

Ormonoterapia e CHT adj nel carcinoma mammario invasivo

Un po' di chiarezza...

- In situ: NON PASSA LA MEMBRANA BASALE (MB)
- Invasivo: passa la MB
- Early: invasivo senza linfonodi (EBC)
- Localmente avanzato: invasivo con compromissione linfonodale (LABC)

In situ (DCIS o LCIS):

- ER/PgR (+): ormonoterapia???
- ER/PgR (-): osservazione
- HER2 (+) o HER2 (-): non importa. Non sognatevi il trastuzumab!!!

TNM

Table 1

**American Joint Committee on Cancer (AJCC)
TNM Staging System For Breast Cancer**

Primary Tumor (T)

Definitions for classifying the primary tumor (T) are the same for clinical and for pathologic classification. If the measurement is made by the physical examination, the examiner will use the major headings (T1, T2, or T3). If other measurements, such as mammographic or pathologic measurements, are used, the subsets of T1 can be used. Tumors should be measured to the nearest 0.1 cm increment.

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple with no tumor
Note: Paget's disease associated with a tumor is classified according to the size of the tumor.	
T1	Tumor 2 cm or less in greatest dimension
T1mic	Microinvasion 0.1 cm or less in greatest dimension
T1a	Tumor more than 0.1 cm but not more than 0.5 cm in greatest dimension
T1b	Tumor more than 0.5 cm but not more than 1 cm in greatest dimension
T1c	Tumor more than 1 cm but not more than 2 cm in greatest dimension
T2	Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor of any size with direct extension to (a) chest wall or (b) skin, only as described below
T4a	Extension to chest wall, not including pectoralis muscle

T4b	Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma

Regional Lymph Nodes (N)

Clinical

NX	Regional lymph nodes cannot be assessed (e.g., previously removed)
N0	No regional lymph node metastasis
N1	Metastasis to movable ipsilateral axillary lymph node(s)
N2	Metastases in ipsilateral axillary lymph nodes fixed or matted, or in <i>clinically apparent</i> * ipsilateral internal mammary nodes in the <i>absence</i> of clinically evident axillary lymph node metastasis
N2a	Metastases in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
N2b	Metastasis only in <i>clinically apparent</i> * ipsilateral internal mammary nodes and in the <i>absence</i> of clinically evident axillary lymph node metastasis
N3	Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in <i>clinically apparent</i> * ipsilateral internal mammary lymph node(s) and in the <i>presence</i> of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
N3a	Metastasis in ipsilateral infraclavicular lymph node(s)
N3b	Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
N3c	Metastasis in ipsilateral supraclavicular lymph node(s)

**Clinically apparent* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.

[Staging continued on next page \(ST-2\)](#)

N

Table 1 (continued)

Pathologic (pN)^a

pNX Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)

pN0 No regional lymph node metastasis histologically, no additional examination for isolated tumor cells (ITC)

Note: Isolated tumor cells (ITC) are defined as single tumor cells or small cell clusters not greater than 0.2 mm, usually detected only by immunohistochemical (IHC) or molecular methods but which may be verified on H&E stains. ITCs do not usually show evidence of malignant activity e.g., proliferation or stromal reaction.

pN0(i-) No regional lymph node metastasis histologically, negative IHC

pN0(i+) No regional lymph node metastasis histologically, positive IHC, no IHC cluster greater than 0.2 mm

pN0(mol-) No regional lymph node metastasis histologically, negative molecular findings (RT-PCR)^b

pN0(mol+) No regional lymph node metastasis histologically, positive molecular findings (RT-PCR)^b

^aClassification is based on axillary lymph node dissection with or without sentinel lymph node dissection. Classification based solely on sentinel lymph node dissection without subsequent axillary node dissection is designated (sn) for "sentinel node," e.g., pN0(i+) (sn).

