一、本共識依下列參考資料修改版本：

(一) NCCN Clinical Practice Guidelines in Oncology- Breast cancer V.2.2015

(二) ASCO文章: American Society of Clinical Oncology Clinical Practice Guideline: Update on Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer. (*Published ahead of print on 7/12/10*)

(網址:http://www.asco.org/guidelines/endocrinebreast)

二、制訂人員：

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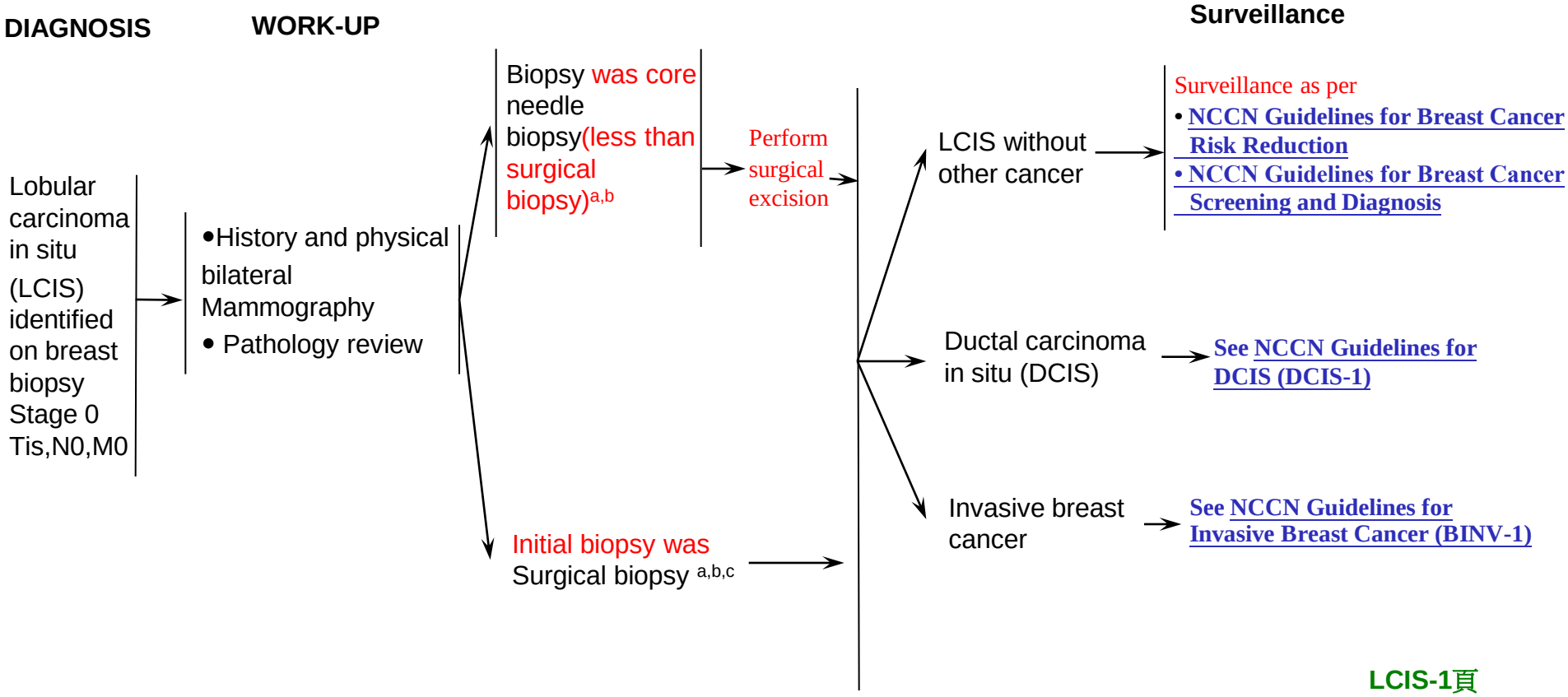
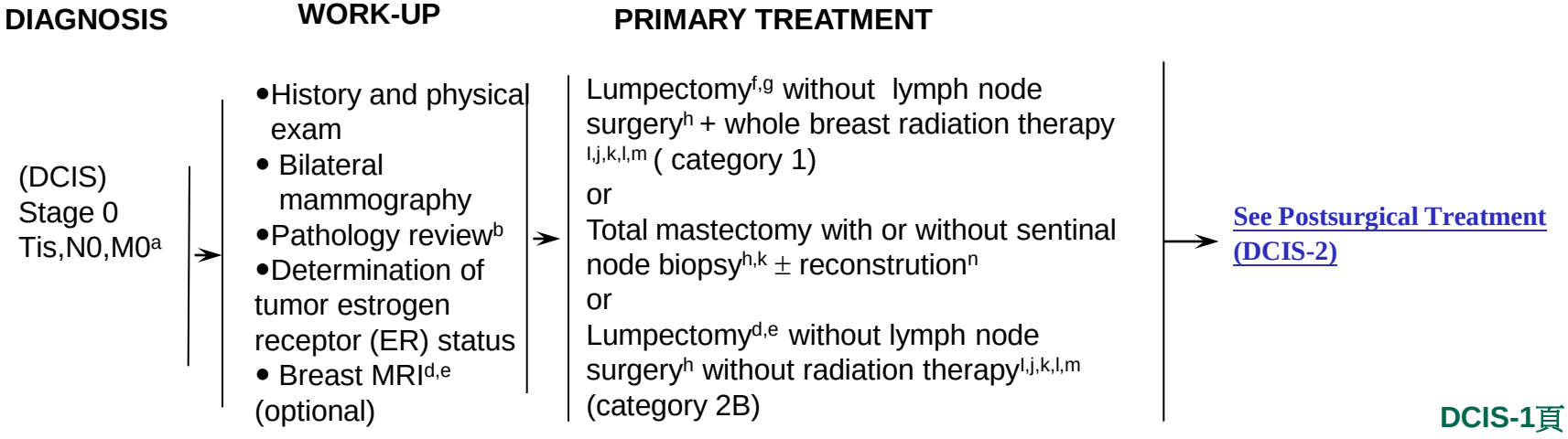
核子醫學 :吳彥雯醫師
個 管 師 :鄭玉琴護理師



