InformedDNA®
Genetics, Decoded.

Somatic Tumor Testing

Policy Number: GT04

Last Review Date: 07/03/2025
Previous Review Date: 10/01/2024

InformedDNA®
Genetics, Decoded.

Table of Contents

Scope

This evidence-based guideline addresses molecular testing, including circulating tumor DNA (ctDNA) and gene expression profiling, of solid and hematologic tumors and malignancies, for the purpose of diagnosis, selecting therapeutic agents, surveillance, and predicting risk of recurrence/prognosis.

This guideline's coverage criteria delineate medically necessary clinical scenarios for molecular testing and may include specific situations when testing is considered never medically necessary. In general, molecular testing is considered never medically necessary when evidence demonstrating its ability to improve diagnosis, management, or clinical outcomes is lacking in peer-reviewed literature.

- Please refer to the General Genetic Testing guideline, for the use of polygenic risk scores for cancer.
- Please refer to the Germline Genetic Testing for Hereditary Cancer guideline, for germline genetic testing to guide treatment selection, e.g. PARP inhibitors.

State Biomarker Legislation

Medical necessity determinations must also take into consideration controlling state coverage mandates that may supersede these guidelines when applicable. When state biomarker legislation requirements impact coverage decisions, this guideline will initially be applied to determine if criteria are met for approval. If an approval cannot be granted based on the criteria in this guideline, some or all of the following sources will be reviewed, as defined by applicable state legislation, to determine if test coverage is supported in a manner that is consistent with the state biomarker legislation requirements:

- Medicare National Coverage Determinations (NCDs)
- Medicare Local Coverage Determinations (LCDs)
- U.S. Food and Drug Administration (FDA) approved or cleared tests
- Tests indicated for an FDA-approved drug
- Nationally recognized clinical practice guidelines
- Consensus statements

Guideline Coverage Criteria

General Coverage Criteria

Somatic tumor testing is medically necessary when all of the following criteria are met:

- Identification of the specific genetic variant or gene expression profile has been demonstrated through prospective research in peer-reviewed literature to improve diagnosis, management, or clinical outcomes for the individual's tumor type and disease characteristics

- Sample type (e.g., formalin-fixed, paraffin embedded (FFPE) tissue, circulating tumor DNA, etc.) has been proven to have clinical utility based on prospective evidence in peer-reviewed literature
- Testing methodology* has been clinically validated and is the most accurate method unless technical limitations (e.g., poor sample quality) necessitate the need for alternate testing strategies
- The clinical benefit of testing outweighs the potential risk of psychological or medical harm to the individual being tested
- The test is as targeted as possible for the clinical situation (e.g., common variants, genes related to phenotype)

*The testing methodology may target DNA and/or RNA.

Multi-Gene Panels

In addition to the above criteria, somatic multi-gene panels for hematology-oncology indications are medically necessary when all of the following are met (please see additional criteria below for circulating tumor DNA testing):

- Sequential testing of individual biomarkers is not practical (i.e., limited tissue available, urgent treatment decisions pending) and more than one target is indicated
- Identification of biomarkers on the panel has been demonstrated to improve diagnosis, management, or clinical outcomes for the individual's tumor type and disease characteristics
- The panel is targeted and limited to genes that are associated with the specific tumor type, unless otherwise specified in tumor site-specific criteria below

Chromosomal Microarray Analysis

In addition to the above criteria, chromosomal microarray analysis is medically necessary in any of the following clinical scenarios:

- To aid diagnosis when part of the initial work-up involves cytogenetic (karyotype) and/or FISH analyses and testing was uninformative or could not be performed
- For methylation analysis (e.g., brain/central nervous system cancer)

Never Medically Necessary Tests

(list may not be all inclusive)

- Whole exome tumor sequencing for any indication (including other genome-wide interrogation strategies, e.g. transcriptome)
- Whole genome tumor sequencing for any indication (including other genome-wide interrogation strategies, e.g. transcriptome)

U.S. Food and Drug Administration (FDA) Companion Diagnostics

Molecular-based testing is considered medically necessary when the requested test is an FDA-approved companion diagnostic (CDx) for a biomarker-directed therapy that is approved for use in the patient's cancer type and stage (*please see the Solid Organ Tumors section below for medically necessary clinical scenarios*).

Molecular-based FDA CDx testing is considered never medically necessary if the patient meets the FDA-label criteria for the medication(s) under consideration without the need for biomarker information.

FDA CDx approvals/retractions issued after this guideline's effective date will be evaluated on an individual basis until criteria can be incorporated into the next iteration of this guideline.

Solid Organ Tumors

Genetic testing for solid tumors may have clinical utility for diagnosis/prognosis or to guide therapeutic decision-making based on the patient's type and stage of cancer and treatment history. The tables below list tests/indications that meet the general coverage criteria or the FDA Companion Diagnostics criteria, when applicable, for the patient's cancer type. The tables are all inclusive. If the patient's cancer type is not listed below, please see the Testing for Tumor Agnostic Therapies section. Broad molecular profiling tests not designated as FDA-approved companion diagnostics are never medically necessary.

Tissue-Based Testing

Indication	Biomarker(s)	Test
Breast Cancer** Advanced† or metastatic	*PIK3CA/AKT1/ESR1/PTEN*	■ Single gene tests ■ FoundationOne CDx (0037U) ■ therascreen *PIK3CA* PCR Kit (0155U) ■ CARIS MI Cancer Seek CDx (0211U)
Breast Cancer Advanced† or metastatic breast cancer with progression on endocrine therapy	*ESR1*	■ Single gene tests
Central Nervous System (CNS) Cancer Suspected or confirmed	*IDH1, IDH2, ATRX, TERT, H3-3A, HIST1H3B, BRAF* [fusion or V600E alteration], *RELA* fusion, *ZFTA* fusion, 1p and 19q codeletion, *MGMT* promoter methylation, Sonic hedgehog (*SHH*) pathway (mutational analysis), *MYC* and *MYCN* (copy number analysis)	■ Single gene tests ■ Phenotype-specific CNS somatic tumor profiling panels (81445) ■ Methylation based testing (0020M) ■ Oncomine DX Target Test (0022U) ■ FoundationOne CDx (0037U)
	RNA fusions	■ RNA sequencing assays (81449) *(when FISH-based or IHC tests are insufficient to establish a diagnosis)*
Cholangiocarcinoma Advanced† or metastatic	*FGFR2*, *IDH1*	■ Single gene tests ■ FoundationOne CDx (0037U) ■ Oncomine DX Target Test (0022U)
Colorectal Cancer Metastatic	*KRAS*, *NRAS*, *BRAF*, *MLH1*, Microsatellite Instability (MSI),	■ Single gene tests ■ MSI Instability Testing (81301)

	MSH2, *MSH6*, *PMS2*, *EPCAM*	■ Targeted multigene panels (81445) ■ cobas *KRAS* Mutation Test, therascreen *BRAF* V600E RGQ PCR, therascreen *KRAS* RGQ PCR ■ CRCdx RAS Mutation Detection Kit (0471U) ■ FoundationOne CDx (0037U) ■ oncoReveal CDx (0523U) ■ Praxis Extended RAS Panel (0111U) ■ xT CDx (0473U) ■ CARIS MI Cancer Seek CDx (0211U)
Stage 0-IIIC	*MLH1*, Microsatellite Instability (MSI), *MSH2*, *MSH6*, *PMS2*, *EPCAM*	■ Single gene tests ■ MSI Instability Testing (81301) ■ Targeted multi-gene panels (81445)
Cutaneous Melanoma Advanced† or metastatic	*BRAF*, *KIT*	■ Single gene tests ■ cobas 4800 *BRAF* V600 Mutation Test, THXID *BRAF* Kit ■ FoundationOne CDx (0037U) ■ CARIS MI Cancer Seek CDx (0211U)
Endometrial Cancer (Uterine Neoplasms)	*POLE, TP53,* Microsatellite Instability (MSI), *MLH1, MSH2, MSH6, PMS2, EPCAM*	■ Single gene tests ■ MSI Instability Testing (81301) ■ Targeted multigene panels (81445) ■ CARIS MI Cancer Seek CDx (0211U)
	RNA fusions	■ RNA sequencing assays (81449) *(when uterine sarcoma is suspected or confirmed and FISH-based or IHC tests are insufficient to establish a diagnosis)*
Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancers Advanced† or metastatic	*BRCA1/BRCA2*	■ Somatic *BRCA1/BRCA2* ■ MyChoice CDx (0172U) ■ FoundationOne CDx (0037U) ■ FoundationFocus CDxBRCA Assay
Gastrointestinal Stromal Tumors (GIST) Suspected or confirmed	*KIT, PDGFRA*	■ Single gene tests ■ therascreen PDGRFA RGQ PCR Kit (81314)
	BRAF, *NF1*, *NTRK*, and *EGFR*	■ Single gene tests ■ Targeted multigene panels (81445) (*when KIT and PDGFRA are negative)*
Lung Cancer** Advanced† or metastatic non-small cell lung cancer at the time of initial diagnosis and/or at the time of progression on a new biopsy sample	*EGFR, ALK, KRAS, ROS1, ERBB2 (HER2), BRAF, RET, MET, NRG1*	■ Single gene tests ■ cobas *EGFR* Mutation test v2 (81235), therascreen *EGFR* RGQ PCR test (81235), therascreen *KRAS* RGQ PCR test (81275, 81276) ■ Targeted multigene panels (81445 and/or 81449) ■ FoundationOne CDx (0037U)

		■ Oncomine DX Target Test (0022U) ■ oncoReveal CDx (0523U) ■ TruSight Oncology (TSO) Comprehensive assay ■ CARIS MI Cancer Seek CDx (0211U)
Lung Cancer Stage IB-IIIA resected non-small cell lung cancer	*EGFR, ALK*	■ Single gene tests ■ Cobas *EGFR* Mutation test v2 (81235), Therascreen *EGFR* RGQ PCR test (81235) ■ FoundationOne CDx (0037U) ■ Oncomine DX Target Test (0022U) ■ ONCO/Reveal Dx Lung & Colon Cancer (0448U) ■ CARIS MI Cancer Seek CDx (0211U)
Pancreatic Cancer *Advanced† or metastatic*	*NRG1*	■ Single gene tests
Prostate Cancer Metastatic, castration-resistant	*BRCA1/BRCA2* and other homologous recombination repair (HRR) genes	■ Single gene tests ■ Targeted multigene panels (81445) ■ FoundationOne CDx (0037U)
Sarcoma Suspected or confirmed	*EGFR, IDH1/IDH2 COL2A1*	■ Single gene tests *(when sarcoma of the bone is suspected or confirmed)*
	Cytogenetic abnormalities or gene fusions	■ DNA (81445) and/or RNA (81449) NGS testing (*when FISH-based or IHC tests are insufficient to establish a diagnosis of soft tissue sarcomas)*
Synovial Sarcoma Advanced† or metastatic	*HLA-A*	■ SeCore CDx HLA A Sequencing System
Salivary Gland Tumors Suspected or confirmed	Cytogenetic abnormalities or gene fusions	■ DNA (81445) and/or RNA (81449) NGS testing (*when FISH-based or IHC tests are insufficient to confirm the subtype of salivary gland tumor)*
Thyroid Cancer Advanced† or metastatic	*BRAF, RET*	■ Single gene tests ■ Oncomine DX Target Test (0022U)
Testing for Tumor Agnostic Therapies Advanced† or metastatic cancer	Tumor Mutation Burden (TMB), Microsatellite Instability (MSI), *NTRK, BRAF, RET*	■ Single gene tests ■ FoundationOne CDx (0037U) ■ TruSight Oncology (TSO) Comprehensive assay ■ CARIS MI Cancer Seek CDx (0211U)
Uveal Melanoma Advanced† or metastatic	*HLA-A*	■ SeCore CDx HLA Sequencing System
Suspected or confirmed	*EIF1AX, SF3B1, BAP1, PRAME*	■ Single gene tests

† Advanced includes unresectable, recurrent, relapsed, or refractory cancers
***Sequential or concurrent testing alongside ctDNA testing is medically necessary*

Circulating Tumor DNA (ctDNA) Testing

Indication	Biomarker(s)	Test
Breast Cancer** Advanced† or Metastatic	*PIK3CA*	■ FoundationOne® Liquid CDx (0239U) ■ therascreen *PIK3CA* PCR Kit (0177U)
	ESR1	■ Guardant360® CDx (0242U)
Colorectal Cancer* Advanced† or Metastatic	*BRAF*	■ FoundationOne® Liquid CDx (0239U)
Lung Cancer** Advanced† or metastatic non-small cell lung cancer at the time of initial diagnosis and/or at the time of progression on a new serum sample	*EGFR, MET, ROS1, ALK, ERBB2, KRAS*	■ cobas v2 EGFR Mutation Test v2 (81235) ■ FoundationOne® Liquid CDx (0239U) ■ Guardant360® CDx (0242U) ■ Agilent Resolution ctDx FIRST
Lung Cancer* Stage IB-IIIA resected non-small cell lung cancer	*EGFR, ALK*	■ FoundationOne® Liquid CDx (0239U) ■ Guardant360® CDx (0242U) ■ cobas v2 EGFR Mutation Test v2 (81235)
Prostate Cancer* Metastatic castration-resistant)	*BRCA1/ BRCA2, ATM*	■ FoundationOne® Liquid CDx (0239U)
Tumor Agnostic* Advanced† or metastatic cancer	*NTRK*	■ FoundationOne® Liquid CDx (0239U)

† Advanced includes unresectable, recurrent, relapsed, or refractory cancers
**Medically necessary when tissue-based testing cannot be performed*
***Sequential or concurrent testing alongside tissue testing is medically necessary*

Gene Expression Classifier Testing

Breast Cancer
Breast cancer assays not listed below are considered never medically necessary.

