Breast cancer Symposium

9/30/2025

NCCN/Older Adults

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2025
Invasive Breast Cancer

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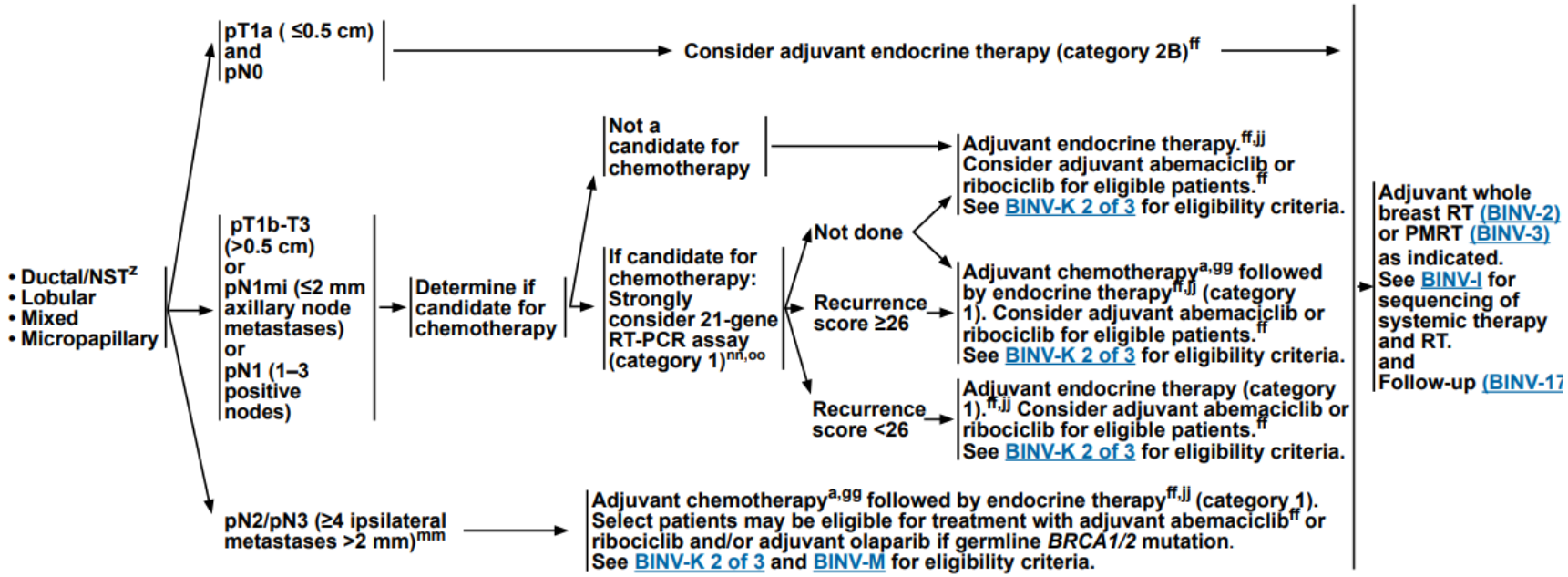
SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE – HER2-NEGATIVE DISEASE[d,v,dd]
POSTMENOPAUSAL[ee] PATIENTS with pT1–3 AND pN0 or pN+ TUMORS



[a] For tools to aid optimal assessment and management of older adults, see NCCN Guidelines for Older Adult Oncology.
[d] Principles of Biomarker Testing (BINV-A).
[v] Special Considerations for Breast Cancer in Males (Sex Assigned at Birth) (BINV-J).
[z] According to WHO, carcinoma of NST encompasses multiple patterns including medullary pattern, cancers with neuroendocrine expression, and other rare patterns.
[dd] Although patients with cancers with 1%–100% ER IHC staining are considered ER-positive and eligible for endocrine therapies, there are more limited data on the subgroup of cancers with ER-low–positive (1%–10%) results. The ER-low–positive group is heterogeneous with