^bRT-PCR: reverse transcriptase/polymerase chain reaction.

pN1 Metastasis in 1 to 3 axillary lymph nodes, and/or in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent*^{**}

pN1mi Micrometastasis (greater than 0.2 mm, none greater than 2.0 mm)

pN1a Metastasis in 1 to 3 axillary lymph nodes

pN1b Metastasis in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent*^{**}

pN1c Metastasis in 1 to 3 axillary lymph nodes and in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent*^{**} (If associated with greater than 3 positive axillary lymph nodes, the internal mammary nodes are classified as pN3b to reflect increased tumor burden)

pN2 Metastasis in 4 to 9 axillary lymph nodes, or in *clinically apparent*^{*} internal mammary lymph nodes in the *absence* of axillary lymph node metastasis

pN2a Metastasis in 4 to 9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)

pN2b Metastasis in *clinically apparent*^{*} internal mammary lymph nodes in the *absence* of axillary lymph node metastasis

pN3 Metastasis in 10 or more axillary lymph nodes, or in infraclavicular lymph nodes, or in *clinically apparent*^{*} ipsilateral internal mammary lymph nodes in the *presence* of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes with clinically negative microscopic metastasis in internal mammary lymph nodes; or in ipsilateral supraclavicular lymph nodes

pN3a Metastasis in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm), or metastasis to the infraclavicular lymph nodes

pN3b Metastasis in *clinically apparent*^{*} ipsilateral internal mammary lymph nodes in the *presence* of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent*^{**}

pN3c Metastasis in ipsilateral supraclavicular lymph nodes

^{*} *Clinically apparent* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

^{**} *Not clinically apparent* is defined as not detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

[Staging continued on next page \(ST-3\)](#)

BC per stadi

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CLINICAL STAGE

WORKUP

Stage I
T1, N0, M0
or
Stage IIA
T0, N1, M0
T1, N1, M0
T2, N0, M0
or
Stage IIB
T2, N1, M0
T3, N0, M0
or
Stage IIIA
T3, N1, M0



General workup including:

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review^a
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status^b
- Genetic counseling if patient is high risk for hereditary breast cancer^c

Optional studies for breast imaging:

- Breast MRI^d

If clinical stage IIIA (T3, N1, M0) consider:

- Bone scan (category 2B)
- Abdominal ± pelvis CT or US or MRI
- Chest imaging

Additional studies as directed by signs or symptoms:

- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvis CT or US or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Chest imaging (if pulmonary symptoms are present)
- Optional FDG PET/CT (for T3,N1,M0) (category 2B)^e
- Consider fertility counseling if indicated^f

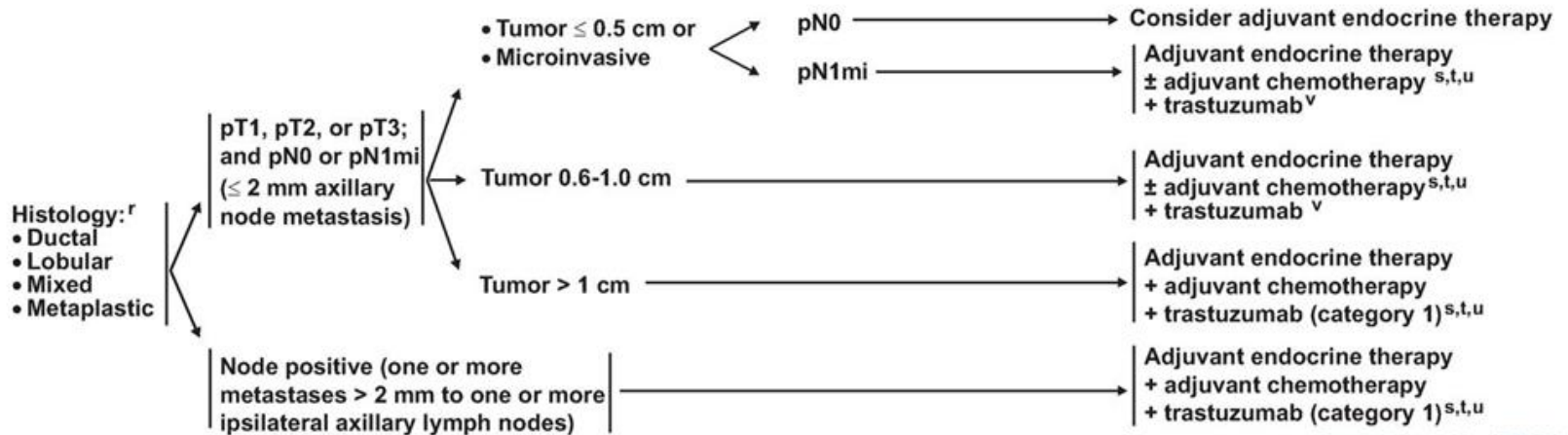


[See Locoregional
Treatment
\(BINV-2\)](#)