Oncotype DX® Breast Recurrence Score Test is medically necessary to assess the need for adjuvant chemotherapy in the following individuals:

- Pre-menopausal women who are axillary-node negative or any axillary-node micrometastasis is no greater than 2.0 millimeters
- Post-menopausal women who are axillary-node negative or have no more than 3 positive lymph nodes
- Men who are axillary-node negative or have no more than 3 positive lymph nodes

AND all of the following criteria are met:

- Patient has undergone surgery and full pathological staging prior to testing

- Breast tumor is anatomic stage 1 or stage 2
- Histologic type is ductal, lobular, mixed (ductal/lobular), or metaplastic
- Tumor size >0.5 cm to ≤1.0 cm plus unfavorable histological features (defined as overall tumor grade 2 or 3; nuclear grade 3; or lymphovascular invasion) **OR** tumor size 1.1-5.0 cm, any grade
- There is no evidence of distant metastatic breast cancer
- Breast tumor is estrogen and/or progesterone receptor-positive
- Breast tumor is *HER2*-negative
- Patient is a candidate for chemotherapy (i.e., chemotherapy not precluded due to other factors)
- Adjuvant chemotherapy is being considered and this testing is being ordered to assess recurrence risk to guide decision making as to whether or not adjuvant chemotherapy will be utilized
- No other breast gene expression classifier (GEC) has been performed

Prosigna™ PAM50, EndoPredict® or Breast Cancer Index testing is medically necessary to assess the risk for recurrence in an individual when all of the following criteria are met:

- Patient has undergone surgery and full pathological staging prior to testing
- Breast tumor is anatomic stage 1 or stage 2
- Histologic type is ductal, lobular, mixed (ductal/lobular), or metaplastic
- Tumor size >0.5 cm to ≤1.0 cm and intermediate or high grade (Grade 2 or 3) **OR** tumor size 1.1-5.0 cm, any grade
- Axillary-node status is negative or any axillary-node micrometastasis is no greater than 2.0 millimeters
- There is no evidence of distant metastatic breast cancer
- Breast tumor is estrogen or progesterone receptor-positive
- Breast tumor is *HER2*-negative
- Female patient is postmenopausal
- Patient is a candidate for chemotherapy (i.e., chemotherapy not precluded due to other factors)
- Adjuvant chemotherapy is being considered and this testing is being ordered to assess recurrence risk to guide decision making as to whether or not adjuvant chemotherapy will be utilized
- No other breast GEC has been performed

MammaPrint® (81521, 81523) is medically necessary to assess the risk for recurrence in an individual when all of the following criteria are met:

- Patient is older than 50 years of age
- Patient has undergone surgery and full pathological staging prior to testing
- Breast tumor is anatomic stage 1 or stage 2
- Histologic type is ductal, lobular, mixed (ductal/lobular), or metaplastic
- Node negative **OR** 1-3 positive node breast cancer
- Breast tumor is estrogen receptor positive and/or progesterone receptor positive
- Breast tumor is *HER2*-negative
- Patient is at high clinical risk for recurrence based on MINDACT categorization
- Patient is a candidate for chemotherapy (i.e., chemotherapy not precluded due to other factors)
- Adjuvant chemotherapy is being considered and this testing is being ordered to assess recurrence risk to guide decision making as to whether or not adjuvant chemotherapy will be utilized

- No other breast GEC has been performed

The Breast Cancer Index™ test is considered medically necessary for an individual diagnosed within the last five years with early stage (T1-T3), hormone receptor positive, *HER2*-negative breast cancer AND all of the following criteria are met:

- EITHER of the following:
  - Axillary node status was negative (micrometastasis no greater than 2.0 mm)
  - Axillary node status was N1(1-3 positive nodes)
- No evidence of distant metastasis
- No evidence of cancer at the time of testing
- Test results will be used in the decision-making for extended endocrine therapy after at least four years of its use

Uveal Melanoma
DecisionDx® - UM (81552) is medically necessary for individuals with confirmed non-metastatic uveal melanoma.

Gene expression profiling is considered never medically necessary in any other clinical setting.

Hematolymphoid Tumors

Diagnostic/Prognostic Testing

The following molecular studies are medically necessary when the General Coverage Criteria or FDA Companion Diagnostics Coverage Criteria are met above.

- Targeted genomic sequencing panels (81450) on a bone marrow biopsy are medically necessary when a hematolymphoid neoplasm or cancer is known or suspected. *Hodgkin lymphoma is excluded from coverage.*
- Targeted genomic sequencing panels (81451) are medically necessary for B-cell acute lymphoblastic leukemia (ALL), T-cell ALL, acute myelogenous leukemia (AML) and eosinophilia only when a diagnosis is known or suspected based on bone marrow biopsy.
- Targeted genomic sequencing panels (*JAK2*, *CALR*, *MPL*) or single gene tests on peripheral blood are medically necessary for essential thrombocythemia or thrombocytosis; polycythemia vera; or primary myelofibrosis, pre-PMF, suspicion for PMF (i.e., myeloproliferative neoplasm is suspected) when 2022 WHO criteria are met.

Minimal Residual Disease (MRD) Monitoring

Hematologic Cancers

Next-generation sequencing (e.g., ClonoSeq, LymphoTrack) for MRD clone identification from bone marrow biopsy is medically necessary for:

- B-cell acute lymphoblastic leukemia (ALL) which is Philadelphia chromosome (*BCR*::*ABL*) negative
- Multiple myeloma

Next-generation sequencing (e.g., ClonoSeq, LymphoTrack) for MRD tracking is medically necessary for B-cell acute lymphoblastic leukemia that is Philadelphia chromosome (BCR::ABL) negative *or* multiple myeloma when all of the following criteria are met:

- A clone for MRD tracking has been identified

- The patient is at the end of a treatment stage when complete remission is likely
- Testing is completed on a bone marrow sample

Targeted molecular MRD testing with prospective evidence of clinical utility for the tumor type and disease characteristics is medically necessary.

Solid Tumors
Molecular testing for MRD (e.g., Signatera) and/or disease monitoring is never medically necessary.

Key Terms and Definitions

Biomarker in genetics typically refers to a DNA or RNA sequence that can aid in diagnosis, prognosis, and treatment decision-making.
Chromosomes carry genetic material known as DNA; humans typically have 23 pairs of chromosomes.
Chromosomal microarray analysis is a genetic test that analyzes the entire genome for small deletions or duplications, known as copy number variants, in the DNA.
Circulating tumor DNA (ctDNA), also known as cell-free tumor DNA or liquid biopsy, refers to small fragments of DNA that originate from tumor cells and are released into the bloodstream.
Cytogenetic (karyotype) analysis is a laboratory technique used to examine and analyze the chromosomes to detect structural and numerical abnormalities.
Deoxyribonucleic acid (DNA) is a molecule that contains the genetic instructions for all living organisms and plays a crucial role in the development and susceptibility to diseases.
Fluorescent in situ hybridization (FISH) is a molecular cytogenetic technique used to visualize and map the location of specific DNA sequences on chromosomes or in cells.
Gene expression classifier testing is a molecular diagnostic technique that evaluates the activity levels of specific genes in a sample to classify or predict certain disease states or outcomes.
Gene expression profile refers to the pattern of gene activity or expression levels in a given cell or tissue sample at a specific time; this provides a snapshot of which genes are being actively transcribed and their associated levels of protein production or cellular activity.
Genes are segments of DNA that contain the instructions for specific traits, characteristics, or functions within an organism.
Genetic (molecular) testing examines a person's DNA or RNA to identify variations that can aid in the diagnosis of disease and/or provide valuable information about a person's risk of developing certain diseases.
Germline genetic testing involves examining the DNA incorporated in every cell of the body derived from reproductive cells (eggs or sperm).
Methylation analysis is a molecular technique used to study DNA methylation patterns in cells and tissue; DNA methylation occurs when a methyl group is added to a DNA segment and does not alter the DNA sequence but can affect gene expression and cellular function.
Minimal residual disease (MRD) monitoring is used to detect and track low levels of cancer cells that persist during or after cancer treatment.
Multi-gene panels simultaneously analyze multiple genes associated with a particular condition or a group of related conditions.
Next-generation sequencing is a technology that enables the rapid and cost-effective sequencing of large amounts of DNA or RNA.

Pathogenic/likely pathogenic variant(s) describe specific genetic changes that are known or highly likely to cause a particular genetic disorder, which can aid in diagnosis and/or guide treatment and management strategies.
Ribonucleic acid (RNA) is a molecule that plays a crucial role in various cellular processes within living organisms, such as cell functioning and regulation.
Somatic variants are genetic changes that arise in a person's DNA during their lifetime. Somatic variants are not inherited or passed onto offspring. Many cancers are associated with the accumulation of somatic variants in specific genes that control cell growth and division.
Somatic tumor testing is a type of genetic testing that focuses on identifying genetic changes that occur spontaneously in cancer cells.

CPT® Codes

Medical necessity review of claims may include evaluation of the submitted codes. Laboratories must accurately represent their services using the most applicable and specific CPT code(s). Tier 1 molecular pathology procedure codes or Proprietary Laboratory Analyses (PLA) codes should be used when available for the specific test. Tier 2 molecular pathology procedure codes should only be used if the American Medical Association (AMA) has specifically assigned the performed test to such a code. Genomic sequencing procedures (GSP) codes (e.g., CPT codes 81410-81471) were developed by the AMA to represent multi-gene panels utilizing DNA or RNA analysis for specific clinical scenarios (e.g., carrier screening, tumor testing, etc.) and should be utilized when applicable.

Coding guidelines can be found in the AMA's CPT manual as well as the Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative (NCCI) policy manuals. NCCI General Correct Coding Policy states that procedures should be reported with the most comprehensive CPT code describing the services performed and that the services described by a CPT code cannot be unbundled into multiple less specific codes. Additionally, GSP codes should be utilized when appropriate for the described test and should not be submitted along with other CPT codes that represent components of the GSP code.

Claims may not be approved if the submitted codes are not the most appropriate for the described procedure (i.e., as accurate and specific as available).

The following code(s) are medically necessary when coverage criteria are met. This list is not all inclusive.

Code	Full Description
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C)
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and

	ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81168	CCND1/IGH (t(11;14)) (eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed
81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81175	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (eg, solid tumors) translocation analysis
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (eg, solid tumors) translocation analysis
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (eg, solid tumors) translocation analysis
81194	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis
81206	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence
81219	CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)

81245	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (ie, exons 14, 15)
81246	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)
81261	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction)
81262	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (eg, Southern blot)
81263	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81264	IGK@ (Immunoglobulin kappa light chain locus) (eg, leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81270	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s)
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)
81277	Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-of-heterozygosity variants for chromosomal abnormalities
81278	IGH@/BCL2 (t(14;18)) (eg, follicular lymphoma) translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative
81279	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme) promoter methylation analysis
81301	Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81305	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
81310	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (eg, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative

81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
81327	SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis
81334	RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10
81340	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (eg, polymerase chain reaction)
81341	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (eg, Southern blot)
81342	TRG@ (T cell antigen receptor, gamma) (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)
81347	SF3B1 (splicing factor [3b] subunit B1) (eg, myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (eg, A672T, E622D, L833F, R625C, R625L)
81348	SRSF2 (serine and arginine-rich splicing factor 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, P95H, P95L)
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)
81357	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, S34F, S34Y, Q157R, Q157P)
81360	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (eg, E65fs, E122fs, R448fs)
81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
81449	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis
81450	Hematolymphoid neoplasm or disorder, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81451	Hematolymphoid neoplasm or disorder, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis
81456	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform

	expression or mRNA expression levels, if performed; RNA analysis
81457	Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, microsatellite instability
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
81520	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score
81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis
81552	Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider.
0023U	Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or nondetection of FLT3 mutation and indication for or against the use of midostaurin
0027U	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis utilizing formalin-fixed paraffin-embedded tissue
0154U	Oncology (urothelial cancer), RNA, analysis by real-time RT-PCR of the FGFR3 (fibroblast growth factor receptor 3) gene analysis (ie, p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3) utilizing formalin-fixed paraffin-embedded urothelial cancer tumor tissue, reported as FGFR gene alteration status
0155U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3- kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y), utilizing formalin-fixed paraffin embedded breast tumor tissue, reported as PIK3CA gene mutation status
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score

0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3- kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements
0364U	Oncology (hematolymphoid neoplasm), genomic sequence analysis using multiplex (PCR) and next-generation sequencing with algorithm, quantification of dominant clonal sequence(s), reported as presence or absence of minimal residual disease (MRD) with quantitation of disease burden, when appropriate
0471U	Oncology (colorectal cancer), qualitative real-time PCR of 35 variants of KRAS and NRAS genes (exons 2, 3, 4), formalin fixed paraffin-embedded (FFPE), predictive, identification of detected mutations
0473U	Oncology (solid tumor), next generation sequencing (NGS) of DNA from formalin-fixed paraffin embedded (FFPE) tissue with comparative sequence analysis from a matched normal specimen (blood or saliva), 648 genes, interrogation for sequence variants, insertion and deletion alterations, copy number variants, rearrangements, microsatellite instability, and tumor-mutation burden
0478U	Oncology (non-small cell lung cancer), DNA and RNA, digital PCR analysis of 9 genes (EGFR, KRAS, BRAF, ALK, ROS1, RET, NTRK 1/2/3, ERBB2, and MET) in formalin-fixed paraffin-embedded (FFPE) tissue, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and reported as actionable detected variants for therapy selection
0481U	IDH1 (isocitrate dehydrogenase 1 [NADP+]), IDH2 (isocitrate dehydrogenase 2 [NADP+]), and TERT (telomerase reverse transcriptase) promoter (eg, central nervous system [CNS] tumors), next-generation sequencing (single-nucleotide variants [SNV], deletions, and insertions)
0523U	Oncology (solid tumor), DNA, qualitative, next-generation sequencing (NGS) of single-nucleotide variants (SNV) and insertion/deletions in 22 genes utilizing formalin-fixed paraffin-embedded tissue, reported as presence or absence of mutation(s), location of mutation(s), nucleotide change, and amino acid change
0534U	Oncology (solid tumor), next generation sequencing of DNA from formalin-fixed paraffin-embedded (FFPE) tissue of 517 genes, interrogation for single nucleotide variants, multinucleotide variants, insertions and deletions from DNA, fusions in 24 genes and splice variants in 1 gene from RNA, and tumor mutation burden

The following code(s) are considered never medically necessary. This list is not all inclusive.

