

Regence

Medical Policy Manual

Genetic Testing, Policy No. 83

Expanded Molecular Testing of Cancers to Select Targeted Therapies

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Next Review: April 2027

Last Review: June 2026

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

A growing number of cancer therapies target specific genetic variants in tumors. Expanded molecular panel tests are used to test tumor tissue for a large number of gene variants, and they are generally not tailored to a specific type of cancer. Tumor profiling with such panels is proposed to aid in treatment selection and to help patients find appropriate clinical trials for experimental therapy.

MEDICAL POLICY CRITERIA

Notes:

- This policy does not address:
 - o Testing for diagnostic purposes (e.g., diagnosis of central nervous system tumors)
 - o Targeted variant testing
 - o Gene expression testing
 - o Testing for hematologic disorders (e.g., leukemia or lymphoma)
 - o Testing of circulating, cell-free tumor DNA (i.e., liquid biopsy) or circulating tumor cells

See Cross References section for relevant policies.

- Clinical documentation to support criteria is required (See Required Documentation)

Medically Necessary

- I. Tumor tissue testing to select targeted cancer treatment using molecular panels, including but not limited to broad tumor profiling panels, may be considered **medically necessary** when all of the following criteria are met:
 - A. The individual has advanced or metastatic (e.g., stage III or IV) solid tumor (non-hematologic) cancer; and
 - B. The test includes one or more genes for which an FDA-approved therapy is available for the cancer indication (see Policy Guidelines); and
 - C. The individual has not decided to forgo targeted cancer treatment.

Investigational

- II. Tumor tissue testing using broad profiling panels for selecting targeted cancer treatment is considered **investigational** when Criterion I. is not met.
- III. Whole genome sequencing, whole exome sequencing, and whole transcriptome sequencing of tumor tissue are considered **investigational**.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

Providers should be aware of the possibility of false positive and false negative results from tumor profiling tests. False positives may lead to a patient receiving an ineffective therapy with the risk of drug-related adverse events. Tests that include normal germline tissue testing for comparison may have a lower incidence of false positives compared with tumor-only tests. It is highly recommended that providers review the test's performance characteristics and discuss this information with patients prior to requesting.

EXAMPLES OF EXPANDED TUMOR PANEL TESTS

Expanded tumor panel tests may utilize DNA and/or RNA analysis. Panel tests for targeted therapy selection that may be considered medically necessary when policy criteria are met include but are not limited to the following:

- FoundationOne® CDx
- GeneTrails® Comprehensive Solid Tumor Panel
- Guardant360® Tissue (previously TissueNext™)
- HopeSeq Solid Tumors Comprehensive
- Illumina TruSeq™
- Ion AmpliSeq™
- MSK-IMPACT™
- NeoTYPE® Lung Tumor Profile
- NeoTYPE® Precision Profile for Solid Tumors

- OnkoMatch™
- Oncomine Comprehensive Assay
- Oncotype MAP
- Symgene™ NGS Cancer Panel
- Tempus xT
- UW OncoPlex Cancer Gene Panel

EXAMPLES OF NON-COVERED WHOLE GENOME, WHOLE EXOME, AND WHOLE TRANSCRIPTOME SEQUENCING TESTS:

- Altera™
- BostonGeneTumor Portrait™
- Tempus xE
- Tempus xR
- Caris Molecular Profiling tests, including the Intelligence Profile Panel and MI Tumor Seek

CANCER INDICATIONS AND GENES WITH TARGETED CANCER TREATMENTS APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Note: This is not an exhaustive list of all genes with FDA-approved targeted treatments. Please consult the [FDA website](#) and/or [National Cancer Institute website](#) for more current or specific information.

Cancer Indications with Targeted Treatments			
Indication	Type	Genes	Medication
Any solid tumor	Advanced or metastatic	<i>BRAF</i> <i>NTRK(1/2/3)</i> <i>RET</i>	Tafinlar , Mekinist , Retevmo , Rozlytrek , Vitrakvi
Breast cancer	HER2-negative	<i>BRCA(1/2)</i>	Lynparza , Talzenna
	HR-positive, HER2-negative, advanced or metastatic	<i>AKT1</i> <i>ESR1</i> <i>PIK3CA</i> <i>PTEN</i>	Trugap , Orserdu , Pigra
	HER2-positive	<i>ERBB2 (HER2)</i>	Herceptin , Kadcyla , Perjeta
Cholangiocarcinoma	Advanced or metastatic	<i>FGFR2</i> <i>IDH1</i>	Pemazyre , Tibsovo
Colorectal cancer	Metastatic	<i>BRAF</i> <i>KRAS</i> <i>NRAS</i>	Braftovi , Erbix , Fruzagla , Tukysa , Vectibix
Gastrointestinal stromal tumor (GIST)	Resected, unresectable, or metastatic	<i>KIT (c-KIT, CD117)</i>	Aykakit , Gleevec

