Introduction

BRAF testing for colorectal cancer is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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What is BRAF

Definition

BRAF is a gene that forms a part of a cell-signaling pathway to help control cell growth. Changes or mutations in the BRAF gene can cause out of control cell growth, which may lead to cancer. The most common BRAF mutation is called V600E which was previously known as V599E.

Prevalence

About 5-9% of colorectal cancer tumors have a V600E BRAF mutation.

Prognosis

Patients with a V600E BRAF mutation appear to have a poorer prognosis. Tumors with BRAF mutations may have less response to anti-EGFR therapies like cetuximab (Erbitux®) and panitumumab (Vectibix®).

Test information

Introduction

Testing for a BRAF mutation may include targeted mutation analysis or sequencing.
Available tests

The following BRAF tests are available to identify mutations.

Note  BRAF mutation analysis has several other test applications with different criteria (such as melanoma therapeutic response, Lynch syndrome tumor screening, or Noonan syndrome diagnosis). Ensure you are reviewing the correct use of the test.

Targeted mutation analysis

Laboratories most commonly test for the BRAF V600E mutation, which accounts for about 90% of activating BRAF mutations. Mutation analysis requires relatively little tumor material for testing and has high sensitivity. It is also relatively inexpensive.

BRAF mutation analysis is done on fresh, frozen, or paraffin-embedded tissue from either a primary tumor or metastasis. Some molecular diagnostic laboratories perform BRAF mutation analysis by laboratory-developed methods, while others use FDA-approved test kits. Laboratory-developed tests may vary in the specimen type required, methodology used, mutations tested, sensitivity, and other test-specific data.

Sequencing

Some laboratories sequence all or part of the BRAF gene, which will find a broader spectrum of mutations than targeted mutation analysis. Laboratories that offer sequencing generally do so for a subset of exons where most BRAF activating mutations have been identified.

Sequence analysis requires more and higher quality tumor material for testing than targeted mutations. This method is typically less efficient and more expensive than targeted mutation analysis.

Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to BRAF testing for colorectal cancer.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2018) states the following.

“Limited data from unplanned retrospective subset analyses of patients with metastatic colorectal cancer treated in the first-line setting suggest that although BRAF V600E mutation confers a poor prognosis regardless of treatment, patients with disease characterized by this mutation may receive some benefit from the addition of cetuximab to front-line therapy.”
“Overall, the panel believes that evidence increasingly suggests that BRAF V600E mutation makes response to panitumumab or cetuximab, as single agents or in combination with cytotoxic chemotherapy, highly unlikely. The panel recommends BRAF genotyping of tumor tissue (either primary tumor or metastasis) at diagnosis of stage VI disease.”

“Despite uncertainty over its role as a predictive marker, it is clear that mutations in BRAF are a strong prognostic marker.”

“Although BRAF genotyping can be considered for patients with tumors characterized by the wild-type KRAS/NRAS genes, this testing is currently optional and not a necessary part of deciding whether to use anti-EGFR agents.”

“The panel strongly recommends genotyping of tumor tissue (either primary tumor or metastasis) in all patients with metastatic colorectal cancer for RAS (KRAS exon 2 or non-exon 2; NRAS) and BRAF at diagnosis of stage IV disease.”

“Testing for KRAS, NRAS, and BRAF mutations should be performed only in laboratories that are certified under the clinical laboratory improvement amendments of 1988 (CLIA-88) as qualifies to perform high complexity clinical laboratory (molecular pathology) testing. No specific methodology is recommended (eg, sequencing, hybridization).”

Criteria
Testing may be considered in individuals who meet the following criteria:

• Individual has been diagnosed with stage IV, metastatic colorectal cancer, AND

• BRAF mutation testing is needed for prognostic purposes.

The following BRAF mutation testing application is considered investigational and experimental:

• BRAF mutation testing for the purpose of decision making regarding the use of anti-EGFR agents.

References
Introduction
These references are cited in this guideline.