Code	Full Description
81458	Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, copy number variants and microsatellite instability
81459	Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements
81462	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants and rearrangements
81463	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis, copy number variants, and microsatellite instability

81464	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements
81525	Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score
81529	Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel lymph node metastasis
81540	Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score
0016M	Oncology (bladder), mRNA, microarray gene expression profiling of 219 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like)
0045U	Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by realtime RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score
0047U	Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score
0048U	Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s)
0244U	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite instability, utilizing formalin-fixed paraffin embedded tumor tissue
0250U	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden
0326U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 83 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0329U	Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene rearrangements, microsatellite instability and tumor mutational burden utilizing DNA and RNA from tumor with DNA from normal blood or saliva for subtraction, report of clinically significant mutation(s) with therapy associations
0334U	Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0340U	Oncology (pan-cancer), analysis of minimal residual disease (MRD) from plasma, with assays personalized to each patient based on prior next-generation sequencing of the patient’s tumor and germline DNA, reported as absence or presence of MRD, with disease-burden correlation, if appropriate

0388U	Oncology (non-small cell lung cancer), next-generation sequencing with identification of single nucleotide variants, copy number variants, insertions and deletions, and structural variants in 37 cancer-related genes, plasma, with report for alteration detection
0422U	Oncology (pan-solid tumor), analysis of DNA biomarker response to anti-cancer therapy using cell-free circulating DNA, biomarker comparison to a previous baseline pre-treatment cell-free circulating DNA analysis using next-generation sequencing, algorithm reported as a quantitative change from baseline, including specific alterations, if appropriate
0485U	Oncology (solid tumor), cell-free DNA and RNA by next-generation sequencing, interpretative report for germline mutations, clonal hematopoiesis of indeterminate potential, and tumor-derived single-nucleotide variants, small insertions/deletions, copy number alterations, fusions, microsatellite instability, and tumor mutational burden

References

CPT Codes

AMA CPT® Professional 2024. American Medical Association

NCCI Policy Manual for Medicare Services. Available at: https://www.cms.gov/Medicare/Coding/NationalCorrectCodInitEd. Accessed quarterly.

NCCI Policy Manual for Medicaid Services. Available at: https://www.medicaid.gov/medicaid/program-integrity/national-correct-coding-initiative/medicaid-ncci reference-documents/index.html

Gene Expression Classifiers

Breast Cancer

Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. Lancet Oncol. 2010 Jan;11(1):55-65. doi: 10.1016/S1470-2045(09)70314-6. Epub 2009 Dec 10. PMID: 20005174.

Andre F, Ismaila N, Allison KH, et al. Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update. J Clin Oncol. 2022 Jun 1;40(16):1816-1837. doi: 10.1200/JCO.22.00069. Epub 2022 Apr 19. PMID: 35439025.

Arpino G, Generali D, Sapino A, et al. Gene expression profiling in breast cancer: a clinical perspective. Breast. 2013 Apr;22(2):109-120. doi: 10.1016/j.breast.2013.01.016. Epub 2013 Feb 23. Erratum in: Breast. 2016 Feb;25:86. Del Matro, Lucia [corrected to Del Mastro, Lucia]. PMID: 23462680.

Ayala de la Peña F, Andrés R, Garcia-Sáenz JA, et al. SEOM clinical guidelines in early stage breast cancer (2018). Clin Transl Oncol. 2019 Jan;21(1):18-30. PMID: 30443868.

Azim HA Jr, Michiels S, Zagouri F, et al. Utility of prognostic genomic tests in breast cancer practice: The IMPAKT 2012 Working Group Consensus Statement. Ann Oncol. 2013 Mar;24(3):647-54. doi: 10.1093/annonc/mds645. Epub 2013 Jan 20. PMID: 23337633.

Bartlett JMS, Sgroi DC, Treuner K, et al. Breast Cancer Index and prediction of benefit from extended endocrine therapy in breast cancer patients treated in the Adjuvant Tamoxifen-To Offer More? (aTTom) trial. Ann Oncol. 2019 Nov 1;30(11):1776-1783. doi: 10.1093/annonc/mdz289. PMID: 31504126; PMCID: PMC6927322.

Blanchette P, Sivajohanathan D, Bartlett J,et al. Clinical Utility of Multigene Profiling Assays in Early-Stage Invasive Breast Cancer: An Ontario Health (Cancer Care Ontario) Clinical Practice Guideline. Curr Oncol. 2022 Apr 9;29(4):2599-2615. doi: 10.3390/curroncol29040213. PMID: 35448187; PMCID: PMC9029123.

Blok EJ, Bastiaannet E, van den Hout WB, et al. Systematic review of the clinical and economic value of gene expression profiles for invasive early breast cancer available in Europe. Cancer Treat Rev. 2018 Jan;62:74-90. Review. PMID: 29175678.

Bombard Y, Bach PB, Offit K. Translating genomics in cancer care. J Natl Compr Canc Netw. 2013 Nov;11(11):1343-53. doi: 10.6004/jnccn.2013.0158. PMID: 24225968.

Bueno-de-Mesquita JM, van Harten WH, Retel VP, et al. Use of 70-gene signature to predict prognosis of patients with node-negative breast cancer: a prospective community-based feasibility study (RASTER). Lancet Oncol. 2007 Dec;8(12):1079-1087. doi: 10.1016/S1470-2045(07)70346-7. Epub 2007 Nov 26. Erratum in: Lancet Oncol. 2008 Jan;9(1):10. PMID: 18042430.

Buus R, Sestak I, Kronenwett R, et al. Comparison of EndoPredict and EPclin With Oncotype DX Recurrence Score for Prediction of Risk of Distant Recurrence After Endocrine Therapy. J Natl Cancer Inst. 2016 Jul 10;108(11):djw149. doi: 10.1093/jnci/djw149. PMID: 27400969.

Buyse M, Loi S, van't Veer L, et al. Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer. J Natl Cancer Inst. 2006 Sep 6;98(17):1183-92. doi: 10.1093/jnci/djj329. PMID: 16954471.

Cardoso F, van't Veer LJ, Bogaerts J, et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. N Engl J Med. 2016 Aug 25;375(8):717-29. doi: 10.1056/NEJMoa1602253. PMID: 27557300.

Chang MC, Souter LH, Kamel-Reid S, et al. Clinical utility of multigene profiling assays in early-stage breast cancer. Curr Oncol. 2017 Oct;24(5):e403-e422. doi: 10.3747/co.24.3595. Epub 2017 Oct 25. PMID: 29089811.

Chen J, Wu X, Christos PJ, et al. Practice patterns and outcomes for patients with node-negative hormone receptor-positive breast cancer and intermediate 21-gene Recurrence Scores. Breast Cancer Res. 2018 Apr 16;20(1):26. doi: 10.1186/s13058-018-0957-3. PMID: 29661221.

Chia SKL. Clinical application and utility of genomic assays in early-stage breast cancer: key lessons learned to date. Curr Oncol. 2018 Jun;25(Suppl 1):S125-S130. doi: 10.3747/co.25.3814. Epub 2018 Jun 13. PMID: 29910655.

Colomer R, Aranda-López I, Albanell J, et al. Biomarkers in breast cancer: A consensus statement by the Spanish Society of Medical Oncology and the Spanish Society of Pathology. Clin Transl Oncol. 2018 Jul;20(7):815-826. doi: 10.1007/s12094-017-1800-5. Epub 2017 Dec 22. Erratum in: Clin Transl Oncol. 2018 Jun 18;: PMID: 29273958; PMCID.

Curigliano G, Burstein HJ, P Winer E, et al. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. Ann Oncol. 2017 Aug 1;28(8):1700-1712. PMID: 28838210.

Dabbs DJ, Clark BZ, Serdy K, et al. Pathologist's health-care value in the triage of Oncotype DX® testing: a value-based pathology study of tumour biology with outcomes. Histopathology. 2018 Oct;73(4):692-700. doi: 10.1111/his.13690. Epub 2018 Aug 6. PMID: 29920746.

Denkert C, Kronenwett R, Schlake W, et al. Decentral gene expression analysis for ER+/Her2- breast cancer: results of a proficiency testing program for the EndoPredict assay. Virchows Arch. 2012 Mar; 460(3):251-259. PubMed PMID: 22371223.

Desmedt C, Piette F, Loi S, et al. Strong time dependence of the 76-gene prognostic signature for node-negative breast cancer patients in the TRANSBIG multicenter independent validation series. Clin Cancer Res. 2007 Jun 1;13(11):3207-14. doi: 10.1158/1078-0432.CCR-06-2765. PMID: 17545524.

Dowsett M, Sestak I, Lopez-Knowles E, et al. Comparison of PAM50 risk of recurrence score with oncotype DX and IHC4 for predicting risk of distant recurrence after endocrine therapy. J Clin Oncol. 2013 Aug 1;31(22):2783-90. doi: 10.1200/JCO.2012.46.1558. Epub 2013 Jul 1. PMID: 23816962.

Drukker CA, Bueno-de-Mesquita JM, Retèl VP, et al. A prospective evaluation of a breast cancer prognosis signature in the observational RASTER study. Int J Cancer. 2013 Aug 15;133(4):929-36. doi: 10.1002/ijc.28082. Epub 2013 Mar 4. PMID: 23371464.

Dubsky P, Filipits M, Jakesz R, et al. EndoPredict improves the prognostic classification derived from common clinical guidelines in ER-positive, HER2-negative early breast cancer. Ann Oncol. 2013 Mar;24(3):640-7. doi: 10.1093/annonc/mds334. Epub 2012 Oct 3. PMID: 23035151.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005 May 14-20;365(9472):1687-717. doi: 10.1016/S0140-6736(05)66544-0. PMID: 15894097.

Eiermann W, Rezai M, Kümmel S, et al. The 21-gene recurrence score assay impacts adjuvant therapy recommendations for ER-positive, node-negative and node-positive early breast cancer resulting in a risk-adapted change in chemotherapy use. Ann Oncol. 2013 Mar;24(3):618-24. doi: 10.1093/annonc/mds512. Epub 2012 Nov 7. PMID: 23136233.

Filipits M, Rudas M, Jakesz R, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. Clin Cancer Res. 2011 Sep 15;17(18):6012-20. doi: 10.1158/1078-0432.CCR-11-0926. Epub 2011 Aug 1. PMID: 21807638.

Giordano SH. Breast Cancer in Men. N Engl J Med. 2018 Jun 14;378(24):2311-2320. doi: 10.1056/NEJMra1707939. PMID: 29897847.

Green N, Al-Allak A, Fowler C. Benefits of introduction of Oncotype DX® testing. Ann R Coll Surg Engl. 2019 Jan;101(1):55-59. doi: 10.1308/rcsann.2018.0173. Epub 2018 Oct 16. PMID: 30322288.

Gustavsen G, Schroeder B, Kennedy P, et al. Health economic analysis of Breast Cancer Index in patients with ER+, LN- breast cancer. Am J Manag Care. 2014 Aug 1;20(8):e302-10. PMID: 25295793.

Hyams DM, Schuur E, Angel Aristizabal J, et al. Selecting postoperative adjuvant systemic therapy for early stage breast cancer: A critical assessment of commercially available gene expression assays. J Surg Oncol. 2017 May;115(6):647-662. doi: 10.1002/jso.24561. Epub 2017 Feb 17. PMID: 28211064.

