Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline

Korde et al.
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Background & Methodology
Introduction

• As our understanding of the biology of breast cancer has evolved in recent decades, it has become clear that optimal therapy for breast cancer is driven by subtype.

• Older neoadjuvant trials that used a one-size-fits-all approach to therapy selection are less relevant in the current era of biologically driven treatment selection.

• The purpose of this guideline is to develop recommendations concerning the optimal use of systemic neoadjuvant therapy, including chemotherapy, endocrine therapy, and targeted therapy for patients with invasive breast cancer.

• The Expert Panel strongly advocates for a multidisciplinary team management approach when considering neoadjuvant therapy for patients with breast cancer.

• The guideline outlines recommendations based on clinical presentation, patient characteristics, and breast cancer subtype.
ASCO Guideline Development Methodology

• The ASCO Clinical Practice Guidelines Committee guideline process includes:
  ▪ a systematic literature review by ASCO guidelines staff
  ▪ an expert panel provides critical review and evidence interpretation to inform guideline recommendations
  ▪ final guideline approval by ASCO CPGC

• The full ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology
Clinical Questions

This clinical practice guideline addresses five overarching clinical questions:

1. Which patients with breast cancer are appropriate candidates for neoadjuvant systemic therapy?
2. How should response be measured in patients receiving neoadjuvant chemotherapy?
3. What neoadjuvant systemic therapy regimens are recommended for patients with triple-negative breast cancer (TNBC)?
4. What neoadjuvant treatment is recommended for patients with HR-positive/HER2-negative breast cancer?
5. What neoadjuvant treatment is recommended for patients with HER2-positive disease?
Target Population and Audience

Target Population

• Patients with nonmetastatic breast cancer

Target Audience

• Medical oncologists, surgical oncologists, radiologists, pathologists, oncology nurses, patients or caregivers or advocates, and oncology advanced practice providers
Summary of Recommendations
Summary of Recommendations

Clinical Question 1

• Which patients with breast cancer are appropriate candidates for neoadjuvant systemic therapy?

Recommendation 1.1

• Neoadjuvant chemotherapy is the treatment of choice for patients with inflammatory breast cancer or those with unresectable or locally advanced disease at presentation whose disease may be rendered resectable with neoadjuvant treatment.

Informal consensus

Evidence Quality
Low

Strength of Recommendation
Strong
Summary of Recommendations

Recommendation 1.2

- Tumor histology, grade, stage and estrogen, progesterone, and HER2 expression should routinely be used to guide clinical decisions as to whether or not to pursue neoadjuvant chemotherapy. There is insufficient evidence to support the use of other immunohistochemical markers, morphological markers (e.g., tumor infiltrating lymphocytes or TILs) or genomic profiles to guide a clinical decision as to whether or not to pursue neoadjuvant chemotherapy.
Summary of Recommendations

Recommendation 1.3

- Neoadjuvant systemic therapy should be offered to patients with high-risk HER2-positive or triple negative breast cancer (TNBC) in whom the finding of residual disease would guide recommendations related to adjuvant therapy.

Evidence-based benefits outweigh harms

Evidence Quality
High

Strength of Recommendation
Strong
Summary of Recommendations

**Recommendation 1.4**

- Neoadjuvant systemic therapy may be offered to reduce the extent of surgery (breast conserving surgery and axillary lymph node dissection). Chemotherapy with or without targeted therapy, or endocrine therapy (if HR+) may be offered.
Summary of Recommendations

Recommendation 1.5

- In patients for whom a delay in surgery is preferable (e.g., for genetic testing required for surgical treatment decision making, to allow time to consider reconstructive options) or unavoidable, neoadjuvant systemic therapy may be offered.
Summary of Recommendations

Clinical Question 2

• How should response be measured in patients receiving neoadjuvant chemotherapy?

Recommendation 2.1

• Patients receiving neoadjuvant therapy should be monitored for response with clinical examination at regular intervals. Breast imaging may be used to confirm clinical suspicion of progression and for surgical planning. When imaging is used, the modality that was most informative at baseline—mammography, ultrasound, or magnetic resonance imaging—should be used at follow-up.

Informal consensus

Evidence Quality: Insufficient

Strength of Recommendation: Moderate
Summary of Recommendations

Recommendation 2.2

• Blood- and tissue-based biomarkers should not be used for monitoring patients receiving neoadjuvant therapy.

Informal consensus

Evidence Quality

Insufficient

Strength of Recommendation

Strong

Recommendation 2.3

• Pathologic complete response (pCR), defined as absence of invasive disease in breast and lymph nodes, should be used to measure response to guide clinical decision making.

Informal consensus

Evidence Quality

Insufficient

Strength of Recommendation

Moderate
Summary of Recommendations

Clinical Question 3

• What neoadjuvant systemic therapy regimens are recommended for patients with TNBC?

Recommendation 3.1

• Patients with TNBC who have clinically node positive and/or at least T1c disease should be offered an anthracycline- and taxane-containing regimen in the neoadjuvant setting.

