Generally, these methods detect the causes of HRD (i.e., alterations in HRR genes) and/or the consequences (i.e., signatures of genomic instability/genomic scarring)[50,56,72,73].

Alterations and prevalence: In a pan-cancer analysis of HRR gene mutations and genomic scar signatures in 8847 tumors across 33 cancer types, 17.5% of tumors were HRD-positive and 4% of tumors were positive for the BRCA1/2 mutation[74]. Specifically, HRD-positive status was observed in over 50% of ovarian serous cystadenocarcinoma and lung squamous cell carcinoma, 35-45% of esophageal carcinoma, uterine carcinosarcoma, sarcoma, and lung adenocarcinoma, 20-30% of stomach adenocarcinoma, bladder urothelial carcinoma, breast invasive carcinoma, and head and neck squamous cell carcinoma, 5-15% of endometrial cancer, mesothelioma, cervical cancer, pancreatic adenocarcinoma, cutaneous melanoma, hepatocellular carcinoma, diffuse large B-cell lymphoma, and adrenocortical carcinoma, and 1-4% of rectum adenocarcinoma, prostate adenocarcinoma, colon adenocarcinoma, testicular germ cell tumors, kidney chromophobe, glioblastoma multiforme, low grade glioma, and renal clear cell carcinoma[74]. Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer, 5-10% of breast cancer, and 1-4% of prostate cancer[7,8,9,10,11,12,13,14]. Somatic alterations in BRCA1 are observed in 5-10% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, and cervical squamous cell carcinoma, 3-4% of lung squamous cell carcinoma, lung adenocarcinoma, stomach adenocarcinoma, ovarian serous cystadenocarcinoma, colorectal adenocarcinoma, and breast invasive carcinoma, and 2% of head and neck squamous cell carcinoma and glioblastoma multiforme[15,16]. Somatic alterations in BRCA2 are observed in 5-15% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, stomach adenocarcinoma, colorectal adenocarcinoma, lung squamous cell carcinoma, lung adenocarcinoma, and uterine carcinosarcoma, 3-4% of cervical squamous cell carcinoma, head and neck squamous cell carcinoma, esophageal adenocarcinoma, ovarian serous cystadenocarcinoma, cholangiocarcinoma, breast invasive carcinoma, renal papillary cell carcinoma, and 2% of renal clear cell carcinoma, hepatocellular carcinoma, thymoma, prostate adenocarcinoma, sarcoma, and glioblastoma multiforme[15,16].

Biomarker Descriptions (continued)

Potential relevance: HRD status is an important biomarker in advanced ovarian and prostate cancer because it predicts response to certain treatments including poly-ADP ribose polymerase (PARP) inhibitors and platinum chemotherapies[5,75,76]. Disruption of HRR or inhibition of PARP, are tolerated by cells through the utilization of complementary DNA repair pathways. However, presence of HRD and subsequent treatment with PARP inhibitors block DNA repair, causing accumulation of DNA damage and cell death through synthetic lethality[50,77,78,79]. Several PARP inhibitors are approved by the FDA for various cancers associated with markers of HRD. Olaparib[20] was the first PARP inhibitor originally approved in 2014 for ovarian cancer with germline mutations in BRCA1/2 (gBRCAm). The utility of olaparib has since expanded to include genomic instability markers and mutations in other HRR genes. Specifically, olaparib as monotherapy is now indicated for gBRCAm and somatic BRCA1/2 mutated (sBRCAm) ovarian cancer and in combination with bevacizumab for BRCA1/2 mutated or genomic instability positive ovarian cancer[20]. In addition, olaparib is approved in prostate cancer with germline or somatic mutations in HRR genes including ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L[20,53,80]. Olaparib is also approved for gBRCAm HER2 negative breast cancer and as maintenance therapies for gBRCAm pancreatic cancers[20]. Other PARP inhibitors that are FDA approved for BRCA mutated cancers include rucaparib[21] (2016) that is indicated for gBRCAm or sBRCAm ovarian and prostate cancers, niraparib[23] (2017) that is indicated for gBRCAm ovarian cancer, and talazoparib[22] (2018) that is indicated for gBRCAm HER2-negative metastatic breast cancer. Niraparib is also recommended for the treatment of HRD-positive ovarian cancer, defined by BRCA1/2 mutations and/or genomic instability[81]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA1/2 mutations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[26], for BRCA1/2, PALB2, or other HRR gene mutations in breast and ovarian cancers. Like PARP inhibitors, pidnarulex[26] causes synthetic lethality but through an alternative mechanism which involves stabilization of G-quadruplexes at the replication fork leading to DNA breaks and genomic instability. Despite tolerability and efficacy, acquired resistance to PARP inhibitors such as olaparib has been clinically reported[24]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[25]. Other potential mechanisms of resistance to PARP inhibitors include restoration of HRR activity, stabilization of the replication forks, inhibition of PARP trapping, increased drug efflux mediated by P-glycoprotein, and cell cycle control alterations[25,82,83,84].

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome[85]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[86,87]. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2[88]. Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250[89]. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)[89]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[90,91,92,93,94]. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes[87]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[86,87,91,95].

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma[86,87,96,97]. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers[96,97].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[98] (2014) and nivolumab[99] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[98] is also approved as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication[98]. Dostarlimab[100] (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer[92,101]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[102] (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location[92,103,104]. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients[104]. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H

Biomarker Descriptions (continued)

tumors[105,106]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[105,106].

Clinical Trials Summary

BRCA1 Q1756Pfs*74 + Genomic Instability

NCT ID	Title	Phase
NCT04518501	Fuzuloparib Plus Arsenic Trioxide in Patients With Platinum Resistance Relapsed Ovarian Cancer	I/II
NCT04890613	Phase Ib Expansion Study of CX-5461 in Patients With Solid Tumours and BRCA2 and/or PALB2 Mutation	I

BRCA1 Q1756Pfs*74

NCT ID	Title	Phase
No NCT ID	Phase II Study To Evaluate The Efficacy And Safety Of Niraparib In Recurrent Or Persistent Rare Gynecologic Malignancies With Homologous Recombination Deficiency (JGOG2052)	II
NCT04261465	The NUVOLA TRIAL: Neoadjuvant Chemotherapy in Unresectable Ovarian Cancer With OLAparib and Weekly Carboplatin Plus Paclitaxel: A Phase II Open-label Multicentre Study	II
NCT05417594	A Modular Phase I/IIa, Open-label, Multi-centre Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Preliminary Efficacy of Ascending Doses of AZD9574 as Monotherapy and in Combination With Anti-cancer Agents in Patients With Advanced Solid Malignancies (CERTIS1)	I/II
NCT04586335	Open Label, Phase Ib Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Clinical Activity of CYH33, an Oral a-specific PI3K Inhibitor in Combination With Olaparib, an Oral PARP Inhibitor in Patients With Advanced Solid Tumors.	I
NCT04673448	Phase IB Trial of Niraparib and TSR-042 in Patients With BRCA-Mutated Breast, Pancreas or Ovary Cancer	I
NCT05445778	Randomized, Multicenter, Open-label, Phase III Study of Mirvetuximab Soravtansine in Combination With Bevacizumab Versus Bevacizumab Alone as Maintenance Therapy for Patients With FRα-positive Recurrent Platinum-sensitive Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancers Who Have Not Progressed After Second Line Platinum-based Chemotherapy Plus Bevacizumab	III
No NCT ID	A Phase I Trial of Niraparib and Pimitespib in Patients with Solid Tumors	I
NCT03278717	International Phase III Randomised Study to Evaluate the Efficacy of Maintenance Therapy With Olaparib and Cediranib or Olaparib Alone in Patients With Relapsed Ovarian Cancer Following a Response to Platinum-based Chemotherapy	III
NCT05255471	Olaparib Beyond Progression Compared to Platinum Chemotherapy After Secondary Cytoreductive Surgery in Recurrent Ovarian Cancer Patients. The Phase III Randomized, Open Label MITO 35b Study: a Project of the MITO-MANGO Groups.	III
NCT03462342	Combination ATR and PARP Inhibitor (CAPRI) Trial With AZD 6738 and Olaparib in Recurrent Ovarian Cancer	II

Clinical Trials Summary (continued)

BRCA1 Q1756Pfs*74 (continued)

NCT ID	Title	Phase
NCT03579316	EFFORT: Efficacy of AZD1775 in Parp Resistance; A Randomized 2-Arm, Non-Comparative Phase II Study of AZD1775 Alone or AZD1775 and Olaparib in Women With Ovarian Cancer Who Have Progressed During PARP Inhibition	II
NCT05225363	A Phase I Study to Evaluate TAG72-Targeting Chimeric Antigen Receptor (CAR) T Cells in Patients With Advanced Epithelial Ovarian Cancer	I
NCT02264678	A Modular Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of Ceralasertib in Combination With Cytotoxic Chemotherapy and/or DNA Damage Repair/Novel Anti-cancer Agents in Patients With Advanced Solid Malignancies.	I
NCT04169841	Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment	II
NCT05002868	A Multi-center, Open-label, Phase I/Ib Study to Assess the Safety, Pharmacokinetics and Anti-tumor Activity of RP12146, a Poly (ADP-ribose) Polymerase (PARP) Inhibitor, in Patients With Locally Advanced or Metastatic Solid Tumors.	I
NCT04507841	Niraparib for the Neoadjuvant Treatment of Unresectable Ovarian Cancer	II
NCT03188965	An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas	I/II
NCT04267939	An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase 2 Dose of the ATR Inhibitor Elimusertib (BAY 1895344) in Combination With PARP Inhibitor Niraparib, in Participants With Recurrent Advanced Solid Tumors and Ovarian Cancer	I
NCT04779151	An Open Label Phase II Basket Trial Exploring The Efficacy And Safety Of The Combination Of Niraparib And Dostarlimab In Patients With DNA Repair-Deficient Or Platinum-Sensitive Solid Tumors	II
NCT04992013	Genomically Guided Phase II Study to Evaluate the Clinical Benefit of Niraparib in Tumors Metastatic to the CNS	II
NCT02029001	A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.	II
NCT03967938	Efficacy of Olaparib in Advanced Cancers Occurring in Patients With Germline Mutations or Somatic Tumor Mutations in Homologous Recombination Genes	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT04550494	A Pharmacodynamics-Driven Trial of Talazoparib, an Oral PARP Inhibitor, in Patients With Advanced Solid Tumors and Aberrations in Genes Involved in DNA Damage Response	II
NCT05327010	Phase II Trial of the Combination of the BET Inhibitor, ZEN003694 (ZEN-3694), and the PARP Inhibitor Talazoparib, in Patients With Molecularly-Selected Solid Tumors (ComBET)	II
NCT04826341	A Phase I/II Study of Sacituzumab Govitecan Plus Berzosertib in Small Cell Lung Cancer, Extra-Pulmonary Small Cell Neuroendocrine and Homologous Recombination-Deficient Cancers Resistant to PARP Inhibitors	I/II

Clinical Trials Summary (continued)

BRCA1 Q1756Pfs*74 (continued)

NCT ID	Title	Phase
NCT05269316	A First-in-human, Phase I/II, Open-label, Multi-center, Dose-escalation and Dose-expansion Study to Evaluate Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of the ATR Inhibitor IMP9064 Monotherapy and in Combination With PARP Inhibitor Senaparib in Patients With Advanced Solid Tumors	I/II
NCT05038839	A Phase I Study of Cabozantinib and Pamiparib to Evaluate Triple Inhibition of PARP, VEGFR and c-MET in Advanced Homologous Recombination Deficient Malignancies	I
NCT03842228	A Phase Ib Biomarker-Driven Combination Trial of Copanlisib, Olaparib, and Durvalumab (MEDI4736) in Patients With Advanced Solid Tumors	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT04266912	DNA Damage Repair (DDR) Inhibitor-Based Basket of Baskets Phase I/II Trial in Patients With Advanced Solid Tumors Harboring Aberrations in DDR Genes (D-BoB)	I/II
NCT03767075	Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours	II
NCT04423185	Platform Study of Genotyping Guided Precision Medicine for Rare Tumors in China	II
NCT04905914	A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors	I/II
NCT04901702	A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma	I/II
NCT04693468	Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)	I

Genomic Instability

NCT ID	Title	Phase
NCT03462342	Combination ATR and PARP Inhibitor (CAPRI) Trial With AZD 6738 and Olaparib in Recurrent Ovarian Cancer	II
NCT04507841	Niraparib for the Neoadjuvant Treatment of Unresectable Ovarian Cancer	II
NCT03579316	EFFORT: Efficacy of AZD1775 in Parp Resistance; A Randomized 2-Arm, Non-Comparative Phase II Study of AZD1775 Alone or AZD1775 and Olaparib in Women With Ovarian Cancer Who Have Progressed During PARP Inhibition	II
NCT05225363	A Phase I Study to Evaluate TAG72-Targeting Chimeric Antigen Receptor (CAR) T Cells in Patients With Advanced Epithelial Ovarian Cancer	I
NCT02264678	A Modular Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of Ceralasertib in Combination With Cytotoxic Chemotherapy and/or DNA Damage Repair/Novel Anti-cancer Agents in Patients With Advanced Solid Malignancies.	I
NCT04423185	Platform Study of Genotyping Guided Precision Medicine for Rare Tumors in China	II
NCT04992013	Genomically Guided Phase II Study to Evaluate the Clinical Benefit of Niraparib in Tumors Metastatic to the CNS	II
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

Clinical Trials Summary (continued)

Genomic Instability (continued)

NCT ID	Title	Phase
NCT04826341	A Phase I/II Study of Sacituzumab Govitecan Plus Berzosertib in Small Cell Lung Cancer, Extra-Pulmonary Small Cell Neuroendocrine and Homologous Recombination-Deficient Cancers Resistant to PARP Inhibitors	I/II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II

TP53 R248Q

NCT ID	Title	Phase
NCT04169841	Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment	II
NCT05002868	A Multi-center, Open-label, Phase I/Ib Study to Assess the Safety, Pharmacokinetics and Anti-tumor Activity of RP12146, a Poly (ADP-ribose) Polymerase (PARP) Inhibitor, in Patients With Locally Advanced or Metastatic Solid Tumors.	I
NCT03188965	An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas	I/II
NCT04267939	An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase 2 Dose of the ATR Inhibitor Elimusertib (BAY 1895344) in Combination With PARP Inhibitor Niraparib, in Participants With Recurrent Advanced Solid Tumors and Ovarian Cancer	I
NCT05631886	A Pilot Clinical Trial of Autologous EphA-2-Targeting Chimeric Antigen Receptor Dendritic Cell Vaccine Loaded With TP53 Mutant Peptide Plus Anti- PD-1 Antibody for Local Advanced/Metastatic Solid Tumors or Relapsed/Refractory Lymphomas.	I
NCT02029001	A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.	II
NCT03767075	Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours	II
NCT04905914	A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors	I/II
NCT04901702	A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma	I/II
NCT04992013	Genomically Guided Phase II Study to Evaluate the Clinical Benefit of Niraparib in Tumors Metastatic to the CNS	II
NCT04693468	Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)	I

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NORTH WEST LABS

Myeloid NGS

NORTH WEST
LABS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Hereditary Cancer Genetics (CGX)

Next Gen Sequencing

Myeloid NGS

North West Labs
(248) 301-6917 | support@nwlabs.com
29580 Northwestern Hwy, Ste 120 | Southfield, MI 48034
www.nwlabs.com

Whole Exome Sequencing (WES)

MYELOID MALIGNANCIES NGS ASSAY

ALL FORM FIELDS REQUIRED

CLIA Certified
CLIA# 23D2126347

NORTHWEST LABS, INC.
29580 NORTHWESTERN HWY | STE 120
SOUTHFIELD, MI 48034-1087
Phone: 248-301-6917 | Fax: 248-301-6805
Lab Director: Dr. Eugene S. Olsowka, MD

NORTH WEST LABS

PATIENT INFORMATION

LAST NAME: _____ FIRST NAME: _____ MI: _____

DOB (MM/DD/YY): ____ / _____ / _____ GENDER: ☐ MALE ☐ FEMALE ☐ OTHER

STREET ADDRESS: _____ APT / BUILDING NUMBER: _____

CITY: _____ STATE: _____ ZIP: _____ PHONE: _____

PATIENT STATUS

☐ NON HOSPITAL ☐ HOSPITAL OUTPATIENT ☐ HOSPITAL INPATIENT (> 24 HOUR STAY)

IF HOSPITAL INPATIENT, DISCHARGE DATE: _____ / _____ / _____

ORDERING PHYSICIAN AND FACILITY INFORMATION

FACILITY / PRACTICE NAME: _____

STREET ADDRESS: _____ STE / BLDG NUMBER: _____

CITY: _____ STATE: _____ ZIP: _____ PHONE: _____

ORDERING PHYSICIAN(S): _____ NPI #. _____

_____ NPI #. _____

BILLING INFORMATION *If Insurance, please attach a copy of the front and back of the patient's insurance card.*

☐ **INSURANCE / MEDICARE** (BILL TO PATIENT'S PRIMARY INSURANCE)
☐ **CLIENT BILL** (BILL DIRECTLY TO THE ORDERING FACILITY)
☐ **PATIENT SELF-PAY** (PLEASE CONTACT LAB FOR SELF-PAY PRICING)

TEST SELECTION

[X] **MI GENETICS MYELOID MALIGNANCIES NGS ASSAY (GENEXUS V2)**

INDICATION FOR USE

The Myeloid Malignancies NGS Assay is intended for the qualitative detection of somatic single nucleotide variants (SNVs), insertions, deletions (indels), and clinically relevant RNA fusions associated with myeloid malignancies. The results generated by this assay are designed to support clinicians in several key areas of patient management, including diagnostic subclassification, prognostic assessment, and therapeutic selection. Furthermore, the assay is also designed to evaluate molecular response and serves as a critical tool for monitoring disease, providing supportive information for minimal residual disease (MRD) assessment by tracking persistent or emergent variants post-therapy. This test is intended for use in patients with a suspected or confirmed myeloid neoplasm and is not indicated for population screening.

DNA TARGETS INCLUDE: ASXL1, BCOR, CALR, CEBPA, CSF3R, DNMT3A, EZH2, FLT3, GATA2, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, PHF6, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1 and others.

RNA FUSION TARGETS INCLUDE: BCR::ABL1, RUNX1::RUNX1T1, CBFB::MYH11, PML::RARA, KMT2A rearrangements and other clinically relevant fusions.

SPECIMEN INFORMATION *Please attach a copy of the patient's most recent CBC and relevant clinical history/pathology reports*

COLLECTION DATE (MM/DD/YY): _____ / _____ / _____ COLLECTION TIME: _____ ☐ AM ☐ PM

SPECIMEN ID / BLOCK ID: _____

SPECIMEN TYPE:
- ☐ BONE MARROW ASPIRATE (PREFERRED: 2-3 mL IN EDTA/PURPLE TOP)
- ☐ EXTRACTED NUCLEIC ACID (DNA/RNA) (VOLUME/CONCENTRATION: _____)
- ☐ OTHER: _____

DIAGNOSTIC ICD-10 CODES

☐ C92.00 - ACUTE MYELOBLASTIC LEUKEMIA (AML)	☐ C94.40 - ACUTE PANMYELOSIS WITH MYELOFIBROSIS	Other
☐ C92.10 - CHRONIC MYELOID LEUKEMIA (CML)	☐ D46.9 - MYELODYSPLASTIC SYNDROME (MDS), UNSPECIFIED	☐
☐ D47.1 - CHRONIC MYELOPROLIFERATIVE DISEASE	☐ D47.3 - ESSENTIAL THROMBOCYTHEMIA	☐

CLINICAL INFORMATION AND DIAGNOSIS

CLINICAL STATUS

- ☐ NEW DIAGNOSIS / SUSPECTED NEOPLASM
- ☐ MONITORING / POST-THERAPY (MRD ASSESSMENT)
- ☐ PROGNOSTIC ASSESSMENT
- ☐ RELAPSE / REFRACTORY

SIGNS/SYMPTOMS / CLINICAL HISTORY: _____

REQUIRED ATTACHMENTS

☐ CBC ☐ PATHOLOGY RECORD ☐ CLINICAL HISTORY ☐ PRIOR MOLECULAR RESULTS ☐ CYTOGENETICS/FISH (IF AVAILABLE) ☐ FLOW CHEMISTRY

PHYSICIAN ACKNOWLEDGMENT & REFERRAL AUTHORIZATION: I, the undersigned healthcare provider, acknowledge that when ordering the Comprehensive Myeloid NGS Panel through Northwest Labs, I understand that testing may be performed by partner facilities and acknowledge this may impact billing and result timelines. I confirm patients have been informed of this arrangement.

Physician Signature: _____ *Date:* _____

PATIENT CONSENT & FINANCIAL RESPONSIBILITY: I authorize the release of medical information for reporting and request benefits be paid to Northwest Labs, Inc. I assume liability for deductibles, co-payments, and non-covered charges. I permit Northwest Labs, Inc. to appeal insurance claims on my behalf. MEDICARE ADVANCE BENEFICIARY NOTICE (ABN): Medicare may deny payment for services deemed not reasonable or necessary for the reported diagnosis. By signing, the patient assumes financial responsibility if payment is denied.

Patient Signature: _____ *Date:* _____

SPECIMEN REQUIREMENTS: Specimens should be refrigerated if not shipped immediately; please utilize a cool pack during transit. For inquiries regarding specimen criteria or logistics, contact Client Services at 248-301-6917 or support@nwlabs.com (Option Y). Detailed specimen specifications are available on our website.

ADDITIONAL BILLING TERMS: Any facility submitting specimens via this Requisition Form ("Client") agrees to the following:

1. Binding Service Order: This form constitutes a binding contract for services; Client assumes full financial responsibility for all tests billed to the Client.

2. Third-Party Billing & Client Responsibility: Client must accurately designate whether Northwest Labs should bill the Client directly or a third-party payer. Client must provide all necessary billing data for third-party claims. Northwest Labs reserves the right to bill the Client directly if: (i) required billing information is not received within ten days of reporting; (ii) the patient lacks coverage*; or (iii) the payer denies responsibility and indicates Client Liability*

North West Labs
29580 Northwestern Hwy
Southfield, MI 48034
Ph: (248) 301-6917
support@nwlabs.com
www.nwlabs.com

Sample Type: Blood
Sample ID: 3456
Primary Tumor Site: Lymph node
Sample Collected: 010101

Sample Cancer Type: Acute Myeloid Leukemia

Relevant Acute Myeloid Leukemia Findings

Gene	Finding	Gene	Finding
ABL1	Not detected	MECOM	Not detected
ASXL1	Not detected	MLLT3	Not detected
CEBPA	Not detected	MYH11	Not detected
CREBBP	Not detected	NPM1	***NPM1 W288fs***
FLT3	***FLT3 ITD mutation***	NUP214	Not detected
IDH1	Not detected	RARA	Not detected
IDH2	Not detected	RUNX1	Not detected
KMT2A	Not detected	TP53	Not detected

Relevant Biomarkers

Prognostic/Diagnostic

Genomic Alteration	Prognostic significance	Diagnostic significance
FLT3 ITD mutation	ELN 2017: Favorable to Intermediate	None
NPM1 W288fs	ELN 2017: Favorable to Intermediate	Acute Myeloid Leukemia

Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

Relevant Biomarkers

Therapeutic

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Clinical Trials
IA	*FLT3 ITD mutation* fms related tyrosine kinase 3 Locus: chr13:28608269 Transcript: NM_004119.2	**gilteritinib** [1, 2] **midostaurin + chemotherapy** [1, 2] sorafenib + chemotherapy venetoclax + chemotherapy	42
IA	*NPM1 W288fs* nucleophosmin 1 Locus: chr5:170837543 Transcript: NM_002520.6	None	4

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	ClinVar[1]
NPM1	p.(W288fs)	c.863_864insTCTG	.	46.15%	NM_002520.6	frameshift Insertion	
FLT3	p.(G583_R595dup)	c.1786_1787insGCTCCTCAGATAATGAGTACTTCTACGTTGATTTCAGAG	.	36.39%	NM_004119.2	nonframeshift Insertion	

[1] Based on Clinvar version 20170404

Biomarker Descriptions

FLT3 (fms related tyrosine kinase 3)

Background: The FLT3 gene encodes the fms related tyrosine kinase 3, a tyrosine kinase receptor that is a member of the class III receptor tyrosine kinase family that also includes PDGFR, FMS, and KIT[1]. FLT3 is highly expressed in hematopoietic progenitor cells[2]. Genomic alterations in FLT3 activate downstream oncogenic pathways including PI3K/AKT/mTOR and RAS/RAF/MEK/ERK pathways which promote cellular proliferation, survival, and inhibition of differentiation[1].

Alterations and prevalence: Somatic mutations occur in approximately 30% of acute myeloid leukemia (AML), 7-10% of melanoma, and up to 8% of uterine cancer[3,4,5,6]. The most common activating FLT3 mutations are internal tandem duplications (ITD) that range from 3 to 400 base pairs in length within exons 14 and 15 in the juxtamembrane (JM) domain[7]. The second most frequent mutations are point mutations in exon 20 within the tyrosine kinase domain (TKD)[8]. FLT3 is amplified in up to 8% of colorectal cancer, 3% of stomach cancer, and is commonly overexpressed in AML[5,6,9].

Potential relevance: The presence of FLT3-ITD confers poor prognosis in myelodysplastic syndrome (MDS) and AML[10,11]. Similarly, the FLT3 TKD mutation D835 confers poor prognosis in MDS[10]. Midostaurin[12] (2017) and gilteritinib[13] (2018) are kinase inhibitors approved for AML patients with FLT3-ITD and TKD mutations including D835 and I836 mutations. The FDA granted fast track designations in 2017 to crenolanib[14] for FLT3 mutation-positive relapsed or refractory AML and in 2018 to quizartinib[15] for AML with FLT3-ITD. A phase II trial testing crenolanib in 34 patients with FLT3-ITD and TKD mutated relapsed/refractory AML, reported that FLT3 inhibitor naïve patients demonstrated a longer overall survival (OS) and event free survival (EFS) in comparison to previously treated patients (median OS: 55 weeks vs 13 weeks; median EFS: 13 weeks vs 7 weeks)[16]. Another phase II trial of crenolanib with chemotherapy in newly diagnosed FLT3 mutated AML reported complete remission in 24/29 (83%) patients[17]. Several multi-targeted tyrosine kinase inhibitors such as sorafenib (2005), sunitinib (2006), cabozantinib (2012), and ponatinib (2012) are FDA approved and include FLT3 as a target. Sorafenib is recommended in combination with chemotherapy in FLT3-ITD mutated AML[11].

NPM1 (nucleophosmin 1)

Background: The NPM1 gene encodes the nucleophosmin protein, a histone chaperone of the nucleophosmin/nucleoplasmin family, which also includes NPM2 and NPM3[18]. NPM1 functions as an oncogene and tumor suppressor, and is important in maintaining genomic stability, DNA repair, and apoptosis[18,19]. NPM1 has a highly conserved N-terminal region which constitutes the core domain responsible for oligomerization, an acidic domain, a nuclear localization signal, and a disorganized C-terminal region which is required for nucleolar localization[18]. Oligomerization of NPM1 localizes the protein in the nucleus of proliferating cells where it binds to Akt in response to growth factor stimulation and escapes proteolytic degradation by caspase activity, thereby promoting cell survival[18,19]. NPM1 is one of the most frequently altered genes in hematological cancers[20]. Most NPM1 mutations occur in the C-terminus, impacting protein folding or the nucleolar localization signal, and result in the localization of NPM1 to the cytoplasm (NPMc) instead of to the nucleus[18].

Alterations and prevalence: NPM1 mutations are observed in 45-60% of AML with a normal karyotype (NK-AML), 28-35% of de novo acute myeloid leukemia (AML) and are frequently co-mutated with DNMT3A and/or FLT3-ITD[11,21,22]. NPM1 fusions are associated with distinct partner genes in acute promyelocytic leukemia (APL), anaplastic large-cell lymphoma (ALCL), AML, and myelodysplasia[20]. Specifically, NPM1-ALK fusion is found in 30% of all ALCL and this specific fusion is observed in 85% of ALK-positive ALCL[18]. The t(5;17)(q35;q21) translocation that results in NPM1-RARA fusion is observed in APL[23].

Potential relevance: NPM1 mutated AML is recognized as a distinct diagnostic disease entity by the World Health Organization (WHO)[24]. NPM1 mutations are associated with better outcomes, increased complete remission, and improved overall survival in AML[11,22]. NPM1 without FLT3-ITD mutations or with <0.5 allelic ratio FLT3-ITD mutations are associated with favorable risk in AML, whereas wild-type NPM1 confers poor/adverse risk[11]. Concurrent NPM1 and with >0.5 allelic ratio FLT3-ITD mutations confer intermediate risk in AML[11]. The NPM1 frameshift mutation W288fs*12 is associated with poor prognosis in myelodysplastic syndrome (MDS)[10].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

FLT3 ITD mutation

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gilteritinib	●	●	●	●	● (III)
midostaurin + cytarabine + daunorubicin	●	●	●	●	✖
midostaurin + cytarabine	✖	●	✖	✖	✖
sorafenib + azacitidine	✖	●	✖	✖	✖
sorafenib + decitabine	✖	●	✖	✖	✖
venetoclax + azacitidine	✖	●	✖	✖	✖
venetoclax + cytarabine	✖	●	✖	✖	✖
venetoclax + decitabine	✖	●	✖	✖	✖
sorafenib	✖	✖	✖	✖	● (IV)
chemotherapy, midostaurin	✖	✖	✖	✖	● (III)
crenolanib, chemotherapy	✖	✖	✖	✖	● (III)
crenolanib, midostaurin, chemotherapy	✖	✖	✖	✖	● (III)
gemtuzumab ozogamicin, chemotherapy, gilteritinib	✖	✖	✖	✖	● (III)
gilteritinib, chemotherapy	✖	✖	✖	✖	● (III)
gilteritinib, midostaurin, chemotherapy	✖	✖	✖	✖	● (III)
chemotherapy	✖	✖	✖	✖	● (II/III)
ibrutinib, sorafenib, chemotherapy	✖	✖	✖	✖	● (II/III)
allogeneic stem cells, chemotherapy	✖	✖	✖	✖	● (II)
chemotherapy, radiation therapy	✖	✖	✖	✖	● (II)
chemotherapy, stem cell therapy, radiation therapy	✖	✖	✖	✖	● (II)
crenolanib	✖	✖	✖	✖	● (II)
midostaurin	✖	✖	✖	✖	● (II)
natural killer cell therapy, stem cell therapy	✖	✖	✖	✖	● (II)
ponatinib	✖	✖	✖	✖	● (II)
quizartinib, chemotherapy	✖	✖	✖	✖	● (II)
venetoclax, chemotherapy	✖	✖	✖	✖	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

FLT3 ITD mutation (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
CC-90009, gilteritinib	✖	✖	✖	✖	● (I/II)
chemotherapy, sorafenib	✖	✖	✖	✖	● (I/II)
FF-10101	✖	✖	✖	✖	● (I/II)
gilteritinib, atezolizumab	✖	✖	✖	✖	● (I/II)
midostaurin, gemtuzumab ozogamicin, chemotherapy	✖	✖	✖	✖	● (I/II)
NMS-P948	✖	✖	✖	✖	● (I/II)
ponatinib, chemotherapy	✖	✖	✖	✖	● (I/II)
stem cell therapy	✖	✖	✖	✖	● (I/II)
venetoclax, gilteritinib, chemotherapy	✖	✖	✖	✖	● (I/II)
venetoclax, quizartinib	✖	✖	✖	✖	● (I/II)
allogeneic double negative T cells	✖	✖	✖	✖	● (I)
clifutinib	✖	✖	✖	✖	● (I)
gemtuzumab ozogamicin, midostaurin, chemotherapy	✖	✖	✖	✖	● (I)
milademetan, quizartinib	✖	✖	✖	✖	● (I)
nintedanib, chemotherapy	✖	✖	✖	✖	● (I)
venetoclax, gilteritinib	✖	✖	✖	✖	● (I)

NPM1 W288fs

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
pembrolizumab, chemotherapy	✖	✖	✖	✖	● (II)
chemotherapy, supplement	✖	✖	✖	✖	● (I/II)
SNDX-5613	✖	✖	✖	✖	● (I/II)
venetoclax, pevonedistat, chemotherapy	✖	✖	✖	✖	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Details

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

FDA information is current as of 2020-11-18. For the most up-to-date information, search www.fda.gov.

