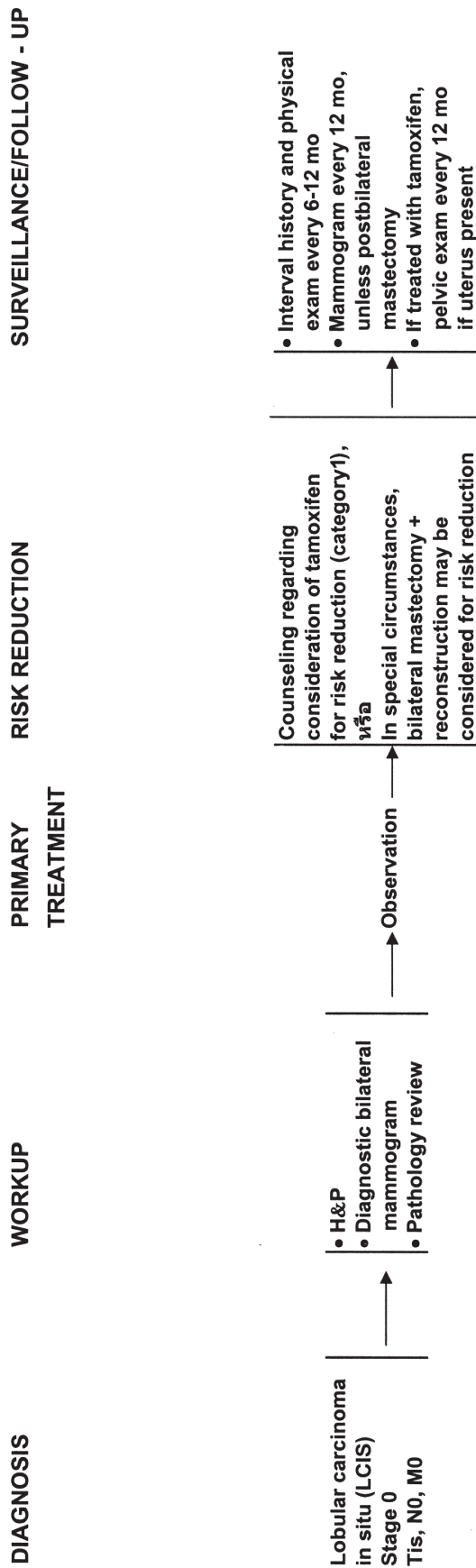
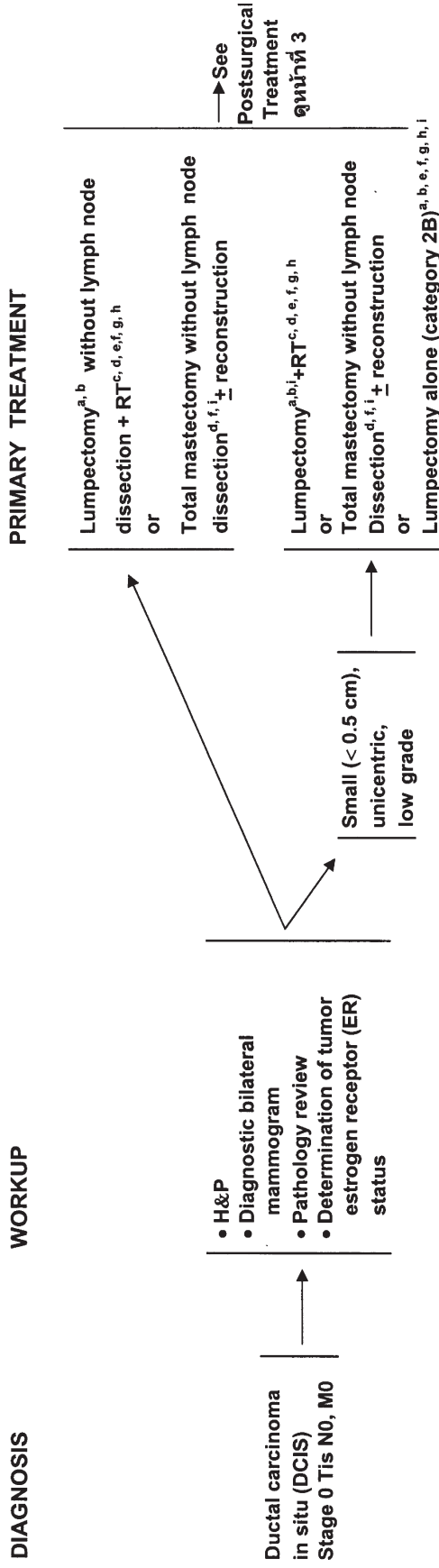


# Lobular Carcinoma In Situ



# Ductal Carcinoma In Situ



<sup>a</sup> Re-resection(s) may be performed in an effort to obtain negative margins in patients desiring breast conserving therapy. Patients not amenable to margin-free  
<sup>b</sup> See Margin Status in DCIS (หน้า 4)

<sup>c</sup> Whole breast irradiation with boost to tumor bed. Boost to tumor bed is especially encouraged in those 50 y of age or younger. Partial breast irradiation should be performed only as part of a high quality prospective clinical trial.

<sup>d</sup> Long-term survival with mastectomy versus excision and irradiation appears to be equivalent.

<sup>e</sup> Complete resection should be documented by analysis of margins, specimen mammography and where appropriate post-excision mammography

<sup>f</sup> Patients found to have invasive disease at total mastectomy or re-excision should be managed as stage II disease, including lymph node staging

<sup>g</sup> See Contraindications to Breast-Conserving Therapy (หน้า 23)

<sup>h</sup> Prospective studies have demonstrated that whole breast radiation lowers the risk of ipsilateral invasive breast cancer recurrence following excision of DCIS. Some patients may be treated with excision alone, particularly if a patient is willing to accept a higher risk of local recurrence. Other factors that should be considered include patient age, comorbidity, tumor margins and tumor grade.

<sup>i</sup> Axillary lymph node staging is discouraged in woman with apparent pure DCIS. However, a small proportion of patients with apparent pure DCIS will be found to have invasive cancer at the time of their definitive surgical procedure. Therefore, the performance of a sentinel lymph node procedure may be considered if the patient with apparent pure DCIS is to be treated with mastectomy or with excision in an anatomic location compromising the performance of a future sentinel lymph node procedure.

# Ductal Carcinoma In Situ

## DCIS POSTSURGICAL TREATMENT

### Adjuvant treatment:

Consider tamoxifen for 5 years for:

- Patients treated with breast-conserving therapy (lumpectomy) and RT (category 1)<sup>1</sup>, especially for those with ER-positive DCIS. The benefit of tamoxifen for ER-negative DCIS is uncertain
- Patients treated with excision alone<sup>1</sup>

### Risk reduction therapy:

- Counseling regarding consideration of tamoxifen for risk reduction (category 2B)

## SURVEILLANCE / FOLLOW-UP

- Interval history and physical exam 6 mo for 5 y, then annually
- Mammogram every 12 mo
- If treated with tamoxifen, pelvic exam every 12 mo if uterus present

<sup>1</sup> Available data suggest tamoxifen provides risk reduction in the ipsilateral breast treated with breast conservation and in the contralateral breast in patients with mastectomy or breast conservation with ER-positive primary tumors. Since a survival advantage has not been demonstrated, individual consideration of risks and benefits is important

# Ductal Carcinoma In Situ

## MARGIN STATUS IN DCIS

- Margins greater than 10 mm. are widely accepted as negative (but may be excessive and may lead to a less optimal cosmetic outcome)
- Margins less than 1 mm are considered inadequate.
- There are insufficient data to make definitive statements regarding margins between 1 and 10 mm.