[ee] Definition of Menopause (BINV-O).
[ff] Adjuvant Endocrine ± CDK/4/6 Inhibitor Therapy and Principles of Adjuvant Endocrine Therapy (BINV-K).
[gg] Preoperative/Adjuvant Therapy Regimens (BINV-M).
[jj] Consider adjuvant bisphosphonate therapy for risk reduction of distant metastasis for 3–5 years in postmenopausal patients (natural or induced) with high-risk node-negative or node-positive tumors.
[mm] There are few data regarding the role of gene expression assays in those with ≥4 ipsilateral axillary lymph nodes. Decisions to administer adjuvant chemotherapy for this group should be based on clinical factors.
[nn] Other prognostic gene expression assays may be considered to help assess risk of

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NCCN Older Adult Oncology Panel Members
Summary of the Guidelines Updates

- Definition and Purpose of the NCCN Guidelines for Older Adult Oncology (OAO-1)
- Approach to Shared Decision-Making in the Older Adult Prior to Therapy (OAO-2)
- Pre-Treatment Evaluation (OAO-3)
- Considerations for Older Adults Undergoing Cancer-Specific Treatment (OAO-4 and OAO-5)
- Management of Common Side Effects in Older Adults Undergoing Cancer-Specific Treatment (OAO-6)
- Life Expectancy of General Population (OAO-A)
- Optimizing Communication with Older Adults (OAO-B)
- Geriatric Screening Tools (OAO-C)
- Geriatric Assessment (OAO-D)
- Falls Assessment and Interventions (OAO-E)
- Assessment of Cognitive Function (OAO-F)
- Insomnia (OAO-G)
- Medications Commonly Used for Supportive Care that Are of Concern in Older Patients (OAO-H)
- Approach to Cancer Screening for Older Adult Cancer Survivors (OAO-I)
- Approach to Surveillance Testing for Older Adult Cancer Survivors with No Evidence of Disease (OAO-J)
- Abbreviations (ABBR-1)

Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Find an NCCN Member Institution: https://www.nccn.org/home/member-institutions.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.

See NCCN Categories of Evidence and Consensus.

NCCN of Older Adults

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DEFINITION AND PURPOSE

Definition of the Older Adult Oncology Population

- There is no chronologic age threshold to define an older adult. Age 65 years and over is generally considered the chronologic definition of an older adult, as this is the usual age of eligibility for Medicare benefits. The guidelines herein focus on physiologic age and function to define the older adult oncology population.

Purpose of the NCCN Guidelines for Older Adult Oncology

- There are unique issues to consider when caring for an older adult with cancer.
- The biologic characteristics of certain cancers and their responsiveness to therapy may be different in older patients compared to their younger counterparts.
- The psychologic and psychosocial changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered in the treatment decision-making process. See NCCN Guidelines for Distress Management.
- Advanced age alone should not be the only criterion to preclude effective treatment that could improve quality of life (QOL) or lead to a survival benefit in older patients.
- Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. See NCCN Guidelines for Supportive Care and NCCN Guidelines for Palliative Care.
- These age-related issues form the basis for the development of NCCN Guidelines for Older Adult Oncology that address special considerations in older patients with cancer.

Introduction

- Increasing age is the most prevalent, primary risk factor for breast cancer.
- Of the approximately 250,000 new cases of female breast cancer diagnosed annually in the United States, almost one-half arise in older women
- Typically defined as age ≥65 years

Practical Challenge

- Wide spectrum of women in the "older" population defined by biological age and by functional status
- Older patients are under-represented in clinical trials
- Relative lack of evidence-based guidelines to inform the treatment of breast cancer in this population

Practical Challenge

- There have been clinical trials specifically for older breast cancer patients
- Subset analyses of trials open to all breast cancer patients, regardless of age
- These results have yielded important information for treatment of older breast cancer patients

Treatment Patterns

- Older women often receive less aggressive treatment
- less often receive guideline therapy compared with younger women
- Decreased rates of breast surgery, axillary surgery, and radiotherapy

TREATMENT PATTERNS

- More often receive upfront mastectomy and primary endocrine therapy
- Adjuvant chemotherapy is used less commonly in older individuals
- More treatment interruption and less treatment completion rate compare to younger patients

Treatment Patterns/SEER database

- Rate of chemotherapy use for stage I or II, HR, node negative ranged from 80% for ages 67 to 69, down to <10% for those above 85
- Less aggressive chemotherapy protocols
- More often hormonal treatment
- Diagnosed at later stages

Factors Contribute to Differences In Treatment Of the older Patient

- Screening programs for early detection of breast cancer focus on women from age 40 and stop by age 70
- Older women are less likely to have screen-detected breast cancers
- More often estrogen receptor positive, human epidermal growth factor receptor 2 negative, and lower grade.

