What is NCCN?

• Arbiter of high-quality cancer care

• Developer and Promoter of National Programs to facilitate the fulfillment of member institution missions in education, research, and patient care and to incrementally advantage NCCN institutions in the marketplace

• Developer and Communicator of scientific, evaluative information to better inform the decision-making process between patients and physicians, ultimately improving patient outcomes

• Seek to enhance the effectiveness and efficiency of cancer care through information resources, outcomes research, clinical trials, and other contributions to the cancer care delivery system

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Integrated Suite of NCCN Information Products
NCCN Guidelines™

• Comprehensive across all stages, modalities and continuum of care
  – 47 multidisciplinary expert panels with 25-30 experts per panel (Volunteer time and expertise)
  – Cancer screening, diagnosis, treatment and supportive care
• Updated at least annually and up to 4 times per year since 1995
• Category of evidence and consensus designated for each recommendation
• Transparent processes
• Centerpiece of suite of tools to support quality oncology care

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Guidelines Available on NCCN.org
Parts of a Guideline

- Panel list
- Table of Contents
- Algorithms including special topics
- Discussion
- References

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Who Develops Guidelines

- Faculty from Member Institutions
  - Multidisciplinary
  - Volunteers
  - Mix of senior, mid-career, and junior faculty

- NCCN Staff Support
  - Oncology scientist
  - Guidelines coordinator
  - Administrative assistants
Guideline Update Process: Continuous Improvement

Institutional Review
Request for Papers
Outside Submissions
Publication
Panel Review
Panel Meeting
Algorithm, Reference, and Discussion Update
Chair Review
Panel Review
Finalize Algorithm and Discussion

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Evidence

- Ongoing process
- The amount of data available differs across disease sites and across clinical decisions within a disease site
- Continuous review of evidence and guideline updates is required
- New studies WILL change the standard of care over time

Data from multiple studies and sources → Expert evaluation → Distill appropriate recommendations © NCCN All rights reserved.
NCCN Categories of Evidence and Consensus

• **Category 1**: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

• **Category 2A**: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

• **Category 2B**: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

• **Category 3**: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

*All recommendations are category 2A unless otherwise noted.*
Critical Analysis and Culling of Data

- NCCN Categories of Evidence
  - 1, 2A, 2B, 3

- Consistency of evidence
  - Highly consistent, single trial, variable data

- Extent of evidence
  - Extensive, less extensive, little, clinical experience

- Quality of evidence
  - Meta analysis/systematic review, RTCs, nonRTCs, clinical experience
Melding Evidence with Expertise

• While data are objective, application of data is not
• Clinical judgement is always subjective
• The specified cutoffs for treatment or no treatment, testing or no testing, the weighing of risk versus benefit reflect the values and preferences of the experts who write the recommendations.

Pamela Hartzband, M.D., and Jerome Groopman, M.D N ENGL J MED 2011;365:1372-1373
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Making Recommendations

Invasive Breast Cancer

SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR POSITIVE - HER2 POSITIVE DISEASE b

Evidence supports the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone-receptor-positive breast cancer similar to that achieved with CMF alone. Early evidence suggests similar benefits from ovarian suppression (i.e., LHRH agonist) as from ovarian ablation. The combination of ovarian ablation/suppression plus endocrine therapy may be superior to suppression alone. The benefit of ovarian ablation/suppression in premenopausal women who have received adjuvant chemotherapy is uncertain.

Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. The benefits of chemotherapy and of endocrine therapy are additive. However, the absolute benefit from chemotherapy may be small. The decision to add chemotherapy to endocrine therapy should be individualized, especially in those with a favorable prognosis where the incremental benefit of chemotherapy may be smaller. Available data suggest that sequential or concurrent endocrine therapy with radiation therapy is acceptable.

There are limited data to make chemotherapy recommendations for those over 70 y old. Treatment should be individualized with consideration of comorbid conditions.