# Invasive Breast Cancer

## CLINICAL STAGE

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  
T3, N1, M0

## WORKUP

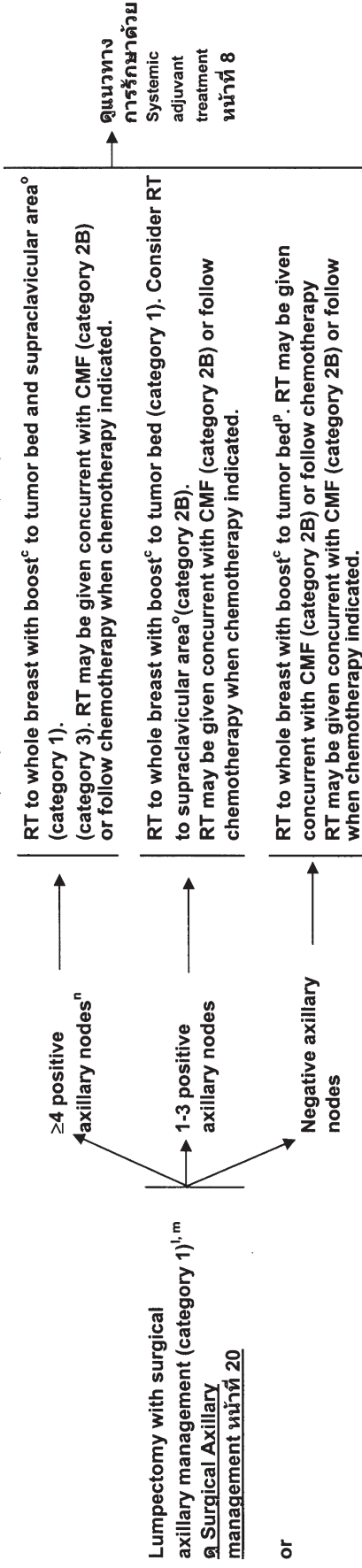
- H&P
- CBC, platelets
- Liver function tests
- Chest imaging
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER-2 status<sup>k</sup>
- Breast MRI with dedicate breast coil may be considered for breast conserving therapy for preoperative evaluation of extent of disease and detection of mammographically occult disease in the breast (optional). Decision making regarding breast conservation should not be made on the basis of MRI imaging alone in the absence of tissue sampling.
- Bone scan (optional) (Indicated if localized symptoms or elevated alkaline phosphatase or if T3, N1, M0) (category 2B)
- Abdominal CT or US or MRI (optional for stage IIA or IIB, indicated if elevated alkaline phosphatase, abnormal LFTs, or if T3, N1, M0) (category 2B)

See  
Locoregional  
Treatment  
(หน้า 6)

<sup>k</sup> HER-2 testing should be done using IHC and/or FISH. An IHC result of 2+ should be confirmed by FISH.

# Invasive Breast Cancer

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



or  
If T2 or T3 and fulfills criteria for breast conserving therapy except for size

<sup>c</sup> Whole breast irradiation with boost to tumor bed. Boost to tumor bed is especially encouraged in those 50 y of age or younger. Partial breast irradiation should be performed only as part of a high quality prospective clinical trial.

<sup>i</sup> See Axillary Dissection (หน้าที่ 21) Margin Status in Infiltrating Carcinoma (หน้าที่ 22)

<sup>m</sup> See Contraindications to Breast-Conserving Therapy (หน้าที่ 23)

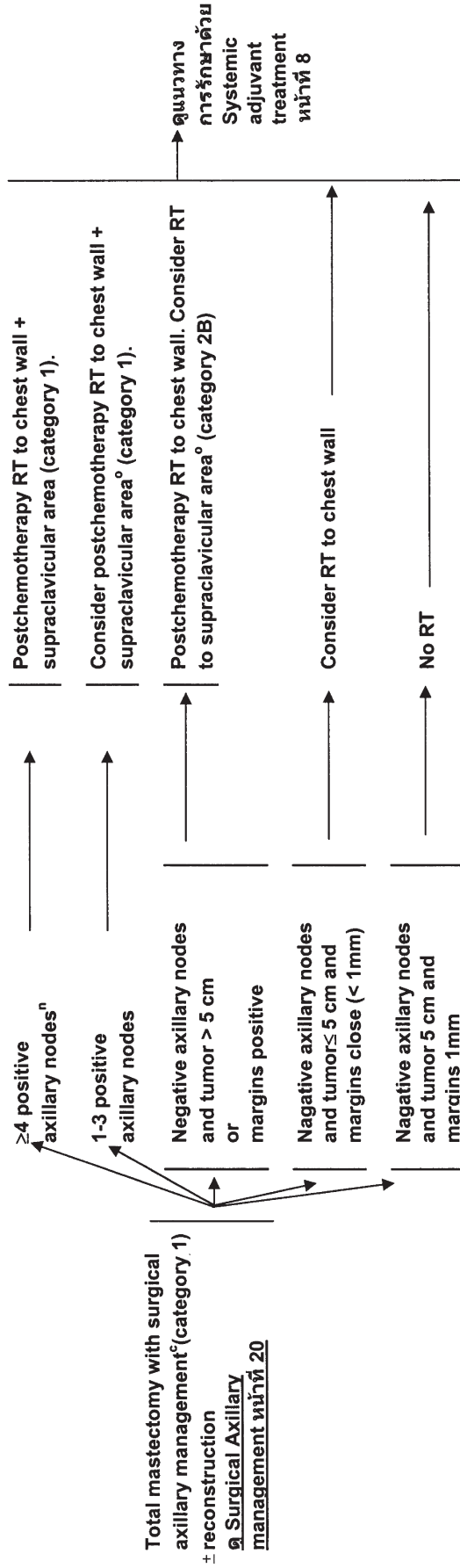
<sup>n</sup> Consideration may be given to additional staging including bone scan and abdominal CT/US/MRI; chest (category 2B)

<sup>o</sup> RT should be given to the internal mammary lymph nodes if they are clinically or pathologically positive, otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where RT is delivered to the internal mammary lymph nodes.

<sup>p</sup> Breast irradiation may be omitted in those 70 y of age or older with estrogen-receptor positive, clinically node negative, T1 tumor who receive adjuvant hormonal therapy (category 1).

# Invasive Breast Cancer

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



<sup>f</sup> See Axillary Dissection (หน้า 21) Margin Status in Infiltrating Carcinoma (หน้า 22)

<sup>n</sup> Consideration may be given to additional staging including bone scan and abdominal CT/US/MRI; chest (category 2B)

<sup>o</sup> RT should be given to the internal mammary lymph nodes if they are clinically or pathologically positive, otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where RT is delivered to the internal mammary lymph nodes.

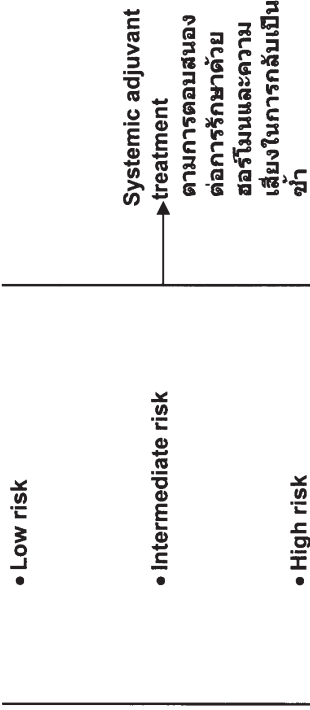
<sup>q</sup> There is inconsistent high-level evidence of survival benefit in this subset.