LCIS-1頁

[a] LCIS is present on initial biopsy (needle or surgical) or on final excision with or without other proliferative changes (atypical ductal or lobular hyperplasia) .
[b] Some variants of LCIS ("pleomorphic LCIS") may have a similar biological behavior to that of DCIS. Clinicians may consider complete excision with negative margins for pleomorphic LCIS, but outcome data regarding the efficacy of surgical excision to negative margins are lacking. There are no data to support using radiotherapy in this setting.
[c] Multifocal/extensive LCIS involving >4 terminal ductal lobular units on a core biopsy may be associated with increased risk of invasive cancer on surgical excision.



[a] See NCCN Breast Cancer Screening and Diagnosis Guidelines.

[b] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http:www.cap.org

[c] See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian.

[d] See Principles of Dedicated Breast MRI Testing (BINV-B).

[e] The use MRI has not been shown to increase likelihood of negative margins or decrease conversion to mastectomy. Data to support improved long-term outcomes are lacking.

[f] 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 lumpectomy should have total mastectomy.

[g] See Margin Status in DCIS (DCIS-A).

[h] Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven metastatic disease in women 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 should be strongly 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.

[i] See Principles of Radiation Therapy (BINV-I).

[j] Complete resection should be documented by analysis of margins and specimen radiography. Post-excision mammography could also be performed whenever uncertainty about adequacy of excision remains.

[k] Patients found to have invasive disease at total mastectomy or re-excision should be managed as having stage l or stage ll disease, including lymph node staging.

[l] See Special Considerations to Breast-Conserving Therapy (BINV-G).

[m] Whole-breast radiation therapy following lumpectomy reduces recurrence rates in DCIS by about 50%. Approximately half of the recurrences are invasive and half are DCIS. A number of factors determine that local recurrence risk: palpable mass, larger size, higher grade, close or involved margins, and age <50 years. If the patient and physician view the individual risk as “low,” some patients may be treated by excision alone. All data evaluating the three local treatments show no differences in patient survival.

[n] See Principles of Breast Reconstruction Following Surgery (BINV-H).

DCIS POSTSURGICAL TREATMENT

Risk reduction therapy for ipsilateral breast following breast-conserving surgery:
Consider tamoxifen[o] for 5 years for:

- Patients treated with breast-conserving therapy (lumpectomy) and radiation therapy[p] (category 1), especially for those with ER-positive DCIS.
- The benefit of tamoxifen for ER-negative DCIS is uncertain
- Patients treated with excision alone[p]

Risk reduction therapy for contralateral breast:

- Counseling regarding risk reduction[o]
  See NCCN Guidelines for Breast Cancer Risk Reduction

SURVEILLANCE/FOLLOW-UP

- Interval history and physical exam every 6-12 mo for 5 y,then annually
- Mammogram every 12 mo (and 6-12 mo postradiation therapy if breast conserved [category 2B])
- If treated with tamoxifen, monitor per NCCN Guidelines for Breast Cancer Risk Reduction

o Some SSRIs like fluoxetine and paroxetine decrease the formation of endoxifen and 4-OH tamoxifen, active metabolites of tamoxifen, and may impact efficacy. Caution is advised about coadministration of these drugs with tamoxifen. However, citalopram and venlafaxine appear to have minimal impact on tamoxifen metabolism. At this time, based on current data the panel recommends against CYP2D6 testing for women being considered for tamoxifen therapy. Coadministration of strong inhibitors of CYP2D6 should be used with caution.

p 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 (See also NCCN Guidelines for Breast Cancer Risk Reduction).

MARGIN STATUS IN DCIS

DCIS-1頁

Substantial controversy exists regarding the definition of a negative pathologic margin in DCIS. Controversy arises out of the heterogeneity of the disease, difficulties in distinguishing the spectrum of hyperplastic conditions, anatomic considerations of the location of the margin, and inadequate prospective data on prognostic factors 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.
With pathologic margins between 1-10 mm, wider margins are generally associated with lower local recurrence rates. However, close surgical
margins (<1 mm) at the fibroglandular boundary of the breast (chest wall or skin) do not mandate surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site (category 2B).