Cancer Indications with Targeted Treatments			
Indication	Type	Genes	Medication
		<i>PDGFRA</i>	
Melanoma, cutaneous	Resected, unresectable, or metastatic	<i>BRAF</i>	Braftovi , Cotellic , Mekinist , Opdivo , Tafinlar , Tecentrig , Zelboraf
Melanoma, uveal	Unresectable, or metastatic	<i>HLA</i>	Kimmtrak
Non-small cell lung cancer (NSCLC)	Advanced or metastatic	<i>ALK</i> <i>BRAF</i> <i>EGFR</i> <i>ERBB2 (HER2)</i> <i>KRAS</i> <i>ROS1</i>	Alcensa , Cyramza , Enhertu , Exkivity , Gavreto , Gilotrif , Iressa , Keytruda , Krazati , Lorbrena , Lumakras , Mekinist , Opdivo , Rozlytrek , Rybrevant , Tafinlar , Tagrisso , Tarceva , Tecentrig , Vizimpro , Xalkori , Zykadia
	Resected	<i>EGFR</i>	Tagrisso
Ovarian cancer (including fallopian tube and primary peritoneal cancer)	Advanced or recurrent	<i>BRCA(1/2)</i>	Lynparza , Rubraca , Zejula
Pancreatic cancer	Metastatic	<i>BRCA(1/2)</i>	Lynparza
Prostate cancer	Metastatic, castration-resistant	<i>BRCA(1/2)</i>	Lynparza , Rubraca
Thyroid cancer	Advanced or metastatic	<i>RET</i>	Gavreto
	Anaplastic and advanced or metastatic	<i>BRAF</i>	Mekinist , Tafinlar
Urothelial carcinoma	Advanced or metastatic	<i>FGFR(2/3)</i>	Balversa

REQUIRED DOCUMENTATION

In order to determine the clinical utility of gene test(s), all of the following information must be submitted for review:

- Name of the genetic test(s) or panel test
- Name of the performing laboratory and/or genetic testing organization (more than one may be listed)
- The exact gene(s) and/or variants being tested
- Relevant billing codes

- Brief description of how the genetic test results will guide clinical decisions that would not otherwise be made in the absence of testing
- Medical records related to this genetic test
 - o Date of sample collection (tumor tissue)
 - o History and physical exam
 - o Conventional testing and outcomes
 - o Additional treatment provided, if any

CROSS REFERENCES

1. [KRAS, NRAS, and BRAF Variant Analysis and MicroRNA Expression Testing for Colorectal Cancer](#), Genetic Testing, Policy No. 13
2. [Gene Expression-Based Assays for Cancers of Unknown Primary](#), Genetic Testing, Policy No. 15
3. [Topographic Genotyping to Classify Cancer Risk](#), Genetic Testing, Policy No. 16
4. [Gene-Based Tests for Screening, Detection, and/or Management of Prostate or Bladder Cancer](#), Genetic Testing, Policy No. 17
5. [Genetic and Molecular Diagnostic Testing](#), Genetic Testing, Policy No. 20
6. [BRAF Genetic Testing to Select Melanoma or Glioma Patients for Targeted Therapy](#), Genetic Testing, Policy No. 41
7. [Targeted Genetic Testing for Selection of Therapy for Non-Small Cell Lung Cancer \(NSCLC\)](#), Genetic Testing, Policy No. 56
8. [Evaluating the Utility of Genetic Panels](#), Genetic Testing, Policy No. 64
9. [Analysis of Proteomic and Metabolomic Patterns for Early Detection or Assessing Risk of Cancer](#), Laboratory, Policy No. 41
10. [Circulating Tumor DNA and Circulating Tumor Cells for Management \(Liquid Biopsy\) of Solid Tumor Cancers](#), Laboratory, Policy No. 46
11. [Urinary Biomarkers for Cancer Screening, Diagnosis, and Surveillance](#), Laboratory, Policy No. 72

BACKGROUND

TRADITIONAL THERAPEUTIC APPROACHES TO CANCER

Tumor location, grade, stage, and the patient's underlying physical condition have traditionally been used in clinical oncology to determine the therapeutic approach to a specific cancer, which could include surgical resection, ionizing radiation, systemic chemotherapy, or combinations thereof. Currently, some 100 different types are broadly categorized according to the tissue, organ, or body compartment in which they arise. Most treatment approaches in clinical care were developed and evaluated in studies that recruited subjects and categorized results based on this traditional classification scheme.

This traditional approach to cancer treatment does not reflect the wide diversity of cancer at the molecular level. While treatment by organ type, stage, and grade may demonstrate statistically significant therapeutic efficacy overall, only a subgroup of patients may derive clinically significant benefit. It is unusual for a cancer treatment to be effective for all patients treated in a traditional clinical trial. Spear et al analyzed the efficacy of major drugs used to treat several important diseases.^[1] They reported heterogeneity of therapeutic responses, noting a low rate of 25% for cancer chemotherapeutics, with response rates for most drugs falling in the range of 50% to 75%. The low rate for cancer treatments is indicative of the need for better identification of characteristics associated with treatment response and better targeting of treatment to have higher rates of therapeutic responses.

TARGETED CANCER THERAPY

Much of the variability in clinical response may result from genetic variations. Within each broad type of cancer, there may be a large amount of variability in the genetic underpinnings of the cancer. Targeted cancer treatment refers to the identification of genetic abnormalities present in the cancer of a particular patient, and the use of drugs that target the specific genetic abnormality. The use of genetic markers allows cancers to be further classified by “pathways” defined at the molecular level. An expanding number of genetic markers have been identified. Dienstmann (2013) categorized these findings into three classes:^[2] (1) genetic markers that have a direct impact on care for the specific cancer of interest, (2) genetic markers that may be biologically important but are not currently actionable, and (3) genetic markers of uncertain importance.