IBC, ER+, HER2+

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



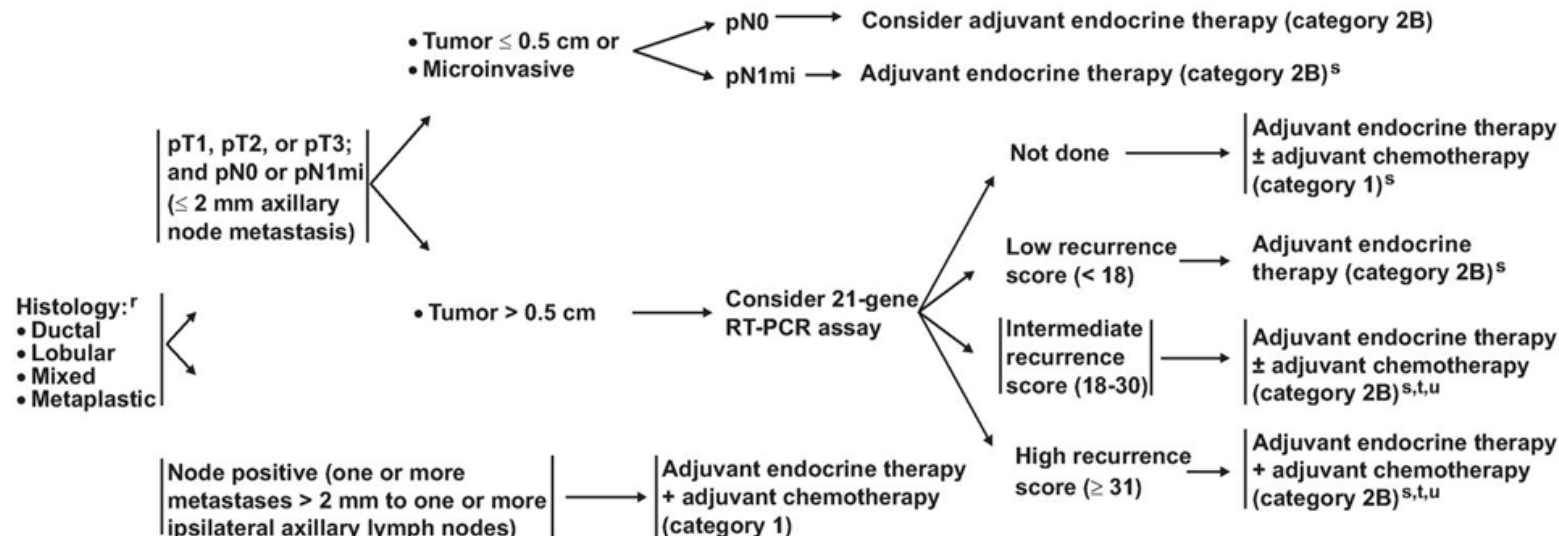
[See Follow-Up \(BINV-16\)](#)

[See Adjuvant Endocrine Therapy \(BINV-J\)](#) and [Adjuvant Chemotherapy \(BINV-K\)](#)

IBC, ER+, HER2-

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



[See Adjuvant Endocrine Therapy \(BINV-J\)](#) and [Adjuvant Chemotherapy \(BINV-K\)](#)

ER-, HER2+

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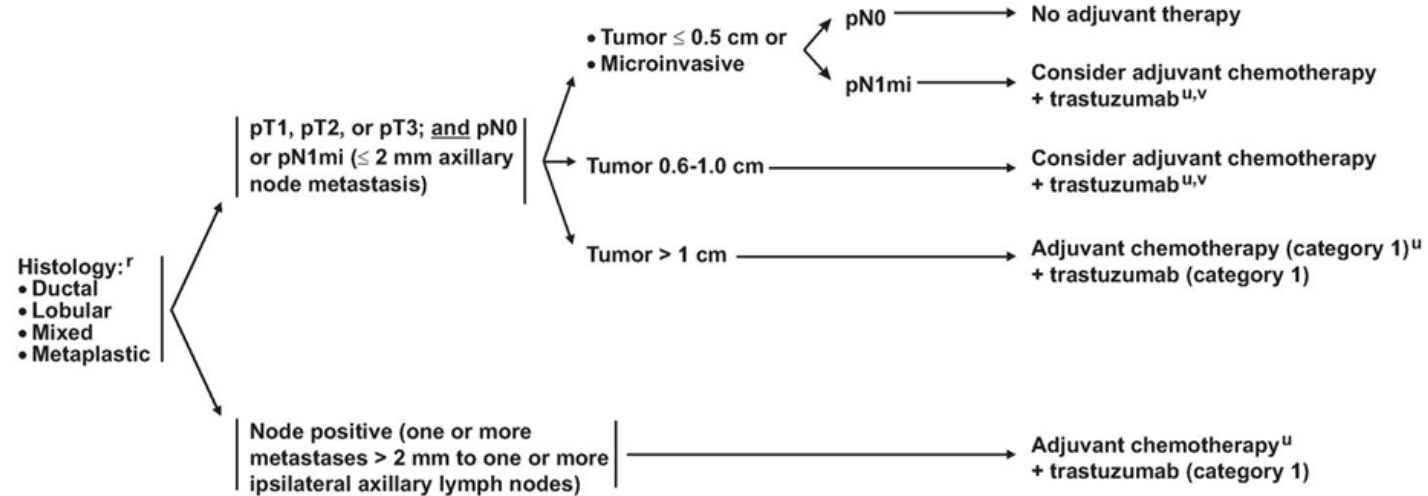