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2019-05-29 **Variant class:** FLT3 ITD mutation

Indications and usage:
XOSPATA® is a kinase inhibitor indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211349s001lbl.pdf

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2020-03-04 **Variant class:** FLT3 ITD mutation

Indications and usage:

RYDAPT® is a kinase inhibitor indicated for the treatment of adult patients with:

- Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.

  Limitations of Use: RYDAPT® is not indicated as a single-agent induction therapy for the treatment of patients with AML.
- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/207997s004lbl.pdf

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2020-11-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Relapsed/Refractory Acute Myeloid Leukemia (Therapy for relapse/refractory)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

● midostaurin + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age <60 years; Intermediate-risk cytogenetics and/or molecular abnormalities (Post-remission therapy)
- Acute Myeloid Leukemia; Age <60 years; Treatment-related disease other than CBF and/or unfavorable cytogenetics and/or molecular abnormalities (Post-remission therapy)
- Acute Myeloid Leukemia; Age ≥60 years; Previous intensive therapy; Complete response (Post-remission therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age <60 years; Intermediate-risk cytogenetics (Induction therapy)
- Acute Myeloid Leukemia; Age <60 years; After standard-dose cytarabine induction; Significant residual disease without a hypocellular marrow or significant cytoreduction with >50% residual blasts (Re-induction therapy)
- Acute Myeloid Leukemia; Age ≥60 years; Candidate for intensive remission induction therapy (Induction therapy)
- Acute Myeloid Leukemia; Age ≥60 years; After standard-dose cytarabine induction; Residual disease (Post-induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

FLT3 ITD mutation (continued)

sorafenib + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age ≥60 years; Not a candidate for intensive remission induction therapy or declines; Low-intensity therapy (Induction therapy) (Other recommended regimen)
- Acute Myeloid Leukemia; Age ≥60 years; Previous lower-intensity therapy; Response (Post-induction therapy)
- Relapsed/Refractory Acute Myeloid Leukemia (Therapy for relapse/refractory)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

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sorafenib + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age ≥60 years; Not a candidate for intensive remission induction therapy or declines; Low-intensity therapy (Induction therapy) (Other recommended regimen)
- Acute Myeloid Leukemia; Age ≥60 years; Previous lower-intensity therapy; Response (Post-induction therapy)
- Relapsed/Refractory Acute Myeloid Leukemia (Therapy for relapse/refractory)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

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venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age ≥60 years; Not a candidate for intensive remission induction therapy or declines (Induction therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

---

venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Acute Myeloid Leukemia; Age ≥60 years; Not a candidate for intensive remission induction therapy or declines (Induction therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

FLT3 ITD mutation (continued)

venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Acute Myeloid Leukemia; Age ≥60 years; Not a candidate for intensive remission induction therapy or declines (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

EMA information is current as of 2020-11-18. For the most up-to-date information, search www.ema.europa.eu/ema.

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2019-11-08 **Variant class:** FLT3 ITD mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/xospata-epar-product-information_en.pdf

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2020-10-12 **Variant class:** FLT3 ITD mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/rydapt-epar-product-information_en.pdf

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2020-11-02. For the most up-to-date information, search www.esmo.org.

FLT3 ITD mutation

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Acute Myeloid Leukemia (Induction therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Relapsed or Refractory Acute Myeloid Leukemia; Not eligible for standard chemotherapy (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Prognostic Details

Current NCCN Information

NCCN information is current as of 2020-11-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

FLT3 ITD mutation + NPM1 W288fs

Prognostic significance: ELN 2017: Intermediate

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

Summary:
- FLT3-ITD^{high}; High defined as allelic ratio (≥0.5).

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

Prognostic significance: ELN 2017: Favorable

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

Summary:
- FLT-ITD^{low}; Low defined as allelic ratio (<0.5).

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2021]

Current ESMO Information

ESMO information is current as of 2020-11-02. For the most up-to-date information, search www.esmo.org.

FLT3 ITD mutation + NPM1 W288fs

Prognostic significance: ELN 2017: Intermediate

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

Summary:
- FLT3-ITD^{High}; High defined as allelic ratio (≥0.5)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Prognostic significance: ELN 2017: Favorable

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

Summary:
- FLT3-ITD^{Low}; Low defined as allelic ratio (<0.5)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Diagnostic Details

Current ESMO Information

ESMO information is current as of 2020-11-02. For the most up-to-date information, search www.esmo.org.

NPM1 W288fs

Diagnostic significance: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Diagnostic notes:
- AML with recurrent genetic abnormalities; WHO classification of AML

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Current Clinical Trials Information

Clinical Trials information is current as of 2020-11-02. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

FLT3 ITD mutation

NCT02156297
Sorafenib to Treat AML Patients With FLT3-ITD Mutation: a Non-interventional Cohort Study

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: ChiCTR-OCH-14004731, SZ3201

Population segments: (N/A), First line, Maintenance/Consolidation

Phase: IV

Therapy: sorafenib

Location: China

NCT04174612
A Phase III, Prospective, Randomized Multi-center Intervention Trial of Early Intensification in AML Patients Bearing FLT3 Mutations Based on Peripheral Blast Clearance: A MYNERVA-GIMEMA Study

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: AMELIORATE, AML1919, MYNERVA-GIMEMA

Population segments: First line, Untreated

Exclusion criteria variant classes: FLT3 ITD mutation, FLT3 TKD mutation, MYH11-CBFB fusion, RUNX1-RUNX1T1 fusion, t(16;16)(p13.1;q22), t(8;21)(q22;q22)

Phase: III

Therapies: chemotherapy, midostaurin

Location: Italy

FLT3 ITD mutation (continued)

NCT03250338
Phase III Randomized, Double-blind, Placebo-controlled Study Investigating the Efficacy of the Addition of Crenolanib to Salvage Chemotherapy Versus Salvage Chemotherapy Alone in Subjects < or = 75 Years of Age With Relapsed/Refractory FLT3 Mutated Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: ARO-013, EudraCT Number: 2017-001600-29, NCI-2018-00334

Population segments: (N/A), Maintenance/Consolidation, Second line, Third line

Phase: III

Therapies: crenolanib, chemotherapy

Locations: France, Germany, Italy, Spain, United States

US States: CA, FL, IL, KS, MI, NC, NY

Contact: General Contact [214-593-0500; info@arogpharma.com]

NCT03258931
Phase III Randomized Study of Crenolanib Versus Midostaurin Administered Following Induction Chemotherapy and Consolidation Therapy in Newly Diagnosed Subjects With FLT3 Mutated Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 17-623, 18-334, 19456, ARO-021, NCI-2018-00266, TX9327

Population segments: First line, Maintenance/Consolidation, Untreated

Phase: III

Therapies: crenolanib, midostaurin, chemotherapy

Location: United States

US States: CA, CT, FL, IA, IL, IN, KS, MA, MI, MN, NC, NJ, NY, OR, VA

Contact: General Contact [214-593-0500; info@arogpharma.com]

NCT04293562
A Phase III Randomized Trial for Patients With De Novo AML Comparing Standard Therapy Including Gemtuzumab Ozogamicin (GO) to CPX-351 With GO, and the Addition of the FLT3 Inhibitor Gilteritinib for Patients With FLT3 Mutations

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: AAML1831, NCI-2020-00546

Population segments: First line, Maintenance/Consolidation, Pediatric or Adolescent, Untreated

Exclusion criteria variant classes: BCR-ABL1 fusion, Trisomy 21

Phase: III

Therapies: gemtuzumab ozogamicin, chemotherapy, gilteritinib

Location: United States

US State: IN

Contact: Site Public Contact [317-338-2194; research@stvincent.org]

FLT3 ITD mutation (continued)

NCT03182244
Phase III Open-label, Multicenter, Randomized Study of ASP2215 Versus Salvage Chemotherapy in Patients With Relapsed or Refractory Acute Myeloid Leukemia (AML) With FLT3 Mutation

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 1512016855, 2215-CL-0303, 2215-CL-0303 34856, CTR20170326, F16099, NMRR-17-895-34856

Population segments: (N/A), Poor-risk, Second line

Phase: III

Therapy: gilteritinib

Locations: China, Malaysia, Russian Federation, Singapore, Thailand

NCT02752035
A Phase III Multicenter, Open-label, Randomized Study of ASP2215 (Gilteritinib), Combination of ASP2215 Plus Azacitidine and Azacitidine Alone in the Treatment of Newly Diagnosed Acute Myeloid Leukemia With FLT3 Mutation in Patients Not Eligible for Intensive Induction Chemotherapy

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 1604017585, 18-033, 2016-0266, 2215-CL-0201, EudraCT Number: 2015-001790-41, IRAS ID: 203823, LACEWING, NCI-2016-00914, UCI-16-100

Population segments: (N/A), First line, Untreated

Phase: III

Therapies: gilteritinib, chemotherapy

Locations: Australia, Belgium, Canada, France, Germany, Italy, Japan, Poland, Republic of Korea, Spain, Taiwan, United States

US States: CA, FL, IL, IN, MO, NJ, NY, SC, UT

Contact: Astellas Pharma Global Development [800-888-7704; astellas.registration@astellas.com]

NCT04027309
A Phase III, Multicenter, Open-label, Randomized, Study of Gilteritinib Versus Midostaurin in Combination With Induction and Consolidation Therapy Followed by One-year Maintenance in Patients With Newly Diagnosed Acute Myeloid Leukemia (AML) or Myelodysplastic Syndromes With Excess Blasts-2 (MDS-EB2) With FLT3 Mutations Eligible for Intensive Chemotherapy (HOVON 156 AML / AMLSG 28-18)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: AMLSG 28-18, EudraCT Number: 2018-000624-33, HO156, HOVON 156 AML, HOVON 156 AML / AMLSG 28-18, NL66038.029.18, Pasha

Population segments: First line, Maintenance/Consolidation, RAEB, RAEB-t, Untreated

Exclusion criteria variant class: PML-RARA fusion

Phase: III

Therapies: gilteritinib, midostaurin, chemotherapy

Location: Netherlands

FLT3 ITD mutation (continued)

NCT03256071
Low Dose Decitabine + Modified BUCY Conditioning Regimen for High Risk Acute Myeloid Leukemia Undergoing Allo-HSCT

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: DAC+BUCY

Population segments: (N/A), Pediatric or Adolescent, Second line

Phase: II/III

Therapy: chemotherapy

Location: China

NCT03642236
Combination of Brutons Tyrosine Kinase (BTK) Inhibitor Overcomes Drug-resistance in Refractory/Relapsed FLT3 Mutant Acute Myeloid Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: BTKi in FLT3 mutant AML

Population segments: (N/A), Second line

Phase: II/III

Therapies: ibrutinib, sorafenib, chemotherapy

Location: China

NCT01760655
A Two Step Approach to Reduced Intensity Allogeneic Hematopoietic Stem Cell Transplantation for High Risk Hematologic Malignancies

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 12D.501, 2012-67, NCI-2012-02762

Population segments: (N/A), Accelerated phase, Aggressive, Blast phase, Classical, Cutaneous T-cell lymphoma (CTCL), Diffuse large B-cell lymphoma (DLBCL), Essential Thrombocythemia, Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), High risk, Indolent, Mantle cell lymphoma (MCL), Nodular lymphocyte-predominant, Other subtype, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Polycythemia Vera, Poor-risk, Primary Myelofibrosis, RAEB, RAEB-t, RCMD, Remission, Second line, Small lymphocytic lymphoma (SLL), T-cell, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapies: allogeneic stem cells, chemotherapy

Location: United States

US State: PA

Contact: Dolores Grosso [215-955-8874]

FLT3 ITD mutation (continued)

NCT03121014
A Phase II Study of Intensity Modulated Total Marrow Irradiation (IM-TMI) in Addition to Fludarabine/ Busulfan Conditioning for Allogeneic Transplantation in High Risk AML and Myelodysplastic Syndromes

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: 2017-0001

Population segments: High risk, Poor-risk, Remission, Second line, del(5q)

Exclusion criteria variant class: t(9;11)

Phase: II

Therapies: chemotherapy, radiation therapy

Location: United States

US State: IL

Contact: Dr. Damiano Rondelli [312-413-3547; drond@uic.edu]

NCT03333486
A Phase II Trial of Haploidentical Allogeneic Stem Cell Transplantation Utilizing Mobilized Peripheral Blood Stem Cells

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other inclusion criteria: Normal cytogenetics

Other identifiers: I 40916, NCI-2017-01949

Population segments: (N/A), Accelerated phase, Aggressive, Chronic phase, Classical, Cutaneous T-cell lymphoma (CTCL), Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), High risk, Indolent, Int-1 risk, Int-2 risk, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Nodular lymphocyte-predominant, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Polycythemia Vera, Primary Myelofibrosis, Remission, Second line, Small lymphocytic lymphoma (SLL), Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapies: chemotherapy, stem cell therapy, radiation therapy

Location: United States

US State: NY

Contact: ASK RPCI [877-275-7724; askrpci@roswellpark.org]

NCT02400255
A Phase II Study of Crenolanib Besylate Maintenance Following Allogeneic Stem Cell Transplantation in Patients with FLT3-positive Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2015-0061, ARO-009, NCI-2015-00677

Population segments: Maintenance/Consolidation, Remission

Phase: II

Therapy: crenolanib

Location: United States

US State: TX

Contact: Vinoo Urity [214-593-0521; vurity@arogpharma.com]

FLT3 ITD mutation (continued)

NCT03836209
Randomized Trial of Gilteritinib vs Midostaurin in FLT3 Mutated Acute Myeloid Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: NCI-2019-04432, PrE0905

Population segments: First line, Maintenance/Consolidation, Second line, Untreated

Exclusion criteria variant classes: inv(16), t(16;16), t(8;21)

Phase: II

Therapies: gilteritinib, midostaurin, chemotherapy

Location: United States

US States: AZ, CA, IL, MD, MI, MN, NE, NY, OH, OK, PA, TN, WA, WI, WV

Contact: Lauren Reilly [267-239-7265; PrE0905@precogllc.org]

NCT03951961
Midostaurin in MRD (Minimal Residual Disease) Positive Acute Myeloid Leukemia After Allogeneic Stem Cell Transplantation

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: EudraCT Number: 2019-000136-26, MAURITIUS

Population segments: (N/A), Second line

Phase: II

Therapy: midostaurin

Location: Germany

NCT03690115
Phase II Study of Ponatinib (Iclusig) for Prevention of Relapse After Allogeneic Stem Cell Transplantation (Allo-SCT) in FLT3-ITD AML Patients: the PONALLO Trial."

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: P1701_ PONALLO

Population segments: Line of therapy N/A, Remission

Phase: II

Therapy: ponatinib

Location: France

FLT3 ITD mutation (continued)

NCT04209725
A Phase II Study Assessing CPX-351 (Vyxeos) With Quizartinib for the Treatment of Relapsed or Refractory FLT3-ITD Mutation-Positive AML

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: SCRI AML 48

Population segments: (N/A), Maintenance/Consolidation, Second line

Exclusion criteria variant class: t(15;17)

Phase: II

Therapies: quizartinib, chemotherapy

Location: United States

US States: CO, MO, TN, TX

Contact: Sarah Cannon [844-710-6157; CANN.InnovationsMedical@sarahcannon.com]

NCT04336982
An Exploratory Phase I/II Open-Label Multi-Arm Trial to Evaluate the Safety and Efficacy of CC-90009 Combinations in Subjects With Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: CC-90009-AML-002, EudraCT Number: 2019-001681-15, NCI-2020-03281, U1111-1247-5619

Population segments: First line, Second line, Untreated

Phase: I/II

Therapies: CC-90009, gilteritinib

Locations: France, United States

US States: MO, TX

Contact: Associate Director Clinical Trial Disclosure [888-260-1599; clinicaltrialdisclosure@celgene.com]

NCT02310321
A Phase I/II Study of ASP2215 in Combination With Induction and Consolidation Chemotherapy in Patients With Newly Diagnosed Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2215-CL-0104, AAAO0661, AML 22, J1494, JapicCTI-195010, STUDY00001793

Population segments: First line, Maintenance/Consolidation, Poor-risk, Untreated

Phase: I/II

Therapies: gilteritinib, chemotherapy

Locations: Japan, Republic of Korea

FLT3 ITD mutation (continued)

NCT04240002
A Phase I/II, Multicenter, Open-Label, Single Arm, Dose Escalation and Expansion Study of Gilteritinib (ASP2215) Combined With Chemotherapy in Children, Adolescents and Young Adults With FMS-like Tyrosine Kinase 3 (FLT3)/Internal Tandem Duplication (ITD) Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2215-CL-0603, EudraCT Number: 2018-002301-61, NCI-2020-04606

Population segments: Pediatric or Adolescent, Second line

Phase: I/II

Therapies: gilteritinib, chemotherapy

Locations: Canada, Italy

NCT04385290
MidOStaurin + Gemtuzumab OzogAmIcin Combination in First-line Standard Therapy for Acute Myeloid Leukemia (MOSAIC)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: EudraCT Number: 2019-003863-23, MOSAIC, TUD-MOSAIC-075

Population segments: (N/A), First line, Maintenance/Consolidation, Untreated

Phase: I/II

Therapies: midostaurin, gemtuzumab ozogamicin, chemotherapy

Location: Germany

NCT03922100
A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients With Relapsed or Refractory AML or CMML

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2018-002793-47, MKIA-088-001

Population segments: Remission, Second line

Exclusion criteria variant class: BCR-ABL1 fusion

Phase: I/II

Therapy: NMS-P948

Location: Italy

NCT02829840
Phase I/II, Dose-Escalation Study of Ponatinib, a FLT3 Inhibitor, With and Without Combination of 5-Azacytidine, in Patients With FLT3-Mutated Acute Myeloid Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2014-1083, ACTRN12614000810617, ALLG AMLM21, AML M21, NCI-2016-01187, PonAZA study

Population segments: (N/A), First line, High risk, Second line

Phase: I/II

Therapies: ponatinib, chemotherapy

Location: United States

US State: TX

FLT3 ITD mutation (continued)

NCT03793478
A Phase I/II, Multicenter, Dose-Escalating Study To Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy Of Quizartinib Administered in Combination with Re-Induction Chemotherapy, and as a Single-Agent Continuation Therapy, in Pediatric Relapsed/Refractory AML Subjects Aged 1 Month to <18 Years (and Young Adults Aged up to 21 Years) with FLT3-ITD mutations.

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: AC220-A-U202, EU/3/09/622, EudraCT Number: 2016-002919-18, NCI-2019-02948, NL65309.078.18, P/102/2018

Population segments: Maintenance/Consolidation, Pediatric or Adolescent, Remission, Second line

Exclusion criteria variant class: t(15;17)(q24;q21)

Phase: I/II

Therapies: quizartinib, chemotherapy

Locations: Belgium, Denmark, France, Israel, Italy, Netherlands, Spain, Sweden, United States

US States: CA, DC, GA, MD, OH, TX

Contact: Daiichi Sankyo Contact for Clinical Information [908-992-6400; CTRinfo@dsi.com]

NCT01203722
Reduced Intensity, Partially HLA Mismatched Allogeneic BMT for Hematologic Malignancies Using Donors Other Than First-degree Relatives

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: CRMS-33771, J1055, NCI-2011-00377

Population segments: (N/A), Aggressive, B-cell, Chronic phase, Classical, Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma (FL), Graft-versus-host disease, Indolent, Mantle cell lymphoma (MCL), Nodular lymphocyte-predominant, Pediatric, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Poor-risk, Second line, Small lymphocytic lymphoma (SLL), Stem cell transplant, T-cell, Third line

Exclusion criteria variant class: t(9;11)

Phase: I/II

Therapy: stem cell therapy

Location: United States

US State: MD

Contact: Dr. Richard Ambinder [410-955-8839; rambind1@jhmi.edu]

NCT04140487
A Phase I/II Study of Azacitidine, Venetoclax, and Gilteritinib for Patients With Acute Myeloid Leukemia or High-Risk Myelodysplastic Syndrome With an Activating FLT3 Mutation

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2019-0366, NCI-2019-04959

Population segments: First line, High risk, Int-2 risk, Second line, Third line

Phase: I/II

Therapies: venetoclax, gilteritinib, chemotherapy

Location: United States

US State: TX

Contact: Nicholas Short [713-563-4485; nshort@mdanderson.org]

FLT3 ITD mutation (continued)

NCT03735875
A Phase Ib/II Study of Venetoclax in Combination With Quizartinib in FLT3-Mutated Acute Myelogenous Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2018-0608, NCI-2018-02396

Population segments: (N/A), Second line

Exclusion criteria variant classes: inv(16), t(8;21)

Phase: I/II

Therapies: venetoclax, quizartinib

Location: United States

US State: TX

Contact: Naval Daver [713-794-4392; ndaver@mdanderson.org]

No NCT ID - see other identifier(s)
Safety and Effective of Prophylactic Infusion of DNT cells in Allogeneic Hematopoietic Stem Cell Transplantation for Patients with Myeloid Malignancies: A Single Center Clinical Research

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifier: ChiCTR1900023499

Population segments: Accelerated phase, High risk, Int-1 risk, Int-2 risk, Poor-risk, Second line

Phase: I

Therapy: allogeneic double negative T cells

Location: China

No NCT ID - see other identifier(s)
A Phase I Study to Assess the Safety of Micro-dose Lenalidomide as Maintenance Therapy Post-allogeneic Haematopoietic Cell Transplantation for Patients with Acute Myeloid Leukaemia or Myelodysplastic Syndromes, at High Risk of Relapse

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: ACTRN12619000556145, MicroLEN

Population segments: High risk, Maintenance/Consolidation, Poor-risk, Remission

Phase: I

Therapy: chemotherapy

Location: Australia

No NCT ID - see other identifier(s)
Phase I Clinical Trial to Assess the Tolerability and Safety, Pharmacokinetic/Pharmacodynamic Characteristics, and Preliminary Efficacy of clifutinib Benzenesulfonate Tablets

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: CTR20180169, CXHL1600156, PCD-DHEC73543-16-001

Population segments: (N/A), Second line

Exclusion criteria variant classes: PML-RARA fusion, t(15;17)(q24;q21)

Phase: I

Therapy: clifutinib

Location: China

FLT3 ITD mutation (continued)

NCT03900949
A Phase I Study to Evaluate the Safety and Tolerability of Gemtuzumab Ozogamicin and Midostaurin When Used in Combination With Standard Cytarabine and Daunorubicin Induction for Newly Diagnosed FLT3-Mutated Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: HEM-18147-L, NCI-2019-01726, STUDY00018684

Population segments: (N/A), First line, Maintenance/Consolidation, Remission, Untreated

Phase: I

Therapies: gemtuzumab ozogamicin, midostaurin, chemotherapy

Location: United States

US States: OR, WA

Contact: Dr. Uma M. Borate [503-494-5058; borate@ohsu.edu]

NCT03552029
A Phase I Study of Milademetan in Combination With Quizartinib in Subjects With FLT3-ITD Mutant Acute Myeloid Leukemia That Are Relapsed/Refractory, or Newly Diagnosed and Unfit for Intensive Chemotherapy

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: 2018-0278, DS3032-A-U105, EudraCT Number: 2019-001344-22, NCI-2018-01454, P 66618

Population segments: First line, Remission, Second line, Untreated

Phase: I

Therapies: milademetan, quizartinib

Location: United States

US States: MI, NC, PA, TX

Contact: Daiichi Sankyo Contact for Clinical Trial Information [908-992-6400; CTRinfo@dsi.com]

NCT03513484
Phase Ib, Open Label, Combination Study of Nintedanib With 5-Azacitidine in Acute Myeloid Leukemia Characterized by HOX Gene Overexpression, That Are Not Candidates of Intensive Chemotherapy

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 ITD mutation

Other identifiers: NCI-2018-00483, NU 17H04

Population segments: (N/A), First line, Second line

Phase: I

Therapies: nintedanib, chemotherapy

Location: United States

US State: IL

Contact: Jessica K. Altman [312-695-6180; j-altman@northwestern.edu]

FLT3 ITD mutation (continued)

NCT02126553
Phase II Study of Lenalidomide Maintenance in Patients With High Risk AML in Remission

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: 2014-0116, NCI-2014-01176

Population segments: Maintenance/Consolidation, Poor-risk, Remission

Exclusion criteria variant classes: inv(16), t(15;17), t(16;16), t(8;21), t(9;22)

Phase: II

Therapy: chemotherapy

Location: United States

US State: TX

Contact: Dr. Tapan Kadia [713-563-3534; tkadia@mdanderson.org]

NCT02727803
Personalized NK Cell Therapy in Cord Blood Transplantation

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: 2015-0313, NCI-2016-00584

Population segments: Accelerated phase, Aggressive, Chronic phase, Classical, High risk, Indolent, Int-1 risk, Int-2 risk, Maintenance/Consolidation, Nodular lymphocyte-predominant, Poor-risk, Remission, Second line, Small lymphocytic lymphoma (SLL), Stage II, Stage III, Third line

Phase: II

Therapies: natural killer cell therapy, stem cell therapy

Location: United States

US State: TX

Contact: Katy Rezvani [713-792-8750; krezvani@mdanderson.org]

NCT04062266
Phase II Study of 5-Azacytidine (AZA) + Venetoclax as Maintenance Therapy in Patients With High Risk AML in Remission

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: 2019-0226, NCI-2019-04987

Population segments: Maintenance/Consolidation, Poor-risk, Remission

Exclusion criteria variant class: t(15;17)

Phase: II

Therapies: venetoclax, chemotherapy

Location: United States

US State: TX

Contact: Tapan M. Kadia [713-563-3534; tkadia@mdanderson.org]

FLT3 ITD mutation (continued)

NCT03194685
A First-in-Human Phase I/IIa Study to Assess the Safety, Tolerability, Efficacy, and Pharmacokinetics of FF-10101-01 in Subjects With Relapsed or Refractory Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: FF-10101-US101/201, NCI-2017-01566

Population segments: (N/A), Second line

Phase: I/II

Therapy: FF-10101

Location: United States

US States: CA, IL, MA, MD, NY, PA

Contact: Study Coordinator [fphucontact@fujifilm.com]

NCT03730012
Phase I/II Study of ASP2215 (Gilteritinib) Combined With Atezolizumab in Patients With Relapsed or Treatment Refractory FLT3 Mutated Acute Myeloid Leukemia (AML)

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: 2215-CL-1101, AAAS0326, NCI-2018-02964, Pro00088311

Population segments: Remission, Second line

Phase: I/II

Therapies: gilteritinib, atezolizumab

Location: United States

US States: CA, IL, KY, NY, OH, SC, TN, TX, WI

Contact: Astellas Pharma Global Development [800-888-7704; astellas.registration@astellas.com]

NCT03625505
A Multicenter, Open-Label Phase 1b Study To Assess Safety And Efficacy Of Venetoclax In Combination With Gilteritinib In Subjects With Relapsed/ Refractory Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 mutation

Other identifiers: 20180388, M16-802

Population segments: Fourth line or greater, Remission, Second line, Third line

Exclusion criteria variant class: BCR-ABL1 fusion

Phase: I

Therapies: venetoclax, gilteritinib

Location: United States

US States: CA, FL, IL, KY, MD, MN, NJ, NY, PA, TX

Contact: ABBVIE CALL CENTER [847-283-8955; abbvieclinicaltrials@abbvie.com]

FLT3 ITD mutation (continued)

NCT03247088
Phase I/II Study Of Sorafenib Added To Busulfan And Fludarabine Conditioning Regimen In Patients With Relapsed/ Refractory AML Undergoing Stem Cell Transplantation

Cancer type: Acute Myeloid Leukemia

Variant class: FLT3 positive

Other identifiers: 2016-0592, NCI-2018-01607

Population segments: (N/A), Second line

Exclusion criteria variant classes: inv(16), t(8;21)

Phase: I/II

Therapies: chemotherapy, sorafenib

Location: United States

US State: TX

Contact: Uday R. Popat [713-745-3055; upopat@mdanderson.org]

NCT02272998
Phase II Study Of Ponatinib For Advanced Cancers With Genomic Alterations In Fibroblastic Growth Factor Receptor (FGFR) And Other Genomic Targets (KIT, Pdgfra, RET FLT3, ABL1)

Cancer type: Unspecified Hematological Cancer

Variant class: FLT3 aberration

Other identifiers: 14078, 2014C0143, NCI-2014-01499, OSU-14078

Population segments: Advanced, Second line, Stage IV

Exclusion criteria variant classes: FGFR3 K652E mutation, FLT3 D835F mutation, FLT3 D835H mutation, FLT3 D835V mutation, FLT3 D835Y mutation, FLT3 Y842C mutation, KIT D816V mutation, PDGFRA D842V mutation

Phase: II

Therapy: ponatinib

Location: United States

US State: OH

Contact: The Ohio State University Comprehensive Cancer Center [800-293-5066; Jamesline@osumc.edu]

NPM1 W288fs

NCT03769532
MRD-guided Treatment With Pembrolizumab and Azacitidine in NPM1mut AML Patients With an Imminent Hematological Relapse

Cancer type: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Other identifiers: EUdraCT Number: 2017-004110-25, PEMAZA, TUD-PEMAZA-068

Population segments: (N/A), Line of therapy N/A

Phase: II

Therapies: pembrolizumab, chemotherapy

Location: Germany

NPM1 W288fs (continued)

NCT03031249
Efficacy and Safety of ATO Plus ATRA in Nucleophosmin-1 Mutated Acute Myeloid Leukemia

Cancer type: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Other identifier: IIT2016007-EC-1-2

Population segments: Line of therapy N/A, Pediatric or Adolescent, Remission

Exclusion criteria variant classes: BCR-ABL1 fusion, NPM1 mutation

Phase: I/II

Therapies: chemotherapy, supplement

Location: China

NCT04065399
AUGMENT-101: A Phase I/II, Open-label, Dose-Escalation and Dose-Expansion Cohort Study of SNDX 5613 in Patients With Relapsed/Refractory Leukemias, Including Those Harboring an MLL/KMT2A Gene Rearrangement or Nucleophosmin 1 (NPM1) Mutation

Cancer type: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Other identifiers: 2019-0997, AUGMENT-101, AUGME-T-101, NCI-2019-07963, SNDX-5613-0700

Population segments: (N/A), Fourth line or greater, Second line, Third line

Phase: I/II

Therapy: SNDX-5613

Location: United States

US States: CA, FL, GA, IL, MA, MO, NY, TX

Contact: Susan Brouwer [781-419-1401; sbrouwer@syndax.com]

NCT03862157
A Phase I/II Study of Azacitidine, Venetoclax and Pevonedistat in Adults With Newly Diagnosed Secondary or Therapy-Related AML

Cancer type: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Other identifiers: 2018-0724, NCI-2018-03465

Population segments: Chronic Eosinophilic Leukemia, Chronic Neutrophilic Leukemia, Essential Thrombocythemia, First line, MDS-U, MPN Unclassifiable, Polycythemia Vera, Poor-risk, Primary Myelofibrosis, RA/RARS, Second line, Untreated

Phase: I/II

Therapies: venetoclax, pevonedistat, chemotherapy

Location: United States

US State: TX

Contact: Nicholas Short [713-792-8760; nshort@mdanderson.org]

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Hereditary Cancer Genetics (CGX)

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Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

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Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Hereditary Cancer Genetics (CGX)

Next Gen Sequencing

Myeloid NGS

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Whole Exome Sequencing (WES)

NORTH WEST LABS

HEREDITARY CANCER TEST REQUISITION FORM

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29580 Northwestern Hwy., Southfield, MI 48034
Phone: (248) 301-6917 Fax: (248) 301-6785 CLIA: 23D2126347
support@nwlabs.com www.nwlabs.com

PATIENT INFORMATION

First name | MI | Last name | Date of birth (MM/DD/YYYY)

Biological sex
☐ Male
☐ Femal

MRN (medical record number)

Ethnicity
☐ Asian ☐Black/African American ☐ White/Caucasian ☐ Ashkenazi Jewish ☐ Hispanic ☐ Other: _____

Email address (for billing contact and report access after clinician releases)

Mobile phone

Address

City | State/Prov | Zip/Postal code | Country

CLINICAL INFORMATION

Organization name | Phone | Fax

Address | City | State/Prov | ZIP/Postal Code | Country

CLINICAL TEAM

Primary clinical contact (contact for general inquires)

Name | NPI | Email address (for report access)

☐ INSURANCE BILLING (attach front and back of insurance card)

Attach clinical notes, medical records, and/or letter of medical necessity (LMN) to prevent delays. We do not accept insurance for certain tests or patients outside the US.