DCIS-A頁

CLINICAL STAGE

Stage I
T1N0M0
or
Stage IIA
T0N1M0
T1N1M0
T2N0M0
or
Stage IIB
T2N1M0
T3N0M0
or
Stage IIIA
T3N0M0

→

WORK-UP

- History and physical exam
- CBC,platelets
- Liver function tests and alkaline phosphatase
- Diagostic 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]
- Breast MRI[d] (optional), with special consideration for mammographically occult tumors)
- Fertility counseling if premenopausal[e]

If clinical stage I-IIB, consider additional studies only if directed by signs or symptoms: [f]

- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT (if pulmonary symptoms present)

If clinical stage IIIA (T3N1M0) consider:

- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or sodium fluoride PET/CT [g] (category 2B)
- FDG PET/CT[h,i] (optional, category 2B)

→ **See Locoregional Treatment (BINV-2)**

BINV-1頁

[a] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http:www.cap.org
[b] See Principle of HER2 Testing (BINV-A) .
[c] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines .
[d] See Principles of Dedicated Breast MRI Testing (BINV-B) .
[e] **See Fertility and Birth Control After Adjuvant Breast Cancer Treatment (BINV-C)**.
[f] Routine systemic staging is not indicated for early breast cancer in the absence of symptoms.
[g] If FDG PET/CT are performed and both clearly indicate bone metastases, bone scan or fluoride PET/CT may not be needed.
[h] FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in LABC when used in addition to standard staging studies.
[i] FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.

LOCOREGIONAL TREATMENT OF CLINICAL STAGE I,IIA, OR IIB DISEASE OR T3N1M0

Lumpectomy with surgery axillary staging (category 1)[j,k,l]

- ≧4 positive[o] Axillary nodes → Radiation therapy to whole breast with or without boost [p] to tumor bed (category 1), infraclavicular region, and supraclavicular area. Consider radiation therapy to internal mammary nodes[q] (category 2B).It is common for radiation therapy to follow chemotherapy when chemotherapy indicated.
- 1-3 positive Axillary nodes → Radiation therapy to whole breast with or without boost[p] to tumor bed (category 1).Strongly consider radiation therapy to infraclavicular region and supraclavicular area (category 2B). It is common for radiation therapy to follow chemotherapy when chemotherapy indicated.

or

- Negative Axillary nodes → Radiation therapy to whole breast with or without boost[p] to tumor bed or consideration of partial breast irradiation (PBI) in selected patients.[p,r] It is common for radiation therapy to follow chemotherapy when chemotherapy indicated.[s]

→ See BINV-4

Total mastectomy with surgery axillary staging[j,k,m] (category 1) ± reconstruction[n] → See Locoregional Treatment (BINV-3)

