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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Sample Selection for Biomarker Testing in Adults with Breast Cancer: Guidelines


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**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

## Research Question

What are the evidence-based guidelines regarding sample selection for biomarker testing to inform treatment decisions in adults with breast cancer?

## Key Findings

Four evidence-based guidelines were identified regarding sample selection for biomarker testing in adults with breast cancer.

## Methods

A limited literature search was conducted on key resources including Medline via OVID, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and January 28, 2019. Internet links were provided, where available.

## Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

### Table 1: Selection Criteria

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| **Population** | Adult patients with breast cancer |
| **Intervention** | Biomarker testing (i.e., ER/PR, and HER2) on core biopsy or definitive tumour samples |
| **Comparator** | No comparator |
| **Outcomes** | Evidence-based guidelines |
| **Study Designs** | Health technology assessments, systematic reviews, meta-analyses, evidence-based guidelines |

## Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by evidence-based guidelines.

Four evidence-based guidelines were identified regarding sample selection for biomarker testing in adults with breast cancer. No relevant health technology assessments, systematic reviews, or meta-analyses were identified.

Additional references of potential interest are provided in the appendix.

## Overall Summary of Findings

Four evidence-based guidelines were identified regarding sample selection for biomarker testing in adults with breast cancer.[1-4] The first guideline from the National Institute of Health and Care Excellence (NICE)[1] recommends that the status of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth receptor 2 (HER2) of all invasive breast cancers should be simultaneously checked at the time of initial histopathological diagnosis using standardized and quality-assured immunohistochemical techniques. They also recommend ER, PR, and HER2 status be recorded at the pre- and postoperative multidisciplinary team meetings when systemic treatment is discussed.[1]

Another guideline from NICE[2] recommends using tumour profiling tests including EndoPredict, Oncotype DX Breast Recurrence Score, and Prosigna as options for guiding adjuvant chemotherapy decisions for people with ER-positive, HER2-negative, and lymph-node (LN)-negative early breast cancer. These are only recommended if the patient has an intermediate risk of distant recurrence. The tests would help with the decision to pursue adjuvant therapy while taking into consideration the patient's preferences for treatment.[2] The tumour profiling test MammaPrint is not recommended for guiding adjuvant chemotherapy decisions in patients with the aforementioned biomarker profile because it is not cost effective; IHC4+C is also not recommended because the analytical validity of the test is uncertain.[2]

The American Society of Breast Surgeons (ASBrS) created an evidence-based guideline of neoadjuvant systemic therapy (NST). They included the following recommendations in the care of patients with breast cancer: "...(2) minimally invasive biopsies of breast and axillary lesions; (3) determination of tumor biomarkers; (4) systemic staging;… (6) initiation of NST; (7) post-NST breast and axillary imaging; and (8) decision for surgery based on extent of disease at presentation, patient choice, clinical response to NST, and genetic testing results, if performed."[3]

The guideline by the American Society of Clinical Oncology/College of American Pathologists provided recommendations on HER2 testing in breast cancer.[4] They recommend that, **"**HER2 status (HER2 negative or positive) be determined in all patients with invasive (early stage or recurrence) breast cancer on the basis of one or more HER2 test results (negative, equivocal, or positive)."[4] Reflex testing should be performed if results are equivocal by using an alternative assay such as immunohistochemistry or in situ hybridization.[4] Lastly, "repeat testing should be considered if results seem discordant with other histopathologic findings."[4]

## References Summarized

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

No literature identified.

### Guidelines and Recommendations

1. National Institute for Health and Care Excellence. Early and locally advanced breast cancer: diagnosis and management. (*NICE guideline NG101)* 2018; https://www.nice.org.uk/guidance/ng101. Accessed 2019 Feb 5.
   *See: Section 1.6 Diagnostic assessment and adjuvant therapy planning, page 13*
2. National Institute for Health and Care Excellence. Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer. *(NICE guideline DG34)* 2018; https://www.nice.org.uk/guidance/dg34. Accessed 2019 Feb 5.
3. Holmes D, Colfry A, Czerniecki B, et al. Performance and practice guideline for the use of neoadjuvant systemic therapy in the management of breast cancer. *Ann Surg Oncol*. 2015;22(10):3184-3190.
   PubMed: PM26224406
4. Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *Arch Pathol Lab Med*. 2014;138(2):241-256.
   PubMed: PM24099077

# Appendix — Further Information

## Previous CADTH Reports

5. Oncotype DX in women and men with ER-positive, HER2-negative early stage breast cancer who are lymph node negative: a review of clinical effectiveness and guidelines. *(CADTH Rapid response report: summary with critical appraisal)*. Ottawa (ON): CADTH; 2014: https://cadth.ca/oncotype-dx-women-and-men-er-positive-her2-negative-early-stage-breast-cancer-who-are-lymph-node-0. Accessed 2019 Feb 5.