Kalinsky K, Barlow W, Meric-Bernstam F, et al. GS3-00. First results from a phase III randomized clinical trial of standard adjuvant endocrine therapy (ET) +/- chemotherapy (CT) in patients (pts) with 1-3 positive nodes, hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer (BC) with recurrence score (RS) ≤25: SWOG S1007 (RxPonder). 2020 Dec 10: San Antonio Breast Cancer Symposium. https://www.sabcs.org/2020-SABCS.

Kalinsky K, Barlow WE, Gralow JR, et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. N Engl J Med. 2021 Dec 16;385(25):2336-2347. doi: 10.1056/NEJMoa2108873. Epub 2021 Dec 1. PMID: 34914339.

Knauer MSM, Rutgers EJT, Bender RA, et al. The 70-gene MammaPrint signature is predictive for chemotherapy benefit in early breast cancer. The Breast 2009;18:S36e7.

Kok M, Koornstra RH, Mook S, et al. Additional value of the 70-gene signature and levels of ER and PR for the prediction of outcome in tamoxifen-treated ER-positive breast cancer. Breast. 2012 Dec;21(6):769-78. doi: 10.1016/j.breast.2012.04.010. Epub 2012 Jun 26. PMID: 22738860.

Korde LA, Somerfield MR, Carey LA, et al. Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline. J Clin Oncol. 2021 Jan 28:JCO2003399. doi: 10.1200/JCO.20.03399. Epub ahead of print. PMID: 33507815.

Kronenwett R, Bohmann K, Prinzler J, et al. Decentral gene expression analysis: analytical validation of the Endopredict genomic multianalyte breast cancer prognosis test. BMC Cancer. 2012 Oct 5;12:456. PubMed PMID: 23039280.

Larson JS, Goodman LJ, Tan Y, et al. Analytical Validation of a Highly Quantitative, Sensitive, Accurate, and Reproducible Assay (HERmark) for the Measurement of HER2 Total Protein and HER2 Homodimers in FFPE Breast Cancer Tumor Specimens. Patholog Res Int. 2010 Jun 28;2010:814176. doi: 10.4061/2010/814176. PMID: 21151530.

Mamounas EP, Bandos H, Rastogi P, et al. Breast Cancer Index and Prediction of Extended Aromatase Inhibitor Therapy Benefit in Hormone Receptor-Positive Breast Cancer from the NRG Oncology/NSABP B-42 Trial. Clin Cancer Res. 2024 May 1;30(9):1984-1991. doi: 10.1158/1078-0432.CCR-23-1977. PMID: 38376912; PMCID: PMC11061597.

Markopoulos C. Overview of the use of Oncotype DX(®) as an additional treatment decision tool in early breast cancer. Expert Rev Anticancer Ther. 2013 Feb;13(2):179-94. doi: 10.1586/era.12.174. PMID: 23406559.

Martin M, Brase JC, Calvo L, et al. Clinical validation of the EndoPredict test in node-positive, chemotherapy-treated ER+/HER2- breast cancer patients: results from the GEICAM 9906 trial. Breast Cancer Res. 2014 Apr 12;16(2):R38. doi: 10.1186/bcr3642. PMID: 24725534.

Massarweh SA, Sledge GW, Miller DP, et al. Molecular Characterization and Mortality From Breast Cancer in Men. J Clin Oncol. 2018 May 10;36(14):1396-1404. doi: 10.1200/JCO.2017.76.8861. Epub 2018 Mar 27. PMID: 29584547.

Müller BM, Keil E, Lehmann A, et al. The EndoPredict Gene-Expression Assay in Clinical Practice – Performance and Impact on Clinical Decisions. PLoS One. 2013 Jun 27;8(6):e68252. doi: 10.1371/journal.pone.0068252. PMID: 23826382.

Paik S, Shak S, Tang G, et al. Multi-gene RT-PCR assay for predicting recurrence in node negative breast cancer patients – NSABP studies B-20 and B-14. Breast Cancer Res Treat. 2003 82(Suppl.)S10–S11.S11

Paik S, Shak S, Tang G, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004 Dec 30;351(27):2817-26. doi: 10.1056/NEJMoa041588. Epub 2004 Dec 10. PMID: 15591335.

Paik S, Tang G, Shak S, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol. 2006 Aug 10;24(23):3726-34. doi: 10.1200/JCO.2005.04.7985. Epub 2006 May 23. PMID: 16720680.

Phung MT, Tin Tin S, Elwood JM. Prognostic models for breast cancer: a systematic review. BMC Cancer. 2019 Mar 14;19(1):230. doi: 10.1186/s12885-019-5442-6. PMID: 30871490; PMCID: PMC6419427.

Piccart M, van ‘t Veer LJ, Poncet C, et al. 70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age. Lancet Oncol. 2021 Apr;22(4):476-488. doi: 10.1016/S1470-2045(21)00007-3. Epub 2021 Mar 12. PMID: 33721561.

Raman G, Avendano EE, Chen M. Update on Emerging Genetic Tests Currently Available for Clinical Use in Common Cancers. Evidence Report/Technology. (Prepared by the Tufts Evidence-based Practice Center under Contract No. 290-2007-10055-I.) Rockville, MD: Agency for Healthcare Research and Quality. July 2013. https://www.ncbi.nlm.nih.gov/books/NBK285327/

Ravdin P. Overview of randomized trials of systemic adjuvant therapy. Cancer Treat Res. 2008;141:55-62. doi: 10.1007/978-0-387-73161-2_4. PMID: 18274082.

Ribnikar D, Cardoso F. Tailoring Chemotherapy in Early-Stage Breast Cancer: Based on Tumor Biology or Tumor Burden? Am Soc Clin Oncol Educ Book. 2016;35:e31-8. doi: 10.1200/EDBK_159077. PMID: 27249737.

Rutgers E, Piccart-Gebhart MJ, Bogaerts J, et al. The EORTC 10041/BIG 03-04 MINDACT trial is feasible: results of the pilot phase. Eur J Cancer. 2011 Dec;47(18):2742-9. doi: 10.1016/j.ejca.2011.09.016. Epub 2011 Nov 1. PMID: 22051734.

Saghatchian M, Mook S, Pruneri G, et al. Additional prognostic value of the 70-gene signature (MammaPrint(®)) among breast cancer patients with 4-9 positive lymph nodes. Breast. 2013 Oct;22(5):682-90. doi: 10.1016/j.breast.2012.12.002. Epub 2013 Jan 21. PMID: 23347730.

Sapino A, Roepman P, Linn SC, et al. MammaPrint molecular diagnostics on formalin-fixed, paraffin-embedded tissue. J Mol Diagn. 2014 Mar;16(2):190-7. doi: 10.1016/j.jmoldx.2013.10.008. Epub 2013 Dec 28. PMID: 24378251.

Scope A, Essat M, Pandor A,et al. Gene Expression Profiling and expanded immunohistochemistry tests to guide selection of chemotherapy regimens in breast cancer management: A Systematic Review. Int J Technol Assess Health Care. 2017 Jan;33(1):32-45. doi: 10.1017/S0266462317000034. Epub 2017 May 10. PMID: 28486999.

Senkus E, Kyriakides S, Ohno S, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015; 26(Suppl 5):v8–v30. PubMed PMID: 26314782.

Sestak I, Buus R, Cuzick J, et al. Comparison of the performance of 6 prognostic signatures for estrogen receptor-positive breast cancer: A secondary analysis of a randomized clinical trial. JAMA Oncol. 2018 Apr 1;4(4):545-553. PMID: 29450494.

Sgroi DC, Sestak I, Cuzick J, et al. Prediction of late distant recurrence in patients with oestrogen-receptor-positive breast cancer: a prospective comparison of the breast-cancer index (BCI) assay, 21-gene recurrence score, and IHC4 in the TransATAC study population. Lancet Oncol. 2013 Oct;14(11):1067-1076. doi: 10.1016/S1470-2045(13)70387-5. Epub 2013 Sep 12. Erratum in: Lancet Oncol. 2018 Apr;19(4):e184. PMID: 24035531.

Sgroi DC, Treuner K, Zhang Y, et al. Correlative studies of the Breast Cancer Index (HOXB13/IL17BR) and ER, PR, AR, AR/ER ratio and Ki67 for prediction of extended endocrine therapy benefit: a Trans-aTTom study. Breast Cancer Res. 2022 Dec 16;24(1):90. doi: 10.1186/s13058-022-01589-x. PMID: 36527133; PMCID: PMC9758861.

Sinn P, Aulmann S, Wirtz R, et al. Multigene Assays for Classification, Prognosis, and Prediction in Breast Cancer: a Critical Review on the Background and Clinical Utility. Geburtshilfe Frauenheilkd. 2013 Sep;73(9):932-940. doi: 10.1055/s-0033-1350831. PMID: 24771945.

Sparano JA, Paik S. Development of the 21-gene assay and its application in clinical practice and clinical trials. J Clin Oncol. 2008 Feb 10;26(5):721-8. doi: 10.1200/JCO.2007.15.1068. PMID: 18258979.

Sparano JA, Gray RJ, Makower DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. 2015 Nov 19;373(21):2005-14. doi: 10.1056/NEJMoa1510764. Epub 2015 Sep 27. PMID: 26412349.

Sparano JA, Gray RJ, Makower DF, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. 2018 Jul 12;379(2):111-121. doi: 10.1056/NEJMoa1804710. Epub 2018 Jun 3. PMID: 29860917.

Sparano JA, Gray RJ, Ravdin PM, et al. Clinical and Genomic Risk to Guide the Use of Adjuvant Therapy for Breast Cancer. N Engl J Med. 2019 Jun 20;380(25):2395-2405. doi: 10.1056/NEJMoa1904819. Epub 2019 Jun 3. PMID: 31157962.

Stoppa-Lyonnet D. The biological effects and clinical implications of BRCA mutations: where do we go from here? Eur J Hum Genet. 2016 Sep;24 Suppl 1(Suppl 1):S3-9. doi: 10.1038/ejhg.2016.93. PMID: 27514841.

Turashvili G, Gonzalez-Loperena M, Brogi E, et al. The 21-Gene Recurrence Score in Male Breast Cancer. Ann Surg Oncol. 2018 Jun;25(6):1530-1535. doi: 10.1245/s10434-018-6411-z. Epub 2018 Mar 8. PMID: 29520654.

Tutt A, Wang A, Rowland C, et al. Risk estimation of distant metastasis in node-negative, estrogen receptor-positive breast cancer patients using an RT-PCR based prognostic expression signature. BMC Cancer. 2008 Nov 21;8:339. doi: 10.1186/1471-2407-8-339. PMID: 19025599.

Varga Z, Sinn P, Seidman AD. Summary of head-to-head comparisons of patient risk classifications by the 21-gene Recurrence Score® (RS) assay and other genomic assays for early breast cancer. Int J Cancer. 2019 Aug 15;145(4):882-893. doi: 10.1002/ijc.32139. Epub 2019 Feb 12. PMID: 30653259.

Wang SY, Dang W, Richman I, et al. Cost-Effectiveness Analyses of the 21-Gene Assay in Breast Cancer: Systematic Review and Critical Appraisal. J Clin Oncol. 2018 Jun 1;36(16):1619-1627. doi: 10.1200/JCO.2017.76.5941. Epub 2018 Apr 16. PMID: 29659329.

Wang Y, Klijn JG, Zhang Y, et al. Gene-expression profiles to predict distant metastasis of lymph-node-negative primary breast cancer. Lancet. 2005 Feb 19-25;365(9460):671-9. doi: 10.1016/S0140-6736(05)17947-1. PMID: 15721472.

Whitney J, Corredor G, Janowczyk A,et al. Quantitative nuclear histomorphometry predicts oncotype DX risk categories for early stage ER+ breast cancer. BMC Cancer. 2018 May 30;18(1):610. doi: 10.1186/s12885-018-4448-9. PMID: 29848291.

Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. 2013 Nov 1;31(31):3997-4013. doi: 10.1200/JCO.2013.50.9984. Epub 2013 Oct 7. PMID: 24101045.

Zhang Y, Schnabel CA, Schroeder BE, et al. Breast cancer index identifies early-stage estrogen receptor-positive breast cancer patients at risk for early- and late-distant recurrence. Clin Cancer Res. 2013 Aug 1;19(15):4196-205. doi: 10.1158/1078-0432.CCR-13-0804. Epub 2013 Jun 11. PMID: 23757354.

Prostate Cancer

Aubin SM, Reid J, Sarno MJ, et al. PCA3 molecular urine test for predicting repeat prostate biopsy outcome in populations at risk: validation in the placebo arm of the dutasteride REDUCE trial. J Urol. 2010 Nov;184(5):1947-52. doi: 10.1016/j.juro.2010.06.098. Epub 2010 Sep 17. PMID: 20850153.

Banerjee, Punnen S. A review on the role of tissue-based molecular biomarkers for active surveillance. World J Urol. 2022 Jan;40(1):27-34. doi: 10.1007/s00345-021-03610-y. Epub 2021 Feb 15. PMID: 33590277.

Bishoff JT, Freedland SJ, Gerber L, et al. Prognostic utility of the cell cycle progression score generated from biopsy in men treated with prostatectomy. J Urol. 2014 Aug;192(2):409-14. doi: 10.1016/j.juro.2014.02.003. Epub 2014 Feb 7. PMID: 24508632.