CONTINUE-

- Marked selection bias among treatment of older women that affects the interpretation of practice patterns in older patients
- Oncotype DX Recurrence Score test would be a highly selective in this group
- Decision on whether to recommend chemotherapy is still being made(rarely includes women over age 75)

Prognosis

- Outcomes among older women with breast cancer tend to be worse than those of younger women with breast cancer
- Breast cancer diagnosis (particularly if early stage) may not affect the life expectancy
- Women with stage I to II breast cancer aged 85 to 89 years had an increased risk of dying due to breast cancer compared with those aged 67 to 69 years

Prognosis:SEER data

- Women diagnosed with (DCIS) or stage I invasive breast cancer had a lower risk of death compared with controls
- Women aged ≥80 years diagnosed with stage II breast cancer, cardiovascular disease is the most common cause of death.
- Women with stage III or IV breast cancer, breast cancer was the most common cause of death

Impact Of Comorbidity

- The number and effect of an individual's other physical and psychological diseases
- Independently associated with decreased life expectancy
- Major role in determining survival in older patients with cancer
- life expectancy is almost halved in the presence of comorbidity

Impact Of Comorbidity

- Comorbid conditions that impose functional limitations are associated with higher mortality
- The adjusted HR of death (from all causes) increased as the severity of comorbidity increased
- The importance of comorbidity on overall prognosis among older women with breast cancer

Impact Of Comorbidity

- The presence and severity of comorbidity must be considered in weighing the risks and benefits when deciding about treatment
- The benefit of chemotherapy was absent in cases of significant comorbidity but still present in another similar study
- This type of retrospective, nonrandomized analyses are however prone to selection bias, making strong conclusions on the impact of frailty on chemotherapy uncertain

General Health Status

- Treatment considerations should be individualized based on general prognostic tumor-related markers
- Global health status (providing information on life expectancy and treatment tolerance)
- Patient preference
- Not on chronological age per se

General Health Status

- Avoid "overtreating" older patients with adjuvant therapies if they are more likely to die from other causes prior to a possible breast cancer recurrence

- Avoid “undertreament”older patiens when treatment can add to life

ePrognosis

- ePrognosis estimates life expectancy based on medical history and has been validated for use among women with early-stage breast cancer
- Providing an estimate of noncancer mortality risk,
- The ePrognosis tool can help frame treatment decisions, especially for adjuvant chemotherapy.

Cancer and Aging Research Group-Breast Cancer (CARG-BC)

- Predict toxicity from chemotherapy specifically in older adults with early breast cancer
- Better prediction than Karnofsky Performance Status (KPS)
- Developed using data prospectively collected from age ≥65 years with stage I to III breast cancer treated with neoadjuvant or adjuvant chemotherapy.

Comprehensive Geriatric Assessment For Patients With Cancer

- The functional status, comorbidity, cognition, nutrition, psychological state, social support, and medication review.
- Various approaches to gathering this information have been used including a mailed or self-administered assessment.
- Comprehensive geriatric assessment (CGA) may help clinicians develop a coordinated plan for breast cancer treatment

Pathologic Features Of The Tumor

- Breast cancers that occur in older women are more often in an advanced stage
- More likely to be HR + and (HER2) negative
- Have more indolent features compared with those that arise in younger women
- The more aggressive subtypes (basal-like)are less common

SURGICAL MANAGEMENT

- Assessment for whether a patient is a good candidate for surgery includes review of life expectancy, comorbidities, and frailty
- In medically fit older women, standard breast cancer surgery options should be offered, given morbidity and mortality benefits
- low postsurgical complication rates (18.9 percent) and average hospital stays (median, three days)