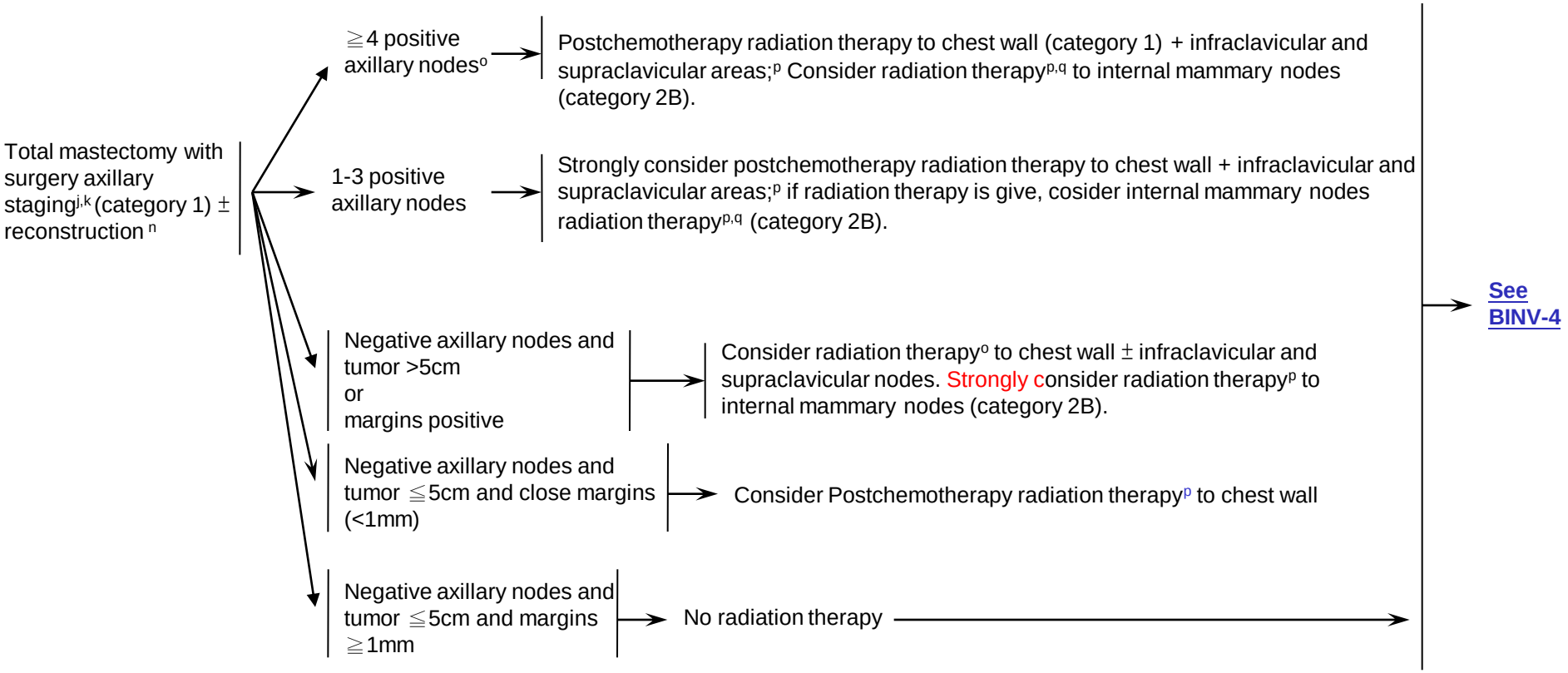
or

If T2 or T3 and fulfills criteria for breast conserving therapy except for size[l] → Consider Properative Chemotherapy Guidelines (BINV-10)

BINV-2頁

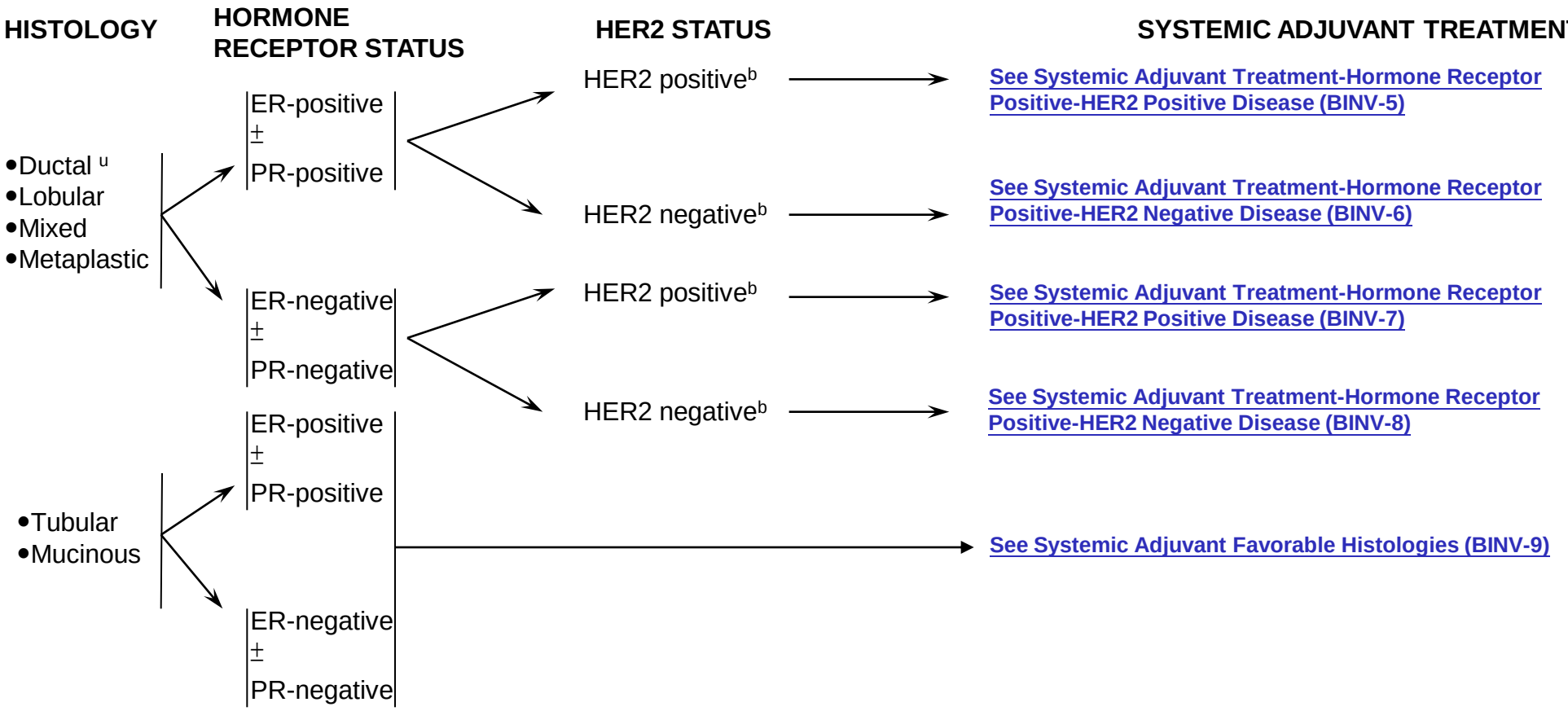
[j] See Surgical Axillary Staging (BINV-D) .
[k] See Axillary lymph Node Staging (BINV-E) and Margin Status in Infiltrating Carcinoma (BINV-F).
[l] See Special Considerations Breast-Converving Therapy (BINV-G) .
[m] Except as outlined in the NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines .and the NCCN Breast Cancer Risk Reduction Guidelines, prophylactic mastectomy of a breast contralateral to a known unilateral breast cancer is discouraged. When considered, the small benefits from contralateral prophylactic mastectomy for women with unilateral breast cancer must be balanced with the risk of recurrent disease from the known ipsilateral breast cancer, psychological and social issues of bilateral mastectomy, and the risk of contralateral mastectomy. The use of prophylactic mastectomy contralateral to a breast treated with breast conserving therapy is very strongly discouraged.
[n] See Principles of Breast Reconstruction Following Surgery (BINV-H)
[o] Consideration may be given to additional staging including bone scan and abdominal CT/US/MRI; chest CT (category 2B). (See BINV-1)
[p] See Principles of Radiation Therapy (BINV-I).
[q] Radiation therapy should be given to the internal mammary lymph nodes if they are clinical 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 radiation therapy is delivered to the internal mammary lymph nodes.
[r] PBI may be administered prior to chemotherapy.
[s] Breast irradiation may be omitted in those 70 y of age or older with estrogen-receptor positive, clinically node negative, T1 tumors who receive adjuvant endocrine therapy (category 1).