Board WCoTE. WHO Classification of Tumours Urinary and Male Genital Tumours. 5th ed. Lyon (France): International Agency for Research on Cancer, 2022

Boström PJ, Bjartell AS, Catto JW, et al. Genomic Predictors of Outcome in Prostate Cancer. Eur Urol. 2015 Dec;68(6):1033-44. doi: 10.1016/j.eururo.2015.04.008. Epub 2015 Apr 23. PMID: 25913390.

Broenimann S, Pradere B, Karakiewicz P, et al. An overview of current and emerging diagnostic, staging and prognostic markers for prostate cancer. Expert Rev Mol Diagn. 2020 Aug;20(8):841-850. doi: 10.1080/14737159.2020.1785288. Epub 2020 Jun 25. PMID: 32552088.

Cooperberg MR, Simko JP, Cowan, et al. Validation of a cell-cycle progression gene panel to improve risk stratification in a contemporary prostatectomy cohort. J Clin Oncol. 2013 Apr 10;31(11):1428-34. doi: 10.1200/JCO.2012.46.4396. Epub 2013 Mar 4. PMID: 23460710.

Crawford ED, Scholz MC, Kar AJ, et al. Cell cycle progression score and treatment decisions in prostate cancer: results from an ongoing registry. Curr Med Res Opin. 2014 Jun;30(6):1025-31. doi: 10.1185/03007995.2014.899208. Epub 2014 Mar 13. PMID: 24576172.

Cucchiara V, Cooperberg MR, Dall'Era M, et al. Genomic Markers in Prostate Cancer Decision Making. Eur Urol. 2018 Apr;73(4):572-582. doi: 10.1016/j.eururo.2017.10.036. Epub 2017 Nov 10. Review. PMID: 29129398.

Cuzick J, Berney DM, Fisher G, et al. Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort. Br J Cancer. 2012 Mar 13;106(6):1095-9. doi: 10.1038/bjc.2012.39. Epub 2012 Feb 23. PMID: 22361632; PMCID: PMC3304411.

Cuzick J, Swanson GP, Fisher G, et al. Prognostic value of an RNA expression signature derived from cell cycle proliferation genes in patients with prostate cancer: a retrospective study. Lancet Oncol. 2011 Mar;12(3):245-55. doi: 10.1016/S1470-2045(10)70295-3. PMID: 21310658; PMCID: PMC3091030.

Cuzick J, Thorat MA, Andriole G, et al. Prevention and early detection of prostate cancer. Lancet Oncol. 2014 Oct;15(11):e484-92. doi: 10.1016/S1470-2045(14)70211-6. PMID: 25281467; PMCID: PMC4203149.

Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline, Part I: Introduction, Risk Assessment, Staging, and Risk-Based Management. J Urol. 2022 Jul;208(1):10-18. doi: 10.1097/JU.0000000000002757. Epub 2022 May 10. PMID: 35536144.

Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline, Part II: Principles of Active Surveillance, Principles of Surgery, and Follow-Up. J Urol. 2022 Jul;208(1):19-25. doi: 10.1097/JU.0000000000002758. Epub 2022 May 10. PMID: 35536148.

Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline. Part III: Principles of Radiation and Future Directions. J Urol. 2022 Jul;208(1):26-33. doi: 10.1097/JU.0000000000002759. Epub 2022 May 10. PMID: 35536141.

Eggener SE, Rumble RB, Armstrong AJ, et al. Molecular Biomarkers in Localized Prostate Cancer: ASCO Guideline. J Clin Oncol. 2020 May 1;38(13):1474-1494. doi: 10.1200/JCO.19.02768. Epub 2019 Dec 12. PMID: 31829902.

Falzarano SM, Ferro M, Bollito E, et al. Novel biomarkers and genomic tests in prostate cancer: a critical analysis. Minerva Urol Nefrol. 2015 Sep;67(3):211-31. Epub 2015 Jun 9. PMID: 26054411.

Feng FY, Huang HC, Spratt DE, et al. Validation of a 22-Gene Genomic Classifier in Patients With Recurrent Prostate Cancer: An Ancillary Study of the NRG/RTOG 9601 Randomized Clinical Trial. JAMA Oncol. 2021 Apr 1;7(4):544-552. doi: 10.1001/jamaoncol.2020.7671. Erratum in: JAMA Oncol. 2021 Apr 1;7(4):639. PMID: 33570548; PMCID: PMC7879385.

Freedland SJ, Gerber L, Reid J, et al. Prognostic utility of cell cycle progression score in men with prostate cancer after primary external beam radiation therapy. Int J Radiat Oncol Biol Phys. 2013 Aug 1;86(5):848-53. doi: 10.1016/j.ijrobp.2013.04.043. Epub 2013 Jun 5. PMID: 23755923; PMCID: PMC3710548.

Geybels MS, Wright JL, Bibikova M, et al. Epigenetic signature of Gleason score and prostate cancer recurrence after radical prostatectomy. Clin Epigenetics. 2016 Sep 15;8:97. doi: 10.1186/s13148-016-0260-z. PMID: 27651837; PMCID: PMC5024414.

Herlemann A, Washington SL 3rd, Eapen RS, et al. Whom to Treat: Postdiagnostic Risk Assessment with Gleason Score, Risk Models, and Genomic Classifier. Urol Clin North Am. 2017 Nov;44(4):547-555. doi: 10.1016/j.ucl.2017.07.003. PMID: 29107271.

Jairath NK, Dal Pra A, Vince R Jr, et al. A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer. Eur Urol. 2021 Mar;79(3):374-383. doi: 10.1016/j.eururo.2020.11.021. Epub 2020 Dec 5. PMID: 33293078.

Kim H, Alshalalfa M, Hoffman-Censits J, et al. Potential Impact on Clinical Decision Making via a Genome-Wide Expression Profiling: A Case Report. Urol Case Rep. 2016 Oct 1;9:51-54. doi: 10.1016/j.eucr.2016.08.010. PMID: 27713863; PMCID: PMC5050262.

Kim SP, Meropol NJ, Gross CP, et al. Physician attitudes about genetic testing for localized prostate cancer: A national survey of radiation oncologists and urologists. Urol Oncol. 2018 Nov;36(11):501.e15-501.e21. doi: 10.1016/j.urolonc.2018.07.002. Epub 2018 Sep 3. PMID: 30190177.

Kretschmer A, Tilki D. Biomarkers in prostate cancer – Current clinical utility and future perspectives. Crit Rev Oncol Hematol. 2017 Dec;120:180-193. doi: 10.1016/j.critrevonc.2017.11.007. Epub 2017 Nov 13. PMID: 29198331.

Lamy PJ, Allory Y, Gauchez AS, et al. Prognostic Biomarkers Used for Localised Prostate Cancer Management: A Systematic Review. Eur Urol Focus. 2018 Dec;4(6):790-803. doi: 10.1016/j.euf.2017.02.017. Epub 2017 Mar 7. PMID: 28753865.

Leapman MS, Nguyen HG, Cowan JE, et al. Comparing Prognostic Utility of a Single-marker Immunohistochemistry Approach with Commercial Gene Expression Profiling Following Radical Prostatectomy. Eur Urol. 2018 Nov;74(5):668-675. doi: 10.1016/j.eururo.2018.08.020. Epub 2018 Sep 1. PMID: 30181067.

Lin DW, Nelson PS. Prognostic Genomic Biomarkers in Patients With Localized Prostate Cancer: Is Rising Utilization Justified by Evidence? JAMA Oncol. 2021 Jan 1;7(1):59-60. doi: 10.1001/jamaoncol.2020.6045. PMID: 33237305.

Moschini M, Spahn M, Mattei A, et al. Incorporation of tissue-based genomic biomarkers into localized prostate cancer clinics. BMC Med. 2016 Apr 4;14:67. doi: 10.1186/s12916-016-0613-7. PMID: 27044421; PMCID: PMC4820857.

Narayan VM, Konety BR, Warlick C. Novel biomarkers for prostate cancer: An evidence-based review for use in clinical practice. Int J Urol. 2017 May;24(5):352-360. doi: 10.1111/iju.13326. Epub 2017 Mar 27. PMID: 28345187.

Paziewska A, Dabrowska M, Goryca K, et al. DNA methylation status is more reliable than gene expression at detecting cancer in prostate biopsy. Br J Cancer. 2014 Aug 12;111(4):781-9. doi: 10.1038/bjc.2014.337. Epub 2014 Jun 17. PMID: 24937670; PMCID: PMC4134497.

Shore N, Concepcion R, Saltzstein D, et al. Clinical utility of a biopsy-based cell cycle gene expression assay in localized prostate cancer. Curr Med Res Opin. 2014 Apr;30(4):547-53. doi: 10.1185/03007995.2013.873398. Epub 2013 Dec 23. PMID: 24320750.

Stewart GD, Van Neste L, Delvenne P, et al. Clinical utility of an epigenetic assay to detect occult prostate cancer in histopathologically negative biopsies: results of the MATLOC study. J Urol. 2013 Mar;189(3):1110-6. doi: 10.1016/j.juro.2012.08.219. Epub 2012 Oct 8. PMID: 22999998.

Trock BJ, Brotzman MJ, Mangold LA, et al. Evaluation of GSTP1 and APC methylation as indicators for repeat biopsy in a high-risk cohort of men with negative initial prostate biopsies. BJU Int. 2012 Jul;110(1):56-62. doi: 10.1111/j.1464-410X.2011.10718.x. Epub 2011 Nov 11. PMID: 22077694; PMCID: PMC3397791.

General Tumor Testing (Solid Tumor)

American Association of Cancer Research. Entrectinib OK'd for Cancers with *NTRK* Fusions, NSCLC. Cancer Discov. 2019 Oct;9(10):OF2. doi: 10.1158/2159-8290.CD-NB2019-101. Epub 2019 Aug 30. PMID: 31471291.

Bombard Y, Bach PB, Offit K. Translating genomics in cancer care. J Natl Compr Canc Netw. 2013 Nov;11(11):1343-53. doi: 10.6004/jnccn.2013.0158. PMID: 24225968.

Chakravarty D, Johnson A, Sklar J, et al. Somatic Genomic Testing in Patients With Metastatic or Advanced Cancer: ASCO Provisional Clinical Opinion. J Clin Oncol. 2022 Feb 17:JCO2102767. doi: 10.1200/JCO.21.02767. Epub ahead of print. PMID: 35175857.

Deverka P, Messner DA, McCormack R, et al. Generating and evaluating evidence of the clinical utility of molecular diagnostic tests in oncology. Genet Med. 2016 Aug;18(8):780-7. doi: 10.1038/gim.2015.162. Epub 2015 Dec 3. Erratum in: Genet Med. 2016 Jun;18(6):650. PMID: 26633547.

Febbo PG, Ladanyi M, Aldape KD, et al. NCCN Task Force report: Evaluating the clinical utility of tumor markers in oncology. J Natl Compr Canc Netw. 2011 Nov;9 Suppl 5:S1-32; quiz S33. doi: 10.6004/jnccn.2011.0137. PMID: 22138009.

Fizazi K, Greco FA, Pavlidis N, et al. Cancers of unknown primary site: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015 Sep;26 Suppl 5:v133-8. doi: 10.1093/annonc/mdv305. PMID: 26314775.

Flaherty KT, Le DT, Lemery S. Tissue-Agnostic Drug Development. Am Soc Clin Oncol Educ Book. 2017;37:222-230. doi: 10.14694/EDBK_173855. PMID: 28561648.

Joseph L. The clinical utility of molecular genetic cancer profiling. Expert Rev Mol Diagn. 2016 Aug;16(8):827-38. doi: 10.1080/14737159.2016.1197120. Epub 2016 Jun 20. PMID: 27253039.

Klauschen F, Heim D, Stenzinger A. Histological tumor typing in the age of molecular profiling. Pathol Res Pract. 2015 Dec;211(12):897-900. doi: 10.1016/j.prp.2015.08.001. Epub 2015 Sep 5. PMID: 26589872.

Nagahashi M, Shimada Y, Ichikawa H, et al. Next generation sequencing-based gene panel tests for the management of solid tumors. Cancer Sci. 2019 Jan;110(1):6-15. Epub 2018 Nov 27. Review. PMID: 30338623.

Strom SP. Current practices and guidelines for clinical next-generation sequencing oncology testing. Cancer Biol Med. 2016 Mar;13(1):3-11. doi: 10.28092/j.issn.2095-3941.2016.0004. PMID: 27144058.

Testing for Tumor Agnostic Therapies

American Association of Cancer Research. Entrectinib OK'd for Cancers with NTRK Fusions, NSCLC. Cancer Discov. 2019 Aug 30. doi: 10.1158/2159-8290.CD-NB2019-101. [Epub ahead of print] PubMed PMID: 31471291.

Bartley AN, Mills AM, Konnick E, et al. Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy. Arch Pathol Lab Med. 2022 Aug 3. doi: 10.5858/arpa.2021-0632-CP. Epub ahead of print. PMID: 35920830.