A smaller number of individual genetic markers fall into the first category (i.e., have established utility for a specific cancer type). The utility of these markers has been demonstrated by randomized controlled trials that select patients with the marker and report significant improvements in outcomes with targeted therapy compared with standard therapy. Testing for individual variants with established utility is not covered in this evidence review. In some cases, limited panels may be offered that are specific to one type of cancer (e.g., a panel of several markers for non-small-cell lung cancer). This review also does not address the use of cancer-specific panels that include a few variants. Rather, this review addresses expanded panels that test for many potential variants that do not necessarily have established efficacy for the specific cancer in question.

When advanced cancers are tested with expanded molecular panels, most patients are found to have at least one potentially pathogenic variant.^[3-5] The number of variants varies widely by types of cancers, different variants included in testing, and different testing methods among the available studies. In a 2015 study, 439 patients with diverse cancers were tested with a 236-gene panel.^[5] A total of 1,813 molecular alterations were identified, and almost all patients (420/439 [96%]) had at least one molecular alteration. The median number of alterations per patient was three, and 85% of patients (372/439) had two or more alterations. The most common alterations were in the genes *TP53* (44%), *KRAS* (16%), and *PIK3CA* (12%).

Some evidence is available on the generalizability of targeted treatment based on a specific variant among cancers that originate from different organs.^[2, 6, 7] There are several examples of variant-directed treatment that was effective in one type of cancer but ineffective in another. For example, targeted therapy for epidermal growth factor receptor (*EGFR*) variants has been successful in non-small cell lung cancer (NSCLC) but not in trials of other cancer types. Treatment with tyrosine kinase inhibitors based on variant testing has been effective for renal cell carcinoma but has not demonstrated effectiveness for other cancer types tested. “Basket” studies, in which tumors of various histologic types that share a common genetic variant are treated with a targeted agent, also have been performed. One such study was published by Hyman (2015).^[8] In this study, 122 patients with *BRAF* V600 variants in nonmelanoma cancers were treated with vemurafenib. The authors reported that there appeared to be antitumor activity for some but not all cancers, with the most promising results seen for NSCLC, Erdheim-Chester disease, and Langerhans cell histiocytosis.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical

Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

EVIDENCE SUMMARY

Human Genome Variation Society (HGVS) nomenclature^[9] is used to describe variants found in DNA and serves as an international standard. It is being implemented for genetic testing medical evidence review updates starting in 2017. According to this nomenclature, the term “variant” is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as “mutation.” Pathogenic variants are variants associated with disease, while benign variants are not. The majority of genetic changes have unknown effects on human health, and these are referred to as variants of uncertain significance.

The evaluation of a genetic test focuses on three main principles: (1) analytic validity (technical accuracy of the test in detecting a variant that is present or in excluding a variant that is absent); (2) clinical validity (diagnostic performance of the test [sensitivity, specificity, positive and negative predictive values] in detecting clinical disease); and (3) clinical utility (how the results of the diagnostic test will be used to change management of the patient and whether these changes in management lead to clinically important improvements in health outcomes). This evidence review focuses on clinical validity and utility.

EXPANDED MOLECULAR PANEL TESTING FOR CANCER

The evidence on the clinical validity of expanded panels is incomplete. Because of the large number of variants contained in expanded panels, it is not possible to determine clinical validity for the panels as a whole. While some variants have a strong association with one or a small number of specific malignancies, none has demonstrated high clinical validity across a wide variety of cancers. Some studies have reported that, after filtering variants by comparison with matched normal tissue and cancer variants databases, most identified variants are found to be false positives. Thus, it is likely that clinical validity will need to be determined for each variant and each type of cancer individually.

The most direct way to demonstrate clinical utility is through controlled trials that compare a strategy of cancer variant testing followed by targeted treatment with a standard treatment strategy without variant testing. Randomized trials are necessary to control for selection bias in treatment decisions, because clinicians may select candidates for variant testing based on clinical, demographic, and other factors. Outcomes of these trials would be the morbidity and mortality associated with cancer and cancer treatment. Overall survival (OS) is most important; cancer-related survival and/or progression-free survival (PFS) may be acceptable surrogates. A quality-of-life (QOL) measurement may also be important if study designs allow for treatments with different toxicities in the experimental and control groups.