SURGICAL MANAGEMENT

- Most older women choose breast conservation surgery over mastectomy(breast-conserving surgery results in less disability in older women)
- Patients with tumors that cannot be treated by breast-conserving surgery (eg, cT4, multifocal tumors, etc) are best treated by mastectomy
- Preoperative (neoadjuvant) systemic therapy can be offered to some patients, especially if they are interested in breast-conserving

Neoadjuvant Endocrine Therapy(NET)

- For the majority of patients with HR-positive disease who warrant neoadjuvant therapy, chemotherapy over endocrine therapy(all age group)
- Neoadjuvant endocrine therapy may allow for less aggressive surgery to be performed at later date for HR+ disease
- Particularly for older patients (eg ≥75 years), those with significant comorbidities, or those with tumors that are strongly HR positive

Neoadjuvant Endocrine therapy(NET)

- NET is associated with similar response rates to neoadjuvant chemotherapy, although it may take longer to achieve a response.
- Survival data with NET versus neoadjuvant chemotherapy are not yet available
- Administer NET for four to six months, though a longer duration of treatment may be utilized

Surgery versus endocrine therapy alone for HR+

- Favor surgery rather than primary endocrine therapy for women with hormone receptor-positive breast cancer
- Surgical resection reduces the risk of a local recurrence and its associated morbidity.
- Breast surgery is well tolerated in older women and if general anesthesia is contraindicated, it can be done under local anesthesia

Surgery And Endocrine Therapy for HR+

- Surgery as the primary treatment is supported by multiple trials and a 2006 meta-analysis
- There was an improvement in progression-free survival favoring surgery alone (hazard ratio [HR] 0.55, 95% CI 0.39-0.77) or surgery plus Tamoxifen
- There was a trend toward an improvement in OS with surgery plus Tamoxifen

Management of the Axilla

- Older women may not require axillary lymph node surgery
- Clinically negative axilla and hormone receptor-positive cancers that will be treated with endocrine therapy
- The 10-year axillary recurrence rate in patients with incomplete axillary staging was 5.2 percent, and the OS was comparable between patients with or without complete axillary staging(patients>75 years)

Adjuvant Systemic Therapy

- Older adult women receiving adjuvant chemotherapy can experience a survival benefit from treatment but more prone to experiencing toxicities
- Patients with more aggressive/advanced disease will derive greater benefit from adjuvant chemotherapy
- Individualized treatment plan based on Geriatric tools

Adjuvant Systemic Therapy:SEER Data

- Adjuvant chemotherapy was associated with a mortality reduction of approximately 15%
- The most pronounced benefits were experienced by those with involved lymph nodes or other high-risk features
- Chemotherapy did not benefit those with significant comorbidity

Adjuvant Systemic Therapy:SEER Database

- Increased risk for toxicity including short-term (eg, drug-induced) mortality when using the same chemotherapy regimens as younger women
- Patients aged >65 years have more than double the risk of being hospitalized for chemotherapy-related reasons
- 2.9% of early breast cancer patients ≥65 years old died within one year after the start of chemotherapy

Tools To Predict benefit

- PREDICT tool may be used for overall survival (OS) estimates with and without chemotherapy
- Applies to women who have had surgery for early breast cancer and are deciding which other treatments to have,likely to apply to neo-adjuvant chemotherapy.
- Not designed for stage 4 or DCIS or LCIS
- Discussion should be in laymen language and documented in patient chart

PREDICT tool

Reset

Predict is not designed to be used in all cases. Click here for more details.
If you are unsure of any inputs or outputs, click on the ℹ buttons for more information.

DCIS or LCIS only? Yes | No

Age at diagnosis – | + | +

Age must be between 25 and 85

Post Menopausal? Yes | No | Unknown

ER status Positive | Negative

HER2/ERRB2 status Positive | Negative | Unknown

Ki-67 status Positive | Negative | Unknown

Positive means more than 10%

Invasive tumour size (mm) – | + | +

If there was more than one tumour, enter the siz of the largest tumour. If neo-adjuvant therapy w undertaken, enter the size before neo-adjuvant therapy.