Policyholder name | Patient relationship to ☐Self ☐ Spouse ☐ Child Other: _____

Primary insurance company name | Primary member ID# | Primary insurance phone | Prior-authorization #

Secondary insurance company name | Secondary member ID# | Secondary insurance phone | Prior-authorization #

Medicare insurance billing only (select one):
☐ Patient was treated as a hospital inpatient in the last 14 days
☐ Not a hospital patient

☐ PATIENT PAY BILLING

North West Labs will send an electronic invoice to the patient email listed above.

☐ INSTITUTIONAL BILLING

North West Labs will send an invoice to the organization address above. Please contact us if this order should be billed to a different location.

☐ PARTNERSHIP PROGRAMS

North West Labs partner code:

Label each tube with the patient's full name, date of birth, and specimen collection date. A requisition form MUST accompany each specimen.

SPECIMEN INFORMATION

Collection date **(MM/DD/YYYY)**

If not provided, date will be 1 day prior to our receipt of specimen. For DNA, provide date retrieved from archive.

Specimen type

☐ Buccal Swab

DNA must be extracted in a CLIA or other suitable certified laboratory. We are unable to accept blood or saliva from patients with allogeneic bone marrow transplants or a blood transfusion <2 weeks prior to specimen collection.

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Custom Hereditary Cancer Genes (124)

ACD, AIP, AKT1, ALK, APC, ATM, AXIN2, BAP, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CASR, CDC73, CDH1, CDK4, CDKN1B, CDKN1C, CDKN2A, CEBPA, CHEK2, CTNNA1, CTRC, DDB2, DICER1, DIS3L2, EGFR, EPCAM, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, FAM175A, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FH, FLCN, GALNT12, GATA2, GPC3, GREM1, HNF1A, HOXB13, HRAS, KIF1B, KIT, LZTR1, MAX, MEN1, MET, MITF, MLH1, MRE11, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NSD1, NTHL1, NTRK1, PALB2, PDGFRA, PHOX2B, PIK3CA, PMS2, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RB1, RECQL4, RET, RHBDF2, RINT1, RUNX1, SDHA, SDHAF2, SDHB, SDHC, SDHD, SLX4, SMAD4, SMARCA4, SMARCB1, SMARCE1, SPINK1, SPRED1, STK11, SUFU, TERC, TERF2IP, TERT, TMEM127, TP53, TSC1, TSC2, VHL, WRN, WT1, XPA, XPC, XRCC2

HEREDITARY CANCER TEST REQUISITION (BLUE SECTIONS REQUIRED)

INDICATIONS FOR TESTING (Check all that apply)

☐ Diagnostic ☐ Family history ☐ Positive or normal control ☐ Other..... ICD-10 code(s):.....

Will Patient management be changed depending on the test results? ☐ Yes ☐ No STAT TEST : Date results needed (if Known): .....

PATIENT CLINICAL HISTORY ☐ No Personal History Of Cancer

Cancer /Tumer	Age at DX	Pathology and Other info
Breast		Type: ER☐ (+)☐(-)☐ unk PR☐ (+)☐ (-) ☐ unk HER2/neu ☐ (+) ☐(-) unk
2nd primary breast		Type: ER☐ (+)☐(-)☐ unk PR☐ (+)☐ (-) ☐ unk HER2/neu ☐ (+) ☐(-) unk
Ovarian		Fallopian tube Primary peritoneal
Prostate		Gleason score:
Hematologic		Type: Allogeneic bone marrow or peripheral stem cell transport
Other Cancer		Type:
Other clinical history:		

PERSONAL HISTORY

Is/was this patient affected or symptomatic†?

☐ Yes ☐ No

If yes, describe below and attach clinical notes. Age at diagnosis: _____

† Symptomatic means the patient has features or signs known or suspected to be related to the genetic testing being ordered and could include findings on physical examination, laboratory tests, or imaging.

Has this patient had genetic testing before?

☐ Yes ☐ No If yes, write test results and attach the report.

FAMILY HISTORY

Is there a family history of disease for which the patient is being tested? ☐ Yes ☐ No
If yes, describe below and attach pedigree and/or clinical notes.

Relationship to patient	Maternal or paternal	Diagnosed condition	Age at diagnosis

ADDITIONAL ICD CODES

_____

_____

_____

This list is intended to be used as a reference to assist ordering Physicians in providing ICD-10 Diagnosis Codes as required by Medicare and other insurers to determine the medical necessity of testing being ordered. This is not an exhaustive list of all applicable diagnoses. Physicians are not required to use these codes but should report the diagnostic codes that best describes the reason for performing the test based on individual patient diagnoses. It is the Physician's Responsibility to determine both the medical need for and the utilization of, all health care services ordered.

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HEREDITARY CANCER PATIENT QUESTIONNAIRE

Please read and answer the questions below. While answering, consider relatives who are living along with those who have passed away who are sick and those in remission, male and female relatives, and relatives on both your mother and father 's side of the family. "Relatives" refer to blood relatives and include mother, father, son, daughter, brother, sister, half-brother, half-sister, uncle, aunt, nephew, niece, grandparent, grandchild, cousin.

1. Have You ever been diagnosed with any these cancers prior to the age listed?
[ ] BREAST CANCER (age 45 or younger)
[ ] COLON CANCER (age 50 or younger)
[ ] ENDOMETRIAL/UTERINE CANCER (age 50 or younger)
[ ] OVARIAN CANCER (any age)

2. Have you ever been diagnosed with either PROSTATE or PANCREATIC cancer? [ ] YES [ ] NO IF YES: Do you also have ONE or more relatives diagnosed with any of these cancers?
[ ] PROSTATE CANCER [ ] PANCREATIC CANCER [ ] BREAST CANCER (age 50 or Younger)

3. Have YOU ever been diagnosed with BREAST cancer between ages 46-50? [ ] YES [ ] NO
IF YES: Do you also have any of following?
[ ] ONE or more relatives diagnosed with BREAST CANCER, PRANCREATIC CANCER or PROSTATE CANCER (at ANY AGE)
[ ] TWO or more relatives on the same side of the family diagnosed with BREAST CANCER AT ANY AGE?

4. Have YOU been diagnosed with BREAST cancer at any age? [ ] YES [ ] NO
IF YES: DO you also have any of the following?
[ ] ONE or relatives diagnosed with BREAST CANCER at age 50 or under?
[ ] TWO or more relatives on the same side of the family diagnosed with BREAST CANCER at ANY AGE?

5. **Have any relatives been diagnosed with BREAST (age 45 and under) or OVARIAN CANCER (any age)?** [ ] YES [ ] NO

6. **Do you have ONE relative that was diagnosed with BREAST cancer (any age)?** [ ] YES [ ] NO
IF YES: Do you also have any of the following on the same side of the family?
[ ] ONE or more additional relatives diagnosed with BREAST CANCER at age 50 or younger
[ ] TWO or more relatives diagnosed with BREAST CANCER at ANY AGE?

7. DO you have ONE relative that was diagnosed with PANCREATIC OR PROSTATE cancer? [ ] YES [ ] NO
IF YOU: Do you also have ONE or more additional relatives on the same side of your family diagnosed with any of these cancers?
[ ] PROSTATE CANCER
[ ] PANCREATIC CANCER
[ ] BREAST CANCER (age 50 or younger)

8. Do you have ONE Relative that was diagnosed with COLORECTAL or ENDOMETRICAL cancer? [ ] YES [ ] NO
IF YES:
[ ] Do you also have ONE or more additional relatives on the same side of family diagnosed at age 50 or younger with any of these cancers: COLORECTAL or ENDOMETRIAL
[ ] Do you have TWO or more additional relatives on the same side of your family diagnosed with any of these Cancers at any age? COLORECTAL, ENDOMETRICAL, PANCREATIC, SMALL BOWEL, HEPATOBILIARY TRACT, LIVER, URINARY TRACT, RENAL PELVIS, URETER, OVARIAN, BRAIN or STOMACH

Answering these questions does not guarantee that your insurance will cover a cancer screening. The screening is a predictive test that can identify if you are at increased risk for certain types of cancer. It does not diagnose cancer or determine definitively if you will develop cancer in your lifetime.

ICD-10 DX Code (s):

Group 1

- ☐ C16.0 - Malignant neoplasm of cardia
- ☐ C16.1 - Malignant neoplasm of fundus of stomach
- ☐ C16.2 - Malignant neoplasm of body of stomach
- ☐ C16.3 - Malignant neoplasm of pyloric antrum
- ☐ C16.4 - Malignant neoplasm of pylorus
- ☐ C16.5 - Malignant neoplasm of lesser curvature of stomach, unspecified
- ☐ C16.6 - Malignant neoplasm of greater curvature of stomach, unspecified
- ☐ C16.8 - Malignant neoplasm of overlapping sites of stomach
- ☐ C16.9 - Malignant neoplasm of stomach, unspecified
- ☐ C17.0 - Malignant neoplasm of duodenum
- ☐ C17.1 - Malignant neoplasm of jejunum
- ☐ C17.2 - Malignant neoplasm of ileum
- ☐ C17.3 - Meckel's diverticulum, malignant
- ☐ C17.8 - Malignant neoplasm of overlapping sites of small intestine
- ☐ C17.9 - Malignant neoplasm of small intestine, unspecified
- ☐ C18.0 - Malignant neoplasm of cecum
- ☐ C18.1 - Malignant neoplasm of appendix
- ☐ C18.2 - Malignant neoplasm of ascending colon
- ☐ C18.3 - Malignant neoplasm of hepatic flexure
- ☐ C18.4 - Malignant neoplasm of transverse colon
- ☐ C18.5 - Malignant neoplasm of splenic flexure
- ☐ C18.6 - Malignant neoplasm of descending colon
- ☐ C18.7 - Malignant neoplasm of sigmoid colon
- ☐ C18.8 - Malignant neoplasm of overlapping sites of colon
- ☐ C18.9 - Malignant neoplasm of colon, unspecified
- ☐ C19 - Malignant neoplasm of rectosigmoid junction
- ☐ C20 - Malignant neoplasm of rectum
- ☐ C21.2 - Malignant neoplasm of cloacogenic zone
- ☐ C21.8 - Malignant neoplasm of overlapping sites of rectum, anus and anal canal
- ☐ C22.0 - Liver cell carcinoma
- ☐ C22.1 - Intrahepatic bile duct carcinoma
- ☐ C22.2 - Hepatoblastoma
- ☐ C22.3 - Angiosarcoma of liver
- ☐ C22.4 - Other sarcomas of liver
- ☐ C22.7 - Other specified carcinomas of liver
- ☐ C22.8 - Malignant neoplasm of liver, primary, unspecified as to type
- ☐ C22.9 - Malignant neoplasm of liver, not specified as primary or secondary
- ☐ C24.0 - Malignant neoplasm of extrahepatic bile duct
- ☐ C24.9 - Malignant neoplasm of biliary tract, unspecified
- ☐ C25.0 - Malignant neoplasm of head of pancreas
- ☐ C25.1 - Malignant neoplasm of body of pancreas
- ☐ C25.2 - Malignant neoplasm of tail of pancreas
- ☐ C25.3 - Malignant neoplasm of pancreatic duct
- ☐ C25.4 - Malignant neoplasm of endocrine pancreas
- ☐ C25.7 - Malignant neoplasm of other parts of pancreas
- ☐ C25.8 - Malignant neoplasm of overlapping sites of pancreas
- ☐ C25.9 - Malignant neoplasm of pancreas, unspecified
- ☐ C54.0 - Malignant neoplasm of isthmus uteri
- ☐ C54.1 - Malignant neoplasm of endometrium
- ☐ C54.2 - Malignant neoplasm of myometrium
- ☐ C54.3 - Malignant neoplasm of fundus uteri
- ☐ C54.8 - Malignant neoplasm of overlapping sites of corpus uteri
- ☐ C54.9 - Malignant neoplasm of corpus uteri, unspecified
- ☐ C55 - Malignant neoplasm of uterus, part unspecified
- ☐ C56.1 - Malignant neoplasm of right ovary
- ☐ C56.2 - Malignant neoplasm of left ovary
- ☐ C56.3 - Malignant neoplasm of bilateral ovaries
- ☐ C56.9 - Malignant neoplasm of unspecified ovary
- ☐ C57.00 - Malignant neoplasm of unspecified fallopian tube
- ☐ C57.01 - Malignant neoplasm of right fallopian tube
- ☐ C57.02 - Malignant neoplasm of left fallopian tube
- ☐ C57.10 - Malignant neoplasm of unspecified broad ligament
- ☐ C57.11 - Malignant neoplasm of right broad ligament
- ☐ C57.12 - Malignant neoplasm of left broad ligament
- ☐ C57.20 - Malignant neoplasm of unspecified round ligament
- ☐ C57.21 - Malignant neoplasm of right round ligament
- ☐ C57.22 - Malignant neoplasm of left round ligament
- ☐ C57.3 - Malignant neoplasm of parametrium
- ☐ C57.4 - Malignant neoplasm of uterine adnexa, unspecified
- ☐ C64.1 - Malignant neoplasm of right kidney, except renal pelvis
- ☐ C64.2 - Malignant neoplasm of left kidney, except renal pelvis
- ☐ C64.9 - Malignant neoplasm of unspecified kidney, except renal pelvis
- ☐ C65.1 - Malignant neoplasm of right renal pelvis
- ☐ C65.2 - Malignant neoplasm of left renal pelvis
- ☐ C65.9 - Malignant neoplasm of unspecified renal pelvis
- ☐ C66.1 - Malignant neoplasm of right ureter
- ☐ C66.2 - Malignant neoplasm of left ureter
- ☐ C66.9 - Malignant neoplasm of unspecified ureter
- ☐ C68.8 - Malignant neoplasm of overlapping sites of urinary organs
- ☐ C71.0 - Malignant neoplasm of cerebrum, except lobes and ventricles
- ☐ C71.1 - Malignant neoplasm of frontal lobe
- ☐ C71.2 - Malignant neoplasm of temporal lobe
- ☐ C71.3 - Malignant neoplasm of parietal lobe
- ☐ C71.4 - Malignant neoplasm of occipital lobe
- ☐ C71.5 - Malignant neoplasm of cerebral ventricle
- ☐ C71.6 - Malignant neoplasm of cerebellum
- ☐ C71.7 - Malignant neoplasm of brain stem
- ☐ C71.8 - Malignant neoplasm of overlapping sites of brain
- ☐ C71.9 - Malignant neoplasm of brain, unspecified
- ☐ D12.0 - Benign neoplasm of cecum
- ☐ D12.1 - Benign neoplasm of appendix
- ☐ D12.2 - Benign neoplasm of ascending colon
- ☐ D12.3 - Benign neoplasm of transverse colon
- ☐ D12.4 - Benign neoplasm of descending colon
- ☐ D12.5 - Benign neoplasm of sigmoid colon
- ☐ D12.6 - Benign neoplasm of colon, unspecified
- ☐ K63.5 - Polyp of colon
- ☐ L85.3 - Xerosis cutis
- ☐ Z85.00* - Personal history of malignant neoplasm of unspecified digestive organ
- ☐ Z85.038* - Personal history of other malignant neoplasm of large intestine
- ☐ Z85.048* - Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus
- ☐ Z85.42* - Personal history of malignant neoplasm of other parts of uterus
- ☐ Z85.43* - Personal history of malignant neoplasm of ovary
- ☐ Z85.53* - Personal history of malignant neoplasm of renal pelvis
- ☐ Z85.54* - Personal history of malignant neoplasm of ureter
- ☐ Z85.59* - Personal history of malignant neoplasm of other urinary tract organ
- ☐ Z85.841* - Personal history of malignant neoplasm of brain
- ☐ Z86.010* - Personal history of colonic polyps

Group 2

- ☐ C25.0 - Malignant neoplasm of head of pancreas
- ☐ C25.1 - Malignant neoplasm of body of pancreas
- ☐ C25.2 - Malignant neoplasm of tail of pancreas
- ☐ C25.3 - Malignant neoplasm of pancreatic duct
- ☐ C25.4 - Malignant neoplasm of endocrine pancreas
- ☐ C25.7 - Malignant neoplasm of other parts of pancreas
- ☐ C25.8 - Malignant neoplasm of overlapping sites of pancreas
- ☐ C25.9 - Malignant neoplasm of pancreas, unspecified
- ☐ C50.011 - Malignant neoplasm of nipple and areola, right female breast
- ☐ C50.012 - Malignant neoplasm of nipple and areola, left female breast
- ☐ C50.019 - Malignant neoplasm of nipple and areola, unspecified female breast
- ☐ C50.021 - Malignant neoplasm of nipple and areola, right male breast
- ☐ C50.022 - Malignant neoplasm of nipple and areola, left male breast
- ☐ C50.029 - Malignant neoplasm of nipple and areola, unspecified male breast
- ☐ C50.111 - Malignant neoplasm of central portion of right female breast
- ☐ C50.112 - Malignant neoplasm of central portion of left female breast
- ☐ C50.119 - Malignant neoplasm of central portion of unspecified female breast
- ☐ C50.121 - Malignant neoplasm of central portion of right male breast
- ☐ C50.122 - Malignant neoplasm of central portion of left male breast
- ☐ C50.129 - Malignant neoplasm of central portion of unspecified male breast
- ☐ C50.211 - Malignant neoplasm of upper-inner quadrant of right female breast
- ☐ C50.212 - Malignant neoplasm of upper-inner quadrant of left female breast
- ☐ C50.219 - Malignant neoplasm of upper-inner quadrant of unspecified female breast
- ☐ C50.521 - Malignant neoplasm of lower-outer quadrant of right male breast
- ☐ C50.522 - Malignant neoplasm of lower-outer quadrant of left male breast
- ☐ C50.529 - Malignant neoplasm of lower-outer quadrant of unspecified male breast
- ☐ C50.611 - Malignant neoplasm of axillary tail of right female breast
- ☐ C50.612 - Malignant neoplasm of axillary tail of left female breast
- ☐ C50.619 - Malignant neoplasm of axillary tail of unspecified female breast
- ☐ C50.621 - Malignant neoplasm of axillary tail of right male breast
- ☐ C50.622 - Malignant neoplasm of axillary tail of left male breast
- ☐ C50.629 - Malignant neoplasm of axillary tail of unspecified male breast
- ☐ C50.811 - Malignant neoplasm of overlapping sites of right female breast
- ☐ C50.812 - Malignant neoplasm of overlapping sites of left female breast
- ☐ C50.819 - Malignant neoplasm of overlapping sites of unspecified female breast
- ☐ C50.821 - Malignant neoplasm of overlapping sites of right male breast
- ☐ C50.822 - Malignant neoplasm of overlapping sites of left male breast
- ☐ C50.829 - Malignant neoplasm of overlapping sites of unspecified male breast
- ☐ C50.911 - Malignant neoplasm of unspecified site of right female breast
- ☐ C50.912 - Malignant neoplasm of unspecified site of left female breast
- ☐ C50.919 - Malignant neoplasm of unspecified site of unspecified female breast
- ☐ C50.921 - Malignant neoplasm of unspecified site of right male breast
- ☐ C50.922 - Malignant neoplasm of unspecified site of left male breast
- ☐ C50.929 - Malignant neoplasm of unspecified site of unspecified male breast
- ☐ C56.1 - Malignant neoplasm of right ovary
- ☐ C56.2 - Malignant neoplasm of left ovary

Group 2 *(Continued)*

- ☐ C50.221 - Malignant neoplasm of upper-inner quadrant of right male breast
- ☐ C50.222 - Malignant neoplasm of upper-inner quadrant of left male breast
- ☐ C50.229 - Malignant neoplasm of upper-inner quadrant of unspecified male breast
- ☐ C50.311 - Malignant neoplasm of lower-inner quadrant of right female breast
- ☐ C50.312 - Malignant neoplasm of lower-inner quadrant of left female breast
- ☐ C50.319 - Malignant neoplasm of lower-inner quadrant of unspecified female breast
- ☐ C50.321 - Malignant neoplasm of lower-inner quadrant of right male breast
- ☐ C50.322 - Malignant neoplasm of lower-inner quadrant of left male breast
- ☐ C50.329 - Malignant neoplasm of lower-inner quadrant of unspecified male breast
- ☐ C50.411 - Malignant neoplasm of upper-outer quadrant of right female breast
- ☐ C50.412 - Malignant neoplasm of upper-outer quadrant of left female breast
- ☐ C50.419 - Malignant neoplasm of upper-outer quadrant of unspecified female breast
- ☐ C50.421 - Malignant neoplasm of upper-outer quadrant of right male breast
- ☐ C50.422 - Malignant neoplasm of upper-outer quadrant of left male breast
- ☐ C50.429 - Malignant neoplasm of upper-outer quadrant of unspecified male breast
- ☐ C50.511 - Malignant neoplasm of lower-outer quadrant of right female breast
- ☐ C50.512 - Malignant neoplasm of lower-outer quadrant of left female breast
- ☐ C50.519 - Malignant neoplasm of lower-outer quadrant of unspecified female breast
- ☐ C56.3 - Malignant neoplasm of bilateral ovaries
- ☐ C56.9 - Malignant neoplasm of unspecified ovary
- ☐ C57.00 - Malignant neoplasm of unspecified fallopian tube
- ☐ C57.01 - Malignant neoplasm of right fallopian tube
- ☐ C57.02 - Malignant neoplasm of left fallopian tube
- ☐ C61 - Malignant neoplasm of prostate
- ☐ D05.00 - Lobular carcinoma in situ of unspecified breast
- ☐ D05.01 - Lobular carcinoma in situ of right breast
- ☐ D05.02 - Lobular carcinoma in situ of left breast
- ☐ D05.10 - Intraductal carcinoma in situ of unspecified breast
- ☐ D05.11 - Intraductal carcinoma in situ of right breast
- ☐ D05.12 - Intraductal carcinoma in situ of left breast
- ☐ D05.80 - Other specified type of carcinoma in situ of unspecified breast
- ☐ D05.81 - Other specified type of carcinoma in situ of right breast
- ☐ D05.82 - Other specified type of carcinoma in situ of left breast
- ☐ D05.90 - Unspecified type of carcinoma in situ of unspecified breast
- ☐ D05.91 - Unspecified type of carcinoma in situ of right breast
- ☐ D05.92 - Unspecified type of carcinoma in situ of left breast
- ☐ Z85.07 - Personal history of malignant neoplasm of pancreas
- ☐ Z85.3 - Personal history of malignant neoplasm of breast
- ☐ Z85.43 - Personal history of malignant neoplasm of ovary
- ☐ Z85.46 - Personal history of malignant neoplasm of prostate

Group 3

- ☐ C16.0 - Malignant neoplasm of cardia
- ☐ C16.1 - Malignant neoplasm of fundus of stomach
- ☐ C16.2 - Malignant neoplasm of body of stomach
- ☐ C16.3 - Malignant neoplasm of pyloric antrum
- ☐ C16.4 - Malignant neoplasm of pylorus
- ☐ C16.5 - Malignant neoplasm of lesser curvature of stomach, unspecified
- ☐ C16.6 - Malignant neoplasm of greater curvature of stomach, unspecified
- ☐ C16.8 - Malignant neoplasm of overlapping sites of stomach
- ☐ C16.9 - Malignant neoplasm of stomach, unspecified
- ☐ C17.0 - Malignant neoplasm of duodenum
- ☐ C17.1 - Malignant neoplasm of jejunum
- ☐ C17.2 - Malignant neoplasm of ileum
- ☐ C17.3 - Meckel's diverticulum, malignant
- ☐ C17.8 - Malignant neoplasm of overlapping sites of small intestine
- ☐ C17.9 - Malignant neoplasm of small intestine, unspecified
- ☐ C18.0 - Malignant neoplasm of cecum
- ☐ C18.1 - Malignant neoplasm of appendix
- ☐ C18.2 - Malignant neoplasm of ascending colon
- ☐ C18.3 - Malignant neoplasm of hepatic flexure
- ☐ C18.4 - Malignant neoplasm of transverse colon

Group 4

- ☐ C43.1 - Malignant melanoma of eyelid, including canthus
- ☐ C43.2 - Malignant melanoma of ear and external auricular canal
- ☐ C43.3 - Malignant melanoma of other and unspecified parts of face
- ☐ C43.4 - Malignant melanoma of scalp and neck
- ☐ C43.5 - Malignant melanoma of trunk
- ☐ C43.0 - Malignant melanoma of lip
- ☐ C43 - Malignant melanoma of skin
- ☐ C43.6 - Malignant melanoma of upper limb, including shoulder
- ☐ C43.7 - Malignant melanoma of lower limb, including hip
- ☐ C43.8 - Overlapping malignant melanoma of skin
- ☐ C43.9 - Malignant melanoma of skin, unspecified
- ☐ C44 - Other malignant neoplasms of skin
- ☐ C44.0 - Skin of lip
- ☐ C44.1 - Skin of eyelid, including canthus
- ☐ C44.2 - Skin of ear and external auricular canal
- ☐ C44.3 - Skin of other and unspecified parts of face
- ☐ C44.4 - Skin of scalp and neck
- ☐ C44.5 - Skin of trunk
- ☐ C44.6 - Skin of upper limb, including shoulder
- ☐ C44.7 - Skin of lower limb, including hip
- ☐ G47.35 - Congenital central alveolar hypoventilation syndrome
- ☐ E66.2 - Morbid (severe) obesity with alveolar hypoventilation
- ☐ G47.36 - Sleep related hypoventilation in conditions classd elswhr
- ☐ G47.34 - Idio sleep related nonobstructive alveolar hypoventilation

Group 5

- ☐ Diabetes due to underlying conditions (codes that start with E08)
- ☐ Drug or chemical induced diabetes (codes that start with E09)
- ☐ Type 1 diabetes (codes that start with E10)
- ☐ Type 2 diabetes (codes that start with E11)
- ☐ Diabetes related to pregnancy (codes that start with 024)
- ☐ Other types of diabetes not covered by the previous categories (codes that start with E13)
- ☐ E31.21 - Multiple endocrine neoplasia [MEN] type I
- ☐ E31.22 - Multiple endocrine neoplasia [MEN] type IIA
- ☐ E31.23 - Multiple endocrine neoplasia [MEN] type IIB
- ☐ E31.20 - Multiple endocrine neoplasia [MEN] syndrome, unspecified
- ☐ Z83.41 - Family history of multiple endocrine neoplasia syndrome
- ☐ E31.0 - Autoimmune polyglandular failure
- ☐ E31.8 - Other polyglandular dysfunction
- ☐ E31.9 - Polyglandular dysfunction, unspecified

Group 6 (Any code from Group A is also qualified)

- ☐ Q85.00 - Neurofibromatosis, unspecified
- ☐ Q85.01 - Neurofibromatosis, type 1
- ☐ Q85.02 - Neurofibromatosis, type 2
- ☐ Q85.09 - Other neurofibromatosis
- ☐ E21.0 - Primary hyperparathyroidism
- ☐ Q85.03 - Schwannomatosis
- ☐ Q85.0 Neurofibromatosis (nonmalignant)
- ☐ Q85.03 - Schwannomatosis

Group 7

- ☐ Q85.1 - Tuberous sclerosis
- ☐ Q85.8 - Other phakomatoses, not elsewhere classified
- ☐ Q85.9 - Phakomatosis, unspecified
- ☐ Q85 - Phakomatoses, not elsewhere classified
- ☐ Q85.00 - Neurofibromatosis, unspecified
- ☐ Q85.01 - Neurofibromatosis, type 1
- ☐ Q85.02 - Neurofibromatosis, type 2
- ☐ Q85.09 - Other neurofibromatosis
- ☐ E21.0 - Primary hyperparathyroidism
- ☐ Q85.03 - Schwannomatosis
- ☐ Q85.0 Neurofibromatosis (nonmalignant)

Group 8

- ☐ G11.3 - Cerebellar ataxia with defective DNA repair
- ☐ G11.10 - Early-onset cerebellar ataxia, unspecified
- ☐ G11.11 - Friedreich ataxia
- ☐ G11.19 - Other early-onset cerebellar ataxia
- ☐ G11.0 - Congenital nonprogressive ataxia
- ☐ G11.2 - Late-onset cerebellar ataxia
- ☐ G11.4 - Hereditary spastic paraplegia
- ☐ G11.8 - Other hereditary ataxias
- ☐ G11.9 - Hereditary ataxia, unspecified
- ☐ Q85.00 - Neurofibromatosis, unspecified
- ☐ Q85.01 - Neurofibromatosis, type 1
- ☐ Q85.02 - Neurofibromatosis, type 2
- ☐ Q85.09 - Other neurofibromatosis
- ☐ E21.0 - Primary hyperparathyroidism
- ☐ Q85.03 - Schwannomatosis
- ☐ Q85.0 Neurofibromatosis (nonmalignant)
- ☐ Q85.03 - Schwannomatosis
- ☐ Q85.1 - Tuberous sclerosis
- ☐ Q85.8 - Other phakomatoses, not elsewhere classified
- ☐ Q85.9 - Phakomatosis, unspecified

_____

Patient Informed Consent for Genetic Testing

I, _____The Patient authorize North West Labs, to conduct genetic testing for CANCER GENETIC TEST (Disease and/or Test Name), as ordered by my physician or authorized healthcare provider or my child's or dependent's physician or autho-rized healthcare provider, and authorize the collection of a sample for the purpose of that testing.