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SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR NEGATIVE - HER2 POSITIVE DISEASE^b



Triplo negative

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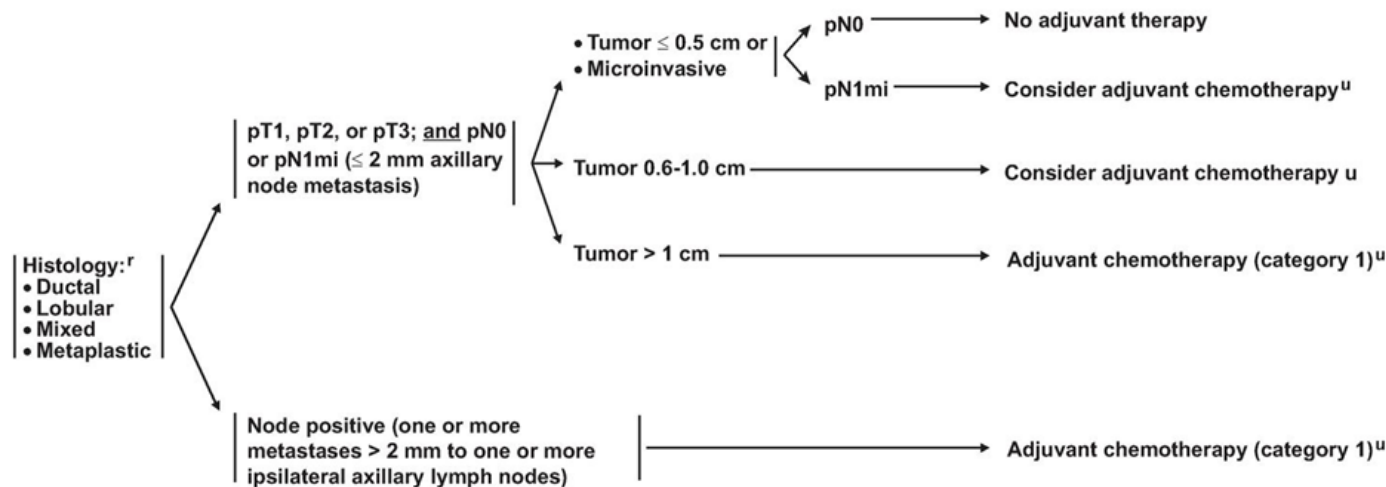


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SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR NEGATIVE - HER2 NEGATIVE DISEASE^b





