

Evidence Based Guideline

Biomarker Genes for Detection of Lymph Node Metastases

File Name: biomarker_genes_for_detection_of_lymph_node_metastases
Guideline Number: EBG.MED1064
Origination: 4/2009
Last CAP Review: 8/2009
Next CAP Review: 8/2011
Last Review: 8/2009

Description of Procedure or Service

Assessing the presence of tumor in axillary lymph nodes of patients with breast cancer is an important aspect in clinical staging of the disease. In addition, the presence of tumor is assessed in sentinel lymph nodes to help determine the extent of lymph node dissection that is needed. Patients with negative findings in the sentinel nodes have a low risk of having other nodes with positive findings and thus can often be spared the morbidity associated with a full axillary lymph node dissection (ALND). Currently, the presence of tumor is identified through traditional pathologic examination using frozen section or touch preparations at the time of surgery as well as the gold standard postoperative histologic examination of formalin-fixed tissue (permanent section) using hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC). If lymph nodes are found positive for metastases by intraoperative assay, ALND is done immediately. If positive findings are not detected until after histopathologic review of a permanent section, a second surgery for full ALND follows. When compared with final permanent histology results, intraoperative frozen section analysis of the sentinel lymph node has a reported sensitivity that varies from 58%–87%.

To improve the accuracy of current methods, newer techniques that yield reliable intraoperative results are being sought. One method identifies metastatic cells by detecting RNA transcribed from genes expressed at high levels in cells of breast origin but only at low levels in normal nodal tissue. Cytokeratin-19 and mammaglobin are two markers that have been studied. These genes are expressed at higher levels in breast tissue, but not in normal nodal tissue. These assays are being proposed as an alternative to the standard intraoperative use of frozen section for sentinel lymph nodes.

The only assay currently approved by the U.S. Food and Drug Administration (FDA) is the GeneSearch™ BLN Test Kit (Veridex, LLC). GeneSearch™ received premarket application approval from the FDA on July 16, 2007, for the “detection of greater than 0.2 mm metastases in nodal tissue removed from sentinel lymph node biopsies of breast cancer patients.” The product information notes that “Post-operative histological evaluation of permanent sections of the tissue specimen, in accordance with usual diagnostic practice and using the Veridex lymph node cutting scheme [alternating sections of <3 mm], is required.” The assay uses real-time polymerase chain reaction (RT-PCR) to qualitatively evaluate nodal sections for the presence of mammaglobin and cytokeratin 19 genes. The assay is automated and performed in a homogeneous, one-step, fully contained reaction; test results are available in about 35 to 40 minutes. The assay cutoff for positivity is designed to allow detection of metastases that are larger than 0.2 mm in size; however, the assay does not discriminate between micrometastases (i.e., between 0.2 mm and 2 mm) and macrometastases (i.e., larger than 2 mm).

*****Note: The Evidence Based Guideline on biomarker genes for the detection of lymph node metastases is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Evidence Based Guideline for Biomarker Genes for Detection of Lymph Node Metastases

The available evidence does not permit conclusions regarding the clinical utility of biomarker genes for detection of lymph node metastases in breast cancer.

Medical Evidence regarding Biomarker Genes for Detection of Lymph Node Metastases indicates it is not recommended in the following situations:

Evaluation of biomarker genes for detection of lymph node metastases in breast cancers is not recommended.

The data available are inadequate to assess the clinical utility and the impact on health outcomes of the GeneSearch™ assay compared to either postoperative histology alone or to alternative intraoperative tests such as imprint cytology and frozen section histology. In addition, the balance of benefits versus harms may require higher specificity to avoid unnecessary ALNDs and their sequelae, whereas the GeneSearch™ design emphasizes sensitivity. Patient preferences should also play a key role in this calculation.

National Cancer Institute Clinical Trials Database

The National Cancer Institute clinical trials database showed a phase IV assay-timing study using the GeneSearch™ assay, with the primary outcome measure to determine assay turn-around-time under clinical use conditions. Estimated enrollment is 320, with estimated study completion date of July 2009. No phase III trials studying the use of molecular pathology techniques in sentinel lymph nodes of breast cancer patients were identified.

National Comprehensive Cancer Network (NCCN) Guidelines

NCCN guidelines acknowledge the revised cancer staging manual by the American Joint Committee on Cancer (January 2003, sixth edition) which addresses the increasing use of novel pathology diagnostic techniques, and the addition of identifiers to indicate the use of sentinel lymph node molecular pathology techniques in staging a patient. However, the NCCN makes no recommendations as how to incorporate molecular testing of a sentinel lymph node into clinical practice.

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the policy.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: There are no specific CPT or HCPCS codes for this service

Policy: Biomarker Genes for Detection of Lymph Node Metastases

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.47, 1/8/2009

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Breast v.1.2000. Retrieved 3/13/09 from http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf.

Senior Medical Director 3/2009

Specialty Matched Consultant Advisory Panel - 8/2009

Policy Implementation/Update Information

4/13/09 New evidence based guideline adopted from the BCBSA. Senior Medical Director review 3/16/2009. The available evidence does not permit conclusions regarding the clinical utility of biomarker genes for detection of lymph node metastases in breast cancer. (btw)

10/12/09 Specialty Matched Consultant Advisory Panel review 8/28/09. No changes to evidence based guideline. (btw)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.