Chakravarty D, Johnson A, Sklar J, et al. Somatic Genomic Testing in Patients With Metastatic or Advanced Cancer: ASCO Provisional Clinical Opinion. J Clin Oncol. 2022 Feb 17:JCO2102767. doi: 10.1200/JCO.21.02767. Epub ahead of print. PMID: 35175857.

Chalmers ZR, Connelly CF, Fabrizio D, et al. Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden. Genome Med. 2017 Apr 19;9(1):34. doi: 10.1186/s13073-017-0424-2. PMID: 28420421; PMCID: PMC5395719.

Cocco E, Scaltriti M, Drilon A. NTRK fusion-positive cancers and TRK inhibitor therapy. Nature Reviews. 2018 Dec;15(12):731-747. PMID: 30333516.

Devereaux KA, Charu V, Zhao S, et al. Immune checkpoint blockade as a potential therapeutic strategy for undifferentiated malignancies. Hum Pathol. 2018 Dec;82:39-45. doi: 10.1016/j.humpath.2018.06.034. Epub 2018 Jul 7. PMID: 30539796.

Flaherty KT, Le DT, Lemery S. Tissue-Agnostic Drug Development. Am Soc Clin Oncol Educ Book. 2017;37:222-230. doi: 10.14694/EDBK_173855. PMID: 28561648.

Food and Drug Administration (FDA), (2015) FDA approves third oncology drug that targets a key genetric driver of cancer, rather than a specific type of tumor. Available from <https://www.fda.gov/news-events/press-announcements/fda-approves-third-oncology-drug-targets-key-genetic-driver-cancer-rather-specific-type-tumor#:~:text=The%20U.S.%20Food%20and%20Drug,there%20are%20no%20effective%20treatments> [11 July 2022]

Food and Drug Administration (FDA), (2018) FDA approves an oncology drug that targets a key genetic driver of cancer, rather than a specific type of tumor. Available from <https://www.fda.gov/news-events/press-announcements/fda-approves-oncology-drug-targets-key-genetic-driver-cancer-rather-specific-type-tumor#:~:text=Vitrakvi%20is%20indicated%20for%20the,morbidity%20and%20have%20no%20satisfactory> [11 July 2022]

Food and Drug Administration (FDA), (2022) FDA grants accelerated approval to dabrafenib in combination with trametinib for unresectable or metastatic solid tumors with BRAF V600E mutation. Available from <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dabrafenib-combination-trametinib-unresectable-or-metastatic-solid> [22 June 2022]

Food and Drug Administration (FDA), (2022) FDA approves selpercatinib for locally advanced or metastatic RET fusion-positive solid tumors. Available from <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-selpercatinib-locally-advanced-or-metastatic-ret-fusion-positive-solid-tumors> [21 Sept 2022]

Furtado LV, Bifulco C, Dolderer D, et al. Recommendations for Tumor Mutational Burden Assay Validation and Reporting: A Joint Consensus Recommendation of the Association for Molecular Pathology, College of American

Pathologists, and Society for Immunotherapy of Cancer. J Mol Diagn. 2024 Jun 6:S1525-1578(24)00115-6. doi: 10.1016/j.jmoldx.2024.05.002. Epub ahead of print. PMID: 38851389.

Haslam A, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs. JAMA Netw Open. 2019 May 3;2(5):e192535. doi: 10.1001/jamanetworkopen.2019.2535. PMID: 31050774; PMCID: PMC6503493.

Hechtman J, Benayed R, Hyman D, et al. Pan-Trk Immunohistochemistry is an efficient and reliable screen for the detection of NTRK fusions. Am J Surg Pathol. 2017 Nov; 41(11): 1547-1551. PMID: 28719467

Kunitomi H, Banno K, Yanokura M, et al. New use of microsatellite instability analysis in endometrial cancer. Oncol Lett. 2017 Sep;14(3):3297-3301. doi: 10.3892/ol.2017.6640. Epub 2017 Jul 20. PMID: 28927079; PMCID: PMC5587995.

Laetsch T, Hawkins D. Larotrectinib for the treatment of TRK fusion solid tumors. Expert Review of Anticancer Therapy. 2018 Oct 23:1-10. PMID: 30350734.

Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. N Engl J Med. 2015 Jun 25;372(26):2509-20. doi: 10.1056/NEJMoa1500596. Epub 2015 May 30. PMID: 26028255; PMCID: PMC4481136.

Luchini C, Bibeau F, Ligtenberg MJL, et al. ESMO recommendations on microsatellite instability testing for immunotherapy in cancer, and its relationship with PD-1/PD-L1 expression and tumour mutational burden: a systematic review-based approach. Ann Oncol. 2019 May 6. pii: mdz116. doi: 10.1093/annonc/mdz116. [Epub ahead of print] PMID: 31056702.

Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol. 2020 Oct;21(10):1353-1365. doi: 10.1016/S1470-2045(20)30445-9. Epub 2020 Sep 10. PMID: 32919526.

McGrail DJ, Pilie PG, Rashid NU, et al. High tumor mutation burden fails to predict immune checkpoint blockade response across all cancer types. Ann Oncol. 2021 May;32(5):661-672. doi: 10.1016/j.annonc.2021.02.006. Epub 2021 Mar 15. PMID: 33736924; PMCID: PMC8053682.

Morris V, Kopetz S. BRAF inhibitors in clinical oncology. F1000Prime Rep. 2013 Apr 2;5:11. doi: 10.12703/P5-11. PMID: 23585929; PMCID: PMC3619157.

Mosele MF, Westphalen CB, Stenzinger A, et al. Recommendations for the use of next-generation sequencing (NGS) for patients with advanced cancer in 2024: a report from the ESMO Precision Medicine Working Group. Ann Oncol. 2024 Jul;35(7):588-606. doi: 10.1016/j.annonc.2024.04.005. Epub 2024 May 27. PMID: 38834388.

Ottaviano M, Giunta EF, Tortora M, et al. BRAF Gene and Melanoma: Back to the Future. Int J Mol Sci. 2021 Mar 27;22(7):3474. doi: 10.3390/ijms22073474. PMID: 33801689; PMCID: PMC8037827.

Raez LE, Santos ES. Tumor Type-Agnostic Treatment and the Future of Cancer Therapy. Target Oncol. 2018 Oct;13(5):541-544. doi: 10.1007/s11523-018-0593-y. PMID: 30302723.

Resser J, Martin D, Miya J, et al. Validation of a targeted RNA sequencing assay for kinase fusion detection in solid tumors. J Mol Diagn. 2017 Sep; 19(5): 682-696. PMID: 28802831.

Romero D. Activity of selpercatinib in RET fusion-positive cancers confirmed. Nat Rev Clin Oncol. 2022 Oct 7. doi: 10.1038/s41571-022-00694-2. Epub ahead of print. PMID: 36207414.

Rousseau B, Foote MB, Maron SB, et al. The Spectrum of Benefit from Checkpoint Blockade in Hypermutated Tumors. N Engl J Med. 2021 Mar 25;384(12):1168-1170. doi: 10.1056/NEJMc2031965. PMID: 33761214.

Rudzinski ER, Lockwood CM, Stohr BA, et al. Pan-trk immunohistochemistry identifies NTRK rearrangements in pediatric mesenchymal tumors. Am J Surg Pathol. 2018 Jul;42(7):927-935. PubMed PMID: 29683818.

Samstein RM, Lee CH, Shoushtari AN, et al. Tumor mutational load predicts survival after immunotherapy across multiple cancer types. Nat Genet. 2019 Feb;51(2):202-206. doi: 10.1038/s41588-018-0312-8. Epub 2019 Jan 14. PMID: 30643254; PMCID: PMC6365097.

Singh N, Daly ME, Ismaila N; Management of Stage III NSCLC Guideline Expert Panel. Management of Stage III Non-Small-Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update. J Clin Oncol. 2023 Sep 20;41(27):4430-4432. doi: 10.1200/JCO.23.01261. Epub 2023 Jul 20. PMID: 37471673.

Strickler JH, Hanks BA, Khasraw M. Tumor Mutational Burden as a Predictor of Immunotherapy Response: Is More Always Better? Clin Cancer Res. 2021 Mar 1;27(5):1236-1241. doi: 10.1158/1078-0432.CCR-20-3054. Epub 2020 Nov 16. PMID: 33199494.

Subbiah V, Wolf J, Konda B, et al. Tumour-agnostic efficacy and safety of selpercatinib in patients with RET fusion-positive solid tumours other than lung or thyroid tumours (LIBRETTO-001): a phase 1/2, open-label, basket trial. Lancet Oncol. 2022 Oct;23(10):1261-1273. doi: 10.1016/S1470-2045(22)00541-1. Epub 2022 Sep 12. PMID: 36108661.

Sung WWY, Chow JCH, Cho WCS. Tumor mutational burden as a tissue-agnostic biomarker for cancer immunotherapy. Expert Rev Clin Pharmacol. 2020 Dec 23:1-3. doi: 10.1080/17512433.2021.1865797. Epub ahead of print. PMID: 33322961.

Sung MT, Wang YH, Li CF. Open the Technical Black Box of Tumor Mutational Burden (TMB): Factors Affecting Harmonization and Standardization of Panel-Based TMB. Int J Mol Sci. 2022 May 3;23(9):5097. doi: 10.3390/ijms23095097. PMID: 35563486; PMCID: PMC9103036.

Toh JWT, de Souza P, Lim SH, et al. The Potential Value of Immunotherapy in Colorectal Cancers: Review of the Evidence for Programmed Death-1 Inhibitor Therapy. Clin Colorectal Cancer. 2016 Dec;15(4):285-291. doi: 10.1016/j.clcc.2016.07.007. Epub 2016 Jul 22. PMID: 27553906.

Vaishnavi A, Le AT, Doebele RC. TRKing down an old oncogene in a new era of targeted therapy. Cancer Discov. 2015 Jan;5(1):25-34. PMID: 25527197.

Vega DM, Yee LM, McShane LM, et al. Aligning tumor mutational burden (TMB) quantification across diagnostic platforms: phase II of the Friends of Cancer Research TMB Harmonization Project. Ann Oncol. 2021 Oct 1:S0923-7534(21)04495-1. doi: 10.1016/j.annonc.2021.09.016. Epub ahead of print. PMID: 34606929.

Verrienti A, Grani G, Sponziello M, et al. Precision oncology for RET-related tumors. Front Oncol. 2022 Aug 24;12:992636. doi: 10.3389/fonc.2022.992636. PMID: 36091144; PMCID: PMC9449844.

Vikas P, Messersmith H, Compton C, et al. Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy: ASCO Endorsement of College of American Pathologists Guideline. J Clin Oncol. 2023 Jan 5:JCO2202462. doi: 10.1200/JCO.22.02462. Epub ahead of print. PMID: 36603179.

WHO Classification of Tumours Editorial Board. Head and neck tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2023. (WHO classification of tumours series, 5th ed.; vol. 9). Available from: https://tumourclassification.iarc.who.int/chapters/52.

Wu YL, Dziadziuszko R, Ahn JS, et al; ALINA Investigators. Alectinib in Resected ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2024 Apr 11;390(14):1265-1276. doi: 10.1056/NEJMoa2310532. PMID: 38598794.

Yan L, Zhang, W. Precision medicine becomes reality-tumor type-agnostic therapy. Cancer Commun (Lond). 2018 Mar 31;38(1):6. PMID: 2976449.

Yarchoan M, Albacker LA, Hopkins AC, et al. PD-L1 expression and tumor mutational burden are independent biomarkers in most cancers. JCI Insight. 2019 Mar 21;4(6):e126908. doi: 10.1172/jci.insight.126908. PMID: 30895946; PMCID: PMC6482991.

Yoshino T, Pentheroudakis G, Mishima S, et al. JSCO-ESMO-ASCO-JSMO-TOS: international expert consensus recommendations for tumour-agnostic treatments in patients with solid tumours with microsatellite instability or NTRK fusions. Ann Oncol. 2020 Apr 6:S0923-7534(20)36386-9. doi: 10.1016/j.annonc.2020.03.299. Epub ahead of print. PMID: 32272210.

Circulating Tumor DNA (ctDNA)

Bradley SH, Barclay ME. “Liquid biopsy” for cancer screening. BMJ. 2021 Jan 4;372:m4933. doi: 10.1136/bmj.m4933. PMID: 33397684.

Chaudhuri AA, Chabon JJ, Lovejoy AF, et al. Early Detection of Molecular Residual Disease in Localized Lung Cancer by Circulating Tumor DNA Profiling. Cancer Discov. 2017 Dec;7(12):1394-1403. doi: 10.1158/2159-8290.CD-17-0716. Epub 2017 Sep 24. PMID: 28899864; PMCID: PMC5895851.

Cheng MM, Palma JF, Scudder S, et al. The Clinical and Economic Impact of Inaccurate EGFR Mutation Tests in the Treatment of Metastatic Non-Small Cell Lung Cancer. J Pers Med. 2017 Jun 28;7(3):5. doi: 10.3390/jpm7030005. PMID: 28657610; PMCID: PMC5618152.

De Rubis G, Krishnan SR, Bebawy M. Circulating tumor DNA – Current state of play and future perspectives. Pharmacol Res. 2018 Oct;136:35-44. doi: 10.1016/j.phrs.2018.08.017. Epub 2018 Aug 22. PMID: 30142423.