# Systemic Adjuvant treatment

พิจารณาการตอบสนองต่อการรักษาทางฮอร์โมน\*

ประเมินความเสี่ยงในการกลับเป็นซ้ำ<sup>†</sup>

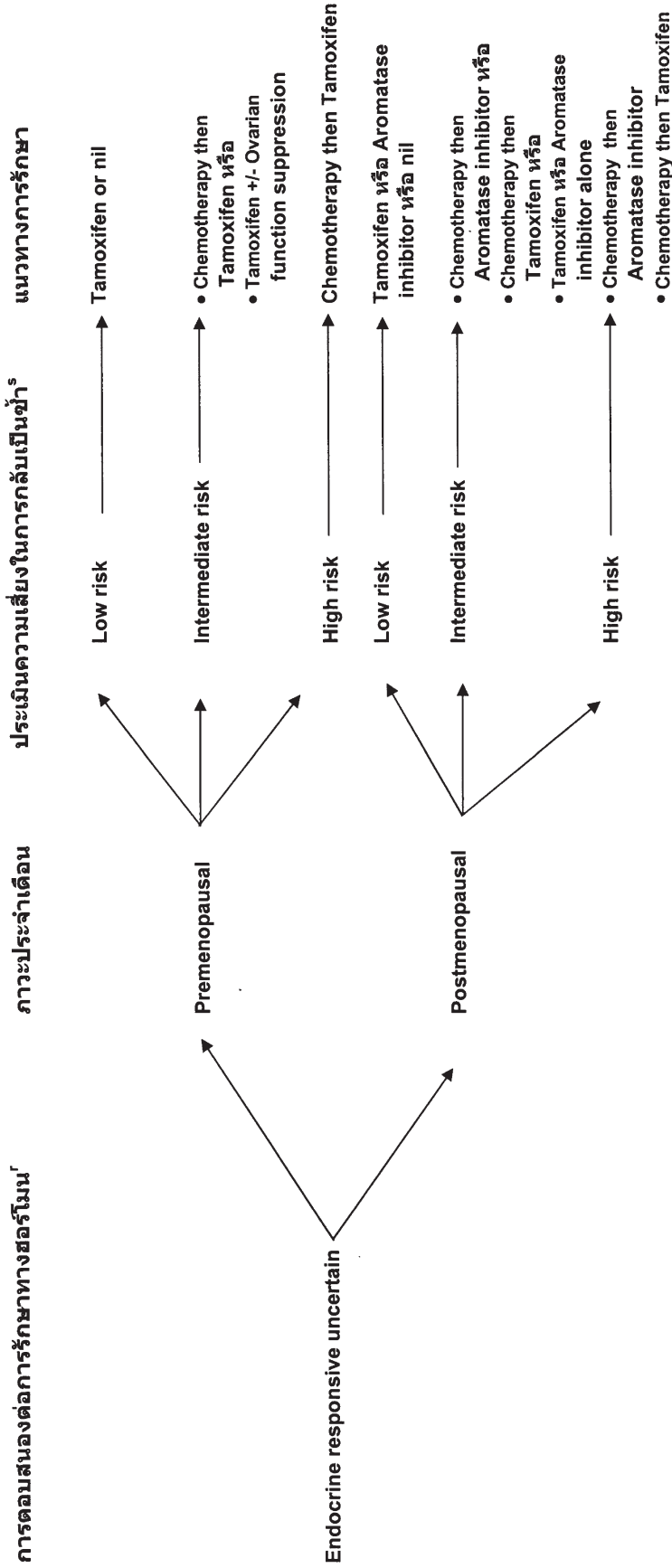
- Endocrine responsive<sup>†</sup>
- Endocrine response uncertain
- Endocrine non-responsive



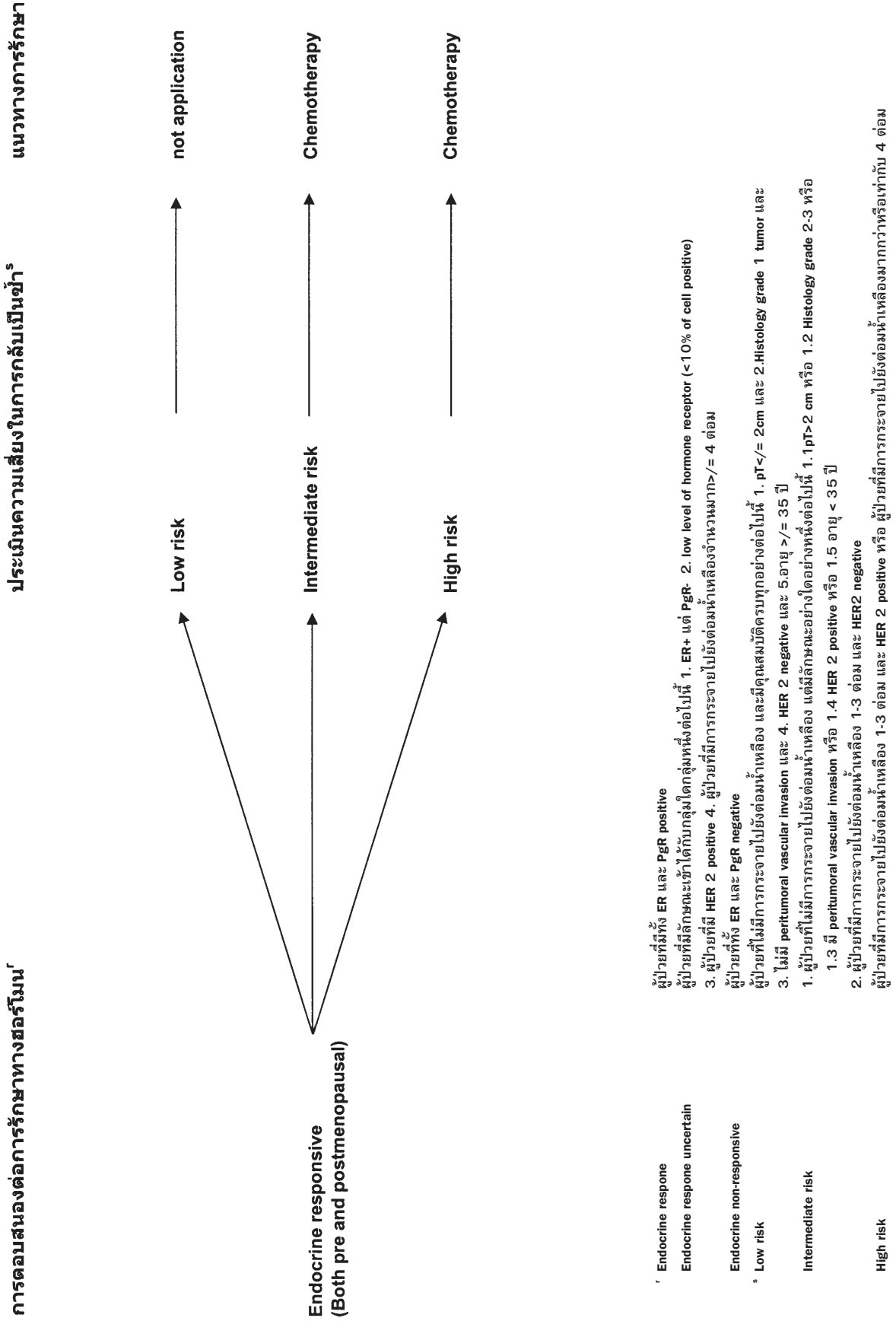
- <sup>†</sup> Endocrine response
- Endocrine response uncertain
- Endocrine non-responsive
- <sup>\*</sup> Low risk
- Intermediate risk
- High risk