I acknowledge and consent to the following:

1. My physician or his/her designee (such as a genetic counselor) has fully covered the following:
(A) purpose, description and nature of the test and its potential uses;
(B) reliability of positive or negative results and the level of certainty that a positive test result for the disease or condition serves as a predictor of such disease, the effectiveness and limitations of the genetic test and the meaning of the genetic test results;
(C) implications of taking the genetic test, including the medical risks and benefit;
(D) description of the disease or condition tested for;
(E) the availability and importance of genetic counseling. I acknowledge that I have been provided with information identifying a genetic counselor or medical geneticist from whom I might obtain such counseling and understand that I may seek counseling prior to signing this consent; and
(F) a positive test result is an indication that I may be predisposed to or have the specific disease or condition tested for and I understand that I may wish to consider further independent testing, consult with my physician or pursue genetic counseling to discuss the test results.

2. I authorize and I understand that I will receive the test results from my physician unless I direct otherwise. I understand that I have a right to confidential treatment of my sample and results and that my test results will only be disclosed as authorized in this consent.

3. Test results will be retained in accordance with applicable laws. I understand that only my physician's office and/or North West Labs. will have access to my sample and that my sample will be used only for the purposes for which I have given my consent.

Patient's Statement

I, the undersigned, have been informed about the test(s) purpose, procedures, possible beneÿts and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to genetic testing.

PATIENT SIGNATURE*	SIGNATURE OF AUTHORIZED REPRESENTATIVE
PRINT NAME*	PRINT NAME
DATE*	DATE

By signing this form, the medical professional acknowledges that the individual/family member authorized to make decisions for the individual (collectively, the "Patient") has been supplied information regarding and consented to undergo genetic testing, substantially as set forth in North West Labs (NWL) Informed Consent for Genetic Testing. For orders originating outside the US, the Patient has been informed their personal information and specimen will be transferred to and processed in the US. The Patient has been informed that NWL may notify them of clinical updates related to genetic test results (in consultation with the ordering medical professional). If insurance billing is selected, the Patient has been informed and authorizes NWL and its designee to release information concerning testing to their insurer. The medical professional agrees to allow NWL (1) to transfer the information from this TRF to a letter of medical necessity and/or other documentation using the medical professional's name as the signature as well as (2) assist the patient in obtaining pre-test genetic counseling from a third-party service, as required by the patient's insurance provider. I acknowledge that the Patient has agreed that if the Patient's insurer does not reimburse NWL in full for any reason then NWL may bill the Patient for the services and the Patient will remit payment to NWL. For amounts the Patient receives from the insurer, the Patient has agreed to remit payment to NWL for services rendered. I acknowledge that I offered pre-test genetic counseling to the Patient, if required by their insurer. I attest that I am authorized under applicable law to order this test.

ORDERING PHYSICIAN SIGNATURE*	DATE: (MM/DD/YYYY)

Patient ID Number: _____

Patient Name: _____,

Notifier: North West Labs

Advance Beneficiary Notice of Non-Coverage (ABN) - All Insurance Providers

Notice to Patients:

Your health insurance plan, whether Medicare or a commercial provider, may not cover all tests or services - including those that you and your healthcare provider consider medically necessary. This notice informs you that one or more of the following North West Labs tests may not be covered, and you may be financially responsible.

Tests That May Not Be Covered:

Test Category	Examples	Reason for non-coverage	Estimated Cost
PharmacoCheck+	Pharmacogenetic testing	Not deemed medically necessary for your diagnosis	Up to $295
Germline Custom Panels	ImmunoCheck+, CancerCheck+, NeuroCheck+, MetabolicCheck+, ThyroidCheck+, etc.	Insurance exclusions, medical necessity, etc.	Up to $295

What You Need to Do:

1. Review this notice carefully to make an informed decision.
2. Ask any questions you may have before proceeding.
3. Select one of the options below to indicate your decision.

Note: If you select Option 1 or 2, we may attempt to coordinate with other insurance carriers you have. However, we are not required to do so by Medicare or other insurers.

Patient Options: (Please select only one option)

☐ Option 1: I want to receive the North West Labs Test(s) listed above. I understand that my insurance provider may not cover these services. I would like a claim submitted to my insurer for an official coverage decision. If denied, I agree to be responsible for payment. I understand that I may appeal the denial in accordance with my insurer's policies.

☐ Option 2: I want to receive the North West Labs Test(s) listed above. I do not want a claim submitted to my insurer. I agree to pay out of pocket and understand that I waive my right to an appeal through my insurance plan.

☐ Option 3: I do not want to receive the North West Labs Test(s) listed above. I understand that I will not be billed for the service and cannot appeal a non-coverage decision.

Additional Information:

-If you choose Option 1, North West Labs will attempt to contact you to discuss your eligibility for financial assistance and may provide you with the option to cancel your order before testing begins. If you have questions about your financial responsibility or coverage, please contact us at (248) 301-6917.

-This form serves as a courtesy and does not represent an official decision by your insurance provider. If you have questions about your insurance policy or billing, contact your provider directly.

-For Medicare-specific questions, call 1-800-MEDICARE (1-800-633-4227 / TTY: 1-877-486-2048).

Patient Acknowledgment:

By signing below, you confirm that you have received, reviewed, and understood this notice. You will also be provided with a copy for your records.

Signature of Patient or Authorized Representative: _____. Date: _____/_____/_____.

NORTH WEST LABS

NORTH WEST LABS

Hereditary Cancer Panel

Patient	Specimen	Ordering Physician
Patient Name:	**Specimen Type:** Buccal Swab	**Physician:**
Date of Birth:	**Collection Date:**	
Accession ID:	**Received Date:**	**Report Date:**
Age:		
Sex:		

Test Result

Positive Result Pathogenic/Likely Pathogenic variant(s) detected.

A positive result indicates the detection of pathogenic or likely pathogenic variant(s) within the coding regions of the genes listed for this assay. This result should be regarded as a preliminary finding. Confirmation by orthogonal method is recommended. Please read the report details and discuss the findings with a qualified health care provider. Genetic counseling and testing for at risk family members is suggested. This result is limited to conditions that are detectable by this targeted DNA sequencing assay and does not rule out all possible genetic conditions.

Primary Findings

GENE/TRANSCRIPT	VARIANT	POSITION	ZYGOSITY	CLASSIFICATION
FANCC NM_000136.2	c.1642C>T p.Arg548Ter	g.97864024G>A	Heterozygous	Pathogenic

Primary Findings Summary

***FANCC* p.Arg548Ter**

This patient is heterozygous for variant p.Arg548Ter in the *FANCC* gene. Nonsense variant p.Arg548Ter in FANCC leads to a premature stop codon and is predicted to undergo nonsense-mediated decay resulting in a truncated or absent protein. Loss of function is an established disease mechanism for this gene. This variant is present in population databases (gnomAD: 0.005%). ClinVar has an entry for this variant and clinical labs have classified this variant as Pathogenic (Variation ID: 12047). This variant has been reported in the literature in individuals with FANCC-related disease, including patients seen homozygous, in trans or phase unknown with other pathogenic variants in the FANCC gene (PMIDs: 9207444, 08103176, 28425259, 31467304, 24584348, 12393516, 20869034). The published individual's features are highly specific for a diagnosis of Fanconi anemia (PMIDs: 9207444, 28425259). Based on the evidence above and according to the ACMG/AMP variant interpretation guidelines, this variant has been classified as Pathogenic for FANCC-related disease.

The Fanconi anemia complementation group (FANC) currently includes FANCA, FANCB, FANCC, FANCD1 (also called BRCA2), FANCD2, FANCE, FANCF, FANCG, FANCI, FANCJ (also called BRIP1), FANCL, FANCM and FANCN (also called PALB2). The previously defined group FANCH is the same as FANCA. Fanconi anemia is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair. The members of the Fanconi anemia complementation group do not share sequence similarity; they are related by their assembly into a common nuclear protein complex. This gene encodes the protein for complementation group C. [provided by RefSeq, Jul 2008]

NORTH WEST LABS

Patient

Patient Name: Date of Birth: Accession ID:

Genes with Negative Findings

Evaluation of the following genes did not reveal pathogenic or likely pathogenic variant(s).

GENE/TRANSCRIPT	COORDINATES (GRCh37/hg19)	FINDINGS
APC	chr5:112043414-112090722	Negative
ATM	chr11:108098351-108098615	Negative
AXIN2	chr17:63526093-63530197	Negative
BAP1	chr3:52436303-52436690	Negative
BARD1	chr2:215593399-215595232	Negative
BLM	chr15:91290622-91293297	Negative
BMPR1A	chr10:88635775-88649981	Negative
BRCA1	chr17:41196311-41199720	Negative
BRCA2	chr13:32890597-32893462	Negative
BRIP1	chr17:59760656-59763526	Negative
CDH1	chr16:68771318-68772314	Negative
CDK4	chr12:58142307-58143100	Negative
CDKN2A	chr9:21968227-21968770	Negative
CHEK2	chr22:29083884-29085203	Negative
COL1A1	chr17:48262862-48263381	Negative
CTNNA1	chr5:138117603-138119071	Negative
DICER1	chr14:95556834-95557446	Negative
EPCAM	chr2:47596644-47600709	Negative
FBN1	chr15:48703186-48704940	Negative
FH	chr1:241661127-241663890	Negative
GREM1	chr15:33022892-33023443	Negative
HNF1A	chr12:121416571-121426835	Negative
HOXB13	chr17:46804155-46805955	Negative
HRAS	chr11:532635-533358	Negative
KIT	chr4:55524181-55561947	Negative
MAX	chr14:65472921-65543381	Negative

Patient

Genes with Negative Findings (CONT.)

GENE/TRANSCRIPT	COORDINATES (GRCh37/hg19)	FINDINGS
MBD4	chr3:129150343-129151449	Negative
MEN1	chr11:64571805-64572670	Negative
MITF	chr3:69788748-69813093	Negative
MLH1	chr3:37035038-37038200	Negative
MSH2	chr2:47630330-47635694	Negative
MSH3	chr5:79950546-79952350	Negative
MSH6	chr2:48010372-48018262	Negative
MUTYH	chr1:45794977-45796229	Negative
NBN	chr8:90947809-90949303	Negative
NF1	chr17:29652837-29654857	Negative
NF2	chr22:29999987-30032865	Negative
NSD1	chr5:176562104-176562201	Negative
NTHL1	chr16:2089924-2090239	Negative
PALB2	chr16:23614779-23619333	Negative
PDGFRA	chr4:55124935-55127579	Negative
PHOX2B	chr4:41747823-41749553	Negative
PMS2	chr7:6012869-6017388	Negative
POLD1	chr19:50902109-50902741	Negative
POLE	chr12:133201272-133201590	Negative
PTEN	chr10:89624226-89653866	Negative
RAD51C	chr17:56770004-56772554	Negative
RAD51D	chr17:33426810-33428384	Negative
RET	chr10:43572706-43596170	Negative
RUNX1	chr21:36164431-36171759	Negative
SDHA	chr5:218470-223683	Negative
SDHB	chr1:17345375-17349225	Negative
SDHC	chr1:161284195-161293460	Negative
SDHD	chr11:111957631-111958697	Negative

Patient

Genes with Negative Findings (CONT.)

GENE/TRANSCRIPT	COORDINATES (GRCh37/hg19)	FINDINGS
SMAD4	chr18:48573416-48575230	Negative
SMARCA4	chr19:11094827-11096081	Negative
STK11	chr19:1206912-1218499	Negative
TERT	chr5:1253842-1254620	Negative
TMEM127	chr2:96919545-96920735	Negative
TP53	chr17:7572926-7574033	Negative
TSC1	chr9:135771621-135772732	Negative
TSC2	chr16:2098616-2100487	Negative
VHL	chr3:10183531-10188320	Negative
WT1	chr11:32410603-32413610	Negative

Test results reviewed and approved by:

Owatha Tatum, Ph.D., HCLD/CC(ABB)

Sep 24, 2024

Patient

Test Methodology

The Hereditary Cancer Panel is designed to detect single nucleotide variants (SNVs) and small insertions and deletions in 65 genes associated with hereditary cancer risk. Targeted regions for this panel include the coding exons and 10 bp intronic sequences immediate to the exon-intron boundary of each coding exon in each of these genes. Extracted patient DNA is prepared using targeted hybrid capture, assignment of a unique index, and sequencing via Illumina sequencing by synthesis (SBS) technology. Data is aligned using human genome build GRCh37. Variant interpretation is performed according to current American College of Medical Genetics and Genomics (ACMG) professional guidelines for the interpretation of germline sequence variants using Fabric Enterprise™ Pipeline 6.6.15. Variant interpretation and reporting is performed by Fabric Clinical (CLIA ID: 45D2281059 and CAP ID: 9619501)), located at 6901 Quaker Avenue, Suite A, Lubbock, Texas, 79413. The following quality filters are applied to all variants: quality <500, allelic balance <0.3, coverage <10x.

Genes Evaluated

APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, COL1A1, CTNNA1, DICER1, EPCAM, FANCC, FBN1, FH, GREM1, HNF1A, HOXB13, HRAS, KIT, MAX, MBD4, MEN1, MITF, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NSD1, NTHL1, PALB2, PDGFRA, PHOX2B, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RET, RUNX1, SDHA, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, TERT, TMEM127, TP53, TSC1, TSC2, VHL, WT1

Test Limitations

This test aims to detect all clinically relevant variants within the coding regions of the genes evaluated. Pathogenic and likely pathogenic variants detected in these genes should be confirmed by orthogonal methods. Detected genetic variants classified as benign, likely benign, or of uncertain significance are not included in this report. Homopolymer regions and regions outside of the coding regions cannot be captured by the standard NGS target enrichment protocols. At this time, the assay does not detect large deletions and duplications. This analysis also cannot detect pathogenic variants within regions which were not analyzed (e.g., introns, promoter and enhancer regions, long repeat regions, and mitochondrial sequence). This assay is not designed to detect mosaicism and is not designed to detect complex gene rearrangements or genomic aneuploidy events. It is important to understand that there may be variants in these genes undetectable using current technology. Additionally, there may be genes associated with hereditary cancer pathology whose clinical association has not yet been definitively established. The test may therefore not detect all variants associated with hereditary cancer pathology. The interpretation of variants is based on our current understanding of the genes in this panel and is based on current ACMG professional guidelines for the interpretation of germline sequence variants. Interpretations may change over time as more information about the genes in this panel becomes available. Qualified health care providers should be aware that future reclassifications of genetic variants can occur as ACMG guidelines are updated. Factors influencing the quantity and quality of extracted DNA include, but are not limited to, collection technique, the amount of buccal epithelial cells obtained, the patient's oral hygiene, and the presence of dietary or microbial sources of nucleic acids and nucleases, as well as other interfering substances and matrix-dependent influences. PCR inhibitors, extraneous DNA, and nucleic acid degrading enzymes may adversely affect assay results.

Regions with Limited Coverage

Validation studies concluded that the following regions may have coverage values below the level required for accurate interpretation.

REGION	GENE	EXON	REGION	GENE	EXON
chr2:179494027-179494170	*TTN*	--	chr13:100755136-100755214	*PCCA*	2 or Intron 1_2
chr7:117229510-117229531	*CFTR*	Intron 12_13	chr20:33068403-33068537	*ITCH*	19

Patient

Regions with Limited Coverage (CONT.)

REGION	GENE	EXON	REGION	GENE	EXON
chr13:32953886-32954050	*BRCA2*	23	chr19:7293802-7293902	*INSR*	1
chr2:179484714-179484839	*TTN*	7	chr9:5073698-5073785	*JAK2*	13 or 14
chr12:40742210-40742311	*LRRK2*	43	chr13:100764094-100764142	*PCCA*	2 or 3
chr9:5077453-5077580	*JAK2*	14 or 15	chr6:129775299-129775433	*LAMA2*	47
chr3:193365858-193365923	*OPA1*	17 or 18	chr6:51611518-51611687	*PKHD1*	59
chr3:193384084-193384178	*OPA1*	25 or 26	chr1:237923075-237923152	*RYR2*	83
chr1:237831182-237831258	*RYR2*	58	chr9:101867487-101867584	*TGFBR1*	1
chr14:64882356-64882457	*MTHFD1*	6	chr16:2185475-2185690	*PKD1*	Intronic
chr14:64855145-64855186	*MTHFD1*	1	chr10:104158485-104158631	*NFKB2*	12 or intron 11_12
chr2:228124508-228124593	*COL4A3*	19	chr11:68080182-68080273	*LRP5*	1
chr11:108164039-108164204	*ATM*	31	chr12:6484711-6484770	*SCNN1A*	Intronic
chr9:5081725-5081861	*JAK2*	18 or 19	chrX:146993468-146993748	*FMR1*	1
chr14:23862874-23863117	*MYH6*	22	chr2:1520654-1520754	*TPO*	14 or 15
chr2:228125797-228125833	*COL4A3*	20	chr13:32903579-32903629	*BRCA2*	8
chr12:40713789-40713977	*LRRK2*	34	chr13:32900237-32900287	*BRCA2*	5

Regulatory Disclosures

This laboratory developed test (LDT) was developed and its performance characteristics were determined by PreCheck Health Services, Inc. This test was performed at PreCheck Health Services, Inc. (CLIA ID: 10D2210020 and CAP ID: 9101993) that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This assay has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Clearance or approval by the FDA is not required for the clinical use of this analytically and clinically validated laboratory developed test. This assay has been developed for clinical purposes and it should not be regarded as investigational or for research.

References

Murer-Orlando M, Llerena JC, Birjandi F, Gibson RA, et al. Lancet (London, England). 1993, Sep 11. FACC gene mutations and early prenatal diagnosis of Fanconi's anaemia. (PMID: 8103176)

Gillio AP, Verlander PC, Batish SD, Giampietro PF, et al. Blood. 1997, Jul 01. Phenotypic consequences of mutations in the Fanconi anemia FAC gene: an International Fanconi Anemia Registry study. (PMID: 9207444)

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References (CONT.)

Hartmann L, Neveling K, Borkens S, Schneider H, et al. American journal of human genetics. 2010, Oct 08. Correct mRNA processing at a mutant TT splice donor in FANCC ameliorates the clinical phenotype in patients and is enhanced by delivery of suppressor U1 snRNAs. (PMID: 20869034)

De Rocco D, Bottega R, Cappelli E, Cavani S, et al. Haematologica. 2014, Jun. Molecular analysis of Fanconi anemia: the experience of the Bone Marrow Failure Study Group of the Italian Association of Pediatric Onco-Hematology. (PMID: 24584348)

Aftab I, Iram S, Khaliq S, Israr M, et al. Turkish journal of medical sciences. 2017, Apr 18. Analysis of FANCC gene mutations (IVS4+4A>T, del322G, and R548X)in patients with Fanconi anemia in Pakistan. (PMID: 28425259)

Dörk T, Peterlongo P, Mannermaa A, Bolla MK, et al. Scientific reports. 2019, Aug 29. Two truncating variants in FANCC and breast cancer risk. (PMID: 31467304)

Patient

Appendix: Sequencing Quality Metrics

QC METRIC	VALUE
% Aligned Reads	0.997436
Fold 80 Base Penalty	1.91051
% of Target with Zero Coverage	0.00674399
Target Coverage Mean	150.93
Target % > 20x	0.98454
Target % > 10x	0.990508
Total Number of Reads	41303200.0

QC PASS by AUTO QC on Sep 20, 2024

NORTH WEST LABS, INC.
Laboratory Director: Eugene Olsowka, M.D. CLIA ID:23D2126347
29580 Northwestern Hwy. Southfield, MI 48034
Phone: (248) 301-6917
www.nwlabs.com

Comprehensive Cancer Panel

Patient
Patient Name:
Date of Birth:
Age: 72
Sex: Female

Specimen

Accession ID: PCHSCgx25-00314
Collection date: 04/09/2025
Received Date: 02/10/2025
Specimen type: Buccal Swab

Order

Physician:
Report Date: April 4, 2026

INCONCLUSIVE RESULT

> *No clinically significant variants detected*

VARIANTS RELEVANT TO THE TEST INDICATION

Gene & transcript	Variant	Genotype	Disease	Inheritance	Evaluation
CDKN1B *NM_004064.5*	c.356T>C p.(Ile119Thr)	Heterozygous	Multiple endocrine neoplasia, type IV	AD	Uncertain Significance
SDHA *NM_004168.4*	c.456+7G>A N/A	Heterozygous	hereditary pheochromocytoma-paraganglioma	AD	Uncertain Significance

AD : Autosomal dominant inheritance

RECOMMENDATIONS

1. These findings support a molecular diagnosis of the listed disorders.
2. Absence of clinically significant variants in genes analyzed does not rule out a genetic basis for the individual's clinical presentation and it is advisable to correlate these findings with the clinical presentation.
3. Please read the report details and discuss the findings with a qualified health care provider.
4. After receiving a positive result, genetic counseling and testing of at risk family members is recommended.

DETAILED VARIANT INFORMATION

CDKN1B - c.356T>C

Uncertain Significance

Interpretation

Variant Description
This variant is present in population databases (0.0009178). Computational algorithms developed to predict the effect of sequence variants are inconclusive (REVEL: 0.320). Functional studies using cell transfection have shown that this variant alters CDKN1B protein function [PMID: 32232325] (PS3_Supporting). This variant has been reported in multiple individuals with CDKN1B related conditions. Due to insufficient evidence, the clinical significance of this variant is uncertain at this time.

Gene Description
The CDKN1B gene provides instructions for making a protein called p27, which acts as a tumor suppressor by regulating cell growth and division. Pathogenic variants in the CDKN1B are associated with autosomal dominant multiple endocrine neoplasia type 4 (OMIM:610755), which is characterized by acromegaly, pituitary tumor, invasive pituitary adenoma with growth hormone hyperproduction, high mitotic activity, and cell atypia (Pellegata NS , 2006 Oct 17)

SDHA - c.456+7G>A

Uncertain Significance

Interpretation

Variant Description
This variant is absent from control populations in gnomAD (PM2_Supporting). Algorithms that predict the potential impact of sequence variants on RNA splicing suggest that this variant may disrupt normal splicing (SpliceAI: 0.29) (PP3). Due to insufficient evidence, the clinical significance of this variant is uncertain at this time.

Gene Description
The SDHA gene encodes one of the four subunits of the succinate dehydrogenase enzyme, which plays a vital role in mitochondria by helping convert energy from food into a usable form for cells. Pathogenic variants in SDHA are associated with autosomal dominant paraganglioma syndrome 5 (OMIM:614165). This condition is characterized by development of nonchromaffin neuroendocrine tumors, including head and neck paragangliomas, adrenal and/or extra adrenal pheochromocytomas, or a combination of both tumor types (Baysal BE , 2002 Sep) , (Burnichon N , 2010 Aug 1)

METHODOLOGY

The Comprehensive Cancer Panel is designed to detect single nucleotide variants (SNVs) and small insertions and deletions in 116 genes associated with cancer risk. Targeted regions for this panel include the coding exons and 10 bp intronic sequences immediate to the exon-intron boundary of each coding exon in each of these genes. Extracted patient DNA is prepared using the Illumina Trusight One Expanded Panel, assigned a unique index, and subjected to sequencing via Illumina sequencing by synthesis (SBS) technology. The SeqOne GermlineVar v2.2 is used to align data to human genome build GRCh38 and make variant calls. Variant annotation and interpretation are performed in the SeqOne platform by qualified variant scientists according to current American College of Medical Genetics and Genomics (ACMG) professional guidelines for the interpretation of germline sequence variants. Variant classification categories include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. Only the variants classified as pathogenic, likely pathogenic, or VUS are reported. The results for each patient are reviewed by an individual who meets Laboratory Director qualifications as stated by CLIA certification and College of American Pathologists (CAP) accreditation requirements. Reportable variants requiring confirmatory testing were reported after confirmatory testing was performed via orthogonal methods.

QUALITY METRICS

Sample name	% of aligned reads	Coverage at 10X	Coverage at 30X	Coverage at 50X	Average coverage	Ti/Tv ratio
PCHSCgx25-00314	99.9%	99.9%	99.7%	99.2%	320.67x	3.55

LIMITATIONS

This test aims to detect all clinically relevant variants within the coding regions of the genes evaluated. Homopolymer regions and regions outside of the coding regions cannot be captured by the standard NGS target enrichment protocols. The assay does not detect large deletions and duplications. This analysis also cannot detect pathogenic variants within regions which were not analyzed (e.g., introns, promoter and enhancer regions, repetitive regions, pseudogenes, and mitochondrial DNA). This assay is not designed to detect mosaicism and is not designed to detect complex gene rearrangements or genomic aneuploidy events. It is important to understand that there may be variants in these genes undetectable using current technology. The interpretation of variants is based on our current understanding of the genes in this panel and is based on current ACMG professional guidelines for the interpretation of germline sequence variants. Interpretations may change over time as more information about the genes in this panel becomes available. Qualified health care providers should be aware that future reclassifications of genetic variants can occur as ACMG guidelines are updated. Factors influencing the quantity and quality of extracted DNA include, but are not limited to, collection technique, the amount of buccal epithelial cells obtained, the patient's oral hygiene, and the presence of dietary or microbial sources of nucleic acids and nucleases, as well as other interfering substances and matrix-dependent influences. PCR inhibitors, extraneous DNA, and nucleic acid degrading enzymes may adversely affect assay results.

EVALUATED GENES

ACD, AIP, AKT1, ALK, APC, ATM, AXIN2, BAP, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CASR, CDC73, CDH1, CDK4, CDKN1B, CDKN1C, CDKN2A, CEBPA, CHEK2, CTNNA1, CTRC, DDB2, DICER1, DIS3L2, EGFR, EPCAM, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, FAM175A, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FH, FLCN, GALNT12, GATA2, GPC3, GREM1, HNF1A, HOXB13, HRAS, KIF1B, KIT, LZTR1, MAX, MEN1, MET, MITF, MLH1, MRE11, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NSD1, NTHL1, NTRK1, PALB2, PDGFRA, PHOX2B, PIK3CA, PMS2, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RB1, RECQL4, RET, RHBDF2, RINT1, RUNX1, SDHA, SDHAF2, SDHB, SDHC, SDHD, SLX4, SMAD4, SMARCA4, SMARCB1, SMARCE1, SPINK1, SPRED1, STK11, SUFU, TERC, TERF2IP, TERT, TMEM127, TP53, TSC1, TSC2, VHL, WRN, WT1, XPA, XPC, XRCC2

REGULATORY DISCLOSURES

This laboratory developed test (LDT) was developed and its performance characteristics were determined by North West Labs, Inc. This test was performed at North West Labs, Inc. (CLIA ID: 23D2126347) that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This assay has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Clearance or approval by the FDA is not required for clinical purposes, and use of this analytically and clinically validated laboratory developed test.

TEST RESULTS REVIEWED AND APPROVED BY

Name: Jessica Moye PhD, HCLD- ABB, MB-ASCP CM, CGMBS

Date: April 5, 2026

This report has been reviewed and approved by the above named individual.