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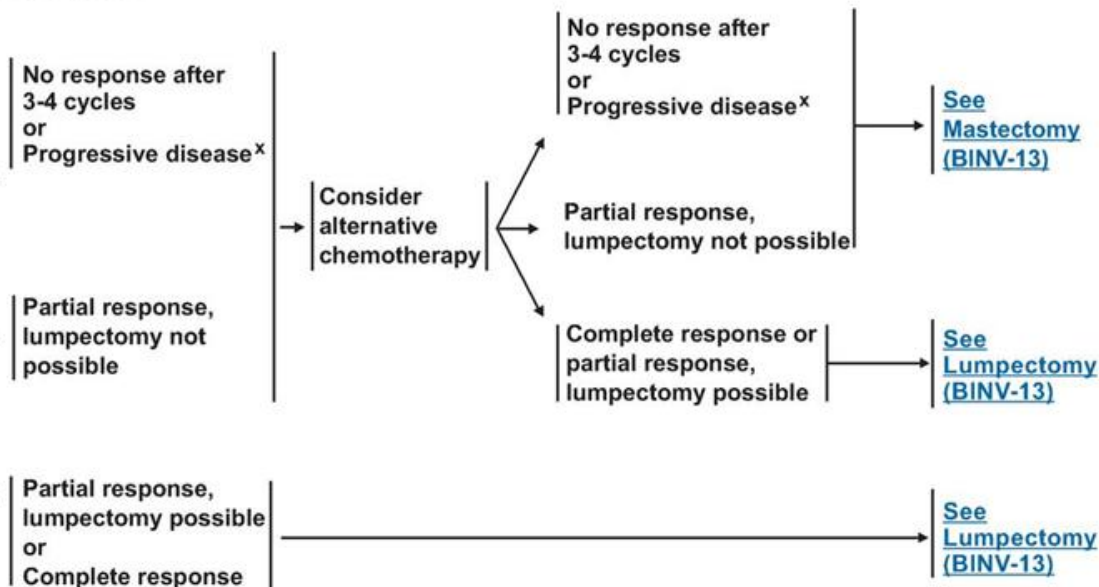
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Preoperative Chemotherapy Guideline

PRIMARY TREATMENT

Preoperative chemotherapy^{x,y,z}
(endocrine therapy alone may be
considered for receptor positive
disease in postmenopausal patients)^{aa}





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Preoperative Chemotherapy Guideline

CLINICAL STAGE

WORKUP

Stage IIA
T2, N0, M0

Stage IIB
T2, N1, M0
T3, N0, M0

Stage IIIA
T3, N1, M0

and

Fulfills criteria for breast
conserving surgery
except for tumor size

General workup including:

- History and physical
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review^a
- Determination of tumor ER/PR status and HER2 status^b
- Genetic counseling if patient is high risk for hereditary breast cancer^c

Optional additional studies for breast imaging:

- Breast MRI^d

If clinical stage IIIA (T3, N1, M0) consider:

- Bone scan (category 2B)
- Abdominal ± pelvis CT or US or MRI
- Chest imaging

Optional studies as directed by signs and symptoms:

- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvis CT or US or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Chest imaging (if pulmonary symptoms are present)
- FDG PET/CT scan (category 2B)^e
- Consider fertility counseling if indicated^f

[See Primary
Treatment
\(BINV-11\)](#)

CHT neoadj in LABC

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LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

CLINICAL STAGE

WORKUP

Stage IIIA
T0, N2, M0
T1, N2, M0
T2, N2, M0
T3, N2, M0

[\(Stage IIIA patients with T3, N1, M0 disease, see BINV-1\)](#)

Stage IIIB
T4, N0, M0
T4, N1, M0
T4, N2, M0

Stage IIIC
Any T, N3, M0

Stage IV
Any T, any N, M1

General workup including:

- History and physical
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review^a
- Determination of tumor ER/PR status and HER2 status^b
- Genetic counseling if patient is high risk for hereditary breast cancer^c

Optional additional studies for breast imaging:

- Breast MRI^d

If clinical stage IIIA (T3, N1, M0) consider:

- Bone scan (category 2B)
- Abdominal ± pelvis CT or US or MRI
- Chest imaging

Optional studies as directed by signs and symptoms:

- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvis CT or US or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Chest imaging (if pulmonary symptoms are present)
- FDG PET/CT scan (category 2B)^e
- Consider fertility counseling if indicated^f

[See Initial Workup for Stage IV Disease \(BINV-16\)](#)

[See Preoperative
Chemotherapy and
Locoregional
Treatment \(BINV-15\)](#)