- ผู้ป่วยที่มีทั้ง ER และ Pgr positive
- ผู้ป่วยที่มีลักษณะเข้าได้กับกลุ่มใดกลุ่มหนึ่งต่อไปนี้ 1. ER+ แต่ Pgr- 2. low level of hormone receptor (<10% of cell positive)
- 3. ผู้ป่วยที่มี HER 2 positive 4. ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลืองจำนวนมากกว่า/= 4 ต่อม
- ผู้ป่วยที่ทั้ง ER และ Pgr negative
- ผู้ป่วยที่ไม่มีการกระจายไปยังต่อมหน้าเหลือง และมีคุณสมบัติครบทุกอย่างต่อไปนี้ 1. pT</= 2cm และ 2. Histology grade 1 tumor และ 3. ไม่มี peritumoral vascular invasion และ 4. HER 2 negative และ 5. อายุ >/= 35 ปี
- 1. ผู้ป่วยที่ไม่มีการกระจายไปยังต่อมหน้าเหลือง แต่มีลักษณะต่อไปนี้ 1.1 pT>2 cm หรือ 1.2 Histology grade 2-3 หรือ 1.3 มี peritumoral vascular invasion หรือ 1.4 HER 2 positive หรือ 1.5 อายุ < 35 ปี
- 2. ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลือง 1-3 ต่อม และ HER 2 positive หรือ ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลืองมากกว่าหรือเท่ากับ 4 ต่อม
- ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลือง 1-3 ต่อม และ HER 2 positive หรือ ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลืองมากกว่าหรือเท่ากับ 4 ต่อม



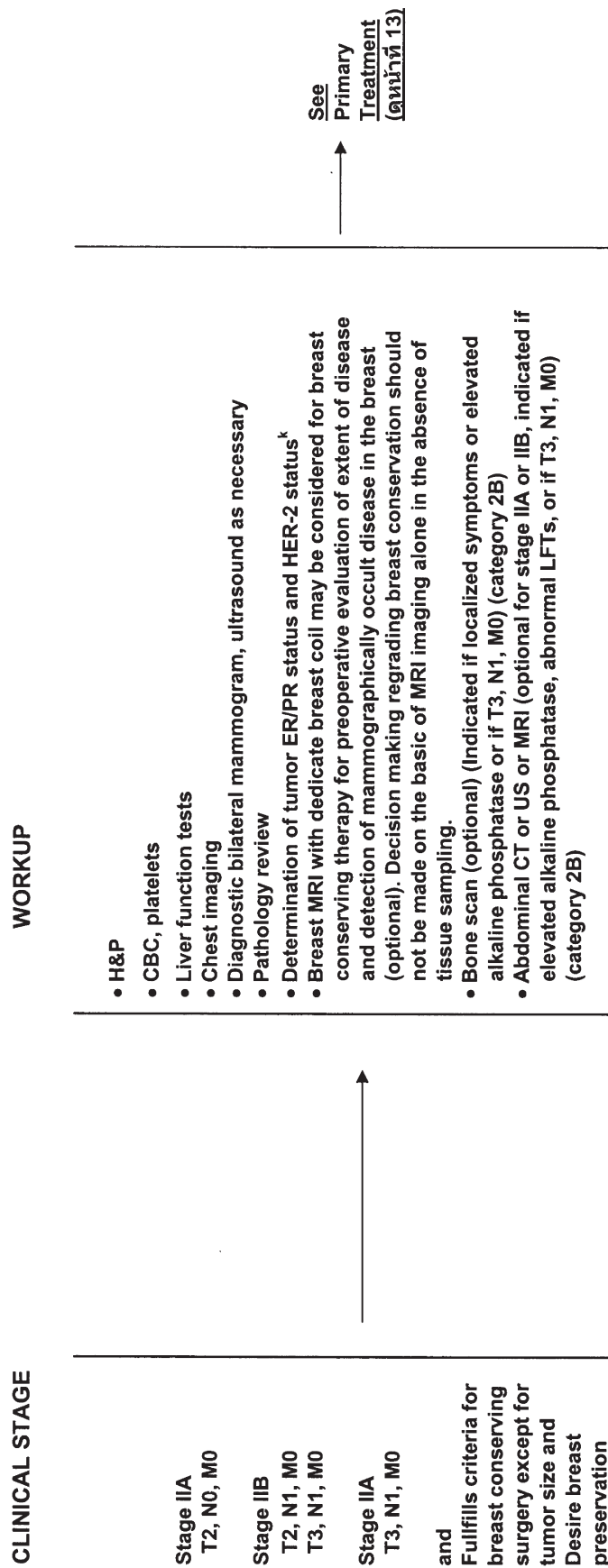


- ผู้ป่วยที่มีทั้ง ER และ Pgr positive
- ผู้ป่วยที่มีลักษณะเข้าได้กับกลุ่มใดกลุ่มหนึ่งต่อไปนี้ 1. ER+ แต่ Pgr- 2. low level of hormone receptor (<10% of cell positive)
- 3. ผู้ป่วยที่มี HER 2 positive 4. ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลืองจำนวนมากกว่า/= 4 ต่อม
- ผู้ป่วยที่ทั้ง ER และ Pgr negative
- ผู้ป่วยที่ไม่มีการกระจายไปยังต่อมหน้าเหลือง และมีคุณสมบัติครบทุกอย่างต่อไปนี้ 1. pT</= 2cm และ 2. Histology grade 1 tumor และ 3. ไม่มี peritumoral vascular invasion และ 4. HER 2 negative และ 5. อายุ >/= 35 ปี
- 1. ผู้ป่วยที่ไม่มีการกระจายไปยังต่อมหน้าเหลือง แต่มีลักษณะอย่างไร้โดย่างหนึ่งต่อไปนี้ 1.1 pT>2 cm หรือ 1.2 Histology grade 2-3 หรือ 1.3 มี peritumoral vascular invasion หรือ 1.4 HER 2 positive หรือ 1.5 อายุ < 35 ปี
- 2. ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลือง 1-3 ต่อม และ HER 2 negative
- ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลือง 1-3 ต่อม และ HER 2 positive หรือ ผู้ป่วยที่มีการกระจายไปยังต่อมหน้าเหลืองมากกว่าหรือเท่ากับ 4 ต่อม