BIBLIOGRAPHY

Pellegata NS, Quintanilla-Martinez L, Siggelkow H, Samson E, Bink K, Höfler H, Fend F, Graw J, Atkinson MJ, Germ-line mutations in p27Kip1 cause a multiple endocrine neoplasia syndrome in rats and humans., Proceedings of the National Academy of Sciences of the United States of America, Volume:103, Issue:42, 2006 Oct 17, Pages:15558-63, DOI:10.1073/pnas.0603877103

NORTH WEST
LABS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Hereditary Cancer Genetics (CGX)

Next Gen Sequencing

Myeloid NGS

North West Labs
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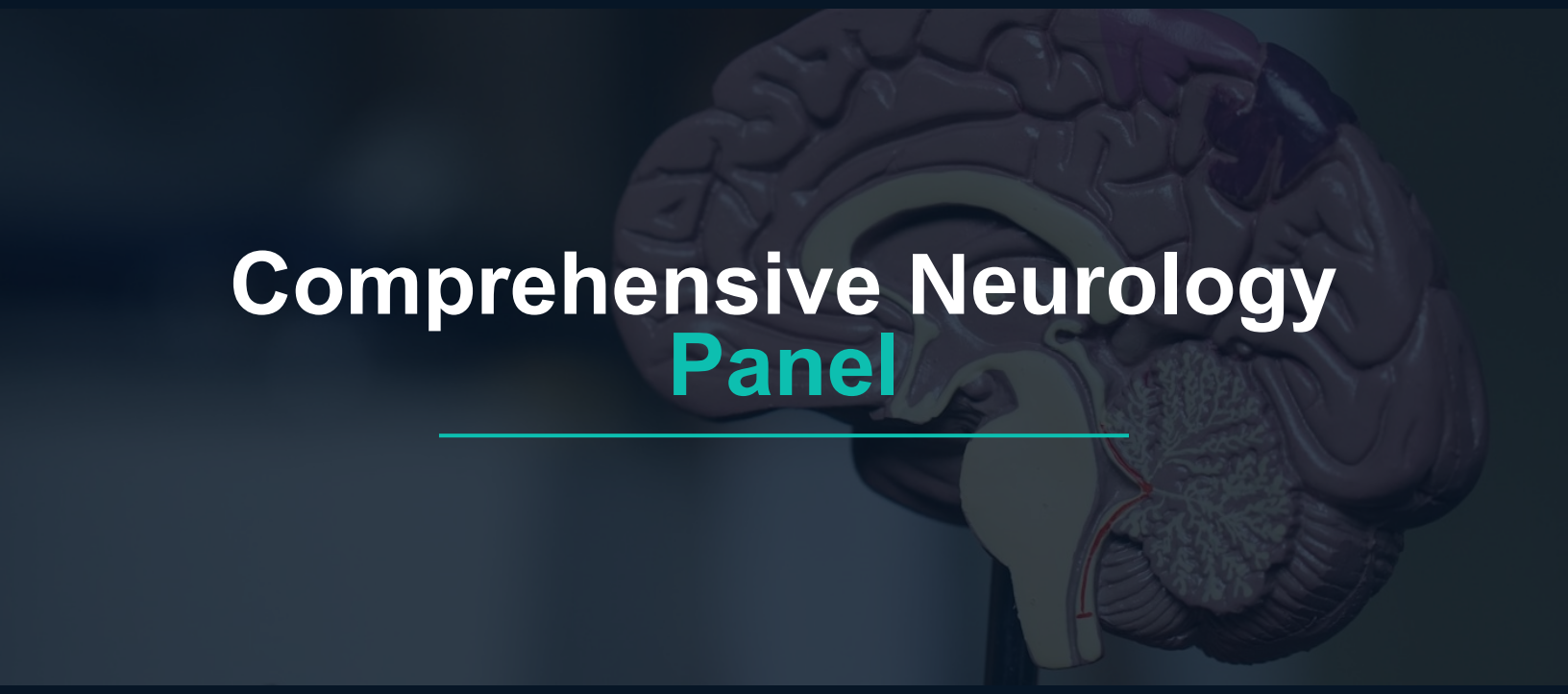
Whole Exome Sequencing (WES)

NORTH WEST LABS



Comprehensive Neurology Panel

NORTH WEST
LABS

Whole Exome Sequencing (WES)

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Myeloid NGS

Next Gen Sequencing

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Neuro NGS

Solid Tumor NGS

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Whole Exome Sequencing (WES)

COMPREHENSIVE NEUROLOGY REQUISITION FORM

NORTH WEST LABS
29580 Northwestern Hwy., Southfield, MI 48034
Phone: (248) 301-6917 Fax: (248) 301-6785 CLIA: 23D2126347
support@nwlabs.com www.nwlabs.com

PATIENT INFORMATION

First name | MI | Last name | Date of birth (MM/DD/YYYY)

Biological sex
☐ Male
☐ Femal

MRN (medical record number)

Ethnicity
☐ Asian ☐Black/African American ☐ White/Caucasian ☐ Ashkenazi Jewish ☐ Hispanic ☐ Other: _____

Email address (for billing contact and report access after clinician releases)

Mobile phone

Address

City | State/Prov | Zip/Postal code | Country

CLINICAL INFORMATION

Organization name | Phone | Fax

Address | City | State/Prov | ZIP/Postal Code | Country

CLINICAL TEAM

Primary clinical contact (contact for general inquires)

Name | NPI | Email address (for report access)

☐ INSURANCE BILLING (attach front and back of insurance card)

Attach clinical notes, medical records, and/or letter of medical necessity (LMN) to prevent delays. We do not accept insurance for certain tests or patients outside the US.

Policyholder name | Patient relationship to ☐Self ☐ Spouse ☐ Child Other: _____

Primary insurance company name | Primary member ID# | Primary insurance phone | Prior-authorization #

Secondary insurance company name | Secondary member ID# | Secondary insurance phone | Prior-authorization #

Medicare insurance billing only (select one):
☐ Patient was treated as a hospital inpatient in the last 14 days
☐ Not a hospital patient

☐ PATIENT PAY BILLING

North West Labs, Inc. will send an electronic invoice to the patient email listed above. Insurance will not be billed.

☐ INSTITUTIONAL BILLING

North West Labs, Inc. will send an invoice to the organization address above. Please contact us if this order should be billed to a different location.

☐ PARTNERSHIP PROGRAMS

North West Labs partner code:

Label each tube with the patient's full name, date of birth, and specimen collection date. A requisition form MUST accompany each specimen.

SPECIMEN INFORMATION

Collection date **(MM/DD/YYYY)**

If not provided, date will be 1 day prior to our receipt of specimen. For DNA, provide date retrieved from archive.

Specimen type

☐ Buccal Swab

DNA must be extracted in a CLIA or other suitable certified laboratory. We are unable to accept blood or saliva from patients with allogeneic bone marrow transplants or a blood transfusion <2 weeks prior to specimen collection.

COMPREHENSIVE NEUROLOGY TESTING

For individuals that meet the eligibility criteria below and wish to receive the program specific genetic testing panels.

REQUIRED: You must select below the appropriate eligibility criteria for this patient.

This program is available to individuals 18 or older suspected of or at risk of having a Comprehensive Neurology disorder based on one or more of the following (please select all that apply)*:

Symptomatic individual with clinical diagnosis or suspicion of one of the following (check one):

- ☐ Amyotrophic Lateral Sclerosis Panel
- ☐ Ataxia Panel
- ☐ Autism Spectrum Disorders Panel
- ☐ Cerebral Cavernous Malformation Panel
- ☐ Charcot-Marie-Tooth Neuropathy Panel
- ☐ Coenzyme q10 Deficiency Panel
- ☐ Collagen Type VI-Related Disorders Panel
- ☐ Comprehensive Epilepsy Panel
- ☐ Comprehensive Muscular Dystrophy / Myopathy Panel
- ☐ Congenital Myasthenic Syndromes Panel
- ☐ Creatine Metabolism Deficiency Panel
- ☐ Dementia Panel
- ☐ Dystonia Panel
- ☐ Emery-Dreifuss Muscular Dystrophy Panel
- ☐ Epileptic Encephalopathy Panel
- ☐ Holoprosencephaly Panel
- ☐ Idiopathic Generalized and Focal Epilepsy Panel
- ☐ Leukodystrophy and Leukoencephalopathy Panel
- ☐ LGMD and Congenital Muscular Dystrophy Panel

Asymptomatic individual with family history of early (<65 years of age) onset diagnosis of one of the following conditions (check one):

- ☐ Lissencephaly Panel
- ☐ Macrocephaly / Overgrowth Syndrome Panel
- ☐ Metabolic Epilepsy Panel
- ☐ Metabolic Myopathy and Rhabdomyolysis Panel
- ☐ Microcephaly and Pontocerebellar Hypoplasia Panel
- ☐ Migraine Panel
- ☐ NCL and Progressive Myoclonic Epilepsy Panel
- ☐ Nemaline Myopathy Panel
- ☐ Neuro-Ophthalmology Panel
- ☐ Neuronal Migration Disorder Panel
- ☐ Parkinson Disease Panel
- ☐ Periodic Paralysis Panel
- ☐ Polymicrogyria Panel
- ☐ Porphyria Panel
- ☐ Septo-Optic Dysplasia Panel
- ☐ Spastic Paraplegia Panel
- ☐ Spinal Muscular Atrophy Panel
- ☐ Tuberous Sclerosis Panel
- ☐ X-linked Intellectual Disability Panel

Family member with known disease-causing variant in one of the genes included on the Combined Hereditary Dementia and Amyotrophic Lateral Sclerosis Panel OR Hereditary Parkinson's Disease and Parkinsonism Panel (list gene): _____

CLINICAL HISTORY (it is strongly encouraged to include notes, reports and/or previous genetic test results for this individual or

Cognitive Features	YES	NO	UNKNOWN
Progressive cognitive decline - amnestic presentation (memory loss, impairment in learning and recall)	☐	☐	☐
Progressive cognitive decline - language presentation (word-finding deficits)	☐	☐	☐
Progressive cognitive decline - visuospatial presentation (spatial cognition-object agnosia, facial recognition, simultagnosia and alexia)	☐	☐	☐
Progressive cognitive decline - executive dysfunction (impaired reasoning, judgment and problem solving)	☐	☐	☐
Behavioral changes (disinhibition/ impulsivity, apathy/inertia, and/or loss of sympathy/empathy)	☐	☐	☐
Behavioral changes (perseverative/compulsive behaviors and/or hyperorality)	☐	☐	☐
Psychiatric illness (psychosis, mania, hallucinations, delusions, etc.)	☐	☐	☐
Other: _____	☐	☐	☐
Motor Features			
Cerebellar ataxia (gait and/or limb ataxia)	☐	☐	☐
Oculomotor dysfunction (ex: oculomotor apraxia, strabismus, and/or nystagmus)	☐	☐	☐
Increased muscle tone and/or increased extremity deep-tendon reflexes/ hyperreflexia (jaw jerk, Hoffman sign, positive Babinski sign, crossed adductors, extensor plantor response)	☐	☐	☐
Spasticity	☐	☐	☐
Pseudobulbar affect (inappropriate laughing/crying/forced yawning)	☐	☐	☐

Motor Features (continued)	YES	NO	UNKNOWN
Progressive muscle weakness and/or atrophy	☐	☐	☐
Muscle fasciculations and/or cramps	☐	☐	☐
Hyporeflexia and/or decreased or absent deep tendon reflexes	☐	☐	☐
Parkinsonism (bradykinesia, postural instability, rigidity, facial masking, resting tremor)	☐	☐	☐
Tardive dyskinesia (irregular, jerky movements), dystonia (patterned/ twisting movements and postures) and/or myoclonus (muscle jerks)	☐	☐	☐
Dysarthria (difficulty speaking)	☐	☐	☐
Dysphagia (swallowing difficulties)	☐	☐	☐

Neuroimaging, biomarkers, genetic and/or neuropathophysiology findings

- ☐ Abnormal MRI
  Major finding(s)? _____
- ☐ Abnormal PET scan or CSF analysis
  Major finding(s)? _____
- ☐ Abnormal brain pathology findings (typically only available post-mortem)
  Major finding(s)? _____
- ☐ Abnormal EMG
  Major finding(s)? _____
- ☐ Previously tested for C9orf72 gene at outside laboratory?
  Test result (positive, negative, intermediate) _____
  [please include copy of previous test result if available]

Other features

- ☐ Paget disease of bone
- ☐ Supranuclear palsy
- ☐ Autonomic dysfunction (ex: orthostatic hypotension, urinary incontinence)
- ☐ Familial insomnia
- ☐ Other relevant clinical features: _____

COMPREHENSIVE NEUROLOGY

Genes# - 98

ABCA7, ALS2, APOE, APP, ARSA, ATM, ATP13A2, ATP1A3, ATP6AP2, ATP7B, ATXN2, C19orf12, C9orf72, CHCHD10, CHCHD2, CHMP2B, COMT, CSF1R, DCTN1, DNAJC13, DNAJC6, DNMT1, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, EIF4G1, ERBB4, FBXO7, FTL, FUS, GALC, GBA, GCH1, GIGYF2, GNAL, GRN, HEXA, HNRNPA1, HNRNPA2B1, HTRA2, ITM2B, LMNB1, LRRK2, MAPT, MATR3, NOTCH3, NPC1, NPC2, OPA1, OPTN, PARK2, PARK7, PDGFB, PDGFRB, PINK1, PLA2G6, PLCG2, PLP1, POLG, PRKRA, PRNP, PSEN1, PSEN2, RAB29, RAB39B, ROGDI, SETX, SIGMAR1, SLC20A2, SLC25A12, SLC30A10, SLC39A14, SLC6A3, SNCA, SNCB, SOD1, SORL1, SPG11, SPR, SQSTM1, SYNJ1, TAF1, TARDBP, TBK1, TBP, TH, TMEM230, TREM2, TTC3, TUBA4A, TYROBP, UBQLN2, UCHL1, VCP, VPS13C, VPS35

INDICATION (S) FOR TESTING — ICD-10 Codes

Inflammatory diseases of the central nervous system (G00-G09)
- ☐ Bacterial meningitis, not elsewhere classified (G00)
- ☐ Meningitis in bacterial diseases classified elsewhere (G01)
- ☐ Meningitis in oth infec/parastc diseases classd elswhr (G02)
- ☐ Meningitis due to other and unspecified causes (G03)
- ☐ Encephalitis, myelitis and encephalomyelitis (G04)
- ☐ Encphlts, myelitis & encephalomyelitis in dis classd elswhr (G05)
- ☐ Intracranial and intraspinal abscess and granuloma (G06)
- ☐ Intcrn & intraspinal abscs & granuloma in dis classd elswhr (G07)
- ☐ Intracranial and intraspinal phlebitis and thrombophlebitis (G08)
- ☐ Sequelae of inflammatory diseases of central nervous system (G09)

Systemic atrophies primarily affecting the central nervous system (G10-G14)
- ☐ Huntington's disease (G10)
- ☐ Hereditary ataxia (G11)
- ☐ Spinal muscular atrophy and related syndromes (G12)
- ☐ Systemic atrophies aff cnsl in diseases classd elswhr (G13)
- ☐ Postpolio syndrome (G14)

Extrapyramidal and movement disorders (G20-G26)
- ☐ Parkinson's disease (G20)
- ☐ Secondary parkinsonism (G21)
- ☐ Other degenerative diseases of basal ganglia (G23)
- ☐ Dystonia (G24)
- ☐ Other extrapyramidal and movement disorders (G25)
- ☐ Extrapyramidal and movement disord in diseases classd elswhr (G26)

Other degenerative diseases of the nervous system (G30-G32)
- ☐ Alzheimer's disease (G30)
- ☐ Oth degenerative diseases of nervous system, NEC (G31)
- ☐ Oth degeneratv disord of nervous sys in dis classd elswhr (G32)

Demyelinating diseases of the central nervous system (G35-G37)
- ☐ Multiple sclerosis (G35)
- ☐ Other acute disseminated demyelination (G36)
- ☐ Other demyelinating diseases of central nervous system (G37)

Episodic and paroxysmal disorders (G40-G47)
- ☐ Epilepsy and recurrent seizures (G40)
- ☐ Migraine (G43)
- ☐ Other headache syndromes (G44)
- ☐ Transient cerebral ischemic attacks and related syndromes (G45)
- ☐ Vascular syndromes of brain in cerebrovascular diseases (G46)
- ☐ Sleep disorders (G47)

Nerve, nerve root and plexus disorders (G50-G59)
- ☐ Disorders of trigeminal nerve (G50)
- ☐ Facial nerve disorders (G51)
- ☐ Disorders of other cranial nerves (G52)
- ☐ Cranial nerve disorders in diseases classified elsewhere (G53)
- ☐ Nerve root and plexus disorders (G54)
- ☐ Nerve root and plexus compressions in diseases classd elswhr (G55)
- ☐ Mononeuropathies of upper limb (G56)
- ☐ Mononeuropathies of lower limb (G57)
- ☐ Other mononeuropathies (G58)
- ☐ Mononeuropathy in diseases classified elsewhere (G59)

Polyneuropathies and other disorders of the peripheral nervous system (G60-G65)
- ☐ Hereditary and idiopathic neuropathy (G60)
- ☐ Inflammatory polyneuropathy (G61)
- ☐ Other and unspecified polyneuropathies (G62)
- ☐ Polyneuropathy in diseases classified elsewhere (G63)
- ☐ Other disorders of peripheral nervous system (G64)
- ☐ Sequelae of inflammatory and toxic polyneuropathies (G65)

Diseases of myoneural junction and muscle (G70-G73)
- ☐ Myasthenia gravis and other myoneural disorders (G70)
- ☐ Primary disorders of muscles (G71)
- ☐ Other and unspecified myopathies (G72)
- ☐ Disord of myoneural junction and muscle in dis classd elswhr (G73)
- ☐ Cerebral palsy and other paralytic syndromes (G80-G83)
- ☐ Cerebral palsy (G80)
- ☐ Hemiplegia and hemiparesis (G81)
- ☐ Paraplegia (paraparesis) and quadriplegia (quadriparesis) (G82)
- ☐ Other paralytic syndromes (G83)

Other disorders of the nervous system (G89-G99)
- ☐ Pain, not elsewhere classified (G89)
- ☐ Disorders of autonomic nervous system (G90)
- ☐ Hydrocephalus (G91)
- ☐ Toxic encephalopathy (G92)
- ☐ Other disorders of brain (G93)
- ☐ Other disorders of brain in diseases classified elsewhere (G94)
- ☐ Other and unspecified diseases of spinal cord (G95)
- ☐ Other disorders of central nervous system (G96)
- ☐ Intraop and postproc comp and disorders of nervous sys, NEC (G97)
- ☐ Other disorders of nervous system not elsewhere classified (G98)
- ☐ Oth disorders of nervous system in diseases classd elswhr (G99)

ADDITIONAL ICD CODES

_____

_____

_____

This list is intended to be used as a reference to assist ordering Physicians in providing ICD-10 Diagnosis Codes as required by Medicare and other insurers to determine the medical necessity of testing being ordered. This is not an exhaustive list of all applicable diagnoses. Physicians are not required to use these codes but should report the diagnostic codes that best describes the reason for performing the test based on individual patient diagnoses. It is the Physician's Responsibility to determine both the medical need for and the utilization of, all health care services ordered.

Patient Informed Consent for Genetic Testing

I, _____The Patient authorize North West Labs, Inc., to conduct genetic testing for NEURO GENETIC TEST (Disease and/or Test Name), as ordered by my physician or authorized healthcare provider or my child's or dependent's physician or autho-rized healthcare provider, and authorize the collection of a sample for the purpose of that testing.

I acknowledge and consent to the following:

1. My physician or his/her designee (such as a genetic counselor) has fully covered the following:

(A) purpose, description and nature of the test and its potential uses;
(B) reliability of positive or negative results and the level of certainty that a positive test result for the disease or condition serves as a predictor of such disease, the effectiveness and limitations of the genetic test and the meaning of the genetic test results;
(C) implications of taking the genetic test, including the medical risks and benefit;
(D) description of the disease or condition tested for;
(E) the availability and importance of genetic counseling. I acknowledge that I have been provided with information identifying a genetic counselor or medical geneticist from whom I might obtain such counseling and understand that I may seek counseling prior to signing this consent; and
(F) a positive test result is an indication that I may be predisposed to or have the specific disease or condition tested for and I understand that I may wish to consider further independent testing, consult with my physician or pursue genetic counseling to discuss the test results.

2. I authorize and I understand that I will receive the test results from my physician unless I direct otherwise. I understand that I have a right to confidential treatment of my sample and results and that my test results will only be disclosed as authorized in this consent.

3. Test results will be retained in accordance with applicable laws. I understand that only my physician's office and/or North West Labs, Inc. will have access to my sample and that my sample will be used only for the purposes for which I have given my consent.

Patient's Statement

I, the undersigned, have been informed about the test(s) purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to genetic testing.

PATIENT SIGNATURE*	SIGNATURE OF AUTHORIZED REPRESENTATIVE
PRINT NAME*	PRINT NAME
DATE*	DATE

By signing this form, the medical professional acknowledges that the individual/family member authorized to make decisions for the individual (collectively, the "Patient") has been supplied information regarding and consented to undergo genetic testing, substantially as set forth in North West Labs, Inc. (NWL) Informed Consent for Genetic Testing. For orders originating outside the US, the Patient has been informed their personal information and specimen will be transferred to and processed in the US. The Patient has been informed that NWL may notify them of clinical updates related to genetic test results (in consultation with the ordering medical professional). If insurance billing is selected, the Patient has been informed and authorizes NWL and its designed to release information concerning testing to their insurer. The medical professional agrees to allow NWL (1) to transfer the information from this TRF to a letter of medical necessity and/or other documentation using the medical professional's name as the signature as well as (2) assist the patient in obtaining pre-test genetic counseling from a third-party service, as required by the patient's insurance provider. I acknowledge that the Patient has agreed that if the Patient's insurer does not reimburse NWL in full for any reason then NWL may bill the Patient for the services and the Patient will remit payment to NWL For amounts the Patient receives from the insurer, the Patient has agreed to remit payment to NWL for services rendered. I acknowledge that I offered pre-test genetic counseling to the Patient, if required by their insurer. I attest that I am authorized under applicable law to order this test.

ORDERING PHYSICIAN SIGNATURE*	DATE: (MM/DD/YYYY)

Patient Name: _____, Patient ID Number: _____
Notifier: North West Labs

Advance Beneficiary Notice of Non-Coverage (ABN) — All Insurance Providers

Notice to Patients: Your health insurance plan, whether Medicare or a commercial provider, may not cover all tests or services — including those that you and your healthcare provider consider medically necessary. This notice informs you that one or more of the following North West Labs tests may not be covered, and you may be financially responsible.

Tests That May Not Be Covered:

Test Category	Examples	Reason for non-coverage	Estimated Cost
PharmacoCheck+	Pharmacogenetic testing	Not deemed medically necessary for your diagnosis	Up to $295
Germline Custom Panels	ImmunoCheck+, CancerCheck+ NeuroCheck+, MetabolicCheck+ ThyroidCheck+, etc.…	Insurance exclusions, medical necessity, etc.	Up to $295

What You Need to Do:

1. Review this notice carefully to make an informed decision.
2. Ask any questions you may have before proceeding.
3. Select one of the options below to indicate your decision.

Note: If you select Option 1 or 2, we may attempt to coordinate with other insurance carriers you have. However, we are not required to do so by Medicare or other insurers.

Patient Options: (Please select only one option)

☐ Option 1: I want to receive the North West Labs Test(s) listed above. I understand that my insurance provider may not cover these services. I would like a claim submitted to my insurer for an official coverage decision. If denied, I agree to be responsible for payment. I understand that I may appeal the denial in accordance with my insurer's policies.

☐ Option 2: I want to receive the North West Labs Test(s) listed above. I do not want a claim submitted to my insurer. I agree to pay out of pocket and understand that I waive my right to an appeal through my insurance plan.

☐ Option 3: I do not want to receive the North West Labs Test(s) listed above. I understand that I will not be billed for the service and cannot appeal a non-coverage decision.

Additional Information:

-If you choose Option 1, North West Labs will attempt to contact you to discuss your eligibility for financial assistance and may provide you with the option to cancel your order before testing begins. If you have questions about your financial responsibility or coverage, please contact us at ***(248) 301-6917.***

-This form serves as a courtesy and does not represent an official decision by your insurance provider. If you have questions about your insurance policy or billing, contact your provider directly.

-For Medicare-specific questions, call ***1-800-MEDICARE*** (1-800-633-4227 / TTY: 1-877-486-2048).

Patient Acknowledgment:

By signing below, you confirm that you have received, reviewed, and understood this notice. You will also be provided with a copy for your records.

Signature of Patient or Authorized Representative: _____. Date: _____/_____/_____.

NORTH WEST LABS

NORTH WEST LABS, INC.
Laboratory Director: Eugene Olsowka, M.D. CLIA ID:23D2126347
29580 Northwestern Hwy. Southfield, MI 48034
Phone: (248) 301-6917
www.nwlabs.com

Comprehensive Neurology Panel

Patient	Specimen	Order
Patient Name:	**Accession ID:**	**Physician:**
Date of Birth:	**Collection date:** 01/20/2026	**Report Date:** April 4, 2026
Age:	**Received Date:** 03/03/2026	
Sex:	**Specimen type:** Buccal Swab	

POSITIVE RESULT

Carrier pathogenic variant detected

VARIANTS RELEVANT TO THE TEST INDICATION

Gene & transcript	Variant	Genotype	Disease	Inheritance	Evaluation
BCS1L *NM_001079866.2*	c.232A>G p.(Ser78Gly)	Heterozygous	GRACILE syndrome	AR	Pathogenic

AR : Autosomal recessive inheritance

RECOMMENDATIONS

1. This individual is heterozygous for a pathogenic variant in the *BCS1L* gene. As this gene is associated with an autosomal recessive disorder and no second variant was identified, this finding does not establish a molecular diagnosis.
2. Absence of clinically significant variants in genes analyzed does not rule out a genetic basis for the individual's clinical presentation and it is advisable to correlate these findings with the clinical presentation.
3. After receiving a positive result, genetic counseling and testing of at risk family members is recommended.

DETAILED VARIANT INFORMATION

BCS1L - c.232A>G Pathogenic

Interpretation

Variant Description
This variant is present in population databases (gnomAD 0.4%). Computational algorithms predict a deleterious effect for this variant (REVEL Score: 0.954) (PP3_Moderate). This variant has been identified in the homozygous and compound state in multiple individuals with BCS1L-related conditions and is commonly reported in individuals of Finnish ancestry (Visapää I , 2002 Oct) , (Hikmat O , 2021 Nov) , (Fellman V , 2008) (PM3). Functional studies have shown that this variant alters BCS1L protein function (Visapää I , 2002 Oct) , (Levéen P , 2011 Feb) , (Purhonen J , 2023) (PS3). Based on the available evidence, this variant is classified as Likely Pathogenic.

Gene Description
The BCS1L gene provides instructions for making a protein that is essential for the assembly of complex III in the mitochondrial respiratory chain, which is critical for cellular energy production. Biallelic pathogenic variants in BCS1L are associated with autosomal recessive Bjornstad syndrome (OMIM:262000), Gracile syndrome (OMIM:603358), and mitochondrial complex iii deficiency, nuclear type 1 (OMIM:124000). These conditions are characterized by mental retardation (Lubianca Neto JF , 1998 May) , hypotonia and seizures (Visapää I , 2002 Oct) , and delayed psychomotor development, mental retardation, mitochondrial encephalopathy, hyperreflexia, spasticity, motor dysfunction, seizures, abnormal EEG, cerebral atrophy, cerebellar atrophy, and white matter lesions (de Lonlay P , 2001 Sep) , respectively.

METHODOLOGY

The Comprehensive Neurology Panel is designed to detect single nucleotide variants (SNVs) and small insertions and deletions in 204 genes associated with neurological disorder risk. Targeted regions for this panel include the coding exons and 10 bp intronic sequences immediate to the exon-intron boundary of each coding exon in each of these genes. This report includes evaluation of two single nucleotide polymorphisms (SNPs) in the APOE gene, rs429358 and rs7412, that define the E4 allele associated with increased risk of Alzheimer's disease. Extracted patient DNA is prepared using the Illumina Trusight One Expanded Panel, assigned a unique index, and subjected to sequencing via Illumina sequencing by synthesis (SBS) technology. The SeqOne GermlineVar v2.2 is used to align data to human genome build GRCh38 and make variant calls. Variant annotation and interpretation are performed in the SeqOne platform by qualified variant scientists according to current American College of Medical Genetics and Genomics (ACMG) professional guidelines for the interpretation of germline sequence variants. Variant classification categories include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. Only the variants classified as pathogenic, likely pathogenic, or VUS are reported. The results for each patient are reviewed by an individual who meets Laboratory Director qualifications as stated by CLIA certification and College of American Pathologists (CAP) accreditation requirements. Reportable variants requiring confirmatory testing were reported after confirmatory testing was performed via orthogonal methods.

QUALITY METRICS

Sample name	% of aligned reads	Coverage at 10X	Coverage at 30X	Coverage at 50X	Average coverage	Ti/Tv ratio
PCHSCgx26-00008	99.8%	99.2%	98.9%	98.5%	296.27x	2.71

LIMITATIONS

This test aims to detect all clinically relevant variants within the coding regions of the genes evaluated. Homopolymer regions and regions outside of the coding regions cannot be captured by the standard NGS target enrichment protocols. The assay does not detect large deletions and duplications. This analysis also cannot detect pathogenic variants within regions which were not

analyzed (e.g., introns, promoter and enhancer regions, long repeat regions, and mitochondrial sequence). This assay is not designed to detect mosaicism and is not designed to detect complex gene rearrangements or genomic aneuploidy events. It is important to understand that there may be variants in these genes undetectable using current technology. Additionally, there may be genes associated with neurological pathology whose clinical association has not yet been definitively established. The test may therefore not detect all variants associated with neurological pathology. The interpretation of variants is based on our current understanding of the genes in this panel and is based on current ACMG professional guidelines for the interpretation of germline sequence variants. Interpretations may change over time as more information about the genes in this panel becomes available. Qualified health care providers should be aware that future reclassifications of genetic variants can occur as ACMG guidelines are updated. Factors influencing the quantity and quality of extracted DNA include, but are not limited to, collection technique, the amount of buccal epithelial cells obtained, the patient's oral hygiene, and the presence of dietary or microbial sources of nucleic acids and nucleases, as well as other interfering substances and matrix-dependent influences. PCR inhibitors, extraneous DNA, and nucleic acid degrading enzymes may adversely affect assay results.

EVALUATED GENES

ABCA7, ALS2, APOE, APP, ARSA, ATM, ATP13A2, ATP1A3, ATP6AP2, ATP7B, ATXN2, C19orf12, C9orf72, CHCHD10, CHCHD2, CHMP2B, COMT, CSF1R, DCTN1, DNAJC13, DNAJC6, DNMT1, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, EIF4G1, ERBB4, FBXO7, FTL, FUS, GALC, GBA, GCH1, GIGYF2, GNAL, GRN, HEXA, HNRNPA1, HNRNPA2B1, HTRA2, ITM2B, LMNB1, LRRK2, MAPT, MATR3, NOTCH3, NPC1, NPC2, OPA1, OPTN, PARK2, PARK7, PDGFB, PDGFRB, PINK1, PLA2G6, PLCG2, PLP1, POLG, PRKRA, PRNP, PSEN1, PSEN2, RAB29, RAB39B, ROGDI, SETX, SIGMAR1, SLC20A2, SLC25A12, SLC30A10, SLC39A14, SLC6A3, SNCA, SNCB, SOD1, SORL1, SPG11, SPR, SQSTM1, SYNJ1, TAF1, TARDBP, TBK1, TBP, TH, TMEM230, TREM2, TTC3, TUBA4A, TYROBP, UBQLN2, UCHL1, VCP, VPS13C, VPS35

REGULATORY DISCLOSURES

This laboratory developed test (LDT) was developed and its performance characteristics were determined by North West Labs, Inc. This test was performed at North West Labs, Inc. (CLIA ID: 23D2126347) that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This assay has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Clearance or approval by the FDA is not required for clinical purposes, and use of this analytically and clinically validated laboratory developed test.

TEST RESULTS REVIEWED AND APPROVED BY

Name: Jessica Moye PhD, HCLD- ABB, MB-ASCP CM, CGMBS

Date: April 5, 2026

This report has been reviewed and approved by the above named individual.