The prognosis of patients with T1a and T1b tumors that are node negative is generally favorable even when HER2 is amplified or over-expressed. This is a population of breast cancer patients that was not studied in the available randomized trials. The decision for use of trastuzumab therapy in this cohort of patients must balance the known toxicities of trastuzumab, such as cardiac toxicity, and the uncertain, absolute benefits that may exist with trastuzumab therapy.

Note: All recommendations are category 2A unless otherwise indicated.

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

See Follow-Up (BINV-16)
See Adjuvant Endocrine Therapy (BINV-J) and Adjuvant Chemotherapy (BINV-K)
Narrower Scope

PubMed Clinical Queries

Results of searches on this page are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

![Search Box]

Clinical Study Categories

Category: Therapy
Scope: Broad

Results: 5 of 53

Hormonal therapy plus bevacizumab in postmenopausal patients who have hormone receptor-positive metastatic breast cancer: a phase II Trial of the Sarah [Clin Breast Cancer. 2011]

Multifactorial central nervous system recurrence susceptibility in patients with HER2-positive breast cancer: epidemiological and clinical data from a population-based cancer registry [Cancer. 2011]

Early breast cancer in the older woman. [Oncologist. 2011]

Lapatinib in breast cancer: clinical experiences and future perspectives. [Cancer Treat Rev. 2010]

Semi-quantitative hormone receptor level influences response to trastuzumab-containing neoadjuvant chemotherapy in HER2-positive breast cancer [Mod Pathol. 2011]

See all (53)

Display citations filtered to a specific clinical study category and scope. These search filters were developed by Harnes RB et al. See more filter information.

Systematic Reviews

Results: 4 of 4

Multifactorial central nervous system recurrence susceptibility in patients with HER2-positive breast cancer: epidemiological and clinical data from a population-based cancer registry [Cancer. 2011]

Impact of treatment characteristics on response of different breast cancer phenotypes: pooled analysis of the German neoadjuvant chemotherapy trials. [Breast Cancer Res Treat. 2011]


See all (4)

Display citations for systematic reviews, meta-analyses, reviews of clinical trials, evidence-based medicine, consensus development conferences, and guidelines. See filter information or additional related sources.

Medical Genetics

Topic: All

Results: 5 of 8

Multifactorial central nervous system recurrence susceptibility in patients with HER2-positive breast cancer: epidemiological and clinical data from a population-based cancer registry [Cancer. 2011]

Multigene assays and isolated tumor cells for early breast cancer treatment: time for biomarkers. [Expert Rev Anticancer Ther. 2010]

HER2 and chromosome 17 effect on patient outcome in the N9831 adjuvant trastuzumab trial. [J Clin Oncol. 2010]

Neoadjuvant chemotherapy with trastuzumab followed by adjuvant trastuzumab versus neoadjuvant chemotherapy alone, in patients with HER2-positive locally advanced breast cancer [Lancet. 2010]

Hormone receptor status and pathologic response of HER2-positive breast cancer treated with neoadjuvant chemotherapy and trastuzumab. [Ann Oncol. 2008]

See all (8)

Display citations pertaining to topics in medical genetics. See more filter information.
Panels’ Clinical Trials Evaluation

- Patient cohort—staging, markers, comorbid conditions, prior therapy, demographics, etc.
- Statistical plan—appropriate, planned analyses
- Appropriate comparator
- Dose, dose adjustments, reporting and management of AEs, etc.
- Response assessment methods and consistency
- Analysis of results

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Use Seminal References

- 1007 citations on adjuvant therapy for HER2 overexpressed breast cancer in PubMed
- NCCN panel judged 11 published papers and 3 abstracts from professional meetings persuasive
- These references are included in the guidelines with links to abstracts
Therapeutic Index

- Each recommendation is considered in light of both safety and efficacy.
- In adjuvant setting, safety and efficacy are equally weighted.
- In potentially curative situation, more toxicity is tolerated for good efficacy.
- In palliative setting, less toxicity is acceptable.
In general:

