Role of Patient and Disease Factors in Adjuvant Systemic Therapy Decision-Making for Early-Stage, Operable Breast Cancer: American Society of Clinical Oncology Endorsement of Cancer Care Ontario Guideline Recommendations
Introduction

• Optimizing the selection of adjuvant systemic therapy for patients with early breast cancer is based on careful evaluation of a range of patient and disease characteristics.

• The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) identified a set of recommendations for endorsement that addressed the role of these patient and disease factors in selecting adjuvant therapy for women with early-stage breast cancer.

• The target recommendations were developed by members of the Cancer Care Ontario (CCO) Early Breast Cancer Systemic Therapy Consensus Panel in 2015 as part of a comprehensive practice guideline on optimal systemic therapy for early breast cancer in women that was published as an article series in *Current Oncology*.

• This ASCO endorsement considers only those recommendations that relate to patient and disease factors, recurrence risk, and selection of patients for adjuvant systemic therapy.
  – A separate ASCO guideline adaptation addresses CCO recommendations on the selection of optimal adjuvant chemotherapy regimens and the selection of adjuvant targeted therapy for HER2-positive cancers (www.asco.org/adaptations/breastsystemictherapy).
ASCO Endorsement Methodology

The ASCO Clinical Practice Guidelines Committee endorsement review process includes:

• a methodological review by ASCO guidelines staff
• a content review by an ad hoc expert panel
• final endorsement approval by ASCO CPGC.

The full ASCO Endorsement methodology supplement can be found at:
www.asco.org/endorsements/breastcancertreatment

CCO Guideline Methodology can be found at:
Clinical Questions

1. Which disease characteristics (histopathological parameters) are considered relevant (either prognostic or predictive) when making a decision regarding adjuvant systemic therapies for breast cancer?

2. What risk stratification tools may be used in determining the utility of certain systemic therapies in patients with early-stage breast cancer?

3. Which patient factors should be considered in making adjuvant systemic therapy decisions?

4. In those patients in whom chemotherapy would likely be tolerated and is acceptable to the patient, adjuvant chemotherapy should be considered for patients with which tumor characteristics?

5. When considering lymph node negative tumors with T>5mm, what should be considered high-risk features (thus considered candidates for chemotherapy)?

6. Patients with which disease characteristics may not benefit from adjuvant chemotherapy?

7. Adjuvant chemotherapy may not be required in patients with HER2−, strongly ER+ and PR+ breast cancer with any of the following additional characteristics?
Target Population and Audience

Target Population
Female patients who are being considered for, or who are receiving, systemic therapy for early-stage invasive breast cancer (stages I to IIA, T1N0–1, T2N0).

Target Audience
Medical oncologists, pathologists, surgeons, oncology nurses, patients/caregivers.
Summary of Recommendations

1. Which disease characteristics (histopathological parameters) are considered relevant (either prognostic or predictive) when making a decision regarding adjuvant systemic therapies for breast cancer?
   - Lymph node status
   - Human epidermal growth factor receptor 2 (HER2) status
   - T stage
   - Tumor grade
   - Estrogen receptor (ER) status
   - Presence of tumor lymphovascular invasion (LVI)
   - Progesterone receptor (PR) status

For making decisions about adjuvant systemic therapy, the CCO guideline recommendations highlight key tumor-related factors that should be considered in order to avoid over- or under-treatment of patients. In addition to the listed factors, the ASCO panel noted that some data suggest that certain uncommon breast cancer subtypes (e.g., tubular, mucinous) have favorable prognoses, and that this histologic information could also be relevant for making decisions about systemic therapy. However, large data sets are not currently available to confirm how best to treat these patients.

Chemotherapy should be considered for selected patients. However, there was no lower size limit provided in the CCO guideline for HER2-positive tumors, and the ASCO panel noted that there are no definitive data for use of chemotherapy and/or trastuzumab for HER2-positive tumors ≤ 5 mm. In addition, in the opinion of the ASCO panel, some of the factors, such as grade 3 and presence of LVI, should generally not be used to drive decision-making when considered in isolation, and need to be interpreted in the overall clinical context.

The ASCO panel also felt, consistent with the 2015 St Gallen International Expert Consensus, that tumors that are well-differentiated, especially those that are “luminal A-like” should also be considered for omission from chemotherapy.
2. What risk stratification tools may be used in determining the utility of certain systemic therapies in patients with early-stage breast cancer?