NORTH WEST LABS

Whole Exome Sequencing (WES)

NORTH WEST
LABS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Hereditary Cancer Genetics (CGX)

Next Gen Sequencing

Myeloid NGS

North West Labs
(248) 301-6917 | support@nwlabs.com
29580 Northwestern Hwy, Ste 120 | Southfield, MI 48034
www.nwlabs.com

Whole Exome Sequencing (WES)

NORTH WEST LABS

WES Testing — Is It Right for Your Child?

Every child with ASD is different. WES helps explain why.

WHO SHOULD CONSIDER WES?

WES may be worth discussing with your doctor if your child has Autism Spectrum Disorder (ASD) or unexplained developmental concerns, especially when additional features are present, such as:

- Intellectual disability or developmental delay
- Seizures or epilepsy
- Congenital anomalies or differences in physical features
- Complex or unclear clinical presentation

These factors can increase the likelihood of identifying a genetic cause.

WHAT CAN WES TELL YOU?

WES may help your family:

- Understand a potential genetic cause behind your child's diagnosis
- Reduce the need for additional specialist visits and repeat testing
- Inform decisions about early intervention and therapy planning
- Provide information relevant to other family members

HOW CAN IT HELP YOUR FAMILY?

Find real answers: WES can identify a genetic cause in up to 30–40% of children with ASD. Testing identifies a cause in up to 1 in 4 children with autism.

Plan more effectively: Genetic findings can guide personalized medical management and early intervention therapies.

Support the whole family: Understanding the genetic basis of ASD can inform family planning and provide valuable information for relatives.

Save time and reduce stress: A clearer diagnosis sooner can reduce unnecessary specialist visits and additional testing.

Diagnostic yield may vary. Based on published literature for WES in children with ASD and complex phenotypes.
(1) Cell. 2020;180(3):568-584 (2) Álvarez-Mora MI, et al. Orphanet J Rare Dis. 2022;17(1):61

HOW DOES THE PROCESS WORK?

1 — Information & Support
Speak with your healthcare provider to discuss whether WES is right for your child.

2 — Saliva Sample Collection
Your physician collects a saliva sample. No blood draw required.

3 — Laboratory Analysis
Your sample undergoes rigorous WES analysis at our state-of-the-art facility.

4 — Results & Next Steps
Receive a detailed report and review findings with your doctor and a genetic counselor.

North West Labs
Full-service clinical laboratory specializing in molecular diagnostics & WES testing.

Contact Us
(248) 301-6917
29580 Northwestern Hwy.
Southfield, MI 48034
support@nwlabs.com
www.nwlabs.com

Scan to Contact Us

NORTH WEST LABS

Could Your Child's DNA Hold the Answers?

For families navigating an Autism Spectrum Disorder diagnosis, real answers matter.

WES Testing by North West Labs

25+	Non-invasive	Covered
Published studies confirm WES across every population	Simple saliva sample — no blood draw required	By Medicaid & commercial payers

WHAT IS WES?

Whole Exome Sequencing (WES) is the most powerful single genetic test available for Autism Spectrum Disorder (ASD). It is evidence-based, covered by insurance plans (including Medicaid), and directly actionable. Over 25 published case studies and cohorts confirm its value across every population.

Using a simple, non-invasive saliva sample, WES provides a comprehensive view of your child's genetic makeup and helps identify potential genetic variations associated with Autism Spectrum Disorders.

WHAT TO KNOW BEFORE TESTING

Insurance Coverage

- WES is a genetic test considered for patients with Autism Spectrum Disorder (ASD).
- Prior-Authorization is easy and seamless — our dedicated team of experts guides you throughout the process.
- Medicaid & Commercial payers have approved this test for all patients with ASD with 1 or more abnormalities.
- Our team helps families understand how WES can be a life-altering genetic test — identifying specific genes that can alter the plan of care and lead to better, more viable outcomes for the future.

Ask your doctor or therapist if WES testing is right for your child.

WES is covered by insurance — including Medicaid.

North West Labs is a local lab option that performs WES testing by partnering with your physician.

North West Labs
Full-service clinical laboratory specializing in molecular diagnostics & WES testing.

Contact Us
(248) 301-6917
support@nwlabs.com
29580 Northwestern Hwy, Ste 120
Southfield, MI 48034
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Version 1.3

NORTH WEST LABS

Transform ABA Outcomes with Whole Exome Sequencing (WES)

Stop Guessing. Start Delivering Precision Care.

What is WES?

Whole Exome Sequencing identifies genetic drivers behind a child's condition — giving real answers, not assumptions.

Why ABA Providers Are Adopting WES

- Faster measurable progress
- Smarter, individualized ABA programs
- Higher-value cases & stronger clinical justification
- Eliminate trial & error
- Build trust with families

Proven Diagnostic Power

25% **diagnostic yield in complex cases,** giving you clarity where others fail.

Competitive Advantage Starts Here

Deliver data-driven, precision ABA care while others rely on outdated methods.

Let's Partner

- Genetic testing coordination
- Clinical integration guidance
- Ongoing support for your team

Partner with North West Labs — Precision Starts Here

Contact Us

North West Labs
(248) 301-6917
29580 Northwestern Hwy, Southfield, MI 48034
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NORTH WEST LABS

WES-Guided ABA Treatment
Pathway Overview

GENE PATHWAY	EXAMPLE GENES	CLINICAL PATTERN	ABA TREATMENT STRATEGY
Synaptic Function	SHANK3, NRXN1, SYNGAP1	Slow learning, weak generalization, attention delays	High repetition, micro-step teaching, strong reinforcement, generalization training
Chromatin / Epigenetic	CHD8, ARID1B, ADNP, KMT2A/C/D	Global developmental delay, uneven cognitive profile	Structured DTT, slower pacing, focus on adaptive skills, caregiver training
Ion Channel / Epilepsy	SCN1A, SCN2A, KCNQ2, CACNA1A	Seizures, fatigue, attention fluctuation	Neurology coordination, shorter sessions, frequent breaks, low overstimulation
Language Pathways	CNTNAP2, FOXP1, FOXP2, SATB2	Severe speech delay, limited expressive language	AAC early, Functional Communication Training (FCT), manding first, NET approach
Neurodevelopmental Syndromes	MECP2, CDKL5, TCF4, FOXG1	Severe ID, possible regression, low imitation	Highly structured ABA, adaptive skills focus, very slow progression, sensory reinforcement
Executive Function	DYRK1A, PTEN, KMT2A	Slow processing, poor working memory, multi-step difficulty	One-step instructions, errorless learning, heavy prompting, visual supports
Behavior Regulation	CHD8, SCN2A, CNTNAP2	Rigidity, irritability, sensory sensitivity	FBA-based ABA, antecedent strategies, reinforcement of calm behavior, sensory supports
Copy Number Variants (CNVs)	16p11.2, 22q11.2 del/dup	Variable ASD severity, mixed cognitive profile	Highly individualized ABA, frequent reassessment, strong parent training, multidisciplinary care

KEY CLINICAL INTERPRETATION NOTES

- WES does not predict ABA success or failure
- ABA is effective across all genetic profiles
- Genetics helps determine:
  - Learning speed
  - Session structure
  - Communication pathway
  - Support intensity

MOST IMPORTANT PREDICTORS OF ABA OUTCOME

- Language ability (expressive + receptive)
- Adaptive functioning (daily living skills)
- Medical stability (sleep, seizures, neurological health)

About North West Labs:
Full-service clinical laboratory specializing in molecular diagnostics and pathology services. Delivering actionable results with fast turnaround times and direct clinical support.

Contact us:
29580 Northwestern Hwy, Suite 120
Southfield, MI 48034
Phone: 248-301-6917
Fax: 248-301-6805
www.nwlabs.com

NORTH WEST LABS

| Whole Exome Sequencing (WES) | Requisition Form

GGID #: Sxp2WSW76ji6vr59

1. PATIENT INFORMATION *

Last Name: Test355 MI: First Name: Test12 Suffix:

Date of Birth: 08/01/2014 Gender: ○ Female ● Male

Email: smarinovsky@gmail.com Phone: (248) 301-6917

Street Address: 29580 Northwestern Hwy

City: Southfield State: MI Zip: 48034

Race/Ethnicity:

- ○ African American/Black
- ● Ashkenazi Jewish
- ○ White (Non-Hispanic)
- ○ Caucasian
- ○ French Canadian
- ○ Hispanic/Latin American
- ○ East Asian
- ○ South Asian
- ○ Southeast Asian
- ○ Mediterranean
- ○ Middle Eastern
- ○ Native American
- ○ Native Hawaiian or other Pacific Islander
- ○ Adopted
- ○ Other_____

2. ORDERING PHYSICIAN *

Name: Eugene Stanley Olsowka, M.D. NPI #: 1407943871

Facility Name: North West Labs

Street Address: 29580 Northwestern Hwy Suite 120

City: Southfield State: MI Zip: 48034

Phone: (248) 301-6917 Fax: (248) 301-6917

3. TEST REQUESTED *

- ○ **Xenome Proband Whole Exome Sequencing**
- ○ **Xenome Duo Whole Exome Sequencing** *Mother OR Father Required for Duo*
- ● **Xenome Trio Whole Exome Sequencing** *Mother AND Father BOTH Required for Trio*

4. Addon Tests *

- ☐ FMR1
- ☐ mtDNA Analysis

5. Personal Symptoms *

Symptom
Congenital malformation syndromes
Failure to thrive
Anxiety
Autistic behavior
Age of Initial Symptoms Onset: 6

6. Personal Conditions *

Condition
Fatigue
Age of Initial Conditions Onset: 5

7. Family Conditions *

Family Member	Condition
Mother	Autism Spectrum Disorder,Family History of Autism Spectrum Disorder

8. Family Member Samples to be Included in Testing *

Family Member	First Name	Last Name	DOB	Symptoms
Biological Mother	Bill	Gates	2026-04-13	○ Asymptomatic ● Symptomatic
Biological Father	Af	Afaf	2026-04-13	● Asymptomatic ○ Symptomatic
Other Affected Sibling/Family Member				○ Asymptomatic ○ Symptomatic

9. Previous Genetic Testing *

Personal or Family History of Genetic Testing: ○ No ● Yes (If yes, please complete the field below)

Relation to patient (self, sibling, etc...), Genetic Test(s) and result (e.g. positive or negative, etc...)
Please attach copy of test result(s)

Proband: negative nana

Mother: afaf

10. STATEMENT OF MEDICAL NECESSITY *

TEST REQUESTS WITHOUT A SIGNATURE WILL NOT BE PROCESSED
I affirm that I am authorized under applicable federal and state laws to order genetic testing and have determined that the requested test(s) are medically necessary based on the patient's clinical presentation, personal and/or family history, or differential diagnosis. I certify that all diagnosis codes have been provided to the best of my clinical knowledge and that I have obtained and documented written informed consent from the patient or their legally authorized representative. This consent includes a clear explanation of the purpose, scope, risks, benefits, limitations, and potential outcomes of the testing, as well as the implications for the patient and their family. The patient has also consented to the release of results to a third-party genetic counselor for interpretation, counseling, and insurance-related purposes. I accept responsibility for interpreting and communicating the results to the patient, ensuring appropriate follow-up care, and retaining all related documentation, including the signed informed consent, in the patient's medical record. I confirm that the information submitted on this requisition form is accurate and complete to the best of my knowledge.

Ordering Physician Signature	Test Ordered Date	Specimen Collected Date
	04/13/2026	04/13/2026

11. ICD-10 CODES *

Patient Selected ICD10: **F41.9 F84.9 R62.50 Q87.9 R53.83**

12. SAMPLE REQUIREMENTS *

● **Mouthwash Sample** OR ○ **Buccal Swab**

13. ITEM CHECKLIST *

- ☐ Proband Sample (Required)
- ☐ Maternal Sample (Required For Duo or Trio WES)
- ☐ Paternal Sample (Required For Duo or Trio WES)
- ☐ Signed Requisition
- ☐ Signed Consent Form
- ☐ Indication For Testing
- ☐ Clinical Note/Summary
- ☐ Patient Medical Records

NORTH WEST LABS

| Whole Exome Sequencing (WES) | Requisition Form

GGID #: Sxp2WSW76ji6vr59

Patient First Name: Test12 Patient Last Name: Test355 Patient MI: ___ Patient DOB: 2014-08-01 Patient Gender: Male

INDICATION FOR TESTING *

Please provide the following clinical information regarding the patient to be tested. Please also submit a clinic note and pedigree, if available. This information is needed to facilitate interpretation of whole exome sequencing results. If the labratory requires additional information, please indicate the health care provider to be contacted.

Pre/Perinatal History

- ☐ Q18.8 Cystic hygroma
- ☐ Q79.0 Congenital diaphragmatic hernia
- ☐ Q01.9 Encephalocele, unspecified
- ☐ Q00.8 Other specified malformations of the central nervous system
- ☐ P05.9 Intrauterine growth restriction
- ☐ P83.9 Nonimmune hydrops fetalis
- ☐ O41.0 Oligohydramnios
- ☐ Q79.2 Omphalocele
- ☐ O41.1 Polyhydramnios
- ☐ P07.30 Premature newborn, gestational age 30-31 weeks
- ☐ P59.9 Neonatal jaundice, unspecified

Structural Brain Abnormalities

- ☐ Q04.3 Cerebellar atrophy, congenital
- ☐ Q04.4 Cerebellar agenesis/hypoplasia
- ☐ Q07.9 Chiari malformation
- ☐ Q06.0 Cerebellar atrophy
- ☐ Q04.9 Abnormalities of cerebral white matter
- ☐ Q05.9 Holoprosencephaly, unspecified
- ☐ G91.9 Hydrocephalus, unspecified
- ☐ E75.9 Leukodystrophy
- ☐ Q04.9 Lissencephaly
- ☐ Q04.9 Pachygyria
- ☐ Q04.9 Polymicrogyria
- ☐ Q04.5 Ventriculomegaly

Endocrine

- ☐ E23.2 Diabetes insipidus
- ☐ E11.9 Type 2 diabetes mellitus, unspecified
- ☐ E05.9 Hyperthyroidism, unspecified
- ☐ E83.30 Hypophosphatemia
- ☐ E03.9 Hypothyroidism, unspecified
- ☐ E16.2 Maturity-onset diabetes of the young
- ☐ E55.9 Rickets, unspecified

Eye Defects/Vision

- ☐ Q11.1 Anophthalmia
- ☐ H25.9 Cataract, unspecified
- ☐ Q11.0 Coloboma of eye
- ☐ H11.9 Corneal opacity
- ☐ H27.9 Lens dislocation
- ☐ H50.8 Other ophthalmoplegia
- ☐ Q11.9 Microphthalmia
- ☐ H52.1 Myopia
- ☐ H55.9 Nystagmus
- ☐ H47.1 Optic atrophy
- ☐ H47.9 Optic neuropathy
- ☐ H02.8 Ptosis (drooping eyelid)
- ☐ H33.0 Retinal detachment
- ☐ H35.5 Retinitis pigmentosa
- ☐ H50.9 Strabismus

Neurological

- ☐ R47.1 Dysarthria (difficulty articulating speech)
- ☐ R26.9 Gait abnormality, unspecified
- ☐ F83 Global developmental delay
- ☐ R27.8 Other lack of coordination
- ☐ F81 Specific developmental disorder of scholastic skills
- ☐ R41.3 Memory loss
- ☐ G47.9 Sleep disorder, unspecified
- ☐ R48.8 Other speech disturbances
- ☐ F84.0 Autistic disorder
- ☐ G40.909 Epilepsy, unspecified, not intractable

Hearing Impairment

- ☐ H90.3 Sensorineural hearing loss, bilateral
- ☐ H90.0 Conductive hearing loss, bilateral
- ☐ H91.9 Unspecified hearing loss
- ☐ H66.9 Otitis media, unspecified
- ☐ H72.9 Perforation of tympanic membrane, unspecified

Family History

- ☐ Z84.89 Family history of other specified conditions
- ☒ **Z81.8 Family history of other mental and behavioral disorders**
- ☐ Z84.9 Family history of other conditions, unspecified

Skin/Hair

- ☐ L63.9 Alopecia areata, unspecified
- ☐ R23.3 Anhidrosis
- ☐ L81.0 Café-au-lait spots
- ☐ Q82.1 Cutis laxa
- ☐ L30.9 Eczema, unspecified
- ☐ D18.9 Hemangioma, unspecified
- ☐ L94.9 Connective tissue disease, unspecified
- ☐ L81.9 Other disorders of pigmentation
- ☐ R23.2 Hypohidrosis
- ☐ L81.9 Other disorders of pigmentation
- ☐ Q80.9 Ichthyosis, unspecified
- ☐ R21 Rash and other nonspecific skin eruption
- ☐ L64.9 Hair loss, unspecified
- ☐ I78.0 Hereditary hemorrhagic telangiectasia
- ☐ L98.9 Disorder of the skin, unspecified
- ☐ Q82.2 Velvety skin syndrome

Craniofacial/Dysmorphism

- ☐ Q75.2 Brachycephaly
- ☐ Q35.9 Cleft lip and palate, unspecified
- ☐ Q75.9 Coarse facial features
- ☐ Q75.3 Craniosynostosis
- ☐ Q75.0 Macrocephaly
- ☐ Q75.1 Microcephaly
- ☐ Q74.9 Short neck syndrome
- ☐ Q75.8 Synophrys (unibrow)

Respiratory

- ☐ J45.9 Asthma, unspecified
- ☐ J47.9 Bronchiectasis, unspecified
- ☐ R06.0 Hyperventilation
- ☐ R06.8 Other abnormal respiratory pattern
- ☐ J93.9 Pneumothorax, unspecified
- ☐ J84.10 Pulmonary fibrosis, unspecified
- ☐ J96.90 Respiratory failure, unspecified

Cancer

- ☐ C80.9 Malignant neoplasm, unspecified
- ☐ C79.9 Secondary malignant neoplasm, unspecified
- ☐ Z00.9 Encounter for general examination, unspecified

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NORTH WEST LABS

| Whole Exome Sequencing (WES) | Requisition Form

GGID #: Sxp2WSW76ji6vr59

Patient First Name: Test12 Patient Last Name: Test355 Patient MI: ___ Patient DOB: 2014-08-01 Patient Gender: Male

INDICATION FOR TESTING - CONTINUED

Musculoskeletal

- ☐ Q87.2 Arachnodactyly (abnormally long fingers and toes)
- ☐ M00.9 Arthralgia, unspecified
- ☐ Q74.0 Arthrogryposis (joint contractures)
- ☐ D69.59 Other thrombocytopenia with bleeding (increased bruising)
- ☐ Q87.3 Clinodactyly (curved fingers or toes)
- ☐ M62.8 Other generalized muscle weakness
- ☐ Q87.3 Ectrodactyly (abnormality of the hands or feet)
- ☐ R53.1 Weakness, unspecified
- ☒ **R53.83 Other fatigue**
- ☐ Q83.9 Hemihypertrophy (abnormal body part growth)
- ☐ G25.0 Hypertonia (muscle stiffness and spasm)
- ☐ G72.9 Hypotonia (low muscle tone)
- ☐ M35.7 Hypermobility of joints
- ☐ M62.81 Muscle weakness, generalized
- ☐ M79.1 Myalgia (muscle pain)
- ☐ Q87.9 Myopathic facies (distinctive facial features)
- ☐ G72.9 Myopathy, unspecified
- ☐ M19.9 Osteoarthritis, unspecified
- ☐ M85.9 Osteopenia (low bone density)
- ☐ R52.9 Pain, unspecified
- ☐ Q67.2 Pectus carinatum (protrusion of the chest)
- ☐ Q67.1 Pectus excavatum (sunken chest)
- ☐ Q87.0 Polydactyly (extra fingers or toes)
- ☐ M80.9 Osteoporosis with fractures, unspecified
- ☐ M62.82 Rhabdomyolysis (muscle breakdown)
- ☐ M41.9 Scoliosis, unspecified
- ☐ R62.52 Short stature (below the 3rd percentile for height)
- ☐ Q78.9 Skeletal dysplasia, unspecified
- ☐ Q87.1 Syndactyly (fusion of fingers or toes)
- ☐ R62.51 Tall stature (above the 97th percentile for height)

Genitourinary

- ☐ Q56.9 Ambiguous genitalia, unspecified
- ☐ Q53.9 Cryptorchidism, unspecified
- ☐ Q62.9 Renal dysplasia, unspecified
- ☐ Q63.0 Horseshoe kidney
- ☐ N13.9 Hydronephrosis, unspecified
- ☐ Q54.9 Hypospadias, unspecified
- ☐ K40.9 Inguinal hernia, unspecified
- ☐ Q55.9 Micropenis, unspecified
- ☐ N20.9 Nephrolithiasis, unspecified
- ☐ Q61.9 Polycystic kidney disease, unspecified

Vascular System

- ☐ I71.9 Aneurysm, unspecified
- ☐ I70.9 Atherosclerosis, unspecified
- ☐ I71.3 Aortic dissection
- ☐ Q87.8 Other congenital malformations of the circulatory system
- ☐ Q27.9 Arteriovenous malformation, unspecified
- ☐ R04.0 Epistaxis (nosebleed)
- ☐ I89.0 Lymphedema (swelling due to lymphatic fluid accumulation)
- ☐ I27.0 Pulmonary hypertension
- ☐ I63.9 Cerebral infarction, unspecified

Hematologic or Immunologic

- ☐ D64.9 Anemia, unspecified
- ☐ D84.9 Immunodeficiency, unspecified
- ☐ D70.9 Neutropenia, unspecified
- ☐ D61.9 Pancytopenia, unspecified
- ☐ A41.9 Sepsis, unspecified
- ☐ D69.9 Thrombocytopenia, unspecified

Gastrointestinal

- ☐ K59.0 Constipation, unspecified
- ☐ R19.7 Diarrhea, unspecified
- ☐ Q41.9 Duodenal atresia, unspecified
- ☐ K86.9 Pancreatic insufficiency, unspecified
- ☐ K21.9 Gastro-esophageal reflux disease, unspecified
- ☐ R16.0 Hepatomegaly (enlarged liver)
- ☐ K50.9 Inflammatory bowel disease, unspecified
- ☐ Q44.6 Intrahepatic biliary atresia
- ☐ Q38.0 Laryngomalacia
- ☐ R11.0 Nausea (feeling of sickness)
- ☐ K85.9 Acute pancreatitis, unspecified
- ☐ Q40.0 Pyloric stenosis
- ☐ R16.1 Splenomegaly (enlarged spleen)
- ☐ Q39.0 Congenital tracheoesophageal fistula
- ☐ R11.10 Vomiting, unspecified

Other Testing/Imaging

- ☐ Z13.6 Encounter for screening for cardiovascular disorders
- ☐ Z13.89 Encounter for screening for neurological disorders
- ☐ Z13.89 Encounter for screening for neurological disorders
- ☐ Z13.89 Encounter for screening for neurological disorders
- ☐ Z13.89 Encounter for screening for neurological disorders
- ☐ Z13.89 Encounter for screening for other diagnostic tests
- ☐ Z13.89 Encounter for screening for diagnostic tests

GENES OF INTEREST:

_____

_____

_____

Additional Clincal Information

Differential Diagnosis

29580 Northwestern Hwy Suite 120 ♦ Southfield, MI ♦ ☎ 2483016917 ♦ FAX 2483016917 ♦ ✉ ♦

NORTH WEST LABS

| Whole Exome Sequencing (WES) | Consent Form

GGID #: Sxp2WSW76ji6vr59

Patient First Name: Test12 Patient Last Name: Test355 Patient MI: ___ Patient DOB: 2014-08-01 Patient Gender: Male

Introduction

This consent form is intended to inform you about Whole Exome Sequencing (WES), a complex genetic test that analyzes the parts of your DNA responsible for producing proteins. It is important that you review this document with your healthcare provider or a certified genetic counselor to understand the scope and implications of this testing.

WES can be performed on you or your child and may identify genetic changes (variants) that cause or increase the risk for disease. The exome, which includes only about 1-2% of the genome, contains the majority of disease-related genetic changes. This test evaluates thousands of genes simultaneously. Variants identified may or may not affect medical care or health outcomes, and some may have implications beyond the current reason for testing. Any results should be discussed in detail with your healthcare provider.

Test Results

- Possible outcomes of the test include:
- Positive: A DNA change (variant) was detected that is known or likely to be associated with disease. This may confirm a diagnosis or indicate increased risk.
- Negative: No disease-causing variants were found in the genes tested. However, this does not eliminate all genetic risk, as not all variants can be detected.
- Variant of Uncertain Significance (VUS): A change was detected, but its role in disease is currently unknown. Additional testing of you or family members may be recommended.
- Secondary/Incidental Findings: Sometimes, testing reveals unrelated but medically important variants. You may choose whether to receive this information.

Reporting of Incidental Findings

Genetic testing can sometimes reveal medically actionable variants—changes in specific genes that are known to be associated with serious health conditions, even if they are not related to the reason for testing or to your (or your child's) current symptoms or clinical presentation.

The reporting of these findings follows the recommendations of the American College of Medical Genetics and Genomics (ACMG). According to the ACMG policy statement (PMID: 25356965) and its updates (PMID: 34012068), laboratories are advised to report pathogenic and likely pathogenic variants found in a curated list of genes considered medically actionable. These recommendations are updated periodically.
These findings may have important implications for early intervention, treatment, prognosis, or risk reduction, and are reported only if you and your healthcare provider choose to opt-in

● I consent to receive secondary findings as defined by ACMG.
○ I do not wish to receive secondary findings.

If you choose to receive updated reports in the future as new data becomes available:
○ I wish to receive updates to my WES report if new clinical interpretations are available.
● I do not wish to receive updates.

Additional Reporting Information

Your results will not include findings related to adult-onset neurological diseases unless specifically requested. If such findings are relevant, please indicate them on the test requisition.

● I consent to receive findings related to adult-onset neurolocical diseases
○ I DO NOT consent to receive findings related to adult-onset neurolocical diseases

Parental samples may assist in interpreting your WES results. If you're undergoing individual (proband-only) testing, your parents' samples may later be tested separately or together for a fee. In trio or duo WES, your sample and one or both biological parents' samples are analyzed simultaneously. Each parent will receive a separate report if secondary findings are identified. Testing for additional relatives may be available.
Additional testing methods (beyond WES) may be ordered to evaluate areas WES does not cover. Results from such tests will be provided in separate reports.

Cancellation Policy

If you wish to cancel testing, contact your provider and North West Labs and its referral labs before 5 PM Eastern Time on the next business day after the lab receives your sample. After that your insurance may be charged the full cost of the test.

Patient Confidentiality

Results will only be released to the ordering provider, individuals authorized by you, or as required by law. You may request your results in writing. Only North West Labs and its referral labs and its contracted labs will have access to your sample for testing purposes.

Genetic testing may have implications for insurance or employment. Federal protections, including the Genetic Information Nondiscrimination Act (GINA), prohibit health insurance and employment discrimination based on genetic information. Learn more at: www.genome.gov/10002077.

Sample Retention and Data Use

Samples are retained according to laboratory policy. De-identified data may be used for research, test validation, or quality control unless you opt out:

● I do not consent to the use of my de-identified data or sample for these purposes.

If you authorize retention:
● I consent to sample retention for internal validation or research use.
○ I do not consent to extended sample retention.

NORTH WEST LABS

| Whole Exome Sequencing (WES) | Consent Form

GGID #: Sxp2WSW76ji6vr59

Patient First Name: Test12 Patient Last Name: Test355 Patient MI: ___ Patient DOB: 2014-08-01 Patient Gender: Male

New York State Samples

I understand that no genetic tests will be performed on my biological sample other than those specifically authorized by me. I also acknowledge that my sample will be destroyed upon completion of testing, or within 60 days from the date of collection, unless I authorize otherwise.

By initialing below, I provide my consent for the laboratory to retain my sample(s) beyond this period in accordance with its retention policy. Retained samples may be used for internal quality assurance purposes and for potential research studies aimed at improving genetic testing.

Furthermore, by signing this consent form, I understand and agree that de-identified information from my results may be submitted to publicly accessible genetic databases, such as ClinVar. These submissions help advance scientific and medical knowledge. I acknowledge that limited clinical details may be required for such submissions, and while every effort will be made to protect my privacy, there is a minimal risk that the information could potentially be linked back to me or my family members.

Initial Here to Authorize Extended Sample Retention: _____

Research Contact Consent

North West Labs and its referral labs may contact you regarding participation in future research:

● Yes, I agree to be contacted.

○ No, I do not want to be contacted.

If no selection is made, this will default to the NO option

PATIENT REPORTING OPTIONS FOR INCIDENTAL AND SECONDARY FINDINGS AND RELEASE OF UPDATED RESULTS

FOR ALL WES

● YES - Report pathogenic and likely pathogenic variants in medically actionable genes per ACMG guidelines.
○ NO - Do NOT report pathogenic or likely pathogenic variants in medically actionable genes.

○ YES - Issue an updated report to my physician if new clinically significant findings become available.
● NO - Do NOT issue an updated report even if new clinically significant findings become available

FOR WES PERFORMED ON ANOTHER FAMILY MEMBER (NOT PROBAND OR PARENTS)

○ YES - Report medically actionable pathogenic/likely pathogenic variants (ACMG)
● NO - Do NOT report medically actionable variants.

FOR DUO AND TRIO WES ONLY

● YES - Report maternal medically actionable findings (ACMG).
○ NO - Do NOT report maternal medically actionable findings.
● YES - Report paternal medically actionable findings (ACMG).
○ NO - Do NOT report paternal medically actionable findings.

Patient Authorization

By signing this statement of consent, I acknowledge that I have read, understand, and hereby grant my informed consent for genetic testing. I have received appropriate explanations from my healthcare provider about the planned genetic test(s) and possible results. I have been informed about the availability and importance of genetic counseling and provided with contact information for a genetic counselor or medical geneticist.

Financial Agreement and Guarantee

● **BILL PATIENT INSURANCE - requires patient and/or patient parent/guardian signature and enlarged copy of both sides of insurance card(s)**

Insurance Carrier: Priority Health MI
Name of Policy Holder: Test12 Test355
DOB: 2014-08-01
Patient Relationship to Policy Holder: Self
Policy ID:
Group ID:

○ **PATIENT SELF PAY**

By signing this form, I accept financial responsibility for all genetic testing ordered by my healthcare provider. I authorize Advanced Molecular Diagnostics to bill my health insurance and to release necessary information for billing. I assign insurance payments directly to North West Labs and its referral labs and will endorse insurance checks received to them within 30 days. If uninsured, I agree to pay based on the provided good faith estimate. A completed Advance Beneficiary Notice (ABN) is required for Medicare patients where applicable.