LOCOREGIONAL TREATMENT OF CLINICAL STAGE I,IIA, OR IIB DISEASE OR T3N1M0



BINV-3頁

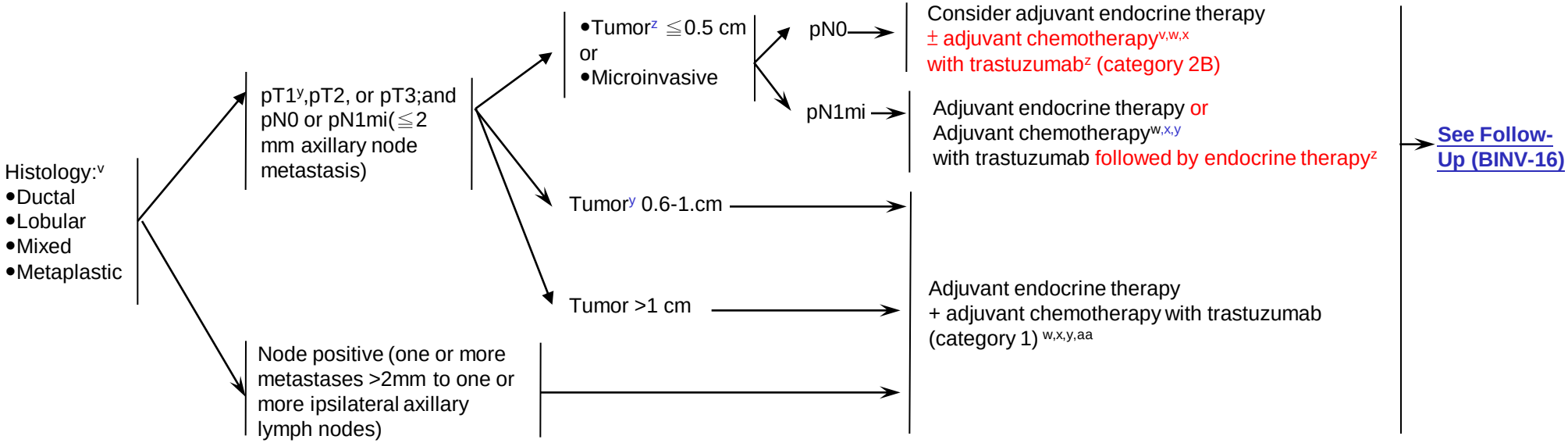
[j] See Surgical Axillary Staging (BINV-D) .
[k] See Axillary lymph Node Staging (BINV-E) and Margin Status in Infiltrating Carcinoma (BINV-F).
[n] See Principles of Breast Reconstruction Following Surgery (BINV-H)
[o] Consideration may be given to additional staging including bone scan and abdominal CT/US/MRI; chest CT (category 2B).
[p] See Principles of Radiation Therapy (BINV-I).
[q] Radiation therapy should be given to the internal mammary lymph nodes if they are clinical 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 radiation therapy is delivered to the internal mammary lymph nodes.



[b] See Principle of HER2 Testing (BINV-A) .
[u] This includes medullary and micropapillary subtypes.

BINV-4頁

SYSTEMIC ADJUVANT TREATMENT – HORMONE RECEPTOR POSITIVE- HER2 POSITIVE DISEASE[b]



See Adjuvant Endocrine Therapy (BINV-J) and Adjuvant Chemotherapy (BINV-K)

BINV-5頁

*cash

[b] See Principle of HER2 Testing (BINV-A) .

[v] Mixed lobular and ductal carcinoma as well as metaplastic carcinoma should be graded based on the ductal component and treated based on this grading. The metaplastic or mixed component does not alter prognosis.

[w] Evidence supports that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone-receptor-positive breast cancer is similar to that achieved with CMF alone. Early evidence suggests similar benefits from ovarian suppression (ie, 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.