Dong S, Wang Z, Zhang et al. Circulating Tumor DNA-Guided De-Escalation Targeted Therapy for Advanced Non-Small Cell Lung Cancer: A Nonrandomized Clinical Trial. JAMA Oncol. 2024 Jun 13. doi: 10.1001/jamaoncol.2024.1779. Epub ahead of print. PMID: 38869865.

Gouton E, Malissen N, Andre N, et al. Clinical Impact of High Throughput Sequencing on Liquid Biopsy in Advanced Solid Cancer. Curr Oncol. 2022 Mar 10;29(3):1902-1918. doi: 10.3390/curroncol29030155. PMID: 35323355; PMCID: PMC8947301.

Hanna N, Johnson D, Temin S, et al. Systemic Therapy for Stage IV Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2017 Oct 20;35(30):3484-3515. doi: 10.1200/JCO.2017.74.6065. Epub 2017 Aug 14. Erratum in: J Clin Oncol. 2018 Jan 20;36(3):304. PMID: 28806116.

Iams WT, Mackay M, Ben-Shachar R, et al. Concurrent Tissue and Circulating Tumor DNA Molecular Profiling to Detect Guideline-Based Targeted Mutations in a Multicancer Cohort. JAMA Netw Open. 2024 Jan 2;7(1):e2351700. doi: 10.1001/jamanetworkopen.2023.51700. PMID: 38252441; PMCID: PMC10804266.

Janku F, Huang HJ, Claes B, et al. BRAF Mutation Testing in Cell-Free DNA from the Plasma of Patients with Advanced Cancers Using a Rapid, Automated Molecular Diagnostics System. Mol Cancer Ther. 2016 Jun;15(6):1397-404. doi: 10.1158/1535-7163.MCT-15-0712. Epub 2016 May 20. PMID: 27207774.

Kalemkerian GP, Narula N, Kennedy EB, et al. Molecular Testing Guideline for the Selection of Patients With Lung Cancer for Treatment With Targeted Tyrosine Kinase Inhibitors: American Society of Clinical Oncology Endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline Update. J Clin Oncol. 2018 Mar 20;36(9):911-919. doi: 10.1200/JCO.2017.76.7293. Epub 2018 Feb 5. PMID: 29401004.

Keller L, Belloum Y, Wikman H, et al. Clinical relevance of blood-based ctDNA analysis: mutation detection and beyond. Br J Cancer. 2021 Jan;124(2):345-358. doi: 10.1038/s41416-020-01047-5. Epub 2020 Sep 24. PMID: 32968207.

Klein EA, Richards D, Cohn A, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Ann Oncol. 2021 Jun 23:S0923-7534(21)02046-9. PMID: 34176681.

Lin LH, Allison DHR, Feng Y, et al. Comparison of solid tissue sequencing and liquid biopsy accuracy in identification of clinically relevant gene mutations and rearrangements in lung adenocarcinomas. Mod Pathol. 2021 Aug 6. doi: 10.1038/s41379-021-00880-0. Epub ahead of print. PMID: 34362997.

Lindeman NI, Cagle PT, Aisner DL, et al. Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors: Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. J Mol Diagn. 2018 Mar;20(2):129-159. doi: 10.1016/j.jmoldx.2017.11.004. Epub 2018 Jan 23. PMID: 29398453.

Merker JD, Oxnard GR, Compton C, et al. Circulating Tumor DNA Analysis in Patients With Cancer: American Society of Clinical Oncology and College of American Pathologists Joint Review. J Clin Oncol. 2018 Jun 1;36(16):1631-1641. doi: 10.1200/JCO.2017.76.8671. Epub 2018 Mar 5. PMID: 29504847.

Pascual J, Attard G, Bidard FC, et al. ESMO recommendations on the use of circulating tumour DNA assays for patients with cancer: a report from the ESMO Precision Medicine Working Group. Ann Oncol. 2022 Aug;33(8):750-768. doi: 10.1016/j.annonc.2022.05.520. Epub 2022 Jul 6. PMID: 35809752.

Post C, Braun TP, Etzioni R, et al. Multicancer Early Detection Tests: An Overview of Early Results From Prospective Clinical Studies and Opportunities for Oncologists. JCO Oncol Pract. 2023 Dec;19(12):1111-1115. doi: 10.1200/OP.23.00260. Epub 2023 Oct 18. PMID: 37851937.

Raoof S, Kennedy CJ, Wallach DA, et al. Molecular cancer screening: in search of evidence. Nat Med. 2021 Jul;27(7):1139-1142. PMID: 34211183.

Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. JAMA Oncol. 2019 May 9;5(8):1124–31. doi: 10.1001/jamaoncol.2019.0528. Epub ahead of print. Erratum in: JAMA Oncol. 2019 Jun 13;: PMID: 31070691; PMCID: PMC6512280.

Rolfo C, Cardona AF, Cristofanilli M, et al. Challenges and opportunities of cfDNA analysis implementation in clinical practice: Perspective of the International Society of Liquid Biopsy (ISLB). Crit Rev Oncol Hematol. 2020 Jul;151:102978. doi: 10.1016/j.critrevonc.2020.102978. Epub 2020 May 5. PMID: 32428812.

Rolfo C, Mack PC, Scagliotti GV, et al. Liquid Biopsy for Advanced Non-Small Cell Lung Cancer (NSCLC): A Statement Paper from the IASLC. J Thorac Oncol. 2018 Sep;13(9):1248-1268. doi: 10.1016/j.jtho.2018.05.030. Epub 2018 Jun 6. PMID: 29885479.

Rossi G, Ignatiadis M. Promises and Pitfalls of Using Liquid Biopsy for Precision Medicine. Cancer Res. 2019 Jun 1;79(11):2798-2804. doi: 10.1158/0008-5472.CAN-18-3402. Epub 2019 May 20. PMID: 31109952.

Rothwell DG, Ayub M, Cook N, et al. Utility of ctDNA to support patient selection for early phase clinical trials: the TARGET study. Nat Med. 2019 May;25(5):738-743. doi: 10.1038/s41591-019-0380-z. Epub 2019 Apr 22. PMID: 31011204.

Sugimoto A, Matsumoto S, Udagawa H, et al. A large-scale prospective concordance study of plasma- and tissue-based next-generation targeted sequencing for advanced non-small cell lung cancer (LC-SCRUM-Liquid). Clin Cancer Res. 2022 Oct 6:CCR-22-1749. doi: 10.1158/1078-0432.CCR-22-1749. Epub ahead of print. PMID: 36201167.

Slavin TP, Banks KC, Chudova D, et al. Identification of Incidental Germline Mutations in Patients With Advanced Solid Tumors Who Underwent Cell-Free Circulating Tumor DNA Sequencing. J Clin Oncol. 2018 Oct 19;36(35):JCO1800328. doi: 10.1200/JCO.18.00328. Epub ahead of print. PMID: 30339520; PMCID: PMC6286162.

Sumbal S, Javed A, Afroze B, et al. Circulating tumor DNA in blood: Future genomic biomarkers for cancer detection. Exp Hematol. 2018 Sep;65:17-28. doi: 10.1016/j.exphem.2018.06.003. Epub 2018 Jun 23. PMID: 29940219.

Wang Y, Li L, Cohen JD, et al. Prognostic Potential of Circulating Tumor DNA Measurement in Postoperative Surveillance of Nonmetastatic Colorectal Cancer. JAMA Oncol. 2019 May 9;5(8):1118–23. doi: 10.1001/jamaoncol.2019.0512. Epub ahead of print. PMID: 31070668; PMCID: PMC6512291.

Xie J, Yao W, Chen L, Zhu W, Liu Q, Geng G, Fang J, Zhao Y, Xiao L, Huang Z, Zhao J. Plasma ctDNA increases tissue NGS-based detection of therapeutically targetable mutations in lung cancers. BMC Cancer. 2023 Mar 31;23(1):294. doi: 10.1186/s12885-023-10674-z. PMID: 37004022; PMCID: PMC10063947.

Zhang L, Zeng J, Zeng Z, et al. MGMT in colorectal cancer: a promising component of personalized treatment. Tumour Biol. 2016 Aug;37(8):11443-56. doi: 10.1007/s13277-016-5014-1. Epub 2016 Mar 22. PMID: 27006309.

General Tumor Testing (Hematologic Malignancies)

Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022 Jul;36(7):1720-1748. doi: 10.1038/s41375-022-01620-2. Epub 2022 Jun 22. PMID: 35732829; PMCID: PMC9214472.

Bombard Y, Bach PB, Offit K. Translating genomics in cancer care. J Natl Compr Canc Netw. 2013 Nov;11(11):1343-53. doi: 10.6004/jnccn.2013.0158. PMID: 24225968.

Febbo PG, Ladanyi M, Aldape KD, et al. NCCN Task Force report: Evaluating the clinical utility of tumor markers in oncology. J Natl Compr Canc Netw. 2011 Nov;9 Suppl 5:S1-32; quiz S33. doi: 10.6004/jnccn.2011.0137. PMID: 22138009.

Taylor J, Xiao W, Abdel-Wahab O. Diagnosis and classification of hematologic malignancies on the basis of genetics. Blood. 2017 Jul 27;130(4):410-423. doi: 10.1182/blood-2017-02-734541. Epub 2017 Jun 9. PMID: 28600336; PMCID: PMC5533199.

Wästerlid T, Cavelier L, Haferlach C, et al. Application of precision medicine in clinical routine in haematology-Challenges and opportunities. J Intern Med. 2022 Aug;292(2):243-261. doi: 10.1111/joim.13508. Epub 2022 Jun 4. PMID: 35599019.

Minimal Residual Disease Monitoring

Multiple Myeloma

Akhlaghi, T.; Firestone, R.; Hultcrantz, M. Minimal Residual Disease in Multiple Myeloma—Current Approaches and Future Clinical Implications. *Hemato* 2022, *3*, 454-465. https://doi.org/10.3390/hemato3030031.

Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022 Jul;36(7):1720-1748. doi: 10.1038/s41375-022-01620-2. Epub 2022 Jun 22. PMID: 35732829; PMCID: PMC9214472.

Avet-Loiseau H, Corre J, Lauwers-Cances V, et al. Evaluation of minimal residual disease (MRD) by next generation sequencing (NGS) is highly predictive of progression free survival in the IFM/DFCI 2009 trial. Blood. 2015 Dec 3;126(23):191.

Bai Y, Orfao A, Chim CS. Molecular detection of minimal residual disease in multiple myeloma. Br J Haematol. 2018 Apr;181(1):11-26. doi: 10.1111/bjh.15075. Epub 2017 Dec 19. PMID: 29265356.

Bal S, Giri S, Godby KN, et al. New regimens and directions in the management of newly diagnosed multiple myeloma. Am J Hematol. 2021 Mar 1;96(3):367-378. doi: 10.1002/ajh.26080. Epub 2021 Jan 20. PMID: 33393136.

Bolli N, Genuardi E, Ziccheddu B, et al. Next-Generation Sequencing for Clinical Management of Multiple Myeloma: Ready for Prime Time? Front Oncol. 2020 Feb 25;10:189. doi: 10.3389/fonc.2020.00189. PMID: 32181154.

Bustoros M, Mouhieddine TH, Detappe A, et al. Established and Novel Prognostic Biomarkers in Multiple Myeloma. Am Soc Clin Oncol Educ Book. 2017;37:548-560. doi: 10.1200/EDBK_175175. PMID: 28561668.

Cavo M, San-Miguel J, Usmani SZ, et al. Prognostic value of minimal residual disease negativity in myeloma: combined analysis of POLLUX, CASTOR, ALCYONE, and MAIA. Blood. 2022 Feb 10;139(6):835-844. doi: 10.1182/blood.2021011101. PMID: 34289038; PMCID: PMC8832474.

Flores-Montero J, Sanoja-Flores L, Paiva B, et al. Next Generation Flow for highly sensitive and standardized detection of minimal residual disease in multiple myeloma. Leukemia. 2017 Oct;31(10):2094-2103. doi: 10.1038/leu.2017.29. Epub 2017 Jan 20. PMID: 28104919.

Fonseca R, Bergsagel PL, Drach J, et al. International Myeloma Working Group molecular classification of multiple myeloma: spotlight review. Leukemia. 2009 Dec;23(12):2210-21. doi: 10.1038/leu.2009.174. Epub 2009 Oct 1. PMID: 19798094.

González D, van der Burg M, García-Sanz R, et al. Immunoglobulin gene rearrangements and the pathogenesis of multiple myeloma. Blood. 2007 Nov 1;110(9):3112-21. doi: 10.1182/blood-2007-02-069625. Epub 2007 Jul 18. PMID: 17634408.

Gormley NJ, Turley DM, Dickey JS, et al. Regulatory perspective on minimal residual disease flow cytometry testing in multiple myeloma. Cytometry B Clin Cytom. 2016 Jan;90(1):73-80. doi: 10.1002/cyto.b.21268. Epub 2015 Jul 25. PMID: 26108351.

Hoang PH, Dobbins SE, Cornish AJ, et al. Whole-genome sequencing of multiple myeloma reveals oncogenic pathways are targeted somatically through multiple mechanisms. Leukemia. 2018 Nov;32(11):2459-2470. doi: 10.1038/s41375-018-0103-3. Epub 2018 Apr 9. PMID: 29654271.