# Invasive Breast Cancer

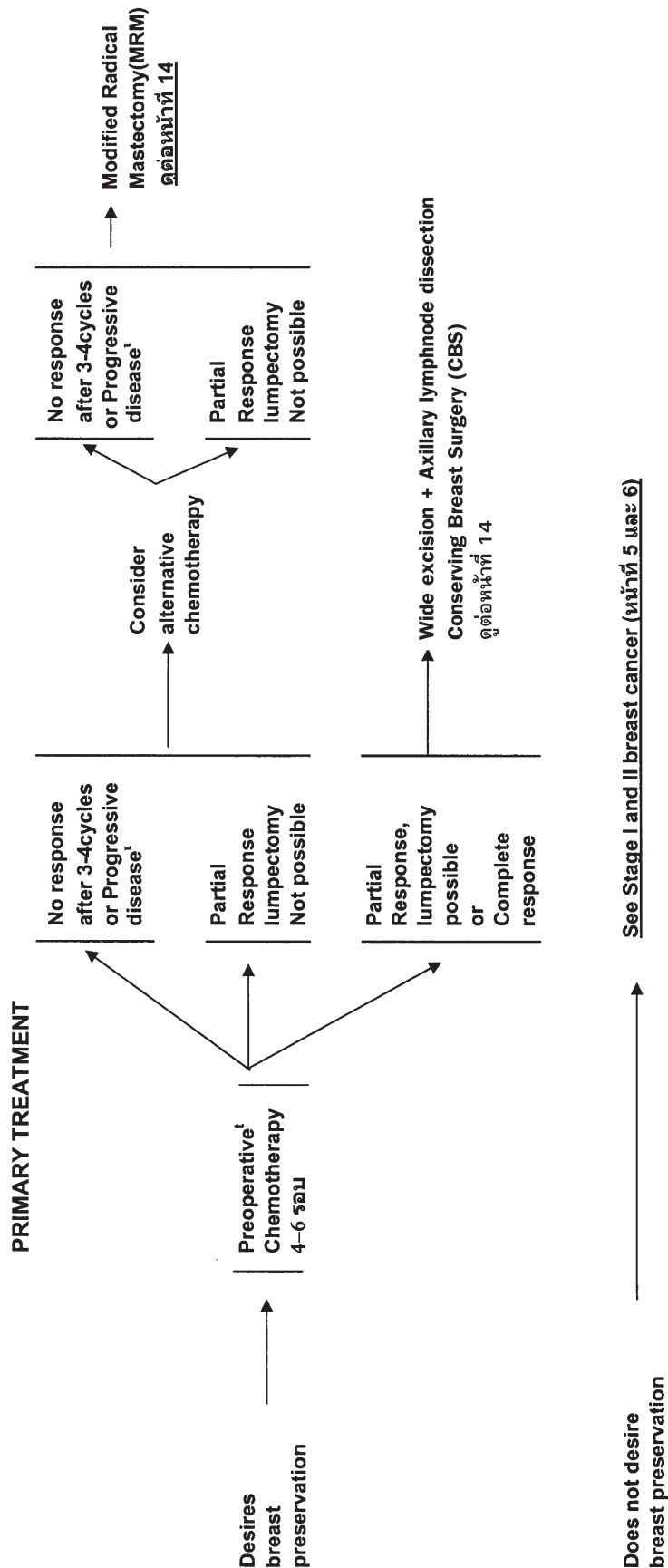
## Preoperative Chemotherapy Guideline



<sup>k</sup> HER-2 testing should be done using IHC and/or FISH. An IHC result of 2+ should be confirmed by FISH.

# Invasive Breast Cancer

## Preoperative Chemotherapy Guideline



<sup>†</sup> In general, those chemotherapy regimens recommended in the adjuvant setting may be considered in the preoperative setting

# Invasive Breast Cancer

## Preoperative Chemotherapy Guideline

### PRIMARY TREATMENT

MRM

→  
Consider additional  
chemotherapy

CBS

→  
Consider additional  
chemotherapy

### ADJUVANT TREATMENT

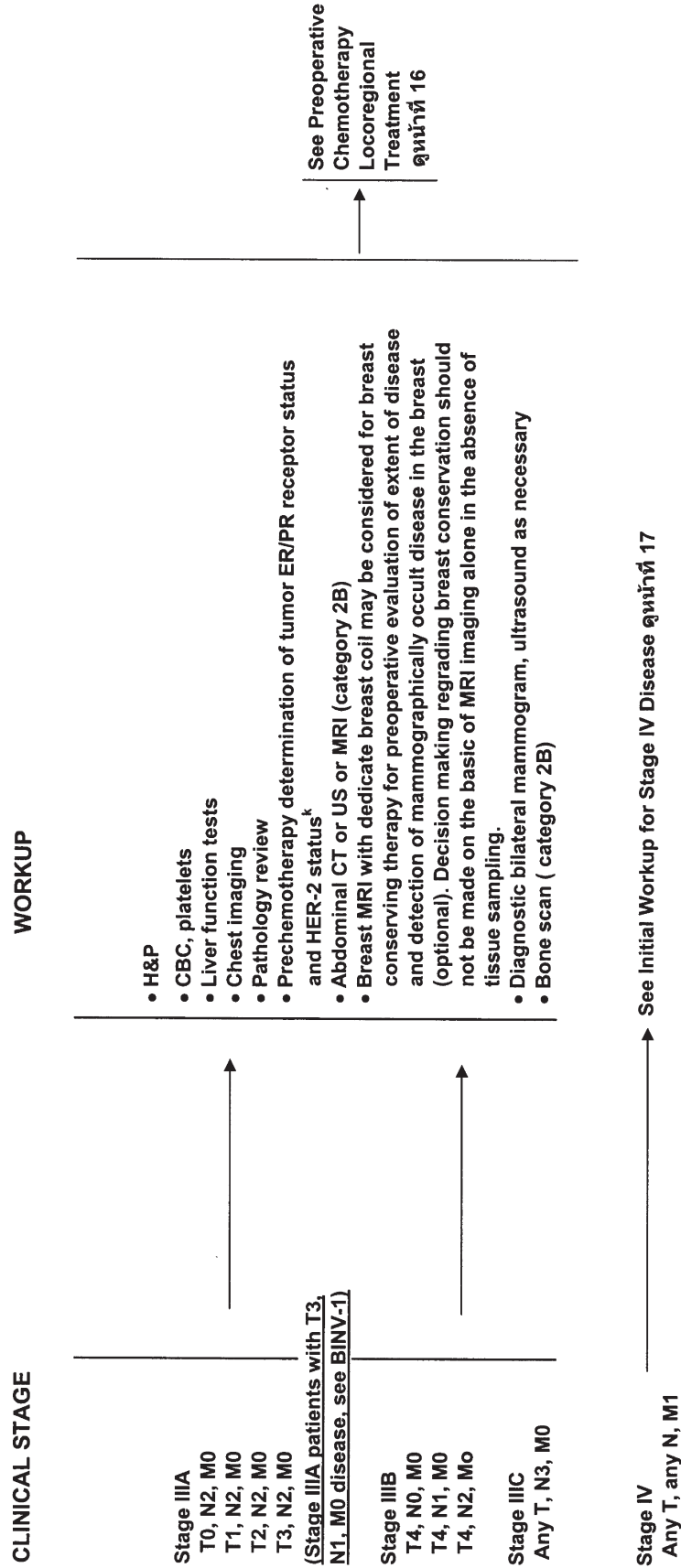
- Adjuvant RT post-mastectomy is based on prechemotherapy tumor characteristics  
ตามหน้าที่ 7  
Hormonal therapy if ER-positive (category 1)<sup>p</sup>  
See Adjuvant Hormonal Therapy (หน้าที่ 24)
- Adjuvant RT post-lumpectomy is based on prechemotherapy tumor characteristics  
ตามหน้าที่ 6  
• Hormonal therapy if ER-positive (category 1)  
See Adjuvant Hormonal Therapy (หน้าที่ 24)

→  
See Surveillance/  
Follow-up หน้าที่ 17

<sup>p</sup> Chemotherapy and hormonal therapy used as adjuvant therapy should be given sequentially with hormonal therapy following chemotherapy. The benefits of chemotherapy and of hormonal therapy are additive. However, the absolute benefit from chemotherapy may be small. The decision to add chemotherapy to hormonal therapy should be individualized, especially in those with a favorable prognosis and in women age 60 y where the incremental benefit of chemotherapy may be smaller. A available data suggest sequential or concurrent hormonal therapy with RT is acceptable.