- **More references:**
  - Large complicated guidelines
  - Large numbers of patients
  - High priority cancers

- **Fewer references**
  - Lower incidence
  - Few innovations
  - Fewer effective interventions
Recommendations per Guideline

Poonacha T K, Go R S JCO 2011;29:186-191
Types of Recommendations

- **Initial therapy** (n = 446; 44%)
- **Work-up** (n = 220; 21%)
- **Salvage therapy** (n = 289; 28%)
- **Follow-up** (n = 70; 7%)

Poonacha TK, Go RS JCO 2011;29:186-191
Recommendations by Evidence Category

IIA (n = 855; 83%)

I (n = 62; 6%)

IIIB (n = 99; 10%)

III (n = 9; 1%)

Poonacha TK, Go RS JCO 2011;29:186-191
Evidence by Type of Recommendation

Poonacha T K, Go R S JCO 2011;29:186-191
Content Relationships

NCCN Guidelines

Biomarkers

NCCN Compendium

Orders Templates

NCCN Outcomes

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Submitting Data to NCCN Panels

- Submissions from community sites, industry, payers, and the advocacy community
- The quality of the data is paramount
- Data submitted to the NCCN (not to individual panel members)
- Panel members interpret the data using their expert judgement
Disclosure

• No industry or any other interest group funds are used to support panel meetings
• No industry representatives allowed at meetings
• Individual panel members disclose conflicts of interest at least annually
• Specific limits on financial relationships
• Financial conflicts of interest published for individuals on nccn.org.
• Members are excused from deliberations when degree of conflict warrants

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Guidelines Implementation
Clinicians Use NCCN Guidelines for Patient Care Decision-Making and As a Reference Tool (n=1,861)
Challenges in Implementation of Guidelines

• Guideline distribution is not enough
• Education alone is not adequate to change practice
• Disease site guidelines are more readily adopted
Strategies to Encourage Implementation

- Coverage policy can encourage adoption
- Incorporation in clinical support tools can help
- Benchmarking concordance against standard increases awareness
- Patient reported outcomes of own patients can improve adoption
Part 7: A step-by-step treatment guide

### Table 6. Chemotherapy regimens for recurrent or metastatic breast cancer

<table>
<thead>
<tr>
<th>Preferred agents</th>
<th>Preferred combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>DAF/PAC (cyclophosphamide/doxorubicin/fluorouracil)</td>
</tr>
<tr>
<td>Estramustine</td>
<td>FEC (fluorouracil/epirubicin/cyclophosphamide)</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>AT (doxorubicin/paclitaxel or doxorubicin/paclitaxel)</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>GEM (cyclophosphamide/erbitaxel/fluorouracil)</td>
</tr>
<tr>
<td>Albumin-bound paclitaxel</td>
<td>Doxetaxel/albumin-bound paclitaxel</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>GT (gemcitabine/paclitaxel)</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>Other combinations</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Ixabepilone and capecitabine</td>
</tr>
<tr>
<td>Erbitux</td>
<td>Preferred agents for HER2-positive tumors</td>
</tr>
<tr>
<td>Paclitaxel with bevacizumab</td>
<td>Trastuzumab and paclitaxel with or without bevacizumab</td>
</tr>
<tr>
<td>Other agents</td>
<td>Trastuzumab and doxorubicin</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Trastuzumab and vinorelbine</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Trastuzumab and capecitabine</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Preferred agents for trastuzumab-treated HER2-positive tumors</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Lapatinib and capecitabine</td>
</tr>
</tbody>
</table>

**HER2 positive and hormone negative/refractory**

**Spread of cancer**

<table>
<thead>
<tr>
<th>Bone or soft tissue only or no symptoms of spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider different hormone therapy if no response to 2 or 3 back-to-back therapies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms of cancer in internal organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab with or without chemotherapy</td>
</tr>
<tr>
<td>Trastuzumab with or without chemotherapy</td>
</tr>
<tr>
<td>Use different chemotherapy or trastuzumab with lapatinib</td>
</tr>
<tr>
<td>Consider supportive care only if no response to third regimen or in poor general health</td>
</tr>
</tbody>
</table>

For hormone therapy, see the next chart. For follow-up hormone therapy, see Part 7.7.9.