- Oncotype DX score (for HR+, N0 or N1mic or ITC, and HER2 negative cancers)
- Adjuvant! Online (www.adjuvantonline.com)

The ASCO panel notes that in addition to the Oncotype DX assay, there are now multiple risk stratification tools available for routine clinical use and that this is a rapidly evolving field. The panel recommends that providers refer to the current ASCO guideline on use of biomarkers for decision-making for treatment of patients with early stage breast cancer (www.asco.org/guidelines/adjuvantbreastmarkers) for recommendations about use of several other risk stratification tools and in the setting of other disease characteristics, such as lymph node positive breast cancer.

The ASCO Panel suggests a slight revision to the CCO language concerning the Oncotype DX intermediate recurrence score, as follows: “The utility of chemotherapy in the intermediate recurrence score zone is currently less clear, although a phase III clinical trial (TAILORx), once reported might help to address that question for patients with a recurrence score 11-25.”
Summary of Recommendations

3. Which patient factors should be considered in making adjuvant systemic therapy decisions?

- Age
- Menopausal status
- Medical comorbidities (including validated tools used to measure health status)

The ASCO panel agreed with the patient factors listed by CCO that should be considered when making decisions about adjuvant systemic therapy. Panel members also felt that the preferences of the patient are an important factor in the selection of adjuvant systemic therapy. In addition, for patients with advanced age, the ASCO panel also recommends measurement of estimated life expectancy and other factors included in validated geriatric assessment tools such as functional status, comorbidity, cognitive function and social support, rather than relying solely on chronologic age when making decisions about adjuvant systemic therapy.
Summary of Recommendations

4. In those patients in whom chemotherapy would likely be tolerated and is acceptable to the patient, adjuvant chemotherapy should be considered for patients with which tumor characteristics?

- In no particular order:
- Lymph node positive: one or more lymph nodes with a macro-metastatic deposit (>2 mm)
- ER− with T size >5mm
- HER2+ tumors
- High-risk lymph node negative tumors with T size >5 mm and another high-risk feature (see next recommendation, R5)
- Adjuvant! Online 10-year risk of death from breast cancer >10% or 15%

The ASCO panel suggests a slight revision to the CCO language concerning the Adjuvant! Online: a 10-year risk of death judged to be greater than 10% or 15% using the Adjuvant! Online model is a reasonable threshold for considering chemotherapy.
Summary of Recommendations

5. When considering lymph node negative tumors with T>5mm, what should be considered high-risk features (thus considered candidates for chemotherapy)?

- Grade 3
- Triple negative (ER−, PR−, and HER2−)
- LVI positive
- An Oncotype DX recurrence score (RS) that is associated with an estimated distant relapse risk of 15% or more at 10 years
- HER2+

The ASCO panel suggests a slight revision to the CCO language concerning the Oncotype DX threshold for this recommendation. Specifically, for lymph node-negative tumors with T > 5mm, Grade 3, triple negative (ER-, PR-, and HER2-), LVI positive, Oncotype DX recurrence score (RS) associated with an estimated distant relapse risk of > 20 % at 10 years, and HER2+ should be considered high-risk features and thus considered candidates for chemotherapy.

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Summary of Recommendations

6. Patients with which disease characteristics may not benefit from adjuvant chemotherapy?
   • T <5 mm, lymph node negative and no other high-risk features (see previous recommendation)

7. Adjuvant chemotherapy may not be required in patients with HER2−, strongly ER+ and PR+ breast cancer with any of the following additional characteristics?
   • Lymph node positive with micrometastasis (<2 mm) only, or
   • T <5 mm, or
   • An Oncotype DX RS with an estimated distant relapse risk of less than 10% at 10 years

The ASCO panel suggests a minor revision from CCO’s “…Oncotype DX RS with an estimated distant relapse risk of less than 15% at 10 years” to “an Oncotype DX RS with an estimated distant relapse risk of less than 10% at 10 years.”
Endorsement Recommendation

ASCO endorses the CCO guideline recommendations on patient and disease factors in selecting adjuvant therapy for women with early-stage breast cancer.
Additional Resources

More information, including a Data Supplement with a reprint of all CCO recommendations, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/endorsements/breastcancertreatment

Link to original guideline:


Patient information is available at www.cancer.net
# ASCO Endorsement Panel Members

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