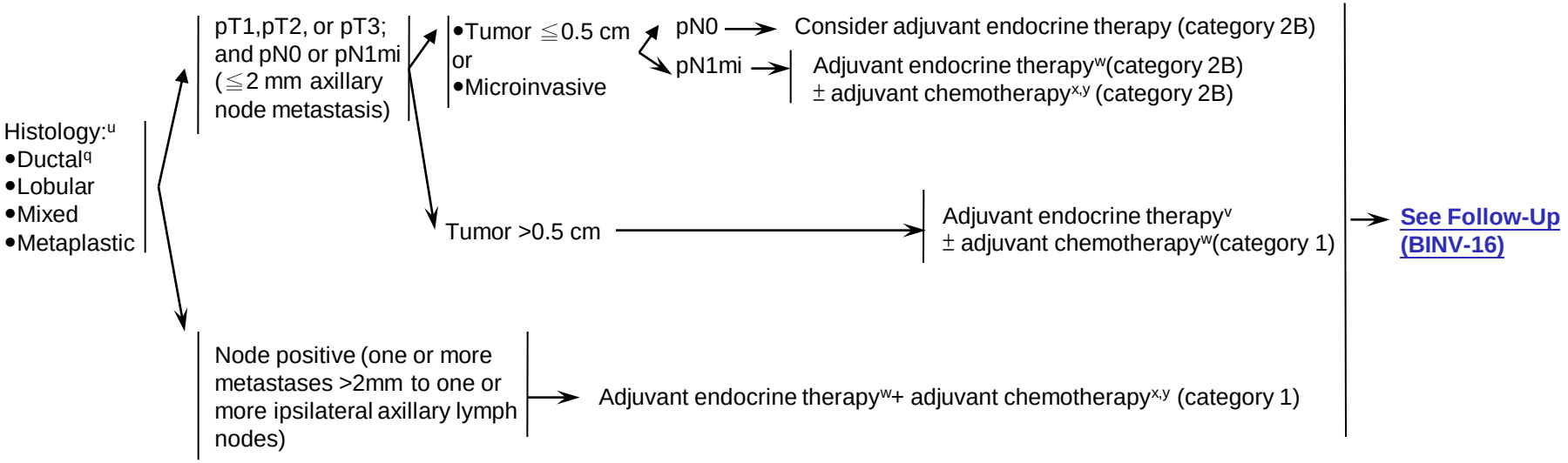
[x] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. The benefits of chemotherapy and of endocrine therapy are additive. However, the absolute benefit from chemotherapy may be small. The decision to add chemotherapy 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 sequential or concurrent endocrine therapy with radiation therapy is acceptable.

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

[z] 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.

[aa] A pertuzumab-containing regimen can be administered to patients with greater than or equal to T2 or greater than or equal to N1, HER2-positive, early-stage breast cancer.

SYSTEMIC ADJUVANT TREATMENT – HORMONE RECEPTOR- POSITIVE- HER2 NEGATIVE DISEASE[b]



See Adjuvant Endocrine Therapy (BINV-J) and Neoadjuvant/Adjuvant Chemotherapy (BINV-K)

BINV-6頁

[b] See Principle of HER2 Testing (BINV-A) .

[v] Mixed lobular and ductal carconoma as well as metaplastic carcinoma should be graded based on the ductal component and treated on this grading. The metaplastic pr mixed component does not after prognosis.

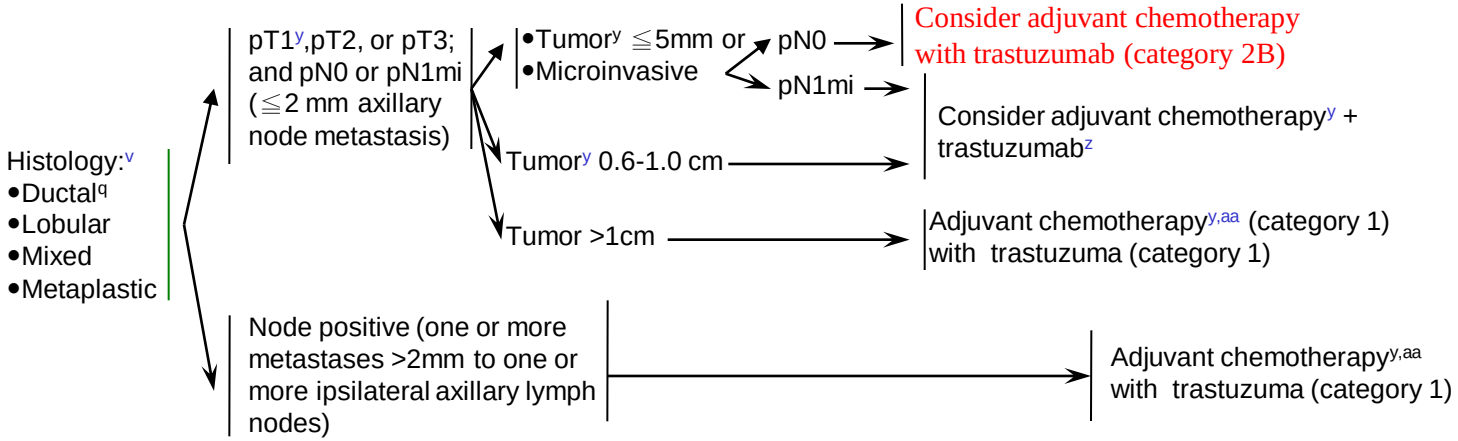
[w] Evidence supports that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone-receptor-positive breast cancer is similar to that achieved with CMF alone. Early evidence suggests similar benefits from ovarian suppression (ie, LHRH agonist) as from 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.