This chart is for women with tumors that are HER2 positive and hormone receptor-negative or that have not responded to hormone therapy. Hormone therapy may be given if your cancer has spread only to the bone or soft tissue, or your cancer has spread to other organs that are still working well. Otherwise, since the tumor is HER2 positive, trastuzumab may be given either alone or with chemotherapy. If your cancer still grows, trastuzumab may be continued with a different chemotherapy drug. Another choice is to try a combination of lapatinib with more trastuzumab or with another chemotherapy drug. If the tumor does not shrink after these different chemotherapy regimens, stopping chemotherapy and receiving supportive care may be your best option.
How is DCIS First Suspected?

- Most often by screening mammography
- Rarely a lump is felt by the woman or the clinician
- Which type of physician interacts with the patient at which stage varies
  - Primary care physician
  - Gynecologist
  - Diagnostic radiologist
  - Interventional radiologist
  - Surgeon
Followup of Abnormal Mammogram

ASSESSMENT CATEGORY

BI-RADS® category 4
Suspicious abnormality

BI-RADS® category 5
Highly suggestive of malignancy

DIAGNOSTIC MAMMOGRAM FOLLOW-UP

Pathology/image concordant

Core needle biopsy

Reassess, repeat imaging + obtain additional tissue, as indicated

Reassess, repeat imaging + obtain additional tissue, as indicated

Pathology/image discordant

Pathology/image concordant

Benign

Mammogram in 6-12 mo for 1-2 y

See Routine Screening (BSCR-1)

Atypical hyperplasia or LCIS or Other pathological findings

Surgical excision

See Follow-up (BSCR-17)

Malignant

Surgical excision

See Follow-up (BSCR-17)

See NCCN Breast Cancer Guidelines

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
# Biopsy Techniques

<table>
<thead>
<tr>
<th>Needle Biopsy</th>
<th>Excisional Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fewer trips to the operating room</td>
<td>Inadequate or indeterminate needle biopsy</td>
</tr>
<tr>
<td>Can sample multiple abnormal areas</td>
<td>Additional tissue needed for pathology review</td>
</tr>
</tbody>
</table>

**Needle Biopsy:**
- Fewer trips to the operating room
- Can sample multiple abnormal areas

**Excisional Biopsy:**
- Inadequate or indeterminate needle biopsy
- Additional tissue needed for pathology review
Needle Biopsies

• FNA: Smaller-bore needle, minimally invasive, low cost, but requires specialized pathologist and may need second core biopsy

• Core Needle Biopsy: Large-bore cutting needle removes 3-5 cores. Can obtain large enough tissue samples for diagnosis. Can place clip to guide further treatment

• Image guided core needle biopsy: Uses ultrasound or mammography to guide sampling
NCCN Database: Rates of Needle vs Excisional Biopsy

<table>
<thead>
<tr>
<th>Initial Biopsy</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>FNA</td>
<td>2</td>
<td>0%</td>
</tr>
<tr>
<td>Needle-Non Image Guided</td>
<td>40</td>
<td>5%</td>
</tr>
<tr>
<td>Needle-Image Guided</td>
<td>567</td>
<td>77%</td>
</tr>
<tr>
<td>Surgical-Non Image Guided</td>
<td>64</td>
<td>9%</td>
</tr>
<tr>
<td>Surgery-Image Guided</td>
<td>64</td>
<td>9%</td>
</tr>
</tbody>
</table>

Clinical Stage 0
Diagnosed January—December 2010
>90 days follow-up
Community and Academic Centers’ rates are similar