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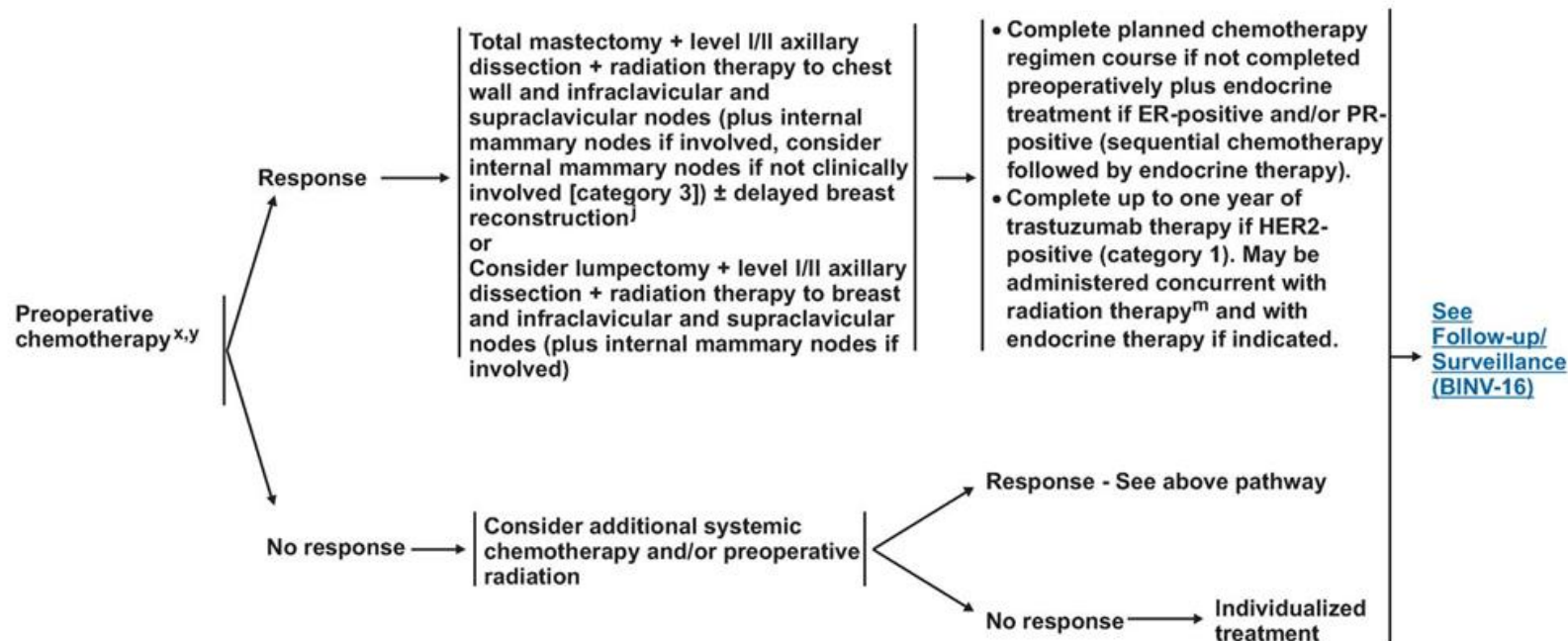
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PREOPERATIVE CHEMOTHERAPY FOR LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

LOCOREGIONAL TREATMENT

ADJUVANT TREATMENT



^mSee Principles of Radiation Therapy (BINV-I).

^jSee Principles of Reconstruction Following Surgery (BINV-H).

^xA number of combination and single agent chemotherapy regimens have activity in the preoperative setting. Those chemotherapy regimens recommended in the adjuvant setting (See BINV-K) may be considered in the preoperative setting. If treated with endocrine therapy, an aromatase inhibitor is preferred for postmenopausal women.

^yPatients with HER2-positive tumors should be treated with preoperative chemotherapy incorporating trastuzumab for at least 9 weeks of preoperative therapy (See BINV-K).

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.

RT: quando?