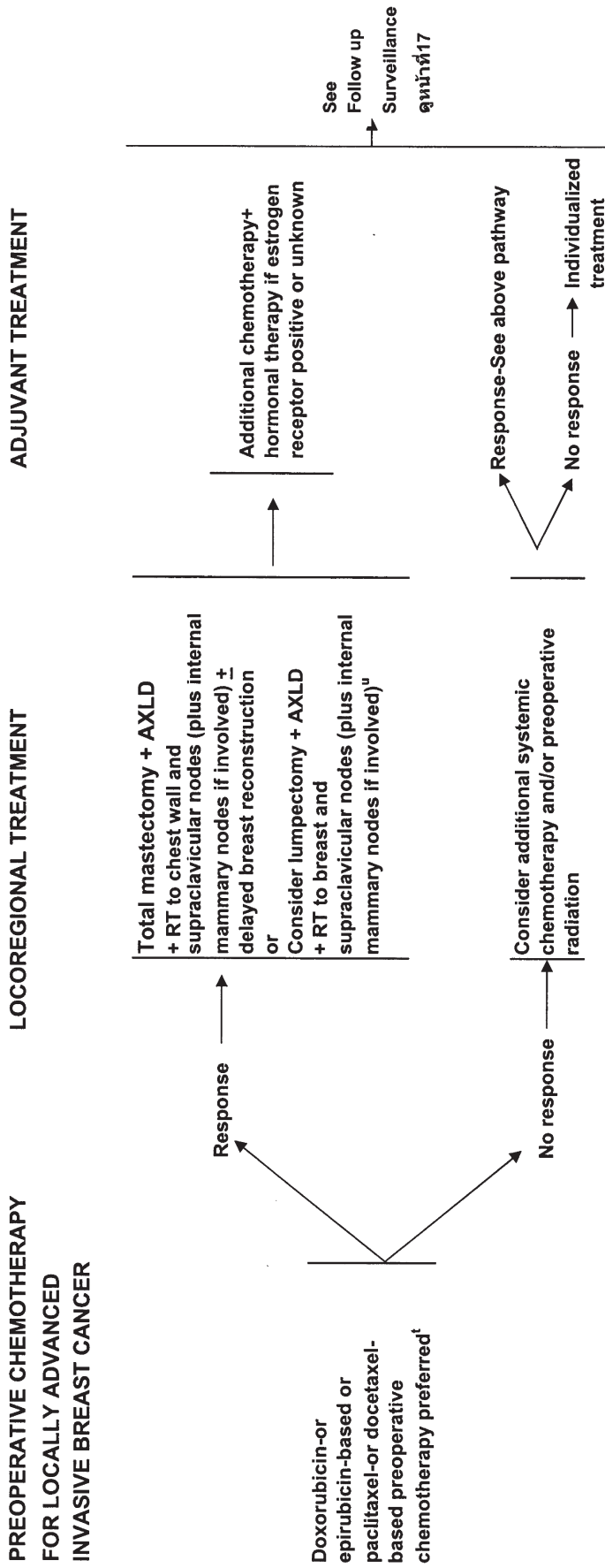
# Invasive Breast Cancer

## LOCALLY ADVANCED INVASIVE BREAST CANCER



<sup>k</sup> HER-2 testing should be done using IHC and/or FISH. An IHC result of 2<sup>+</sup> should be confirmed by FISH.

# Invasive Breast Cancer



<sup>†</sup> In general, those chemotherapy regimens recommended in the adjuvant setting may be considered in the preoperative setting

<sup>‡</sup> There are no data regarding breast conserving surgery in the management of inflammatory breast cancer.

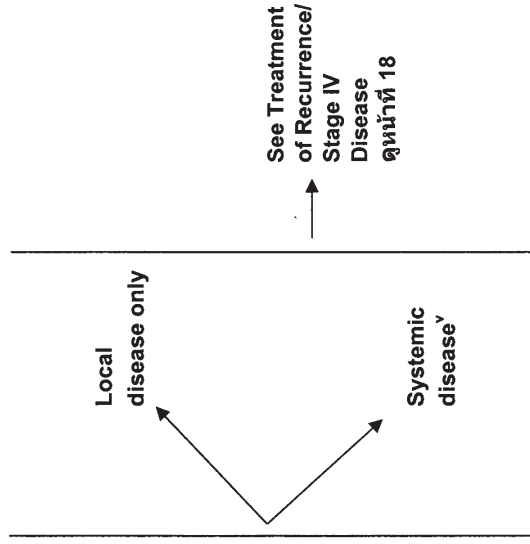
# Invasive Breast Cancer

## SURVEILLANCE/FOLLOW-UP

- Interval history and physical exam every 4-6 mo for 5 y, then every 12 mo
- Mammogram every 12 mo (and 6-12 mo post-RT if breast conserved) (category 2B)
- Woman on tamoxifen pelvic exam every 12 mo if uterus present
- Woman on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health

## RECURRENCE WORKUP or INITIAL WORKUP FOR STAGE IV DISEASE

- H&P
- CBC, platelets
- Liver function tests
- Chest imaging
- Bone scan
- X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan
- Consider abdominal CT or MRI
- Biopsy documentation of first recurrence, if possible
- Consider determination of tumor ER/PR and HER-2 status if unknown, originally negative or not over-expressed<sup>k</sup>

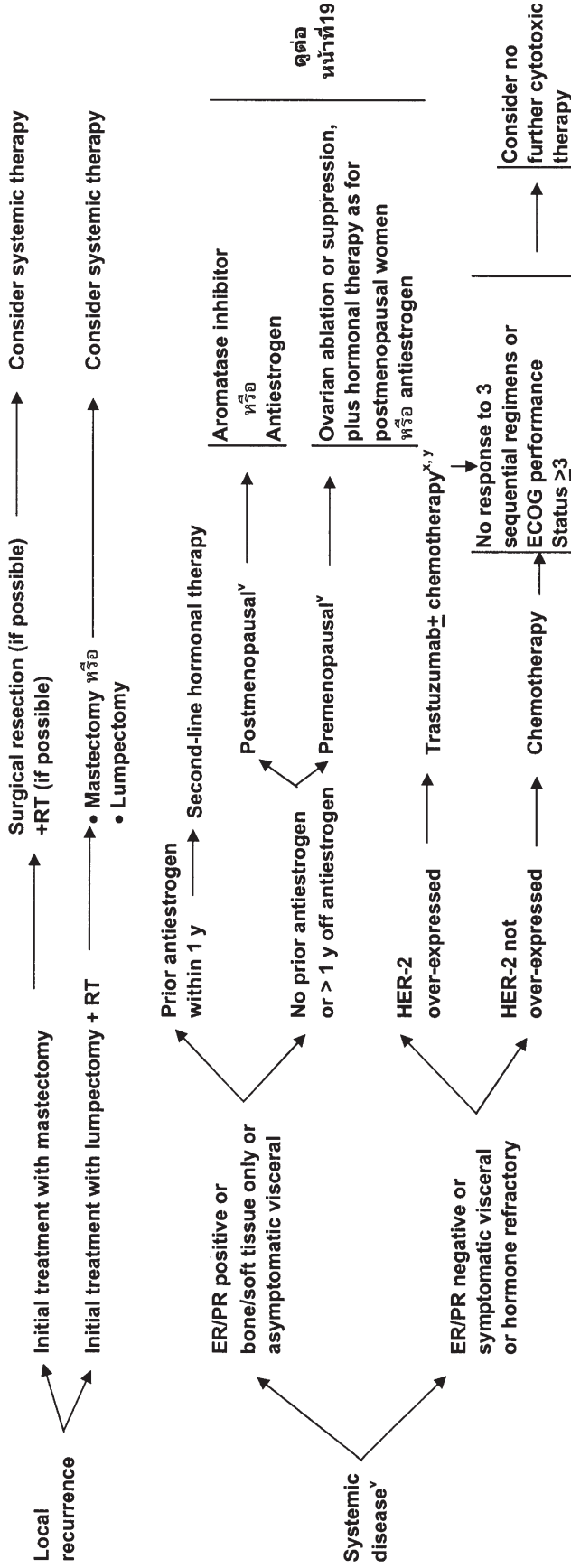


<sup>k</sup> HER-2 testing should be done using IHC and/or FISH. An IHC result of 2+ should be confirmed by FISH.