Systematic Reviews

Kazmi (2025) conducted a systematic review and meta-analysis to evaluate the benefits and harms of using comprehensive genetic profiling via NGS for matched targeted therapies in individuals with advanced cancers from randomized controlled trials (35 studies, n=9,819).^[10] Outcomes of interest were PFS, OS, overall response rates (ORR), serious (grade 3 or 4) adverse events, and QOL. The meta-analysis compared matched targeted therapy with and without standard-of-care (SOC) to SOC treatment only, non-matched targeted therapies, or no treatment (best supportive care). Matched therapy compared with standard systemic therapy

reduced the risk of disease progression by 34% (hazard ratio [HR] 0.66, 95% confidence interval [CI] 0.59 to 0.74), however, there was no significant difference in the risk of death (HR 0.85, 95% CI 0.75 to 0.97) with limited evidence to suggest an improved QOL for the matched therapy patients. Matched therapy in combination with SOC compared to SOC alone decreased the risk of disease progression by 39% (HR 0.61, 95% CI 0.53 to 0.70) and risk of death by 21% (HR 0.79, 95% CI 0.70 to 0.89) but had limiting evidence to demonstrate an improved QOL. Matched versus non-matched targeted therapy exhibited a reduction in the risk of disease progression by 24% (HR 0.76, 95% CI 0.64 to 0.89) and risk of death by 25% (HR 0.75, 95% CI 0.65 to 0.86). Matched therapy compared to best supportive care reduced the risk of disease progression by 61% (HR 0.37, 95% CI 0.28 to 0.50) but no clear evidence to suggest a difference in OS between the groups. The overall risk of bias was judged low for eight studies, unclear for two studies, and the remaining 27 studies were high risk. Therapy selection guided by NGS for individuals with advanced cancer slows down cancer progression compared to standard therapies, however, there is limited evidence to suggest that it prolongs overall survival, improves the quality of life or decreases adverse events.

Zerdes (2025) performed systematic review and meta-analysis on data compiled from real-world evidence (144 studies, n=54,739) to investigate the applicability and clinical impact of tumor profiling in individuals with metastatic cancer.^[11] For individuals treated with NGS-guided therapy, the pooled median PFS was 4.41 months (95% CI 3.71 to 5.24, 35 studies) and OS was 13.14 months (95% CI 9.56 to 18.06, 16 studies) for all cancer types. NGS-guided treatment was correlated with statically significant increase in ORR (odds ratio [OR] 2.75, 95% CI 1.84 to 4.13, 16 studies, n=1,109), PFS (pooled HR 0.63, 95% CI 0.56 to 0.70, 18 studies, n=3,269), and OS (pooled HR 0.60, 95% CI 0.51 to 0.70, 21 studies, n=2,772) when compared to conventional treatment. Despite these promising results, the authors note there was a low certainty of evidence, mainly due to clinical heterogeneity and low internal validity of eligible studies.

Limaye (2025) carried out a systematic review on the clinical utility of tumor profiling for treatment selection from randomized clinical trials (RCTs), non-randomized, and observational studies (14 studies, n=35,975) encompassing all cancer types and different therapeutic interventions using OS and PFS as the primary outcome.^[12] Targeted therapy that was based on genomically matched scores and/or molecular tumor board (MTB) recommendations enhanced OS, PFS, and yielded better clinical outcomes when compared to standard chemotherapy or physician's choice regimens. Improved OS and PFS were reported when testing guided treatment decisions, but its clinical utility varied among cancer types. Furthermore, while most of the studies in this review incorporated tumor profiling testing during the study, the actual treatment based on the testing was limited to subgroup analysis only, which was limited by low sample size, statistical insignificance, and heterogeneity in the matching scores.

Labaki (2025) evaluated clinical studies that assessed targeted therapy in the management of individuals with cancers of unknown primary, as compared to empiric treatment, and performed a meta-analysis using OS and PFS as the endpoints.^[13] Only one study used tumor profiling methodology to determine what targeted therapy individuals received, and the results of that study did not indicate a significant difference in OS.^[14] Of note, the study was a randomized phase 2 clinical trial that enrolled 436 individuals with 326 patients receiving targeted therapy as a result of molecular testing and 110 patients receiving empirical chemotherapy.

Schwaederle (2015) published a meta-analysis of studies comparing personalized treatment with nonpersonalized treatment.^[15] Their definition of personalized treatment was driven by a biomarker, which could be genetic or nongenetic. Therefore, this analysis not only included studies of matched versus unmatched treatment based on genetic markers, but also included studies that personalized treatment based on nongenetic markers. A total of 111 arms of identified trials received personalized treatment, and they were compared with 529 arms that received nonpersonalized treatment. On random-effects meta-analysis, the personalized treatment group had a higher response rate (31% vs 10.5%, $p<0.001$), and a longer PFS (5.9 months vs 2.7 months, $p<0.001$) compared with the nonpersonalized treatment group. Another meta-analysis (2015) by this group compared outcomes from 44 Food and Drug Administration-regulated drug trials that used a personalized treatment approach to 68 trials that used a nonpersonalized approach to cancer treatment.^[16] Response rates were significantly higher in the personalized treatment trials (48%) than in the nonpersonalized approach (23%; $p<0.001$). PFS was 8.3 months in the personalized treatment trials compared with 5.5 months in the nonpersonalized approach ($p<0.001$). For trials that used a personalized treatment strategy, OS was significantly longer (19.3 months) than in trials that did not (13.5 months, $p=0.01$). Personalized treatment in these studies was based on various biomarkers, both genetic and nongenetic.

Randomized Controlled Trials

Randomized controlled trials (RCT) have been published that compare molecular profiling techniques to assess the utility of detecting actionable gene variants in advanced or metastatic cancers, and some of these studies have reported that outcomes are better in patients receiving targeted therapy. However, there are potential limitations with these designs that could compromise the validity these studies, which include the following: (1) differences in clinical and demographic factors, (2) differences in the severity of disease or prognosis of disease (i.e., patients with more undifferentiated anaplastic cancers might be less likely to express genetic markers), and (3) differences in the treatments received. It is possible that one of the "targeted" drugs could be more effective than standard treatment even in unmatched patients.