## Clinical Practice Guidelines

### *Unspecified Methdology*

6. Alberta Health Services. Adjuvant systemic therapy for early stage (lymph node negative and lymph node positive) breast cancer; 2018: https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-adjuvant-systemic-therapy-breast.pdf. Accessed 2019 Feb 5.
See: Table 2. Genomic testing for systemic therapy decision making, page 4

7. Krop I, Ismaila N, Andre F, et al. Use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer: American Society of Clinical Oncology clinical practice guideline focused update. *J Clin Oncol*. 2017;35(24):2838-2847.
PubMed: PM28692382

8. UHN Princess Margaret Cancer Centre. Princess Margaret Cancer Centre clinical practice guidelines: breast site. 2015; https://www.uhn.ca/PrincessMargaret/Health_Professionals/Programs_Departments/Breast/Documents/CPG_Breast_BreastCancer.pdf. Accessed 2019 Feb 5.
*See estrogen receptor (ER), progesterone receptor (PR), HER2 testing page 23.*

9. Eastern Health Breast Site Disease Group. Molecular biomarker discordance between primary and recurrent/metastatic breast cancer; 2014. http://cancercare.easternhealth.ca/wp-content/plugins/download-attachments/includes/download.php?id=6735. Accessed 2019 Feb 5.

### *Consensus Statements*

10. Cardoso F, Senkus E, Costa A, et al. 4th ESO–ESMO international consensus guidelines for advanced breast cancer (ABC 4). *Ann Oncol*. 2018; 29: 1634–1657.
PubMed: PM30032243

11. Colomer R, Aranda-Lopez I, Albanell J, et al. Biomarkers in breast cancer: a consensus statement by the Spanish Society of Medical Oncology and the Spanish Society of Pathology. *Clin Transl Oncol.* 2018;20(7):815-826.
PubMed: PM29273958

12. CancerCare Manitoba Breast Disease Site Group. Provincial consensus recommendations for adjuvant systemic therapy for breast cancer; 2017. https://www.cancercare.mb.ca/export/sites/default/For-Health-Professionals/.galleries/files/treatment-guidelines-rro-files/practice-guidelines/breast/Adjuvant_Breast_Guideline_July_2017.pdf. Accessed 2019 Feb 5.

## Review Articles

13. Ballinger TJ, Sanders ME, Abramson VG. Current HER2 testing recommendations and clinical relevance as a predictor of response to targeted therapy. *Clin Breast Cancer*. 2015;15(3):171-180.
PubMed: PM25516402

14. Bethune GC, Veldhuijzen van Zanten D, MacIntosh RF, et al. Impact of the 2013 American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 (HER2) testing of invasive breast carcinoma: a focus on tumours assessed as 'equivocal' for HER2 gene amplification by fluorescence in-situ hybridization. *Histopathology*. 2015;67(6):880-887.
PubMed: PM25913507

## Additional References

15. Biomarker-based tests for the decision for or against adjuvant systemic chemotherapy in primary breast cancer – addendum to Commission D14-01. Cologne (DE): Institute for Quality and Efficiency in Health Care; 2016. https://www.iqwig.de/download/D18-01_Biomarkers-in-breast-cancer_Executive-summary-of-addendum_V1-1.pdf. Accessed 2019 Feb 5.

16. Cimino-Matthews A, Park BH, Emens LA, Tsangaris TN. 'Smarter' ordering of breast biomarker tests could save millions in health care dollars, study reveals. Johns Hopkins Medicine; 2015: https://www.hopkinsmedicine.org/news/media/releases/smarter_ordering_of_breast_biomarker_tests_could_save_millions_in_health_care_dollars_study_reveals. Accessed 2019 Feb 5.