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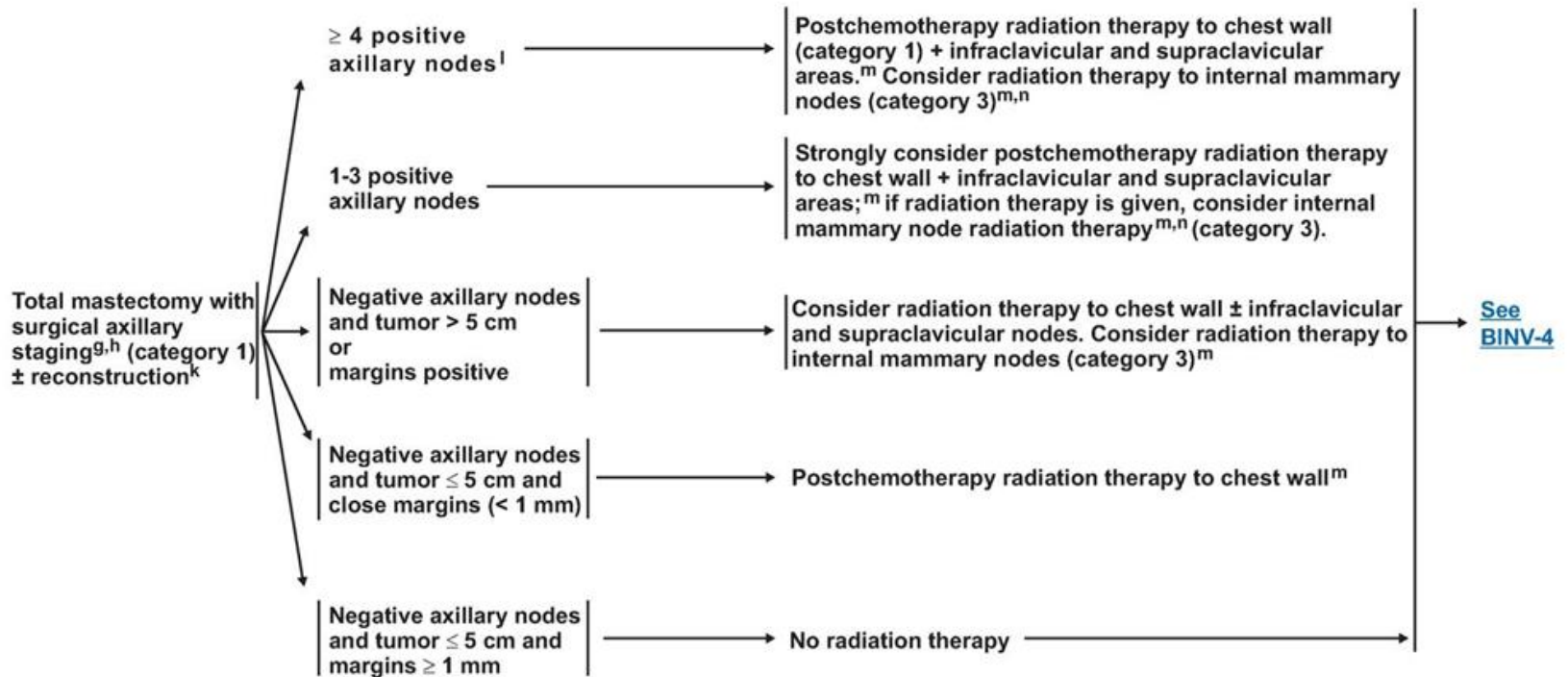


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LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



Ormonoterapia

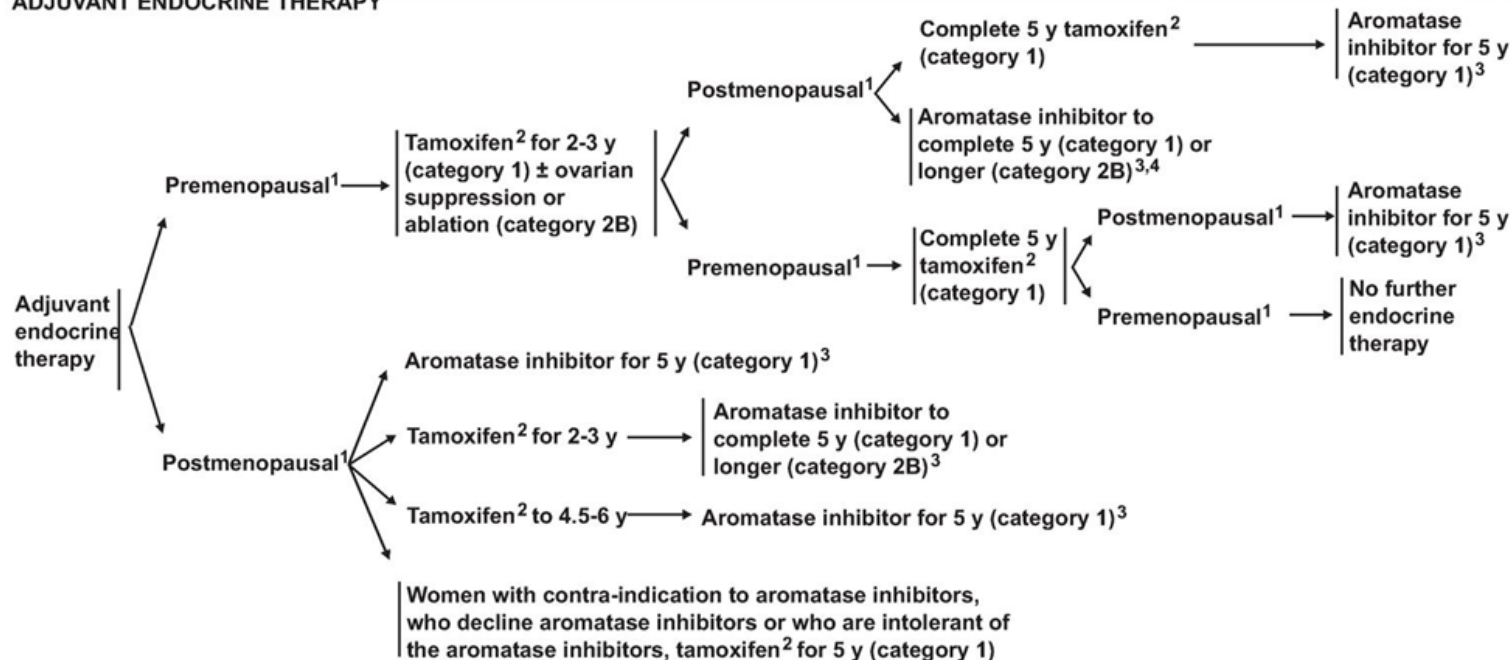
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ADJUVANT ENDOCRINE THERAPY