Trédan (2025) examined molecular alterations via a panel of 324-cancer genes (Foundation One® CDx) or a smaller panel of 87-genes of single-nucleotide and copy number variants, which were subsequently reviewed by a molecular tumor board to identify actionable gene variants.^[17] Significantly more actionable gene variants were identified using the larger panel (51.65) versus the smaller panel (36.9%, $p<0.001$), but no differences in clinical outcomes were observed.

SHIVA was a randomized trial of treatment directed by cancer variant testing vs standard care, with the first results published in 2015 (see Table 2).^[18, 19] In this study, 195 patients with a variety of advanced cancers refractory to standard treatment were enrolled from eight academic centers in France. Variant testing included comprehensive analysis of three molecular pathways (hormone receptor pathway, PI3K/AKT/mTOR pathway, RAF/MEK pathway) performed by targeted next-generation sequencing, analysis of copy number variations, and hormone expression by immunohistochemistry. Based on the pattern of abnormalities found, nine different regimens of established cancer treatments were assigned to the experimental treatment arm. The primary outcome was PFS analyzed by intention to treat. Baseline clinical characteristics and tumor types were similar between groups.

Table 2. Treatment Algorithm for Experimental Arm, From the SHIVA Trial^[18]

Molecular Abnormalities	Molecularly Targeted Agent
<i>KIT, ABL, RET</i>	Imatinib
<i>AKT, mTORC1/2, PTEN, PI3K</i>	Everolimus
<i>BRAF V600E</i>	Vemurafenib
<i>PDGFRA, PDGFRB, FLT-3</i>	Sorafenib
<i>EGFR</i>	Erlotinib
<i>HER2</i>	Lapatinib and trastuzumab
<i>SRC, EPHA2, LCK, YES</i>	Dasatinib
Estrogen receptor, progesterone receptor	Tamoxifen (or letrozole if contraindications)
Androgen receptor	Abiraterone

Ninety-nine patients were randomized to the targeted treatment group, and 96 to standard care. Baseline clinical characteristics and tumor types were similar between groups. Molecular alterations affecting the hormonal pathway were found in 82 (42%) of 195 patients; alterations affecting the PI3K/AKT/mTOR pathway were found in 89 (46%) of 195 patients; and alterations affecting the RAF/MED pathway were found in 24 (12%) of 195 patients. After a median follow-up of 11.3 months, the median PFS was 2.3 months (95% confidence interval [CI] 1.7 to 3.8 months) in the targeted treatment group vs 2.0 months (95% CI 1.7 to 2.7 months) in the standard care group (hazard ratio, 0.88; 95% CI 0.65 to 1.19, $p=0.41$). Objective responses were reported for four (4.1%) of 98 assessable patients in the targeted treatment group vs three (3.4%) of 89 assessable patients in the standard care group. In subgroup analysis by molecular pathway, there were no significant differences in PFS between groups.

A 2017 crossover analysis of the SHIVA trial evaluated the PFS ratio from patients who failed standard of care therapy and crossed over from molecularly targeted agents (MTA) therapy to treatment at physician's choice (TPC) or vice versa.^[20] The PFS ratio was defined as the PFS on MTA (PFSMTA) to PFS on TPC (PFSTPC) in patients who crossed over. Of the 95 patients who crossed over, 70 patients crossed over from the TPC to MTA arm while 25 patients crossed over from MTA to TPC arm. In the TPC to MTA crossover arm, 26 (37%) of patients and 15 (61%) of patients in the MTA to TPC arm had a PFSMTA/PFSTPC ratio greater than 1.3. The post hoc analysis of the SHIVA trial has limitations because it only evaluated a subset of patients from the original clinical trial but used each patient as his/her control by using the PFS ratio. The analysis would suggest that patients may have benefited from the treatment algorithm evaluated in the SHIVA trial.

Nonrandomized Controlled Trials

Numerous nonrandomized studies have been published that use some type of control.^[21-25] Some of these studies had a prospective, interventional design. For example, Wheler (2016) reported a prospective comparative trial of patients who had failed standard treatment and had been referred to their tertiary center for admission into phase 1 trials.^[24] Comprehensive molecular profiling (FoundationOne® panel) was performed on 339 patients, of whom 122 went onto a phase 1 therapy that was matched to their genetic profile; based on physician evaluation of additional information, 66 patients went onto a phase 1 trial not matched to their genetic profile. There was a significant benefit for the time to treatment failure and a trend for an increased percentage of patients with stable disease and median OS in patients matched to their genetic profile. When exploratory analysis divided patients into groups that had high matching results or low matching results (number of molecular matches per patient divided by the number of molecular alterations per patient), the percentage of patients with stable disease and the median time to failure were significantly better in the high-match group. Median OS did

not differ significantly between groups. Notably, those patients had failed multiple prior therapies (median four) and had a number (median five, range 1 to 14) of gene alterations in the tumors. For comparison, response rates in phase 1 trials with treatment-resistant tumors are typically 5% to 10%.