NORTH WEST LABS

| Whole Exome Sequencing (WES) | Consent Form

GGID #: Sxp2WSW76ji6vr59

Patient First Name: Test12 Patient Last Name: Test355 Patient MI: Patient DOB: 2014-08-01 Patient Gender: Male

Patient Consent and Signatures

By signing below, I confirm that I understand the benefits, limitations, and potential results of WES. I have had the opportunity to ask questions and have received information about genetic counseling services. I voluntarily consent to proceed with WES testing.

I hereby give permission to North West Labs and its referral labs to conduct genetic testing as recommended by my physician.

Test12 Test355		04/13/2026
Patient Name	Patient's Signature	Date Signed (MM/DD/YYYY)
Bill Gates		04/13/2026
Patient's Parent/Personal Representative Name	Patient's Parent/Personal Representative Signature	Date Signed (MM/DD/YYYY)

Father
Relationship of Personal Representative to the Patient

FOR DUO AND TRIO WES ONLY:

Bill Gates		04/13/2026
Maternal Name	Maternal Signature	Date Signed (MM/DD/YYYY)
Af Afaf		04/13/2026
Paternal Name	Paternal Signature	Date Signed (MM/DD/YYYY)

FOR AFFECTED SIBLING OR OTHER FAMILY MEMBER WES ONLY:

Affected Sibling/Other Family Member Name	Affected Sibling/Other Family Member Signature	Date Signed (MM/DD/YYYY)

Relationship of Affected Sibling/Other Family Member to Patient

Affected Sibling/Other Family Member Parent/Personal Representative Name	Affected Sibling/Other Family Member Parent/Personal Representative Signature	Date Signed (MM/DD/YYYY)

Relationship of Personal Representative to Affected Sibling/ Other Family Member

Letter of Medical Necessity for Trio Whole Exome Sequencing

Patient Information

Date: 2026-04-13
Patient Name: Test12 Test355
Patient DOB: 2014-08-01
Insurance Company Name: Priority Health MI
Policy Number:
Group Number:

ICD10 Codes: F41.9 F84.9 R62.50 Q87.9

Test Name: Xenome (Trio) Whole Exome Sequencing
CPT Codes: 81415, 81416x2
Laboratory: North West Labs
NPI: 1568994879
TAXID: 813538903
CLIA: 23D2126347
29580 Northwestern Highway
Southfield, MI 48034
Telephone: (248) 301-6917
Fax: (248) 301-6785

Purpose of This Letter

This letter supports my request for insurance authorization and full coverage of Whole Exome Sequencing (WES) for my patient , Test12 Test355 , to be performed at North West Labs. Based on the patient's clinical history and extensive prior evaluations, this testing is medically necessary and will provide clinically actionable insights that directly influence diagnosis, medical management, and prognosis.

Clinical History and Medical Justification

The patient presents with a complex clinical phenotype, including but not limited to:

Congenital malformation syndromes	**Failure to thrive**	**Anxiety**	**Autistic behavior**
Fatigue			

Age of initial Sypmtoms Onset: **6**

Age of initial Conditions Onset: **5**

The patient's family history is:
☐ negative for related conditions
☐ unknown
☒ remarkable for the following related clinical features:

Anxiety	**Autistic behavior**	**Autism Spectrum Disorder**	**Family History of Autism Spectrum Disorder**

Previous genetic and metabolic testing have not yielded a diagnosis, including:

negative nana

Despite this extensive diagnostic workup, the etiology remains unknown, and a genetic diagnosis is strongly suspected based on clinical features and early-onset presentation.

Rationale for Whole Exome Sequencing - Trio

WES is the most comprehensive, cost-effective, and efficient method for identifying monogenic conditions associated with the patient's phenotype, particularly when prior targeted tests have failed. A trio approach (proband and both biological parents) maximizes diagnostic yield by:

- Clarifying inheritance patterns (de novo vs inherited)
- Reducing variants of uncertain significance (VUS)
- Improving interpretation confidence and diagnostic specificity

Letter of Medical Necessity for Trio Whole Exome Sequencing

Clinical Evidence and Guidelines for Testing

The American College of Medical Genetics and Genomics (ACMG) recommends exome sequencing for patients with a disorder that has a suspected genetic etiology when the patient's phenotype is not consistent with a specific disorder that has more targeted genetic testing currently available, the testing currently available for the patient's phenotype has failed to arrive at a diagnosis, or the suspected genetic condition is associated with a high degree of genetic heterogeneity.[1]

Overall, the diagnostic yield of exome sequencing has been reported to range from 25-37% for individuals with a broad range of clinical phenotypes, specifically including neurodevelopmental disorders, epilepsy and other neurologic disorders, multiple congenital anomalies, and other suspected monogenic disorders.[2-6] The diagnostic yield is highest when parental samples or other relevant family members are included in the analysis.[2-6]

A recent multidisciplinary consensus statement recommended exome sequencing as a first-tier genetic test for individuals with neurodevelopmental disorders including intellectual disability, global developmental delay, and autism spectrum disorder due to the high diagnostic yield.[2] Multiple studies have found that exome sequencing is more cost effective than traditional testing approaches such as sequential single gene testing, multi-gene panels, serial imaging, biopsies, and other diagnostic approaches, and is most cost-effective when done early in the testing process.[7-12]

Patient Clinical Utility and Medical Management Implications

The test results will guide and tailor appropriate medical management and treatment for this patient, which would not be possible without this testing. Whole Exome Sequencing can lead to direct changes in medical management, including modifications to medications, surgical interventions, surveillance regimens, or preventative measures that may be life-saving, and can eliminate the need for other expensive and often invasive diagnostic procedures.[8-10]

Summary

Given the complexity of this patient's presentation and the failure of prior testing, Whole Exome Sequencing with parental analysis is medically necessary. This testing offers a high probability of achieving a diagnosis that will significantly influence medical management and long-term outcomes. Xenome Whole Exome Sequencing at North West Labs is a highly sensitive and cost-effective genetic test. I am requesting coverage for this medically necessary test in order to establish appropriate medical management for this patient. Without testing, treatment would be suboptimal.

Request for Authorization

I respectfully request coverage and authorization for:

- 81415 - Whole Exome Sequencing, Proband
- 81416 x2 - Parental comparator sequencing (biological mother and father)

Please do not hesitate to contact me with any questions or if additional clinical documentation is required.

Sincerely,

Ordering Provider's Name: Eugene Stanley Olsowka M.D.

Ordering Provider's NPI: 1407943871

Ordering Provider's Phone Number: 1407943871

Ordering providers signature:

References

1. ACMG Board of Directors. ACMG Policy Statement: Points to consider in the clinical application of genomic sequencing. Genet Med. 2012 14(8):759-61. (PMID: 22863877)
2. Srivastava S et al. Meta-analysis and multidisciplinary consensus statement: exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders. Genet Med. 2019 (PMID: 31182824)
3. Retterer K et al. Clinical application of whole-exome sequencing across clinical indications. Genet Med. 2016 18(7):696-704. (PMID: 26633542)
4. Farwell KD et al. Enhanced utility of family-centered diagnostic exome sequencing with inheritance model-based analysis: results from 500 unselected families with undiagnosed genetic conditions. Genet Med. 2015 17(7):578-86. (PMID: 25356970)
5. Lee H et al. Clinical exome sequencing for genetic identification of rare Mendelian disorders. JAMA. 2014 312(18):1880-7. (PMID: 25326637)
6. Yang Y et al. Molecular findings among patients referred for clinical whole-exome sequencing. JAMA. 2014 312(18):1870-9. (PMID: 25326635)
7. Vrijenhoek T et al. Whole-exome sequencing in intellectual disability; cost before and after a diagnosis. Eur. J. Hum. Genet. 2019 26 (11):1566-1571 (PMID: 29959382)
8. Tan TY et al. Diagnostic Impact and Cost-effectiveness of Whole-Exome Sequencing for Ambulant Children with Suspected Monogenic Conditions. JAMA Pediatr 2017 171 (9):855-862 (PMID: 28759686)
9. Vissers et al. A clinical utility study of exome sequencing versus conventional genetic testing in pediatric neurology. Genet. Med. 2017 19 (9):1055-1063 (PMID: 28333917)
10. Stark Z et al. A prospective evaluation of whole-exome sequencing as a first-tier molecular test in infants with suspected monogenic disorders. Genet Med. 2016 Nov 18(11):1090-1096. (PMID: 26938784)
11. Stark Z et al. Prospective comparison of the cost-effectiveness of clinical whole-exome sequencing with that of usual care overwhelmingly supports early use and reimbursement. Genet. Med. 2017 19 (8):867-874. (PMID: 28125081)
12. Monroe GR, et al. Effectiveness of whole-exome sequencing and costs of the traditional diagnostic trajectory in children with intellectual disability. Genet Med. 2016 18(9):949-56. (PMID: 26845106)

NORTH WEST LABS

WHOLE EXOME SEQUENCING

CONFIDENTIAL

PATIENT	SPECIMEN	HEALTHCARE PROVIDER
Name: **Patient Demo** Date of Birth: **02/17/2015** Gender: **Female** Accession #: **WES-2025-12356** Test Type: **Whole Exome** **Ordering Physician: Joseph Medic, MD**	Specimen Type: **Saliva** Collection Date: **06/15/2025** Completion of Testing: **07/02/2025**	Joseph Medic, MD Office New Jersey

TEST RESULT: POSITIVE - Clinically relevant variant(s) identified.

INTERPRETATION SUMMARY

The patient tested positive for two variants in the **ALG6 (alpha-1,3-glucosyltransferase)** gene, confirming a diagnosis of **ALG6-congenital disorder of glycosylation (ALG6-CDG)**, also known as **congenital disorder of glycosylation type Ic (CDG-Ic)**. This condition follows an **autosomal recessive** inheritance pattern, meaning that disease manifestations occur when both copies of the gene carry pathogenic variants. In this case, the patient is a **compound heterozygote**, having inherited two different pathogenic variants—one from each parent.

ALG6-CDG is the second most common subtype within the CDG spectrum and is typically characterized by **global developmental delays**, including **psychomotor retardation**, **delayed speech and walking**, **hypotonia**, **seizures**, and, in some cases, **protein-losing enteropathy**. Clinical severity and symptoms may vary between individuals.

At present, there are **no specific or curative therapies** available for ALG6-CDG. Management is focused on **symptom-based treatment** and the **prevention of complications**, requiring a multidisciplinary approach involving neurology, gastroenterology, physical therapy, and other supportive services as needed.

SEQUENCE VARIANTS RELATED TO THE INDICATION

GENE	GENOMIC LOCATION (GRCh38)	VARIANT	ZYGOSITY/ INHERITANCE	CLASSIFICATION	CONDITION
ALG6	chr1:63414136TTAA>T	NM_013339.4: c.897_899del (p.Ile299del)	**HET**	Likely Pathogenic	Congenital disorder of glycosylation, type Ic (Autosomal Recessive)
ALG6	chr1:63411333T>G	NM_013339.4: c.680+2T>G	**HET**	Pathogenic	Congenital disorder of glycosylation, type Ic (Autosomal Recessive)

COPY NUMBER VARIANTS RELATED TO THE INDICATION

No clinically significant copy number variants were detected.

INDIVIDUAL VARIANT INTERPRETATIONS

ALG6 c.897_899del, p.Ile299del, Likely Pathogenic

SUMMARY: Inframe Deletion, Rare, ClinVar Likely Pathogenic, Partial Autosomal Recessive

The chr1:63414136TTAA>T (GRCh38), c.897_899del, p.Ile299del inframe deletion was identified in the heterozygous state in the *ALG6* gene. *ALG6* is associated with: Congenital disorder of glycosylation, type Ic (OMIM: 603147);

In silico predictions for this variant are inconclusive; the conservation at this position is moderate; the splice prediction at this position is low. The total AF among gnomAD exomes and genomes is 0.00004. This variant is not present in the homozygous

state in gnomAD. The variant is present in ClinVar (Variation ID: 30420) and absent from HGMD.
According to the ACMG guidelines, the variant is classified as Likely pathogenic. ACMG tags applied:
- BP4: Multiple lines of computational evidence suggest no impact on gene or gene product (conservation, evolutionary, splicing impact, etc.)
- PM2: Absent from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, ExAC or gnomAD (not comprising gnomAD other)
- PM4: Protein length changes as a result of in-frame deletions/insertions in a nonrepeat region or stop-loss variants
- PP5: Reputable source recently reports variant as pathogenic, but the evidence is not available to the laboratory to perform an independent evaluation (Based on ClinVar submissions with 1-4 stars)
- PS3: Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product (Based on ClinVar submissions with 1-4 stars)

ALG6 c.680+2T>G , Pathogenic

SUMMARY: Splice Donor, Rare, ClinVar Likely Pathogenic, Partial Autosomal Recessive
The chr1:63411333T>G (GRCh38), c.680+2T>G splice donor variant was identified in the heterozygous state in the *ALG6* gene. *ALG6* is associated with: Congenital disorder of glycosylation, type Ic (OMIM: 603147);
In silico tools predict this variant to be damaging; the conservation at this position is high; the splice prediction at this position is high. The total AF among gnomAD exomes and genomes is 0. This variant is not present in the homozygous state in gnomAD. The variant is present in ClinVar (Variation ID: 30421) and absent from HGMD.
According to the ACMG guidelines, the variant is classified as Pathogenic. ACMG tags applied:
- PM2: Absent from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, ExAC or gnomAD (not comprising gnomAD other)
- PP5: Reputable source recently reports variant as pathogenic, but the evidence is not available to the laboratory to perform an independent evaluation (Based on ClinVar submissions with 1-4 stars)
- PS3: Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product (Based on ClinVar submissions with 1-4 stars)
- PVS1: Null variant in a gene where LOF is a known mechanism of disease (Based on ClinVar submissions with 1-4 stars)

SECONDARY FINDINGS

GENE	GENOMIC LOCATION (GRCh38)	VARIANT	ZYGOSITY/ INHERITANCE	CLASSIFICATION	CONDITION
GAA	chr17:80112920G>A	NM_000152.5: c.1933G>A (p.Asp645Asn)	**HET**	Pathogenic	Glycogen storage disease II (Autosomal Recessive)

GAA c.1933G>A, p.Asp645Asn, Pathogenic

SUMMARY: Missense, Rare, ClinVar Pathogenic, Partial Autosomal Recessive
The chr17:80112920G>A (GRCh38), c.1933G>A, p.Asp645Asn missense variant was identified in the heterozygous state in the *GAA* gene. *GAA* is associated with: Glycogen storage disease II (OMIM: 232300);
In silico tools predict this variant to be damaging; the conservation at this position is high; the splice prediction at this position is low. The total AF among gnomAD exomes and genomes is 0.00002. This variant is not present in the homozygous state in gnomAD. The variant is present in ClinVar (Variation ID: 188728) and absent from HGMD.
According to the ACMG guidelines, the variant is classified as Pathogenic. ACMG tags applied:
- PM2: Absent from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, ExAC or gnomAD (not comprising gnomAD other)

- PM5: Novel missense change at an amino acid residue where this change or a different missense change determined to be pathogenic has been seen before (Based on ClinVar submissions with any amount of stars)
- PP2: Missense variant in a gene that has a low rate of benign missense variation and in which missense variants are a common mechanism of disease (Based on ClinVar submissions)
- PP3: Multiple lines of computational evidence support a deleterious effect on the gene or gene product (conservation, evolutionary, splicing impact, etc.)
- PS3: Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product (Based on ClinVar submissions with 1-4 stars)

ADDITIONAL COMMENTS

Secondary findings: The patient is a heterozygous carrier of a variant in the **GAA** gene. This gene encodes the enzyme **acid alpha-glucosidase**, which plays a critical role in breaking down **glycogen** into glucose within lysosomes. Mutations in the *GAA* gene lead to **Pompe disease**, a rare **autosomal recessive** metabolic disorder characterized by the accumulation of glycogen in cells, particularly in cardiac and skeletal muscle tissues. This buildup can impair normal cellular and organ function, especially in muscles.
As a **carrier**, the patient has one normal and one altered copy of the *GAA* gene. Carriers do not develop symptoms of Pompe disease. However, there are important **reproductive implications**. If the patient's reproductive partner is also a carrier of a pathogenic *GAA* variant, there is a **25% chance** with each pregnancy that the child will inherit both altered copies of the gene and be affected by Pompe disease. Genetic counseling and, if appropriate, partner testing are recommended to assess the risk to future offspring and to guide reproductive planning.

TEST METHODOLOGY

This test was developed and its performance characteristics determined by North West Labs. It has not been cleared or approved by the US Food and Drug Administration. Advanced Molecular Diagnostics is a CLIA-certified Laboratory accredited by the College of American Pathologists.

Genomic DNA was extracted from the submitted specimen and quantified using fluorometric methods. Prepared libraries are enriched for exonic regions using the Illumina DNA Prep with Exome 2.5 Enrichment kit. This panel targets approximately 37 Mb of coding regions (exons) and flanking intronic sequences from more than 20,000 genes, based on RefSeq and Ensembl annotations. Target enrichment was followed by high-throughput sequencing on the Illumina NextSeq 2000 platform using (2 × 100 bp or 2 × 151 bp)paired-end reads and XLEAP-SBS chemistry. Illumina sequencing by synthesis (SBS) technology ensures high accuracy and uniform coverage, with ≥80% of bases typically achieving Q30 or higher quality scores.
Sequence data were processed using the Illumina DRAGEN Bio-IT Platform for alignment to the GRCh38/hg38 human reference genome, variant calling, and initial quality control. The assay achieved an average sequencing depth of >100x, with >95% of targeted bases covered at a minimum of 20x.
Variant annotation and interpretation were conducted using Emedgene, an AI-powered clinical decision support platform that integrates multiple databases and predictive tools (including ClinVar, HGMD, gnomAD, OMIM, and in silico prediction algorithms). The results were curated and reviewed by molecular geneticists in accordance with the ACMG/AMP 2015 guidelines for variant classification. Variants are classified as Pathogenic (P), Likely Pathogenic (LP), Variant of Uncertain Significance (VUS), Likely Benign (LB), or Benign (B Confirmatory testing by an orthogonal method (e.g., Sanger sequencing) was performed when necessary for clinically significant findings.

LIMITATIONS

This WES assay is optimized for the detection of single nucleotide variants (SNVs), small insertions/deletions (indels), and selected copy number variants (CNVs) within the targeted coding regions. However, several limitations apply:

- The test may not reliably detect variants in low-complexity or high GC-content regions, or in genes with closely related pseudogenes. It targets exonic regions included in the Illumina Exome 2.5 panel. Variants outside these regions (e.g., deep intronic, intergenic, regulatory elements) are not assessed.
- It does not detect balanced rearrangements, such as translocations or inversions, repeat expansions, or deep intronic or regulatory variants outside the target regions.

- Detection of CNVs is bioinformatically inferred and limited to multi-exon events. Single-exon deletions/duplications, low-level mosaicism, and somatic variants are not reliably identified.
- Structural variants, mitochondrial DNA changes, and epigenetic alterations are not evaluated in this assay.
- Poor quality or degraded DNA may compromise assay performance, resulting in failed libraries or incomplete data.
- Interpretation is dependent on currently available data sources. Variants of uncertain significance (VUS) do not confirm or exclude a diagnosis and should not be used for clinical decision-making without further validation. Classifications may evolve as new evidence emerges.
- The use of AI-assisted interpretation (Emedgene) augments variant prioritization but still requires expert human review. Final interpretation is based on a combination of automated analysis and expert curation. Some rare or novel variants may not be fully captured or correctly prioritized, especially if phenotypic information is incomplete or if variant calling is suboptimal for certain variant types
- A negative result does not exclude a genetic diagnosis, particularly in cases where the causative variant is in a region not covered, not yet associated with disease, or beyond current interpretive capabilities.

Secondary findings are reported only if explicitly consented for ACMG SF v3.1 genes.

REFERENCES

1. Richards S et al. Genetics in medicine. *Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.* 2015 May;17(5):405-24 (PMID: 25741868)

COMMENTS

It is recommended that test results be interpreted in the context of clinical findings, family history, and other diagnostic studies. Genetic counseling is advised before and after testing to address clinical implications and test limitations. Negative results do not exclude genetic etiology; additional testing may be warranted for unresolved cases.

SIGNATURE

Dr. Daniel Cohen, M.D., Laboratory Director

This report was electronically signed.

Date: 07/02/2025

NORTH WEST
LABS

Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

Whole Exome Sequencing (WES)

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Next Gen Sequencing

Myeloid NGS

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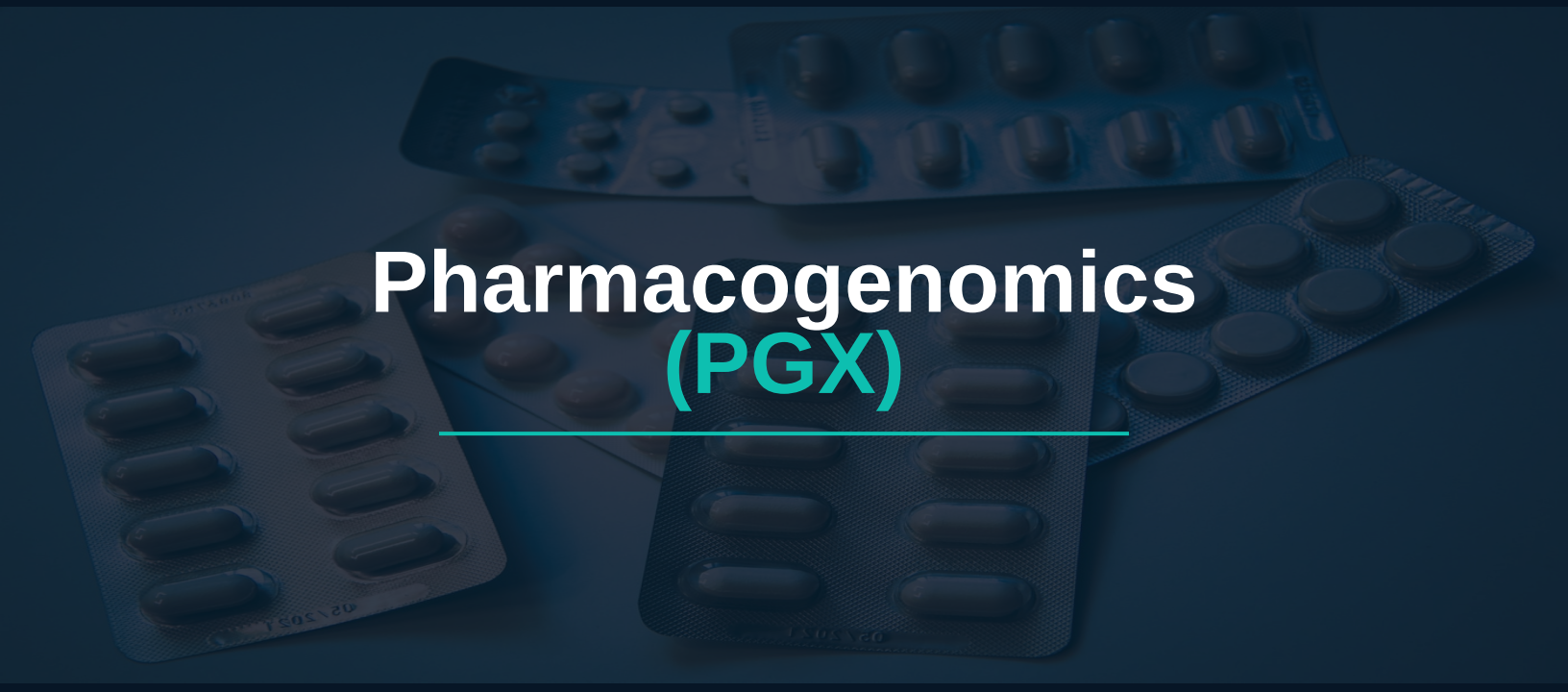
Whole Exome Sequencing (WES)

NORTH WEST LABS



Pharmacogenomics (PGX)

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Whole Exome Sequencing (WES)

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Pharmacogenomics (PGX) Drug Response Testing

What are the Benefits of PGX Drug Response Testing?

- Your DNA doesn't change, so a one-time test is all you'll ever need
- Reduce overall prescriptions
- No more trial-and-error means getting the right medication the first time
- Avoid costly hospitalizations by decreasing patient falls and adverse drug reactions

Traditional Method of Prescribing
A standard dose that works for most people

Standard Dose

Same for everyone

- This is the correct dose
- This medication may not work at all for some patients
- This dose is too high for some patients
- This dose is too low for some patients

Prescribing With PGX Drug Response Testing
Identifying the best medication at the optimal dose

Personalized Dosing

Based on YOUR DNA

- Standard Dose — correct for this patient
- Different Medication — matched to DNA
- Lower Dose — optimized for metabolism
- Higher Dose — optimized for metabolism

Drug response testing tells your doctor how YOU will respond to a certain medication.
Your doctor can then use that information to prescribe the right dose or an alternative medication based on your DNA.

What is Drug Response Testing?

Pharmacogenomic (PGX), or drug response testing, is a simple, non-invasive cheek swab that tests to see how you will personally respond to medications based on your genetic makeup/DNA.

Cost Savings

- The potential savings over time outweigh the cost of Drug Response testing by more than two-fold.
- On average, residents saved $1,863 after utilizing PGX results to guide treatment.

Figure 1: Average savings by category over 2–3 years

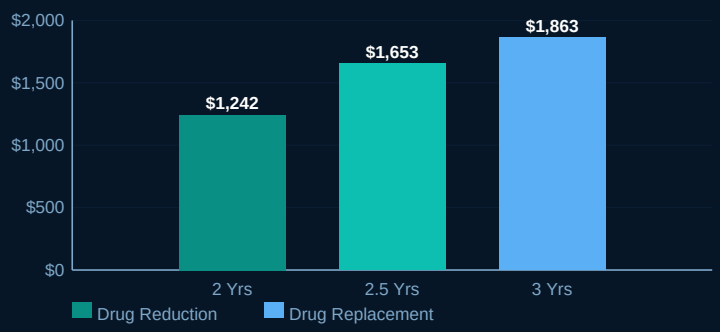
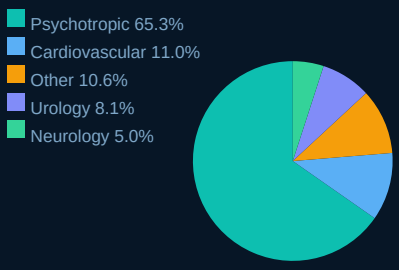


Figure 2: Savings by drug class



Saldivar J, Taylor D, Sugarman E, Cullors A, Garces J, Oades K, Centeno J. Initial assessment of the benefits of implementing pharmacogenetics into the medical management of patients in a long-term care facility. Pharmacogenomics Pers Med. 2016;9:1–6 https://doi.org/10.2147/PGPM.S91480

NORTH WEST LABS

Postpartum PGx Benefits

Pharmacogenomic Testing for New Mothers

How PGX Testing Helps with Postpartum Depression

For new mothers dealing with postpartum depression, finding the right medication quickly is critical. PGx testing analyzes a patient's genetic profile to predict how she will respond to specific psychiatric medications — reducing delay, risk, and uncertainty in treatment.

Key Benefits of PGx-Guided Care:

- Shorter time to an effective medication
- Personalized treatment based on genetics
- Safer medication choices for breastfeeding
- Fewer adverse drug reactions
- More durable remission outcomes

> *"PGx testing for postpartum depression can improve treatment outcomes by reducing the trial-and-error approach to medication selection. By analyzing how a person's genes affect their response to medication, PGx tests help providers choose a more effective medication and dosage with fewer side effects."*

Who Should Be Offered PGx Testing?

- **New mothers with PPD symptoms**
  Especially when initiating antidepressant therapy
- **Breastfeeding mothers**
  Minimize infant exposure to drug metabolites
- **Prior medication failures**
  History of poor response or adverse effects to medication
- **History of mood disorders**
  Improve long-term medication management genetically

1 in 5
new mothers experience postpartum depression

50%+
of PPD cases go untreated or inadequately treated

2x
more likely to achieve remission with PGx-guided prescribing

Reduced Trial & Error

Many psychiatric medications, particularly antidepressants, have a low initial success rate. PGx testing can shorten the time to an effective treatment — critical for new mothers experiencing the severe and time-sensitive symptoms of postpartum depression.

Personalized Treatment Plan

PGx testing can inform medication choices for mood disorders like PPD. By revealing how a patient's unique genetic profile affects medication response, it helps create a more personalized and effective treatment plan.

Durable Effects

Studies have suggested that PGx-guided treatment for depression can lead to more lasting symptom improvement and higher remission rates compared to traditional prescribing methods.

Informed Decision-Making for Breastfeeding

Test results can help alleviate a mother's anxiety about drug metabolites passing into breast milk. With genetic information, a provider can select a medication and dose less likely to cause drug toxicity in the infant, supporting the mother's confidence in breastfeeding.

Reduced Adverse Effects

PGx can identify gene variants that cause a person to metabolize medications too slowly or too quickly — leading to adverse drug reactions or ineffective treatment. For a new mother, avoiding these side effects increases compliance and confidence in her treatment plan.

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Phone: 248 301 6917
Fax: 248 301 6805
support@nwlabs.com

NORTH WEST LABS

PATIENT INFORMATION ☐ Demographics Attached			PROVIDER INFORMATION
FIRST NAME:			
LAST NAME:			
DOB:	SEX: ☐ MALE ☐ FEMALE		
ADDRESS:			
CITY:	STATE:	ZIP:	
EMAIL:	PHONE:		

ANCESTRY			SPECIMEN INFORMATION	
☐ African American	☐ Hispanic	☐ East Asian	DATE OF COLLECTION:	TIME: ☐ AM ☐ PM
☐ Caucasian	☐ Pacific Islander	☐ South Asian	SPECIMEN TYPE: ☐ Buccal Swab ☐ Other: _____	COLLECTOR:
☐ Native American	☐ North African	☐ Other		

INSURANCE INFORMATION		
☐ Insurance	☐ Client Bill	☐ Self-Pay
CARRIER:	GROUP #:	POLICY #:
NAME OF INSURED:	DOB OF INSURED:	RELATIONSHIP:

Please attach a copy of the insurance card & other demographics

TEST SELECTION

Current RX or Considering RX: Please put a check mark next to the medications you want to order a test on in either Current RX indicating that you are currently prescribing the medication or Considering RX if you are evaluating the medication for the patient.

ICD10: Please put the diagnosis code that is the reason for the current/considered RX.

Provider Notes: Please describe in as much detail as possible why you are evaluating the medication for Selection, Avoidance or Dosage. e.g. if you are evaluating a current RX for avoidance, please indicate the adverse reaction.

Dosage, Avoidance or Selection: Please select D for Dosage, A for Avoidance or S for selection, you may be evaluating this for all 3 reasons or just one, please indicate which.