Evidence-based benefits outweigh harms

Evidence Quality
High

Strength of Recommendation
Strong
Summary of Recommendations

Recommendation 3.2

- Patients with cT1a or cT1bN0 TNBC should not routinely be offered neoadjuvant therapy outside of a clinical trial.

Evidence-based benefits outweigh harms

Evidence Quality: High
Strength of Recommendation: Strong

Recommendation 3.3

- Carboplatin may be offered as part of a neoadjuvant regimen in patients with TNBC to increase likelihood of pCR. The decision to offer carboplatin should take into account the balance of potential benefits and harms.

Evidence-based benefits outweigh harms

Evidence Quality: Intermediate
Strength of Recommendation: Moderate
Summary of Recommendations

Recommendation 3.4

• There is insufficient evidence to recommend routinely adding the immune checkpoint inhibitors to neoadjuvant chemotherapy in patients with early-stage TNBC.

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<tr>
<th>Evidence Quality</th>
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Informal consensus
Summary of Recommendations

Clinical Question 4

• What neoadjuvant treatment is recommended for patients with HR-positive/HER2-negative breast cancer?

Recommendation 4.1

• Neoadjuvant chemotherapy can be used instead of adjuvant chemotherapy in any patient with HR-positive, HER2-negative breast cancer in whom the chemotherapy decision can be made without surgical pathology data and/or tumor specific genomic testing.

Informal consensus

Evidence Quality
Low

Strength of Recommendation
Moderate
Recommendation 4.2

- For postmenopausal patients with HR-positive, HER2-negative disease, neoadjuvant endocrine therapy with an aromatase inhibitor may be offered to increase locoregional treatment options. If there is no intent for surgery, endocrine therapy may be used for disease control.

Evidence-based benefits outweigh harms

Evidence Quality: Intermediate
Strength of Recommendation: Moderate

Recommendation 4.3

- For premenopausal patients with HR-positive, HER2-negative early-stage disease, neoadjuvant endocrine therapy should not be routinely offered outside of a clinical trial.
Summary of Recommendations

Clinical Question 5

• What neoadjuvant treatment is recommended for patients with HER2-positive disease?

Recommendation 5.1

• Patients with node-positive or high-risk node-negative, HER2-positive disease should be offered neoadjuvant therapy with an anthracycline and taxane or non-anthracycline-based regimen in combination with trastuzumab. Pertuzumab may be used with trastuzumab in the neoadjuvant setting.

Evidence-based benefits outweigh harms

Evidence Quality
High

Strength of Recommendation
Strong
Summary of Recommendations

Recommendation 5.2

- Patients with T1a N0 and T1b N0, HER2-positive disease should not be routinely offered neoadjuvant chemotherapy or anti-HER2 agents outside of a clinical trial.

Informal consensus

Evidence Quality
Intermediate

Strength of Recommendation
Moderate
Discussion
Patient and Clinician Communication

• Communication topics of particular relevance to neoadjuvant therapy for breast cancer include the need to:
  ▪ clarify the goals of treatment so that the patient understands likely outcomes and can relate the goals of treatment to their goals of care (eg, downstaging to enable BCS, desire for immediate surgery)
  ▪ ensure the patient’s understanding of the potential benefits and burdens of any proposed treatment.

• Communicating the goals of treatment with patients in the neoadjuvant setting can be challenging. Patients for whom neoadjuvant treatment is proposed begin treatment very quickly after diagnosis, which leaves very little time to ask questions about the therapy they are about to receive.

• Many patients feel like they do not receive adequate information to make decisions or manage the side effects of neoadjuvant therapy.\(^1\)

• It is crucial for the clinicians and healthcare system to promote multidisciplinary treatment of breast cancer patients.
Health Disparities

- The literature search conducted to inform this section of the neoadjuvant therapy guideline identified 14 articles (from a total of 101 abstracts) on the topic of health disparities.²-¹⁵

- It is possible that for some patients, especially those with poor access to the multiple healthcare providers involved in breast cancer care, earlier initiation of therapy may reduce delays in care.

- Delays in care have been associated with poor breast cancer outcomes among minorities and patients with low socioeconomic status,¹⁶ particularly those with TNBC.

- Research is underway to determine if reducing delays in care for high-risk women by early administration of neoadjuvant chemotherapy improves outcomes.
Cost Implications

• Increasingly, individuals with cancer are required to pay a larger proportion of their treatment costs through deductibles and co-insurance.\textsuperscript{17,18} Higher patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended cancer treatments.\textsuperscript{19,20}

• Discussion of cost can be an important part of shared decision-making.\textsuperscript{21}

• Patient out-of-pocket costs may vary depending on insurance coverage. When discussing financial issues and concerns, patients should be made aware of any financial counseling services available to address this complex and heterogeneous landscape.\textsuperscript{21}

• The decision of giving a treatment in the adjuvant or neoadjuvant setting does not alter the overall costs of care; however, limiting the extent of surgery, introducing radiation, and extending therapy after neoadjuvant therapy do have the potential to alter the total financial burden.
Additional Resources

• More information, including a supplement and clinical tools and resources, is available at www.asco.org/breast-cancer-guidelines

• Patient information is available at www.cancer.net
# Guideline Panel Members

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<tr>
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References

References

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