Another type of study compares patients matched to targeted treatment with patients not matched. In this type of study, all patients undergo comprehensive genetic testing, but only a subset is matched to targeted therapy. Patients who are not matched continue to receive standard care. An individual study of this type was published by Tsimberidou (2012).^[25] In it, patients with advanced or metastatic cancer refractory to standard therapy underwent molecular profiling. Of 1,144 patients, 460 had a molecular aberration based on a panel of tests, 211 of whom were given “matched” treatment and 141 given nonmatched treatment. The principal analysis presented was of a subgroup of the 460 patients who had only one molecular aberration (n=379). Patients were enrolled in one of 51 phase 1 clinical trials of experimental agents. In the list of trials in which patients were enrolled, it appears that many of the investigational agents were inhibitors of specific kinases, and thus a patient with a particular aberration of that kinase would probably be considered a match for that agent. Among the 175 patients treated with matched therapy, the overall response rate was 27%. Among the 116 patients treated with nonmatched therapy, the response rate was 5% ($p<0.001$ for the difference in response rates). The median time to failure was 5.2 months for patients on matched therapy and 2.2 months for those on nonmatched therapy ($p<0.001$). At a median 15-month follow-up, survival was 13.4 months vs 9.0 months ($p=0.017$) in favor of matched therapy.

There are significant limitations inherent in using these and other types of nonrandomized trials to assess the clinical utility of molecular profiling, which are detailed in a review by Freidlin (2019).^[26] Comparisons of patients that receive therapy based on molecular profiling to those that receive do not receive profiling-selected therapy are confounded by the fact that these patient groups are likely to differ in a number of ways other than type of therapy selection. As stated in the review, “the very mechanism by which some patients are separated into the two groups is likely to introduce bias. For example, patients who were treated with MP therapy were selected into that group based on their willingness to accept additional (possibly invasive) MP testing; their willingness to wait for results to come back (and the tumor board to issue a recommendation, if there was one); and their willingness to accept a potentially more aggressive, prolonged, and/or logistically challenging treatment course.”^[26] Additionally, patients with certain molecular variants may have a better prognosis regardless of type of treatment, and certain treatments (which may be more commonly prescribed in the profiled patients) may be more efficacious regardless of molecular status. Other common, nonrandomized study designs, such as comparisons of PFS between a selected, targeted therapy and a previously failed therapy, or “basket” trials have similar issues that limit interpretation.

Whole Genome, Whole Exome, and Whole Transcriptome Testing of Cancers to Identify Targeted Therapies

No systematic reviews, randomized controlled trials, or nonrandomized controlled trials were identified that evaluated the use of whole genome, whole exome, or whole transcriptome sequencing of cancer tissue to guide treatment options.

NATIONAL COMPREHENSIVE CANCER NETWORK

The National Comprehensive Cancer Network guidelines for many cancer types include recommendations for molecular profiling. Some examples of indications for which the guidelines recommend somatic, multigene panel testing for advanced or metastatic disease include:

- Breast cancer^[27]
- Colon cancer^[28]
- Non-small-cell lung cancer^[29]
- Chondrosarcoma^[30]
- Ovarian cancer^[31]
- Biliary tract cancer^[32]
- Pancreatic adenocarcinoma^[33]
- Rectal cancer^[34]

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

In 2022, the American Society of Clinical Oncology (ASCO) published a provisional clinical opinion based on informal consensus in the absence of a formal systematic review on the appropriate use of tumor genomic testing in patients with metastatic or advanced solid tumors.^[35] The opinion notes the following:

- PCO 1.1. Genomic testing should be performed for patients with metastatic or advanced solid tumors with adequate performance status in the following 2 clinical scenarios:
 - When there are genomic biomarker–linked therapies approved by regulatory agencies for their cancer.
 - When considering a treatment for which there are specific genomic biomarker-based contraindications or exclusions (strength of recommendation: strong).
- PCO 1.2.1. For patients with metastatic or advanced solid tumors, genomic testing using multigene genomic sequencing is preferred whenever patients are eligible for a genomic biomarker–linked therapy that a regulatory agency has approved (strength of recommendation: moderate).
- PCO 1.2.2. Multigene panel–based genomic testing should be used whenever more than one genomic biomarker is linked to a regulatory agency–approved therapy (strength of recommendation: strong).
- PCO 2.1. Mismatch repair deficiency status (dMMR) should be evaluated on patients with metastatic or advanced solid tumors who are candidates for immunotherapy. There are multiple approaches, including using large multigene panel-based testing to assess microsatellite instability (MSI). Consider the prevalence of dMMR and/or MSI-H status in individual tumor types when making this decision (strength of recommendation: strong).

- PCO 2.2. When tumor mutational burden (TMB) may influence the decision to use immunotherapy, testing should be performed with either large multigene panels with validated TMB testing or whole-exome analysis (strength of recommendation: strong).
- PCO 4.1. Genomic testing should be considered to determine candidacy for tumor-agnostic therapies in patients with metastatic or advanced solid tumors without approved genomic biomarker–linked therapies (strength of recommendation: moderate).

