BRAF Testing for Colorectal Cancer

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 in their tumor 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.

BRAF testing may sometimes be performed as part of a multi-mutation/multi-gene targeted panel to detect mutations in the KRAS, NRAS, and BRAF genes that are relevant for predictive and/or prognostic purposes in patients with colon cancer.

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.

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, 2019) states the following: "All patients with metastatic colorectal cancer should have tumor tissue genotyped for RAS (KRAS and NRAS) and BRAF mutations individually or as part of a next-generation sequencing (NGS) panel. Patients with any known KRAS mutation (exon 2, 3, 4) or NRAS mutation (exon 2,3,4) should not be treated with either cetuximab or..."
panitumumab.44-46 BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

“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 or predictive purposes.

References
Introduction
These references are cited in this guideline.