Holstein SA, Bahlis N, Bergsagel PL, et al. The 2020 BMT CTN Myeloma Intergroup Workshop on Immune Profiling and Minimal Residual Disease Testing in Multiple Myeloma. Transplant Cell Ther. 2021 Jun 6:S2666-6367(21)00946-5. doi: 10.1016/j.jtct.2021.05.027. Epub ahead of print. PMID: 34107340.

Kortuem KM, Braggio E, Bruins L, et al. Panel sequencing for clinically oriented variant screening and copy number detection in 142 untreated multiple myeloma patients. Blood Cancer J. 2016 Feb 26;6(2):e397. doi: 10.1038/bcj.2016.1. PMID: 26918361.

Kuiper R, Broyl A, de Knegt Y, et al. A gene expression signature for high-risk multiple myeloma. Leukemia. 2012 Nov;26(11):2406-13. doi: 10.1038/leu.2012.127. Epub 2012 May 8. Erratum in: Leukemia. 2014 May;28(5):1178-80. doi: 10.1038/leu.2014.53. PMID: 22722715.

Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016 Aug;17(8):e328-e346. doi: 10.1016/S1470-2045(16)30206-6. PMID: 27511158.

Maclachlan KH, Came N, Diamond B, et al. Minimal residual disease in multiple myeloma: defining the role of next generation sequencing and flow cytometry in routine diagnostic use. Pathology. 2021 Apr;53(3):385-399. doi: 10.1016/j.pathol.2021.02.003. Epub 2021 Mar 3. PMID: 33674146.

Mateos MV, Dimopoulos MA, Cavo M, et al. Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma. N Engl J Med. 2018 Feb 8;378(6):518-528. doi: 10.1056/NEJMoa1714678. Epub 2017 Dec 12. PMID: 29231133.

Mina R, Oliva S, Boccadoro M. Minimal Residual Disease in Multiple Myeloma: State of the Art and Future Perspectives. J Clin Med. 2020 Jul 7;9(7):E2142. doi: 10.3390/jcm9072142. PMID: 32645952.

Misiewicz-Krzeminska I, Krzeminski P, Corchete LA, et al. Factors Regulating microRNA Expression and Function in Multiple Myeloma. Noncoding RNA. 2019 Jan 16;5(1):9. doi: 10.3390/ncrna5010009. PMID: 30654527.

Morè S, Corvatta L, Manieri VM, et al. Current Main Topics in Multiple Myeloma. Cancers (Basel). 2023 Apr 8;15(8):2203. doi: 10.3390/cancers15082203. PMID: 37190132; PMCID: PMC10136770.

Moreau P, San Miguel J, Sonneveld P, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017 Jul 1;28(suppl_4):iv52-iv61. doi: 10.1093/annonc/mdx096. PMID: 28453614.

Nishihori T, Shain K. Insights on Genomic and Molecular Alterations in Multiple Myeloma and Their Incorporation towards Risk-Adapted Treatment Strategy: Concise Clinical Review. Int J Genomics. 2017;2017:6934183. doi: 10.1155/2017/6934183. Epub 2017 Nov 8. PMID: 29250532.

Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. J Clin Oncol. 2015 Sep 10;33(26):2863-9. doi: 10.1200/JCO.2015.61.2267. Epub 2015 Aug 3. PMID: 26240224.

Pawlyn C, Davies FE. Toward personalized treatment in multiple myeloma based on molecular characteristics. Blood. 2019 Feb 14;133(7):660-675. doi: 10.1182/blood-2018-09-825331. Epub 2018 Dec 26. PMID: 30587529; PMCID: PMC6384187.

Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. Am J Hematol. 2020 May;95(5):548-567. doi: 10.1002/ajh.25791. Erratum in: Am J Hematol. 2020 Nov;95(11):1444. PMID: 32212178.

Rasche L, Kortüm KM, Raab MS, et al. The Impact of Tumor Heterogeneity on Diagnostics and Novel Therapeutic Strategies in Multiple Myeloma. Int J Mol Sci. 2019 Mar 12;20(5):1248. doi: 10.3390/ijms20051248. PMID: 30871078.

Scherer F, Kurtz DM, Diehn M, et al. High-throughput sequencing for noninvasive disease detection in hematologic malignancies. Blood. 2017 Jul 27;130(4):440-452. doi: 10.1182/blood-2017-03-735639. Epub 2017 Jun 9. PMID: 28600337.

Soekojo CY, de Mel S, Ooi M, et al. Potential Clinical Application of Genomics in Multiple Myeloma. Int J Mol Sci. 2018 Jun 10;19(6):1721. doi: 10.3390/ijms19061721. PMID: 29890777.

Ubels J, Sonneveld P, van Beers EH, et al. Predicting treatment benefit in multiple myeloma through simulation of alternative treatment effects. Nat Commun. 2018 Jul 27;9(1):2943. doi: 10.1038/s41467-018-05348-5. PMID: 30054467.

Willenbacher W, Seeber A, Steiner N, et al. Towards Molecular Profiling in Multiple Myeloma: A Literature Review and Early Indications of Its Efficacy for Informing Treatment Strategies. Int J Mol Sci. 2018 Jul 18;19(7). pii: E2087. doi: 10.3390/ijms19072087. Review. PMID: 30021955.

Acute Lymphoblastic Leukemia

Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022 Jul;36(7):1720-1748. doi: 10.1038/s41375-022-01620-2. Epub 2022 Jun 22. PMID: 35732829; PMCID: PMC9214472.

Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. Blood. 2022 Sep 15;140(11):1200-1228. doi: 10.1182/blood.2022015850. PMID: 35767897; PMCID: PMC9479031.

Berry DA, Zhou S, Higley H, et al. Association of minimal residual disease with clinical outcome in pediatric and adult acute lymphoblastic leukemia: a meta-analysis. JAMA Oncol. 2017 July 13;3(7):e170580. doi: 10.1001/jamaoncol.2017.0580. Epub 2017 Jul 13. PMID: 28494052; PMCID: PMC5824235.

Brüggemann M, Kotrová M, Knecht H, et al. Standardized next-generation sequencing of immunoglobulin and T-cell receptor gene recombinations for MRD marker identification in acute lymphoblastic leukaemia; a EuroClonality-NGS validation study. Leukemia. 2019 Sep;33(9):2241-2253. doi: 10.1038/s41375-019-0496-7. Epub 2019 Jun 26. PMID: 31243313; PMCID: PMC6756028.

Chen J, Gale RP, Hu Y, et al. Measurable residual disease (MRD)-testing in haematological and solid cancers. Leukemia. 2024 Jun;38(6):1202-1212. doi: 10.1038/s41375-024-02252-4. Epub 2024 Apr 18. PMID: 38637690; PMCID: PMC11147778.

Duffield AS, Mullighan CG, Borowitz MJ. International Consensus Classification of acute lymphoblastic leukemia/lymphoma. Virchows Arch. 2023 Jan;482(1):11-26. doi: 10.1007/s00428-022-03448-8. Epub 2022 Nov 24. PMID: 36422706.

Eckert C, Groeneveld-Krentz S, Kirschner-Schwabe R, et al. Improving Stratification for Children With Late Bone Marrow B-Cell Acute Lymphoblastic Leukemia Relapses With Refined Response Classification and Integration of Genetics. J Clin Oncol. 2019 Dec 20;37(36):3493-3506. doi: 10.1200/JCO.19.01694. Epub 2019 Oct 23. PMID: 31644328.

Food and Drug Administration (FDA), (2018). FDA approval brings first gene therapy to the United States. Available from <https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states> [03 Mar 2018].

Gökbuget N, Boissel N, Chiaretti S, et al. Diagnosis, prognostic factors, and assessment of ALL in adults: 2024 ELN recommendations from a European expert panel. Blood. 2024 May 9;143(19):1891-1902. doi: 10.1182/blood.2023020794. PMID: 38295337.

Heikamp EB, Pui CH. Next-Generation Evaluation and Treatment of Pediatric Acute Lymphoblastic Leukemia. J Pediatr. 2018 Dec;203:14-24.e2. doi: 10.1016/j.jpeds.2018.07.039. Epub 2018 Sep 10. PMID: 30213460; Central PMCID: PMC6261438.

Horowitz NA, Akasha D, Rowe JM. Advances in the genetics of acute lymphoblastic leukemia in adults and the potential clinical implications. Expert Rev Hematol. 2018 Aug 16:1-11. doi: 10.1080/17474086.2018.1509702.

Kansagra AJ, Frey NV, Bar M, et al. Clinical utilization of Chimeric Antigen Receptor T-cells (CAR-T) in B-cell acute lymphoblastic leukemia (ALL)-an expert opinion from the European Society for Blood and Marrow Transplantation (EBMT) and the American Society for Blood and Marrow Transplantation (ASBMT). Bone Marrow Transplant. 2019 May 15. doi: 10.1038/s41409-019-0451-2. [Epub ahead of print] PMID: 31092900.

Liu RB, Guo JG, Liu TZ, et al. Meta-analysis of the clinical characteristics and prognostic relevance of NOTCH1 and FBXW7 mutation in T-cell acute lymphoblastic leukemia. Oncotarget. 2017 Jun 19;8(39):66360-66370. doi: 10.18632/oncotarget.18576. PMID: 29029518; PMCID: PMC5630418.

Mahadeo KM, Khazal SJ, Abdel-Azim H, et al. Management guidelines for paediatric patients receiving chimeric antigen receptor T cell therapy. Nat Rev Clin Oncol. 2019 Jan;16(1):45-63. doi: 10.1038/s41571-018-0075-2. PMID: 30082906; PMCID: PMC7096894.

Marke R, van Leeuwen FN, Scheijen B. The many faces of IKZF1 in B-cell precursor acute lymphoblastic leukemia. Haematologica. 2018 Apr; 103(4):565-574. Epub 2018 Mar 8. PMID: 29519871; PMCID: PMC5865415.

Mohseni M, Uludag H, Brandwein JM. Advances in biology of acute lymphoblastic leukemia (ALL) and therapeutic implications. Am J Blood Res. 2018 Dec 10;8(4):29-56. eCollection 2018. Review. PMID: 30697448; Central PMCID: PMC6334189.

Shah S, Martin A, Turner M, et al. A systematic review of outcomes after stem cell transplantation in acute lymphoblastic leukemia with or without measurable residual disease. Leuk Lymphoma. 2020 Jan 21:1-11. doi: 10.1080/10428194.2019.1709834. [Epub ahead of print] PMID: 31960716.

Valecha GK, Ibrahim U, Ghanem S, et al. Emerging role of immunotherapy in precursor B-cell acute lymphoblastic leukemia. Expert Rev Hematol. 2017 Sep; 10(9):783-799. doi: 10.1080/17474086.2017.1350165. Epub 2017 Jul 10. PMID: 28666090.

Change Summary

Version	Review Date	Effective Date	Summary of Revisions
Created	CSC: 8/11/2022 PAB: 9/12/2022	November 2022	Not applicable
v1.2023	COOC: 2/15/2023 PAB: 3/16/2023	April 1, 2023	Semi-annual review. No criteria changes.
v2.2023	COOC: 8/16/2023 PAB: 9/25/2023	October 1, 2023	Semi-annual review. FDA CDx criteria were revised to limit testing to single gene EGFR analysis in the setting of stage IB-IIIA resected NSCLC or advanced/metastatic NSCLC with progression on EGFR TKI therapy (excluding osimertinib).
v1.2024	COOC: 2/14/2024 PAB: 3/25/2024	April 1, 2024	Semi-annual review. Criteria were updated to allow concurrent tissue/ctDNA testing in metastatic breast cancer and NSCLC; 81523 is considered MN; AKT1, PTEN and ESR1 were added to the list of biomarkers for breast cancer tumor testing; additional ctDNA and tissue testing criteria were clarified. Updates were made to the scope, CPT code and reference sections.
v2.2024	COOC:08/19/2024 PAB: 09/20/2024	October 1, 2024	Semi-annual review. FDA CDx criteria were clarified. Criteria were updated to allow ALK testing for NSCLC, methylation based testing for CNS Cancer and the CRCdx RAS Mutation Detection Kit for metastatic colorectal cancer; repeat testing for NSCLC was clarified; FoundationOne Liquid CDx testing for BRCA1/BRCA2 was removed from the ctDNA testing table. Hematolymphoid tumor testing criteria were clarified. CPT codes and references were updated. TruSight Oncology (TSO) Comprehensive Assay was added to the Lung Cancer (Advanced or metastatic NSCLC) testing and to the Testing for Tumor Agnostic Therapies testing. 81455 was removed from the never medically necessary CPT code table. It was not added to the medically necessary table as it will only be considered medically necessary if used to code for this test.
v1.2025	COOC: 02/17/2025 PAB: 03/24/2025	July 3, 2025	Semi-annual review. Criteria were revised for repeat testing in the metastatic setting. Tissue testing table was updated to reflect FDA approvals. Gene expression profiling never medically necessary criteria were streamlined. Oncotype DX® Breast Recurrence Score Test criteria were clarified. CPT codes and references were updated.