ALERT (need to know!!!!)

- CYP2D6 e TAM
- ATAC (anastrozolo)
- BIG 1-98 (letrozolo)
- IES (ITA) (exemestane)

Da San Antonio 2010....

NCIC CTG MA 27

Figura 1 - Disegno dello studio

IN APERTO

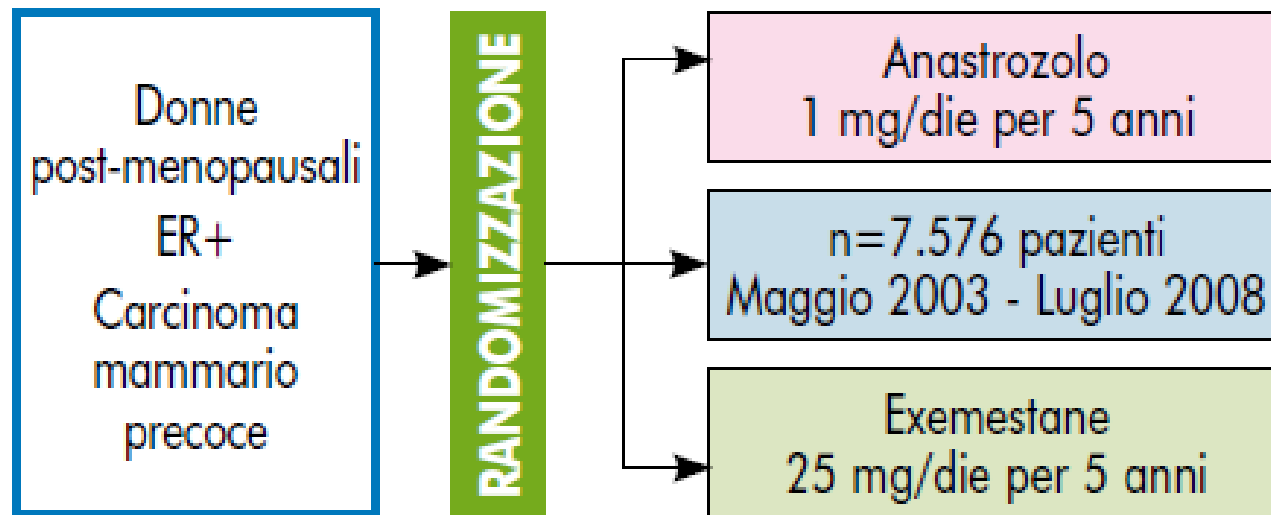


Tabella 1 - Risultati

Stratificazione di exemestane su anastrozolo				
	Eventi (%)	Eventi (%)	HR (IC 95%)	p
EFS	350 (9,2)	343 (9,1)	1,02 (0,87-1,18)	0,85
OS	208 (5,5)	224 (5,9)	0,93 (0,77-1,13)	0,64
DDFS	157 (4,1)	164 (4,3)	0,95 (0,76-1,18)	0,46
DSS	89 (2,4)	98 (2,6)	0,93 (0,70-1,24)	0,62