[x] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy following chemotherapy. The benefit of 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 sequential or concurrent endocrine therapy with radiation therapy is acceptable.

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

[bb] The 21-gene RT-PCR assay recurrence score can be considered in select patients with 1–3 involved ipsilateral axillary lymph nodes to guide the addition of combination chemotherapy to standard hormone therapy. A retrospective analysis of a prospective randomized trial suggests that the test is predictive in this group similar to its performance in node-negative disease.

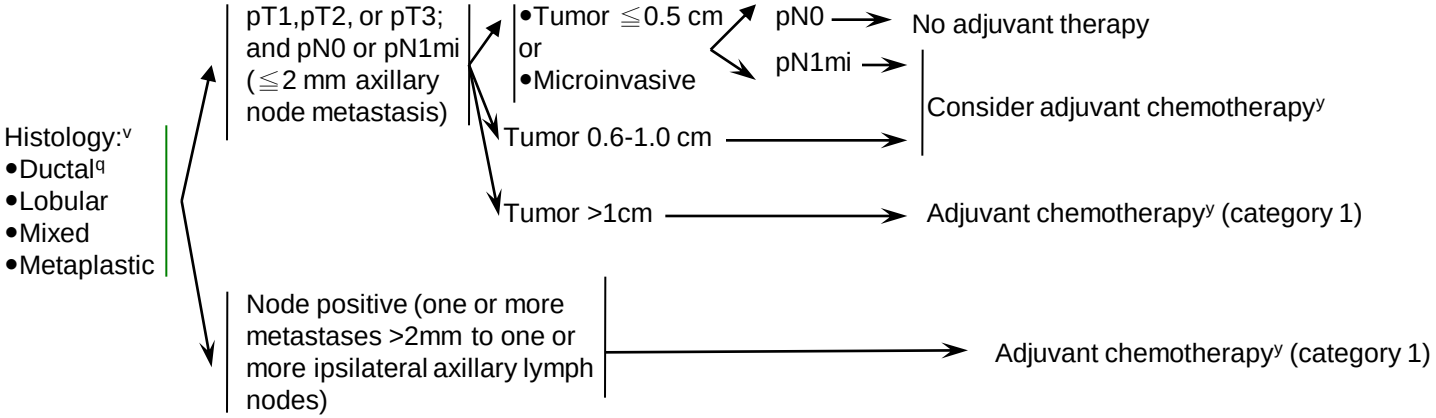
SYSTEMIC ADJUVANT TREATMENT – HORMONE RECEPTOR NEGATIVE- HER2 POSITIVE DISEASE[b]



See Follow-Up (BINV-16)

BINV-7頁

SYSTEMIC ADJUVANT TREATMENT – HORMONE RECEPTOR- NEGATIVE- HER2 NEGATIVE DISEASE [b]



See Follow-Up (BINV-16)

See Adjuvant Chemotherapy (BINV-K)

BINV-8頁

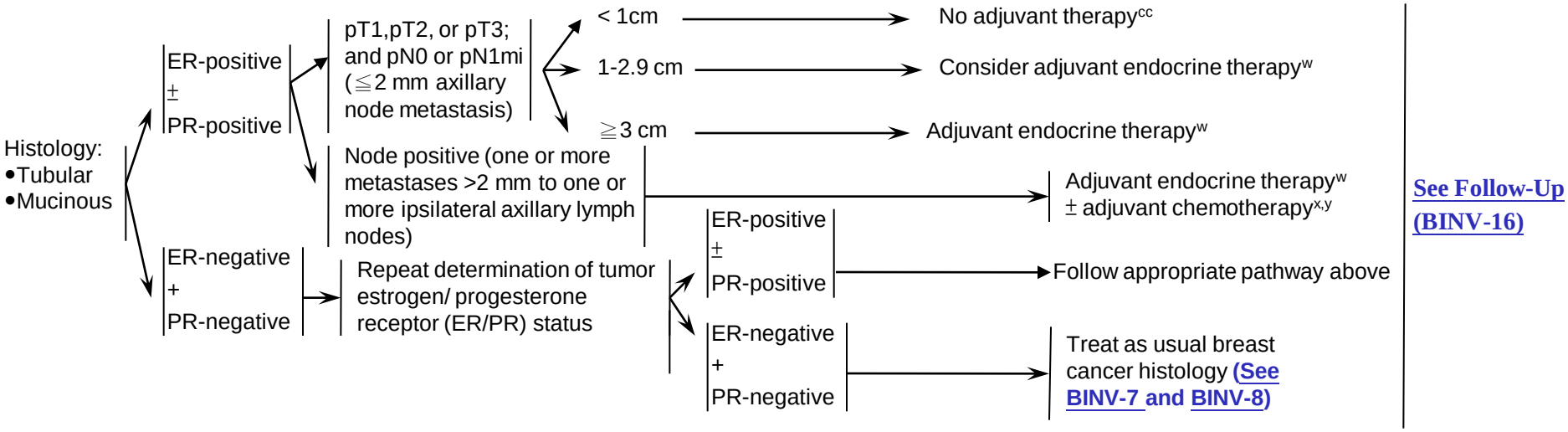
[b] See Principle of HER2 Testing (BINV-A) .