SUMMARY

Medically Necessary

There is limited evidence that molecular profiling of tumor tissue can improve health outcomes for patients with any type of cancer. However, for certain patients with advanced or metastatic cancer, this type of testing may help to identify targeted treatments or clinical trials for which a patient may be eligible. In addition, current clinical guidelines recommend broad molecular profiling for certain patients with advanced cancers. Therefore, tumor testing using molecular panels, including expanded tumor profiling panels, may be considered medically necessary for patients with advanced or metastatic disease who meet the policy criteria.

Investigational

There is not enough evidence that tumor profiling with expanded panels can improve health outcomes for patients that do not have advanced or metastatic (i.e., stage III or IV) cancers, when the testing is not associated with an FDA-approved targeted treatment, or when an individual has already decided not to pursue targeted therapy. Therefore, expanded tumor tissue panel testing is considered investigational for patients that do not meet the policy criteria.

There is not enough evidence that tumor profiling with whole genome, whole exome, or whole transcriptome sequencing can improve health outcomes for patients with cancer compared to more targeted testing. Clinical guidelines based on evidence do not currently recommend these types of tumor testing. Therefore, whole genome, whole exome, or whole transcriptome testing is considered investigational.

REFERENCES

1. Spear BB, Heath-Chiozzi M, Huff J. Clinical application of pharmacogenetics. *Trends in molecular medicine*. 2001;7(5):201-4. PMID: 11325631
2. Dienstmann R, Rodon J, Barretina J, et al. Genomic medicine frontier in human solid tumors: prospects and challenges. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2013;31(15):1874-84. PMID: 23589551
3. Drilon A, Wang L, Arcila ME, et al. Broad, hybrid capture-based next-generation sequencing identifies actionable genomic alterations in lung adenocarcinomas otherwise negative for such alterations by other genomic testing approaches. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2015;21(16):3631-9. PMID: 25567908

4. Johnson DB, Dahlman KH, Knol J, et al. Enabling a genetically informed approach to cancer medicine: a retrospective evaluation of the impact of comprehensive tumor profiling using a targeted next-generation sequencing panel. *The oncologist*. 2014;19(6):616-22. PMID: 24797823
5. Schwaederle M, Daniels GA, Piccioni DE, et al. On the road to precision cancer medicine: analysis of genomic biomarker actionability in 439 patients. *Molecular cancer therapeutics*. 2015;14(6):1488-94. PMID: 25852059
6. National Comprehensive Cancer Network (NCCN). NCCN Biomarkers Compendium. [cited 6/2/2026]. 'Available from:' <https://www.nccn.org/professionals/biomarkers/default.aspx>.
7. O'Brien CP, Taylor SE, O'Leary JJ, et al. Molecular testing in oncology: Problems, pitfalls and progress. *Lung Cancer*. 2014;83(3):309-15. PMID: 24472389
8. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. *The New England journal of medicine*. 2015;373(8):726-36. PMID: 26287849
9. den Dunnen JT, Dalgleish R, Maglott DR, et al. HGVS Recommendations for the Description of Sequence Variants: 2016 Update. *Human mutation*. 2016;37(6):564-9. PMID: 26931183
10. Kazmi F, Shrestha N, Liu TFD, et al. Next-generation sequencing for guiding matched targeted therapies in people with relapsed or metastatic cancer. *Cochrane Database Syst Rev*. 2025;3(3):Cd014872. PMID: 40122129
11. Zerdes I, Filis P, Fountoukidis G, et al. Comprehensive genome profiling for treatment decisions in patients with metastatic tumors: real-world evidence meta-analysis and registry data implementation. *Journal of the National Cancer Institute*. 2025;117(6):1117-24. PMID: 39842854
12. Limaye S, Deshmukh J, Rohatagi N, et al. Usefulness of Comprehensive Genomic Profiling in Clinical Decision-Making in Oncology: A Systematic Review. *J Immunother Precis Oncol*. 2025;8(1):55-63. PMID: 39811425
13. Labaki C, Eid M, Bakouny Z, et al. Molecularly directed therapy in cancers of unknown primary: A systematic review and meta-analysis. *Eur J Cancer*. 2025;222:115447. PMID: 40318263
14. Krämer A, Bochtler T, Pauli C, et al. Molecularly guided therapy versus chemotherapy after disease control in unfavourable cancer of unknown primary (CUPISCO): an open-label, randomised, phase 2 study. *Lancet*. 2024;404(10452):527-39. PMID: 39096924
15. Schwaederle M, Zhao M, Lee JJ, et al. Impact of precision medicine in diverse cancers: a meta-analysis of phase II clinical trials. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2015;33(32):3817-25. PMID: 26304871
16. Jardim DL, Schwaederle M, Wei C, et al. Impact of a biomarker-based strategy on oncology drug development: a meta-analysis of clinical trials leading to FDA approval. *Journal of the National Cancer Institute*. 2015;107(11):djv253. PMID: 26378224
17. Trédan O, Pouessel D, Penel N, et al. Broad versus limited gene panels to guide treatment in patients with advanced solid tumors: a randomized controlled trial. *Nat Med*. 2025;31(5):1502-08. PMID: 40195451
18. Le Tourneau C, Kamal M, Tredan O, et al. Designs and challenges for personalized medicine studies in oncology: focus on the SHIVA trial. *Targeted oncology*. 2012;7(4):253-65. PMID: 23161020
19. Le Tourneau C, Delord JP, Goncalves A, et al. Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a

- multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. *The Lancet Oncology*. 2015;16(13):1324-34. PMID: 26342236
20. Belin L, Kamal M, Mauborgne C, et al. Randomized phase II trial comparing molecularly targeted therapy based on tumor molecular profiling versus conventional therapy in patients with refractory cancer: cross-over analysis from the SHIVA trial. *Annals of oncology : official journal of the European Society for Medical Oncology*. 2017;28(3):590-96. PMID: 27993804
 21. Tsimberidou AM, Hong DS, Wheler JJ, et al. Long-term overall survival and prognostic score predicting survival: the IMPACT study in precision medicine. *Journal of hematology & oncology*. 2019;12(1):145. PMID: 31888672
 22. Pishvaian MJ, Blais EM, Brody JR, et al. Overall survival in patients with pancreatic cancer receiving matched therapies following molecular profiling: a retrospective analysis of the Know Your Tumor registry trial. *The Lancet Oncology*. 2020;21(4):508-18. PMID: 32135080
 23. Ibrahim T, Ahmadi A, Rassy E, et al. Comprehensive tumor profiling-guided therapy in rare or refractory solid cancer: A feasibility study in daily clinical practice. *Bulletin du cancer*. 2020;107(4):410-16. PMID: 32145962
 24. Wheler JJ, Janku F, Naing A, et al. Cancer therapy directed by comprehensive genomic profiling: a single center study. *Cancer research*. 2016;76(13):3690-701. PMID: 27197177
 25. Tsimberidou AM, Iskander NG, Hong DS, et al. Personalized medicine in a phase I clinical trials program: the MD Anderson Cancer Center initiative. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2012;18(22):6373-83. PMID: 22966018
 26. Freidlin B, Allegra CJ, Korn EL. Moving Molecular Profiling to Routine Clinical Practice: A Way Forward? *Journal of the National Cancer Institute*. 2019. PMID: 31868907
 27. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
 28. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf.
 29. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
 30. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Bone Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf.
 31. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf.
 32. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Biliary Tract Cancers. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf.
 33. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf.

34. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer. [cited 6/2/2026]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf.
35. Chakravarty D, Johnson A, Sklar J, et al. Somatic Genomic Testing in Patients With Metastatic or Advanced Cancer: ASCO Provisional Clinical Opinion. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2022;40(11):1231-58. PMID: 35175857

CODES

Codes	Number	Description
CPT	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/or absence of variants and associated therapy(ies) to consider
	0036U	Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses
	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
	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)
	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
	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
	0297U	Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification
	0298U	Oncology (pan tumor), whole transcriptome sequencing of paired malignant and normal RNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and expression level and chimeric transcript identification
	0300U	Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification
	0329U	Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene

Codes	Number	Description
		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
	0379U	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA (523 genes) and RNA (55 genes) by next-generation sequencing, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability, and tumor mutational burden
	0391U	Oncology (solid tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded (FFPE) tissue, 437 genes, interpretive report for single nucleotide variants, splice site variants, insertions/deletions, copy number alterations, gene fusions, tumor mutational burden, and microsatellite instability, with algorithm quantifying immunotherapy response score
	0444U	Oncology (solid organ neoplasia), targeted genomic sequence analysis panel of 361 genes, interrogation for gene fusions, translocations, or other rearrangements, using DNA from formalin-fixed paraffin-embedded (FFPE) tumor tissue, report of clinically significant variant(s)
	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
	0498U	Oncology (colorectal), nextgeneration sequencing for mutation detection in 43 genes and methylation pattern in 45 genes, blood, and formalin-fixed paraffin-embedded (FFPE) tissue, report of variants and methylation pattern with interpretation
	0499U	Oncology (colorectal and lung), DNA from formalin-fixed paraffinembedded (FFPE) tissue, nextgeneration sequencing of 8 genes (NRAS, EGFR, CTNNB1, PIK3CA, APC, BRAF, KRAS, and TP53), mutation detection
	0648U	Oncology (solid tumor), targeted genomic sequencing analysis, to detect deletions, insertions, and substitutions in 42 genes, copy number amplifications in 10 genes, and fusions and splice variants in 18 driver genes from DNA and RNA extracted from formalinfixed paraffin-embedded (FFPE) tissue
	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, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
	81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
	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)
	81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)

Codes	Number	Description
	81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)
	81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
	81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
	81298	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
	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)
	81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
	81321	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
	81400	Molecular pathology procedure, Level 1
	81401	Molecular pathology procedure, Level 2
	81402	Molecular pathology procedure, Level 3
	81403	Molecular pathology procedure, Level 4
	81404	Molecular pathology procedure, Level 5
	81405	Molecular pathology procedure, Level 6
	81406	Molecular pathology procedure, Level 7
	81407	Molecular pathology procedure, Level 8
	81408	Molecular pathology procedure, Level 9
	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 DNE 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
	81455	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, DNA analysis or combined DNA and 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
	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

Codes	Number	Description
		number variants, microsatellite instability, tumor mutation burden, and rearrangements
	81479	Unlisted molecular pathology procedure
HCPCS	None	

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