PGX INSTRUMENT PANEL:							
	ABCG2 CYP3A4 CYP3A5	CYP2B6 CYP2C9 CYP2C19	CYP2D6 VKORC1 SLCO1B1	OPRM1 G6PD	Factor I Factor II	COMT MTHFR	CYP4F2 2C Cluster

To ensure that **medical necessity** requirements are met, **at least one medication and corresponding diagnosis (ICD-10) code must be selected** from the options below. An additional area is included for any other medications, diagnoses, or notes not listed in the table for comprehensive documentation of the patient's care.

PHYSICIAN AUTHORIZATION

I, the undersigned healthcare provider, acknowledge that when ordering a PGX panel through North West Labs, located at 29580 Northwestern Hwy., Suite 120, Southfield, MI 48034 (NPI: 1568994879, Tax ID: 813538903) I understand and agree to the following terms:

In some or all instances PGX panels and their associated tests will be forwarded to PCR Labs of America (1464 E Whitestone Blvd, Ste 2401, Cedar Park, TX 78613; Phone: (512) 456-0071; Fax: (512) 456-0072) for processing and analysis.

I attest that I am the ordering physician and treating clinician for the patient identified on this requisition.

I confirm that the medical necessity for each test ordered is documented in the patient's record, and I will provide supporting documentation within 72 hours when requested.

I attest that all tests ordered are medically necessary, individualized to the patient's condition, clinically appropriate in frequency, and will guide patient care decisions. I have attached all prescribed medications, over-the-counter drugs, and herbal products that may impact test results. I certify that all information provided, including ICD-10 codes, is accurate and complies with applicable payer medical necessity policies. I confirm that the patient (or their legal guardian) has provided informed consent for this genetic test, and a record of this consent is maintained or attached. I authorize the laboratory to bill the patient and/or their insurance for the ordered tests. I acknowledge that testing will be performed in compliance with all applicable healthcare regulations, including HIPAA and CLIA, as required.

PHYSICIAN SIGNATURE:_____DATE:_____

PATIENT AUTHORIZATION

I voluntarily consent to the collection and testing of my specimen and authorize the laboratory to perform the ordered test and release my test results to the ordering clinician. If I have provided my insurance information, I authorize performing lab to bill my insurance directly, receive payment on my behalf, and act as my designated representative to appeal any denial of health benefits. I understand that I am responsible for any amounts not covered by my insurance, including deductibles, copayments, and coinsurance, and for forwarding any payments I may receive from my insurer to performing lab for services rendered. I confirm that I have an ongoing provider-patient relationship with the ordering provider and that test results will be used in the provision of my healthcare.

You understand that "de-identified" means removal of direct identifiers (e.g., name, medical record number, social security number) so that your identity cannot reasonably be determined. Personal identifiers will be replaced with a unique code. Unless you authorize otherwise, your sample will be destroyed within thirty (30) days of test completion and will not be used for any other purpose. Granting or withholding this authorization is optional and will not affect your testing or results.

Database Participation: You acknowledge that de-identified medical and genetic information may be shared with scientists, health care providers, or databases to advance understanding of human health and disease. No personal identifying information will be shared. While the risk of re-identification is low, it may increase if you have made genetic or medical data publicly available.

Research Participation: If you consent to both database and research participation, NWL may share your de-identified sample and raw data for research purposes, including test development, drug discovery, validation studies, clinical trials, and scientific publications. Your provider, or you directly, if necessary, may be contacted regarding research findings. You acknowledge that any resulting discoveries, tests, or products will be owned by PCHS and its collaborators and may have commercial value. You and your heirs will not receive compensation for such value.

PATIENT SIGNATURE:_____DATE:_____

MEDICATIONS & ICD-10 CODES REQUIRED FOR PHARMACOGENOMIC TESTING (Select all that apply)

Provider Notes: Please describe in as much detail as possible why you are evaluating the medication for Selection, Avoidance or Dosage. e.g. if you are evaluating the current RX for avoidance, please indicate an adverse reaction. ICD List Disclaimer: It is the sole responsibility of the ordering clinician to diagnose the patient accurately and faithfully. The diagnosis codes provided below are published by the CMS for ease of ordering. Any diagnosis codes on the requisition should also be documented in the patients' clinical medical records. Please provide a copy of those records along with the order.

Note - CPT code 81418 will be billed for the following tests: (*CYP2C19, CYP2D6, APOE, COMT, CYP3A4 & CYP1A2*). All other CPT codes associated with additional tests will be billed separately.

CYP2D6

TRICYCLIC ANTIDEPRESSANTS

☐ Amitriptyline (Elavil)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Clomipramine (Anafranil)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F60.5
☐ Other: _____

☐ Desipramine (Norpramin)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Doxepin (Silenor)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ G47.09
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Imipramine (Tofranil)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Nortriptyline (Pamelor, Aventyl)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Trimipramine (Surmontil)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2
☐ F32.4 ☐ F33.3
☐ Other: _____

CNS STIMULANTS

☐ Amphetamine (Eveko, Dyanavel XR, Adzenys XR-ODT)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F90.1 ☐ F90.2 ☐ F90.8
☐ Other: _____

☐ Atomoxetine (Strattera)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F90.1 ☐ F90.2 ☐ F90.8
☐ Other: _____

☐ Pitolisant (Wakix)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G47.411 ☐ G47.419
☐ Other: _____

ADRENERGIC AGENTS

☐ Carvedilol (Coreg)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ I50.1 ☐ I50.40 ☐ I50.9
☐ I50.20 ☐ I50.89 ☐ I10
☐ I50.30 ☐ Other: _____

☐ Lofexidine (Lucemyra)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F11.23 ☐ Other:_____

SSRI's

☐ Citalopram (Celexa)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Escitalopram (Lexapro)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F41.1
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Fluvoxamine (Luvox)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F60.5 ☐ Other_____

☐ Paroxetine (Paxil)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F33.2 ☐ F41.0
☐ F32.2 ☐ F33.3 ☐ F41.1
☐ F32.3 ☐ F33.41 ☐ F43.11
☐ F32.4 ☐ F33.9 ☐ F43.12
☐ F32.9 ☐ F40.01 ☐ F32.81
☐ F33.1 ☐ F40.11
☐ Other: _____

☐ Sertraline (Zoloft)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F33.1 ☐ F40.11
☐ F32.2 ☐ F33.2 ☐ F41.0
☐ F32.3 ☐ F33.3 ☐ F43.11
☐ F32.4 ☐ F33.41 ☐ F43.12
☐ F32.81 ☐ F33.9 ☐ F60.5
☐ F32.9 ☐ F40.01
☐ Other: _____

☐ Venlafaxine (Effexor)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

VMAT2 INHIBITORS

☐ Deutetrabenazine (Austedo)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G10 ☐ G24.01
☐ Other: _____

☐ Tetrabenazine (Nitoman, Xenazine)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G10 ☐ Other: _____

☐ Valbenazine (Ingrezza)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G24.01 ☐ Other: _____

ANTICHOLINERGICS

☐ Tolterodine (Detrol)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ N32.81 ☐ N39.41 ☐ N39.46
☐ Other: _____

CHOLINERIC AGENTS

☐ Cevimeline (Evoxac)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ M35.00 ☐ Other: _____

ANTINEOPLASTICS/ONCOLOGY

☐ Gefitinib (Iressa)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ C34.90 ☐ Other: _____

☐ Tamoxifen (Soltamox, Nolvadex)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ C50.919 ☐ C50.929
☐ Other: _____

ANTIARRHYTHMICS

☐ Propafenone (Rythmol)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ I48.0 ☐ I48.11 ☐ I48.19
☐ Other: _____

ANTIEMETICS/PROKINETICS

☐ Meclizine (Antivert)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ T75.3XXA ☐ T75.3XXS ☐ T75.3XXD
☐ R11.2 ☐ Other: _____

☐ Metoclopramide (Reglan, Metozolv)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ R11.2 ☐ K21.00 ☐ K21.9
☐ K31.84 ☐ K21.01
☐ Other: _____

☐ Ondansetron (Zofran)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ R11.2 ☐ Other_____

☐ Tropisetron (Navoban)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ R11.2 ☐ Other_____

ENZYME INHIBITORS

☐ Eliglustat (Cerdelga)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ E75.22 ☐ Other: _____

ANTIPSYCHOTICS

☐ Aripiprazole (Abilify)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F33.1 ☐ F31.4
☐ F20.1 ☐ F33.2 ☐ F31.5
☐ F20.2 ☐ F33.3 ☐ F31.61
☐ F20.3 ☐ F33.41 ☐ F31.62
☐ F20.5 ☐ F33.9 ☐ F31.63
☐ F20.81 ☐ F31.0 ☐ F31.64
☐ F20.89 ☐ F31.11 ☐ F31.71
☐ F32.1 ☐ F31.12 ☐ F31.73
☐ F32.2 ☐ F31.13 ☐ F31.75
☐ F32.3 ☐ F31.2 ☐ F31.77
☐ F32.4 ☐ F31.31 ☐ F84.0
☐ F32.9 ☐ F31.32 ☐ F95.2
☐ Other: _____

☐ Pimozide (Orap)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F95.2 ☐ Other_____

ANTIPSYCHOTICS (CONT)

☐ Aripiprazole Lauroxil (Aristrada)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.3 ☐ F20.89
☐ F20.1 ☐ F20.5 ☐ F20.81
☐ F20.2 ☐ Other: _____

☐ Brexpiprazole (Rexulti)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.89 ☐ F33.1
☐ F20.1 ☐ F32.1 ☐ F33.2
☐ F20.2 ☐ F32.2 ☐ F33.3
☐ F20.3 ☐ F32.3 ☐ F33.41
☐ F20.5 ☐ F32.4 ☐ F33.9
☐ F20.81 ☐ F32.9
☐ Other: _____

☐ Clozapine (Clozaril, Versacloz, FazaClo ODT)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.3 ☐ F20.89
☐ F20.1 ☐ F20.5 ☐ R45.851
☐ F20.2 ☐ F20.81
☐ Other: _____

☐ Iloperidone (Fanapt)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.3 ☐ F20.89
☐ F20.1 ☐ F20.5 ☐ F20.81
☐ F20.2 ☐ Other: _____

☐ Perphenazine (Trilafon, Etrafon, Triavil, Triptafen)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.3 ☐ F20.89
☐ F20.1 ☐ F20.5 ☐ R11.2
☐ F20.2 ☐ F20.81
☐ Other: _____

☐ Thioridazine (Mellaril)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ F20.0 ☐ F20.2 ☐ F20.5
☐ F20.1 ☐ F20.3 ☐ F20.81
☐ Other: _____

☐ Codeine (Nelx AC, VroveX CB, BroveX CBX, EndaCof-AC)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G89.11 ☐ G89.29 ☐ G89.18
☐ R52 ☐ Other: _____

☐ Hydrocodone (Vicodin, Loratab, Lorcet-HD, Hycodan, Vicoprofen)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G89.11 ☐ G89.29 ☐ G89.18
☐ R52 ☐ Other: _____

☐ Oliceridine (Olinvyk)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G89.11 ☐ G89.18 ☐ R52
☐ Other: _____

☐ Tramadol (Ultram)
☐ Current ☐ Considering ☐ D ☐ A ☐ S
☐ G89.11 ☐ G89.29 ☐ G89.18
☐ R52 ☐ Other: _____

Note- CPT code 81418 will be billed for the following tests: (*CYP2C19, CYP2D6, APOE, COMT, CYP3A4 & CYP1A2*). All other CPT codes associated with additional tests will be billed separately.

CYP2C19

ANTICONVULSANTS

☐ Brivaracetam (Briviact)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ G40.101 ☐ G40.119 ☐ G40.211
☐ G40.109 ☐ G40.201 ☐ G40.219
☐ G40.111 ☐ G40.209
☐ Other: _____

☐ Clobazam (Onfi)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ G40.811 ☐ G40.813
☐ G40.812 ☐ G40.814
☐ Other: _____

SNRIS & OTHER SEROTONERGIC AGENTS

☐ Flibanserin (Addyl)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F52.0 ☐ Other: _____

ANTIPLATELETS

☐ Clopidogrel (Plavix)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ I20.0 ☐ I21.4 ☐ I69.30
☐ I21.01 ☐ I21.A1 ☐ Z86.73
☐ I21.02 ☐ I21.A9 ☐ Z98.61
☐ I21.09 ☐ I22.0 ☐ Z98.62
☐ I21.11 ☐ I22.1 ☐ I21.B
☐ I21.19 ☐ I22.2 ☐ I25.2
☐ I21.29 ☐ I22.8
☐ Other: _____

ANTINEOPLASTICS/ONCOLOGY

☐ Belzutifan (Welireg)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ C25.4 ☐ C67.3 ☐ D13.7
☐ C64.1 ☐ C67.4 ☐ D18.02
☐ C64.2 ☐ C67.5 ☐ D32.0
☐ C65.1 ☐ C67.6 ☐ D32.1
☐ C65.2 ☐ C67.7 ☐ D33.0
☐ C66.1 ☐ C67.8 ☐ D33.1
☐ C66.2 ☐ C68.0 ☐ D33.3
☐ C67.0 ☐ C68.1 ☐ D33.4
☐ C67.1 ☐ C68.8 ☐ D33.7
☐ C67.2 ☐ C7A.093
☐ Other: _____

TRICYCLIC ANTIDEPRESSANTS

☐ Amitriptyline (Elavil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Clomipramine (Anafranil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F60.5 ☐ Other: _____

☐ Desipramine (Norpramin)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Doxepin (Silenor)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ G47.09
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Imipramine (Tofranil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Nortriptyline (Pamelor, Aventyl)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Trimipramine (Surmontil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

SSRI's

☐ Citalopram (Celexa)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F33.3
☐ F32.4 ☐ Other: _____

☐ Escitalopram (Lexapro)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F32.9 ☐ F33.41
☐ F32.2 ☐ F33.1 ☐ F33.9
☐ F32.3 ☐ F33.2 ☐ F41.1
☐ F32.4 ☐ F33.3
☐ Other: _____

☐ Fluvoxamine (Luvox)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F60.5 ☐ Other: _____

☐ Paroxetine (Paxil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F33.2 ☐ F41.0
☐ F32.2 ☐ F33.3 ☐ F41.1
☐ F32.3 ☐ F33.41 ☐ F43.11
☐ F32.4 ☐ F33.9 ☐ F43.12
☐ F32.9 ☐ F40.01 ☐ F32.81
☐ F33.1 ☐ F40.11
☐ Other: _____

☐ Sertraline (Zoloft)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F33.1 ☐ F40.11
☐ F32.2 ☐ F33.2 ☐ F41.0
☐ F32.3 ☐ F33.3 ☐ F43.11
☐ F32.4 ☐ F33.41 ☐ F43.12
☐ F32.81 ☐ F33.9 ☐ F60.5
☐ F32.9 ☐ F40.01
☐ Other: _____

ANTIFUNGALS

☐ Voriconazole (Vfend)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ B37.81 ☐ B44.0 ☐ B37.81
☐ B37.89 ☐ B48.8
☐ Other: _____

PROTON PUMP INHIBITORS (PPIS)

☐ Dexlansoprazole (Dexilant)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E16.4 ☐ K21.9 ☐ K26.6
☐ E31.20 ☐ K22.10 ☐ K26.7
☐ K21.00 ☐ K22.11 ☐ K26.9
☐ K21.01 ☐ K25.9
☐ Other: _____

☐ Lansoprazole (Prevacid)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E16.4 ☐ K21.9 ☐ K26.6
☐ E31.20 ☐ K22.10 ☐ K26.7
☐ K21.00 ☐ K22.11 ☐ K26.9
☐ K21.01 ☐ K25.9
☐ Other: _____

☐ Omeprazole (Prilosec)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E16.4 ☐ K21.9 ☐ K26.6
☐ E31.20 ☐ K22.10 ☐ K26.7
☐ K21.00 ☐ K22.11 ☐ K26.9
☐ K21.01 ☐ K25.9
☐ Other: _____

☐ Pantoprazole (Protonix)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E16.4 ☐ K21.9 ☐ K26.6
☐ E31.20 ☐ K22.10 ☐ K26.7
☐ K21.00 ☐ K22.11 ☐ K26.9
☐ K21.01 ☐ K25.9
☐ Other: _____

IMMUNOSUPPORESSANTS

☐ Abrocitinib (Cibinqo)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ L20.89 ☐ Other: _____

CARDIOVASCULAR AGENTS

☐ Mavacamten (Camzyos)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ I42.1 ☐ Other:

CYP2C9

ANTICONVULSANTS

☐ Fosphenytoin (Cerebyx)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ G40.201 ☐ G40.309 ☐ G40.411
☐ G40.209 ☐ G40.311 ☐ G40.419
☐ G40.211 ☐ G40.319 ☐ Z48.811
☐ G40.219 ☐ G40.401 ☐ G40.409
☐ G40.301 ☐ Other: _____

☐ Phenytoin (Dilantin, Phenytek)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ G40.201 ☐ G40.309 ☐ G40.411
☐ G40.209 ☐ G40.311 ☐ G40.419
☐ G40.211 ☐ G40.319 ☐ Z48.811
☐ G40.219 ☐ G40.401 ☐ G40.409
☐ G40.301 ☐ Other: _____

NSAIDs

☐ Celecoxib (Celebrex)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

☐ Flurbiprofen (Ansaid)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

☐ Ibuprofen (Advil, Motrin, Nurofen)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

☐ Lornoxicam (Xefo)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

NSAIDs (CONT)

☐ Meloxicam (Mobic, Vivlodex)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

☐ Piroxicam (Feldene)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

☐ Tenoxicam (Tilcotil)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ M06.8A ☐ M19.09 ☐ M19.29
☐ Other: _____

ANTIEMETICS/PROKINETICS

☐ Dronabinol (Marinol, Syndros)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ Other: _____

ANTINEOPLASTICS/ONCOLOGY

☐ Erdafitinib (Balversa)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ Other: _____

ANTIDIABETIC AGENTS

☐ Nateglinide (Starlix)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ T38.3X5A ☐ Other: _____

IMMUNOSUPPORESSANTS

☐ Siponimod (Mayzent)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ Other: _____

STATINS

☐ Fluvastatin (Lescol)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8 ☐ E78.1 ☐ Z86.73
☐ E11.9 ☐ E78.2 ☐ Z86.79
☐ E78.00 ☐ E78.49 ☐ I25.10
☐ E78.01 ☐ Z86.39
☐ Other: _____

CYP2B6

SSRI's

☐ Sertraline (Zoloft)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ F32.1 ☐ F33.1 ☐ F40.11 ☐ F32.4 ☐ F33.41 ☐ F43.12
☐ F32.2 ☐ F33.2 ☐ F41.0 ☐ F32.81 ☐ F33.9 ☐ F60.5
☐ F32.3 ☐ F33.3 ☐ F43.11 ☐ F32.9 ☐ F40.01

☐ Other: _____

ANTIRETROVIRAL

☐ Efavirenz (Sustiva)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ B20

☐ Other: _____

CYP3A5

IMMUNOSUPPORESSANTS

☐ Tacrolimus (Prograf, Envarsus XR, Astagraf XL)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ Z94.0 ☐ Z94.1 ☐ Z94.4

☐ Other: _____

SLCO1B1

STATINS

☐ Atorvastatin (Lipitor)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Pravastatin (Pravachol)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Lovastatin (Mevacor, Altoprev)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Fluvastatin (Lescol)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Pitavastatin (Livalo, Zypitamag)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Simvastatin (Zocor)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

☐ Rosuvastatin (Crestor)

☐ Current ☐ Considering ☐ D ☐ A ☐ S

☐ E11.8	☐ E78.1	☐ Z86.73
☐ E11.9	☐ E78.2	☐ Z86.79
☐ E78.00	☐ E78.49	☐ I25.10
☐ E78.01	☐ Z86.39	

☐ Other: _____

OTHER MEDICATIONS, NOTES, AND DIAGNOSTIC CODES (ICD-10)

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

☐ Medications Attached

_____
_____
_____
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_____
_____
_____
_____
_____
_____

☐ ICD-10 Codes & Notes Attached

FACTOR II & FACTOR V (DIAGNOSTIC GENES INDEPENDENT OF MEDICATION)

ICD List Disclaimer: It is the sole responsibility of the ordering clinician to diagnose the patient accurately and faithfully. The diagnosis codes provided below are published by the CMS for ease of ordering. Any diagnosis codes on the requisition MUST also be documented in the patients' clinical medical records. Please provide a copy of those records along with the order.

☐ I81.0	☐ I82.4Z1	☐ I82.612	☐ I82.0	☐ I82.4Z2	☐ I82.613	☐ I82.1	☐ I82.4Z3	☐ I82.621	☐ I82.210	☐ I82.501	☐ I82.622
☐ I82.211	☐ I82.502	☐ I82.623	☐ I82.220	☐ I82.503	☐ I82.701	☐ I82.221	☐ I82.511	☐ I82.702	☐ I82.290	☐ I82.512	☐ I82.703
☐ I82.291	☐ I82.513	☐ I82.711	☐ I82.3	☐ I82.521	☐ I82.712	☐ I82.401	☐ I82.522	☐ I82.713	☐ I82.402	☐ I82.523	☐ I82.721
☐ I82.403	☐ I82.531	☐ I82.722	☐ I82.411	☐ I82.532	☐ I82.723	☐ I82.412	☐ I82.533	☐ I82.A11	☐ I82.413	☐ I82.541	☐ I82.A12
☐ I82.421	☐ I82.542	☐ I82.A13	☐ I82.422	☐ I82.543	☐ I82.A21	☐ I82.423	☐ I82.551	☐ I82.A22	☐ I82.431	☐ I82.552	☐ I82.A23
☐ I82.432	☐ I82.553	☐ I82.B11	☐ I82.433	☐ I82.561	☐ I82.B12	☐ I82.441	☐ I82.562	☐ I82.B13	☐ I82.442	☐ I82.563	☐ I82.B21
☐ I82.443	☐ I82.591	☐ I82.B22	☐ I82.451	☐ I82.592	☐ I82.B23	☐ I82.452	☐ I82.593	☐ I82.C11	☐ I82.453	☐ I82.5Y1	☐ I82.C12
☐ I82.461	☐ I82.5Y2	☐ I82.C13	☐ I82.462	☐ I82.5Y3	☐ I82.C21	☐ I82.463	☐ I82.5Z1	☐ I82.C22	☐ I82.491	☐ I82.5Z2	☐ I82.C23
☐ I82.492	☐ I82.5Z3	☐ I82.811	☐ I82.493	☐ I82.601	☐ I82.812	☐ I82.4Y1	☐ I82.602	☐ I82.813	☐ I82.4Y2	☐ I82.603	☐ I82.890
☐ I82.4Y3	☐ I82.611	☐ I82.91									

NORTH WEST LABS

PGx Report

Provider: **Dr Test Test**

Patient:
Jane Doe | DOB 01/01/2001

Specimen Type:
Buccal Swab

Received Date:
2025-04-08

Accession #:
123498979

Sample Collected:
2025-04-07

Reported Date
2025-04-08

CURRENT MEDICATIONS

* According to the Lab Report

- Clopidogrel
- Metoprolol
- Omeprazole
- Fluoxetine

RELEVANT GENE PHENOTYPES

* According to the Lab Report

- CYP2C19
Intermediate metabolizer

- CYP2D6
Normal metabolizer

INTERPRETATION SCOPE

* Basis of current interpretation

- [x] PGx Drug–Gene Guidance
- [x] Current Medications
- [ ] Current Diagnosis
- [x] Drug–Drug Interactions
  - [ ] Lab-Provided DDI Only
  - [ ] AI-Derived DDI Only
  - [x] Combined DDI (Lab + AI)

RECOMMENDED ACTIONS

Drug	Overall Priority	Recommended action
Clopidogrel	Major	Avoid reduced-activation risk: consider an alternative antiplatelet strategy or change interacting acid-suppression therapy (DDI-driven).
Metoprolol	Moderate	Monitor for exaggerated beta-blocker effects; consider dose adjustment or alternative if clinically indicated (DDI-driven)
Omeprazole	Moderate	Prefer an alternative acid-suppression option that does not meaningfully reduce clopidogrel activation (DDI-driven)
Fluoxetine	Moderate	If therapy is required, be aware it can drive interaction risk for multiple meds; consider alternatives if medication review indicates safer options (DDI-driven)

***Note:** Overall Priority reflects combined DGI severity and DDI significance.*

JUSTIFICATION (DGI Based)

Drug	Gene / Phenotype	DGI Severity	Clinical impact
Clopidogrel	CYP2C19 - Intermediate metabolizer	Moderate	Reduced activation potential → reduced antiplatelet effect risk
Metoprolol	CYP2D6 - Normal metabolizer	Mild or No	Genotype alone suggests typical metabolism
Omeprazole	CYP2C19 - Intermediate metabolizer	Moderate	Altered exposure/tolerability considerations possible
Fluoxetine	-	Unknown	No clinically actionable PGx guidance identified in the source report.

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PGx Report

Provider: **Dr Test Test**

Patient:
Jane Doe | DOB 01/01/2001

Specimen Type:
Buccal Swab

Received Date:
2025-04-08

Accession #:
123498979

Sample Collected:
2025-04-07

Reported Date
2025-04-08

JUSTIFICATION (DDI Based)

Regimen-level Interaction

Drugs involved	DDI Significance	Interaction summary	Clinical Consideration
Clopidogrel + Omeprazole + Fluoxetine	Major	Combined CYP pathway inhibition may further reduce clopidogrel activation beyond genetic effect	Prioritize avoiding avoidable CYP inhibition when antiplatelet efficacy is critical
Metoprolol + Fluoxetine	Moderate	CYP-mediated inhibition may increase metoprolol exposure and enhance beta-blocker effects	Monitor heart rate and blood pressure; consider dose adjustment or alternative therapy if clinically indicated

**** Interpretation Note:*** *Multiple drugs affect CYP pathways and may cumulatively alter activation or exposure.*

Pairwise contributors

Drugs involved	Clinical impact
Clopidogrel <> Omeprazole	May reduce activation (efficacy risk).
Clopidogrel <> Fluoxetine	May further reduce activation (efficacy risk).
Metoprolol <> Fluoxetine	May increase beta-blocker exposure (safety/ tolerability risk).

CLINICAL NOTES & NUANCES

- **Phenoconversion:** Enzyme inhibitors or inducers can functionally alter metabolism regardless of genotype.
- **Regimen Effects:** Combined interactions may have greater impact than individual pairwise estimates.
- **Optimization Strategy:** When possible, modify the most flexible or lower-priority medication rather than essential therapy.
- **Monitoring:** If changes are not feasible, increase monitoring for efficacy and adverse effects.
- **Clinical Integration:** Interpret PGx and DDI findings in the context of overall patient risk and treatment goals.

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Whole Exome Sequencing (WES)

Pharmacogenomics (PGX)

Myeloid NGS

Next Gen Sequencing

Hereditary Cancer Genetics (CGX)

Neuro NGS

Solid Tumor NGS

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Whole Exome Sequencing (WES)

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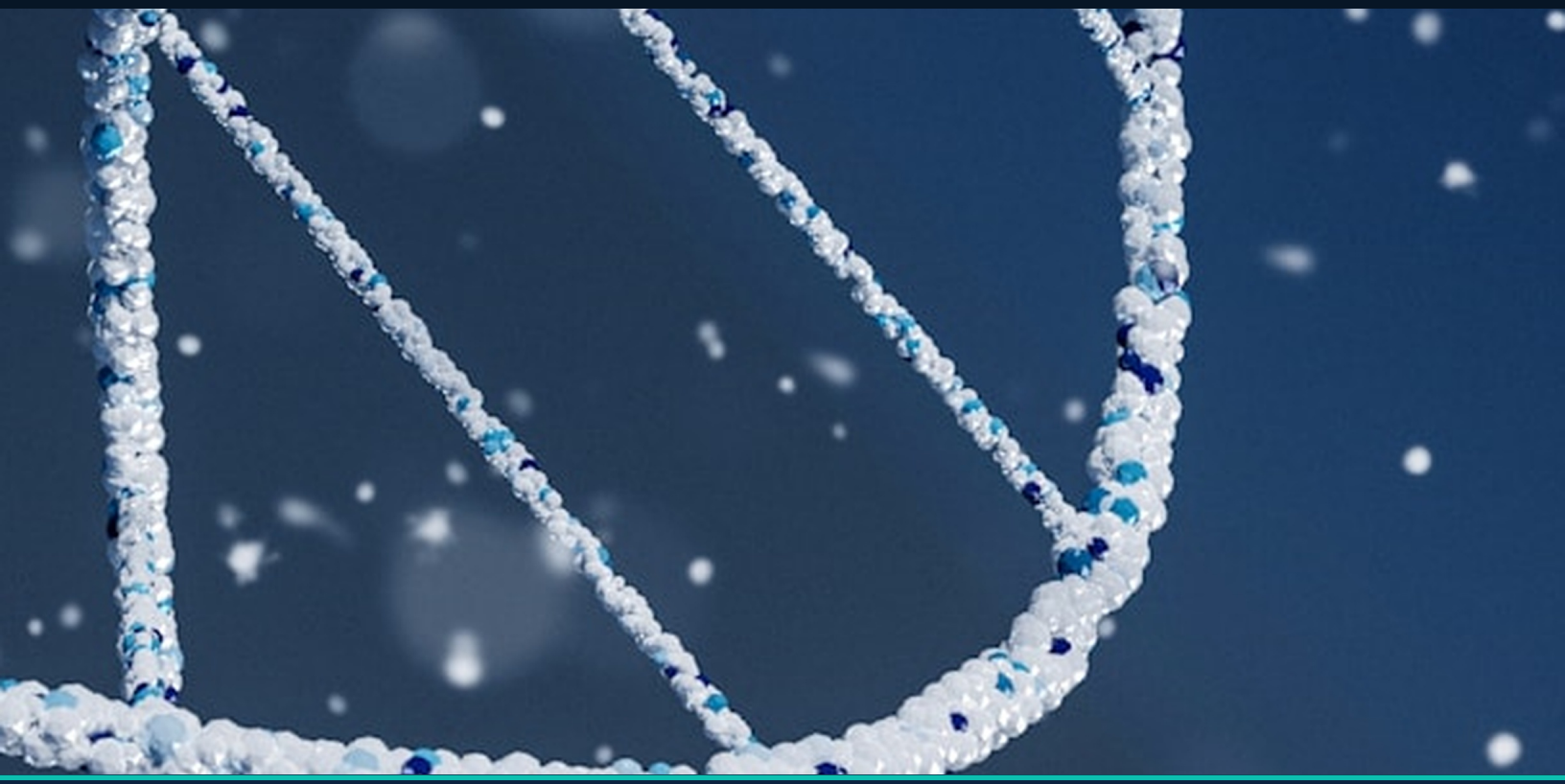

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