<sup>v</sup> Pamidronate or zoledronic acid (with calcium citrate 500 mg and vitamin D 400 IU supplement) should be given (category 1) in addition to chemotherapy or hormonal therapy if bone metastasis present, expected survival > 3 months, and creatinine < 3.0 mg/dL.

# Invasive Breast Cancer

## TREATMENT OF RECURRENCE/STAGE IV DISEASE



<sup>y</sup> Pamidronate or zoledronic acid (with calcium citrate 500 mg and vitamin D 400 IU supplement) should be given (category 1) in addition to chemotherapy or hormonal therapy if bone metastasis present, expected survival > 3 months, and creatinine < 3.0 mg/dL.

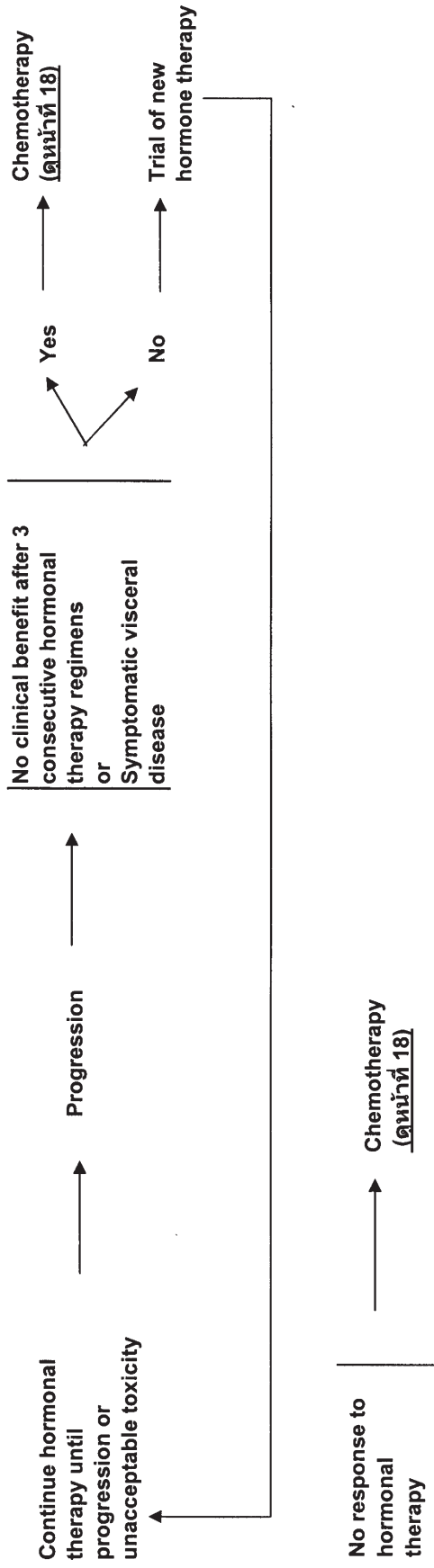
<sup>x</sup> The value of continued trastuzumab following progression on first line-trastuzumab containing chemotherapy for metastatic breast cancer is unknown.

The optimal duration of trastuzumab in patients with long-term control of disease is unknown.

<sup>y</sup> Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity.

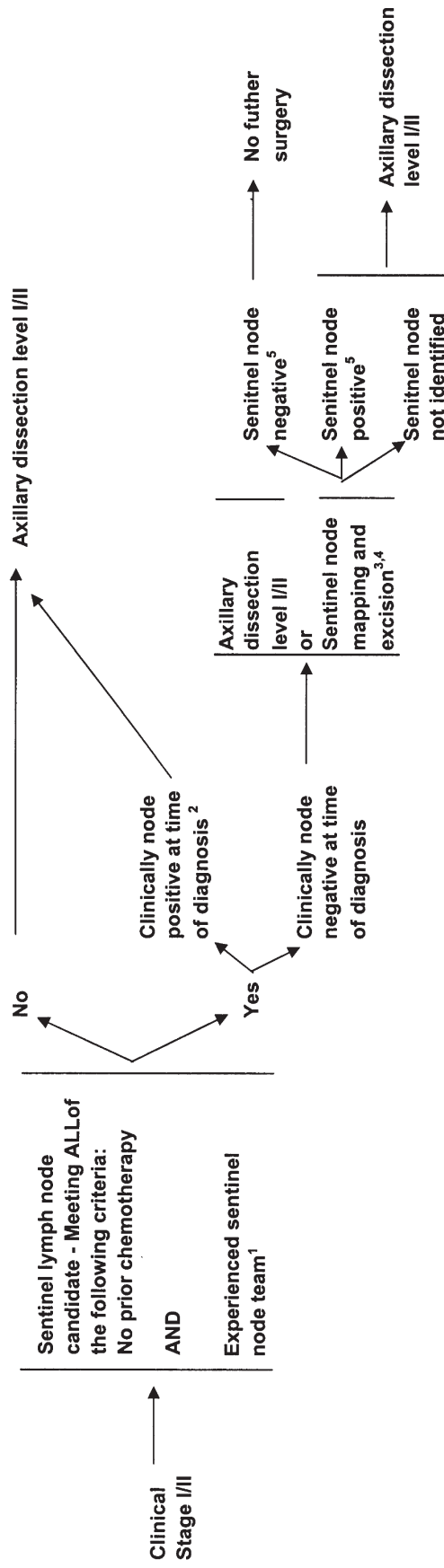
# Invasive Breast Cancer

## FOLLOW-UP THERAPY FOR HORMONE TREATMENT OF RECURRENCE/STAGE IV DISEASE



# Invasive Breast Cancer

## SURGICAL AXILLARY MANAGEMENT - STAGE I, IIA, AND IIB



<sup>1</sup> Sentinel node team must have documented experience with sentinel node biopsy in breast cancer. Team includes surgeon, radiologists, nuclear medicine physician, pathologist, and prior discussion with medical and radiation oncologists on use of sentinel node for treatment decisions.

<sup>2</sup> Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound guided FNA or core biopsy in determining if patient needs axillary lymph node dissection.

<sup>3</sup> Axillary sentinel node biopsy in all cases; internal mammary sentinel node biopsy optional if drainage maps to internal mammary nodes (category 3).

<sup>4</sup> Sentinel lymph node mapping injections may be peritumoral, subareolar or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).

<sup>5</sup> Sentinel node involvement defined by multilevel node sectioning with hematoxylin and eosin staining. Cytokeratin immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is controversial (category 3).

# Invasive Breast Cancer

## AXILLARY DISSECTION

In the absence of definitive data demonstrating superior survival from the performance of axillary lymph node dissection, patients who have particularly favorable tumors, patients for whom the selection of adjuvant systemic therapy is unlikely to be affected, for the elderly, or those with serious comorbid conditions, the performance of axillary lymph node dissection may be considered optional. The axillary dissection should be extended to include level III nodes only if there is gross disease apparent in the level II nodes.