Tumour grade 1 | 2 | 3

Detected by Screening | Symptoms | Unknown

Positive nodes – | + | +

Micrometastases only Yes | No | Unknown

Enabled when positive nodes is 1.

ℹ All boxes with a pink outline need to be filled in. Treatment options and results will only appear here when you have entered information into all of them.

Treatment (HER2-negative disease)

- Standard chemotherapy regimens, such TC;for fit women with higher-risk disease, anthracycline-taxane regimens.
- The older regimen, cyclophosphamide, methotrexate, and fluorouracil (CMF), may be considered in those who have contraindications both to anthracyclines and taxanes.
- Other nonstandard regimens have either been associated with worsened toxicities and/or efficacy among older adults

Treatment (HER2-positive disease)

- Addition of trastuzumab improves survival and diminishes recurrence risk compared with chemotherapy alone and is tolerated in older patients
- Older adult patients receiving trastuzumab had 47% relative risk reduction in compared with chemotherapy alone
- Cardiac function should be monitored every 3 months

Treatment (HER2-positive disease)

- Insufficient data to recommend adjuvant trastuzumab without chemotherapy in early breast cancer
- Cardiac toxicity is a particular issue when anthracyclines and Herceptin used
- Taxane-anti-HER2 combinations **without** anthracyclines are favored for older patients like TCH or Taxol and Herceptin only

Treatment (HER2-positive disease)

- Significant proportion of older patients with HER2-positive early breast cancer do not receive trastuzumab
- CHF occurs more frequently with versus without trastuzumab: 29% in ≥66-year-old trastuzumab users versus 19% in non-trastuzumab
- One year of adjuvant trastuzumab should be administered in the older patient(can consider 6 months for high risk patinets)

Treatment (HER2-positive disease)

- The absolute benefit of Pertuzumab addition in terms of decreased invasive DFS was rather minor
- Pertuzumab-associated diarrhea may be more debilitating for older than younger persons
- Aphinity evaluated pertuzumab only in combination with Herceptin and anthracycline-taxane or TCH regimen(very few patients)

Endocrine Therapy for HR+

- Should be offered to all women with ER-positive breast tumors >0.5 cm, regardless of age
- Aromatase inhibitor (AI) in older women favored because of its benefits in the adjuvant setting compared with Tamoxifen
- Tamoxifen is a reasonable alternative for risk for cardiovascular complications or bone loss, and those unable to tolerate an AI

Adjunctive Systemic Treatments

- Growing interest in the use of bisphosphonates in the adjuvant setting
- Reducing the relapse risk
- Decreasing the risk of therapy-induced osteoporotic fractures
- Renal function declines with age, and the dose of zoledronic acid needs to be adapted to renal function

Adjuvant Radiation

- Well tolerated and the cosmetic results are excellent, even in older women
- Studies show that the risk of a local recurrence is lower in older women, and the benefits of RT following breast conservation surgery decline with age
- Still may have short term and medium to long term risks

Omission of Adjuvant Radiation

- Small, estrogen receptor-positive breast cancer and no evidence of nodal disease who agree to take endocrine therapy.
- Should be counseled that they may have a slightly higher risk of an in-breast cancer recurrence compared with those who undergo RT
- life expectancy plays a role in the true benefit of adjuvant RT; in frail patients with higher-risk tumors, adjuvant RT will provide little, if any, benefit

Non-Surgical Candidate (HR+)

- Patients with hormone-positive disease who are not surgical candidates are offered primary endocrine therapy(palliative intent)

- Patients with a limited life expectancy (due to comorbidities) and those who wish to avoid treatment-related toxicity referral to palliative care

Non-Surgical Candidate (Her2 + or triple negative))

- Observe without systemic treatment for asymptomatic nonsurgical patients
- For symptomatic patients anti-HER2 therapy with single-agent chemotherapy (or potentially with endocrine therapy
- Short course of radiotherapy can be considered to avoid/treat local symptoms.

- Thanks for attending Mercy Health 3rd Annual Oncology Symposium