CellSearch Circulating Tumor Cell Count for Breast Cancer Prognosis

Introduction

CellSearch circulating tumor cell count 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 are circulating tumor cells

Definition

Circulating tumor cells (CTCs) are cells whose source is unknown, but may have broken away from tumor tissue and are circulating in the blood stream.\(^1\)\(^2\)\(^3\) CTCs are rare in healthy individuals, but often present in people with metastatic cancer.\(^1\)

CTCs and breast cancer

The presence of CTCs in breast cancer patients may predict metastasis of an aggressive primary tumor.\(^1\)\(^2\)

A 2004 study found that individuals undergoing treatment for metastatic breast cancer with greater than or equal to 5 CTCs/7.5 mL had shorter progression-free survival (PFS) and shorter overall survival (OS) than individuals with less than 5 CTCs/7.5 mL.\(^2\)

The results of these and other studies suggest that measuring CTCs could be a useful prognostic tool for individuals with metastatic breast cancer.

CTCs may be measured before the start of therapy, and then after each therapy cycle (usually 4-5 weeks).\(^3\)
Test information

Introduction

The CellSearch® Circulating Tumor Cells Test measures CTC levels in the blood of breast cancer patients to identify risk for distant metastasis.\textsuperscript{3}

CellSearch

The purpose of CellSearch is to distinguish normal cells from CTCs with fluorescent nucleic acid dye.\textsuperscript{3}

Results are generally reported at number of CTCs per 7.5 ml of whole blood.\textsuperscript{2,4}

It has been reported that CellSearch correctly measures the levels of CTCs in 99.7\% of breast cancer patients.\textsuperscript{1}

CellSearch was cleared by the FDA in 2004.\textsuperscript{4}

Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to circulating tumor cells.

National Comprehensive Cancer Network

The NCCN Guidelines for Breast Cancer (2019) state that the clinical use of CTC in metastatic breast cancer is “not yet included in the NCCN Guidelines for Breast Cancer for disease assessment and monitoring.” They also state that “In spite of its prognostic ability, CTC count has failed to show a predictive value.”\textsuperscript{5}

American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO, 2016) states the following regarding circulating tumor cells with regard to early stage invasive breast cancer:\textsuperscript{6}


The American Society of Clinical Oncology (ASCO, 2015) states the following regarding circulating tumor cells with regard to metastatic breast cancer:\textsuperscript{7}

- "There is no evidence at this time that changing therapy based solely on circulating biomarker results improves health outcomes, quality of life, or cost effectiveness."
...comparison of progression-free survival and overall survival showed no difference in outcome when patients were switched to an alternate regimen on the basis of CTC level. These data also illustrate the frequency observed result that biomarkers may be prognostic but not predictive of clinical benefit when used to guide or influence decisions on systemic therapy for breast cancer."

Literature Review

The evidence is insufficient to support the use of CellSearch as a prognostic or predictive test. The clinical utility of CellSearch to predict or monitor treatment response has not been established.8-17

Results of several observational studies suggest that the use of CellSearch in metastatic breast cancer patients has prognostic value to assess risk of disease progression. Study results showed that enumerated CTC levels by CellSearch were significantly associated with overall survival outcomes in metastatic breast cancer patients. However, results of an RCT reported that use of CellSearch had no impact on survival outcomes in metastatic breast cancer patients who either maintained first-line treatment or opted to change treatment based on CTC levels. A good quality RCT reported that use of CellSearch had no impact on survival outcomes in metastatic breast cancer patients who were undergoing first-line treatment. Thus, clinical utility of CellSearch to predict and monitor treatment response has not been established. There is a lack of evidence regarding how CellSearch compares with variant analysis of tumor biopsy tissue. It is unclear whether molecular subtypes of breast cancer affect the status of CTC under various treatments. There is also a lack of evidence evaluating the use of CellSearch in early stage or non-metastatic breast cancer, or in screening settings.

Criteria

Introduction

Requests for CellSearch circulating tumor cell count are reviewed using these criteria.

Criteria

This test is considered investigational and/or experimental.

- Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.
• In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References

Introduction

These references are cited in this guideline.