Sentinel lymph node biopsy may be considered an option if there is an experienced sentinel node team and the patient is an appropriate sentinel lymph node biopsy candidate (ดูหน้า 20).

# Invasive Breast Cancer

## MARGIN STATUS IN INFILTRATING CARCINOMA

The use of breast conserving therapy is predicated on achieving a pathologically negative margin of resection. Cases where there is a positive margin should undergo further surgery, either a re-excision to achieve a negative margin or a mastectomy. If re-excision is technically feasible to allow for breast conserving therapy, this can be done with resection of the involved margin guided by the orientation of the initial resection specimen or re-excision of the entire original excision cavity. If multiple margins remain positive, mastectomy may be required for optimal local control.

It may be reasonable to treat selected cases with breast conserving therapy with a microscopically focally positive margin in the absence of an extensive intraductal component<sup>1</sup>. For these patients, the use of a higher radiation boost dose to the tumor bed should be considered.

Margins should be evaluated on all surgical specimens from breast conserving surgery. Requirements for optimal margin evaluation include:

- Orientation of the surgical specimens.
- Description of the gross and microscopic margin status
- Reporting of the distance, orientation, and type of tumor (invasive or DCIS) in relation to the closest margin

<sup>1</sup> An extensive intraductal component is defined as an infiltrating ductal cancer where greater than 25% of the tumor volume is DCIS and DCIS extend beyond the invasive cancer into surrounding normal breast parenchyma.

# Invasive Breast Cancer

## CONTRAINDICATIONS TO BREAST-CONSERVING THERAPY REQUIRING RADIATION THERAPY

Contraindications for breast-conserving therapy requiring radiation therapy include:

**Absolute:**

- Prior RT to the breast or chest wall
- RT during pregnancy
- Diffuse suspicious or malignant appearing microcalcifications
- Widespread disease that cannot be incorporated by local excision through a single incision that achieves negative margins with a satisfactory cosmetic result.
- Positive pathologic margin<sup>1</sup>

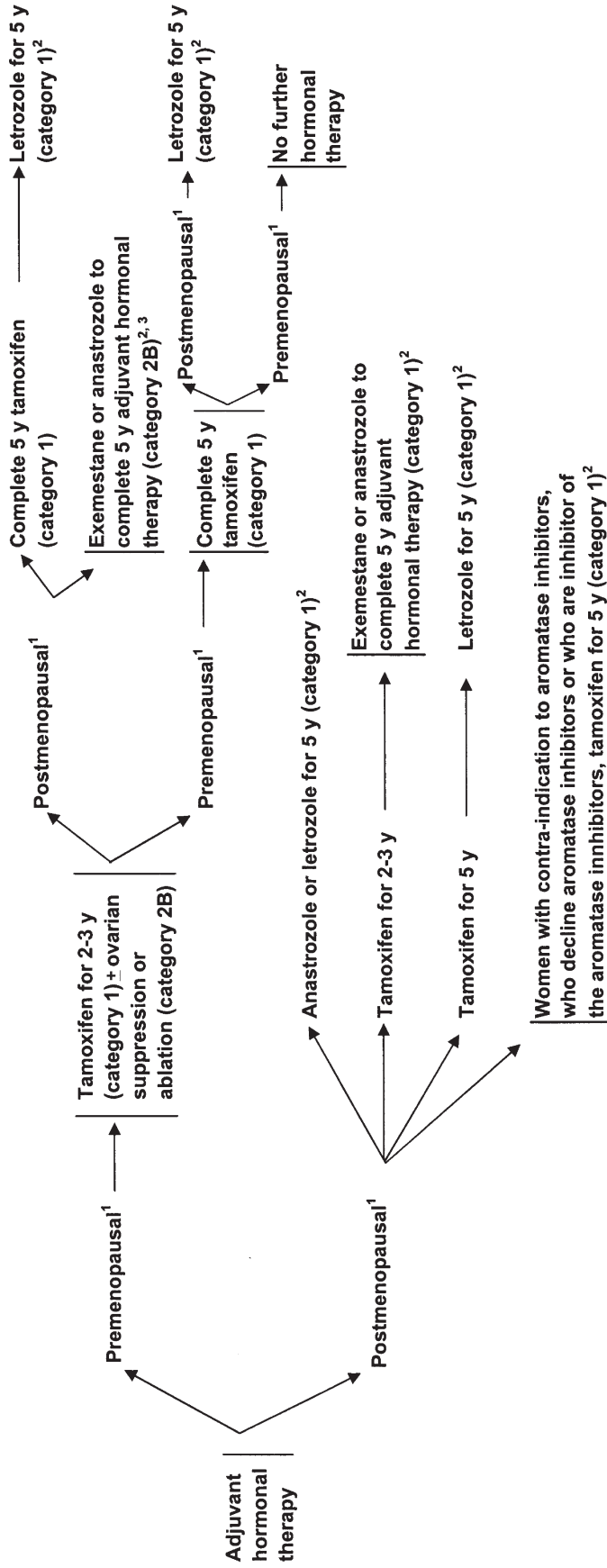
**Relative:**

- Active connective tissue disease involving the skin (especially scleroderma and lupus)
- Tumors >5cm (category 2B)
- Focally positive margin<sup>1</sup>

<sup>1</sup> See Margin Status in Infiltrating Carcinoma (หน้า 22)

# Invasive Breast Cancer

## ADJUVANT HORMONAL THERAPY



<sup>1</sup> See Definition of Menopause(หน้า 25)

<sup>2</sup> The panel believes the three selective aromatase (anastrozole, letrozole, exemestane) have similar antitumor efficacy and similar toxicity profiles. The aromatase inhibitor (s) specified is that used in the clinical trial(s) that most closely approximates the clinical situation.

<sup>3</sup> This specific patient subset was not included in the trials of aromatase inhibitors given sequentially with adjuvant tamoxifen. Some women who appear to become postmenopausal on tamoxifen therapy have resumption of ovarian function after discontinuation of tamoxifen and initiation of an aromatase inhibitor. Therefore, serial monitoring of plasma estradiol and FSH levels is encouraged in this clinical setting. Should ovarian function resume, the aromatase inhibitor should be discontinued and tamoxifen resumed. See Definition of Menopause(หน้า 25)

# Invasive Breast Cancer

## DEFINITION OF MENOPAUSE

Clinical trials in breast cancer have utilized a variety of definitions of menopause. Menopause is generally the permanent cessation of menses, and as the term is utilized in breast cancer management includes a profound and permanent decrease in ovarian estrogen synthesis. Reasonable criteria for determining menopause include any of the following:

- Prior bilateral oophorectomy
- Age  $\geq$  60 y
- Age < 60 y and amenorrheic for 12 or more months in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression and FSH and estradiol in the postmenopausal range
- If taking tamoxifen or toremifene, and age < 60 y, then FSH and plasma estradiol level in postmenopausal ranges

It is not possible to assign menopausal status to women who are receiving an LH-RH agonist or antagonist. In women premenopausal at the time of adjuvant chemotherapy, amenorrhea is not a reliable indicator of menopausal status.

# Invasive Breast Cancer

## SUBSEQUENT HORMONAL THERAPY FOR SYSTEMIC DISEASE

(For first-line hormonal therapy ดูหน้า 18)

Premenopausal patients with ER-positive disease should have ovarian ablation/suppression and follow postmenopausal guideline

### POSTMENOPAUSAL PATIENTS

- Non-steroidal aromatase inhibitor (anastrozole, letrozole) or steroidal aromatase inactivator (exemestane)
- Fulvestrant
- Tamoxifen or Toremifene
- Megestrol acetate
- Fluoxymesterone
- Ethinyl estradiol