[v] Mixed lobular and ductal carconoma as well as metaplastic carcinoma should be graded based on the ductal component and treated on this grading. The metaplastic pr mixed component does not after prognosis.

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

[z] 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 with trastuzumab therapy.

SYSTEMIC ADJUVANT - FAVORABLE HISTOLOGIES



See Adjuvant Endocrine Therapy (BINV-J) and Adjuvant Chemotherapy (BINV-K)

[w] Evidence supports that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone-receptor-positive breast cancer is similar to that achieved with CMF alone. Early evidence suggests similar benefits from ovarian suppression (ie, LHRH agonist or antagonist) 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.

[x] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with radiation therapy is acceptable.

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

[cc] If EF-positive consider endocrine therapy for risk reduction and to diminish the small risk of disease recurrence.

Preoperative Systemic Therapy Guideline

CLINICAL STAGE

Stage IIA
T2N0M0

Stage IIB
T2N1M0
T3N0M0

Stage IIIA
T3N1M0

and

Fulfills criteria for breast conserving surgery except for tumor size[dd]

WORK-UP

- History and physical
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagostic 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]
- Breast MRI[d] (optional), with special consideration for mammographically occult tumors)
- Fertility counseling if premenopausal[e]

Consider systemic staging (particularly if signs and symptoms are present):[f]

- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or sodium fluoride PET/CT [g] (category 2B)
- FDG PET/CT[h,i] (optional, category 2B)

See Preoperative Systemic Therapy Breast and Axillary Evaluation (BINV-11)

第BINV-10頁

[a] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http:www.cap.org
[b] See Principle of HER2 Testing (BINV-A) .
[c] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines .
[d] See Principles of Dedicated Breast MRI Testing (BINV-B) .
[e] See Fertility and Birth Control After Adjuvant Breast Cancer Treatment (BINV-C).
[f] Routine systemic staging is not indicated for early breast cancer in the absence of symptoms.

[g] If FDG PET/CT are performed and both clearly indicate bone metastases, bone scan or fluoride PET/CT may not be needed.
[i] FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.
[dd] In cases where breast-conserving surgery may not be possible but patient will need chemotherapy, neoadjuvant treatment remains an acceptable option..

Preoperative Systemic Therapy Breast and Axillary Evaluation

Preoperative systemic therapy → Core biopsy with placement of image-detectable marker(s), if not previously performed, must be done to demarcate the tumor bed for post-chemotherapy surgical mamagement

- Clinically negative axillary lymph node(s), should have axillary imaging; suspicious nodes should be sampled by FNA or core biopsy prior to neoadjuvant therapy[ee]
- Clinically positive axillary lymph node(s), should be sampled by FNA or core biopsy prior to neoadjuvant therapy[ee].

→ See Preoperative Systemic Therapy - Primary Treatment (BINV-12)

Surgical resection → See Locoregional Treatment of Clinical Stage I, IIA, or IIB Disease or T3, N1, M0 (BINV-3)

第BINV-11頁

Preoperative Systemic Therapy Guideline (Stage IIA-IIIA)

PRIMARY TREATMENT	RESPONSE[ll]	
Preoperative chemotherapy[gg,hh,ii,jj] (endocrine therapy alone may be considered for receptor-positive disease in postmenopausal patients)[kk]	Confirmed-progressive disease any time	→ See Mastectomy (BINV-13)
	Partial response, lumpectomy not possible	→ See Mastectomy (BINV-13)
	Partial response, lumpectomy possible or Complete response	→ See Lumpectomy (BINV-13)

第BINV-12頁

[gg] A number of combination and single-agent chemotherapy regimens have activity in the preoperative setting. In general, 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.

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

[jj] Administration of all chemotherapy prior to surgery is preferred.

[kk] Definition of Menopause (See BINV-L).

[ll] The accurate assessment of in-breast tumor or regional lymph node response to preoperative chemotherapy is difficult, and should include physical examination and performance of imaging studies that were abnormal at the time of initial tumor staging.

ee Marking of sampled axillary nodes with a tattoo or clip should be considered to permit verification that the biopsy-positive lymph node has been removed at the time of definitive surgery.

ff Among patients shown to be node-positive prior to neoadjuvant systemic therapy, SLNB has a >10% false-negative rate when performed after neoadjuvant systemic therapy. This rate can be improved by marking biopsied lymph nodes to document their removal, using dual tracer, and by removing more than 2 sentinel nodes.

PREOPERATIVE CHEMOTHERAPY GUIDELINE

LOCAL TREATMENT

Mastectomy and surgical axillary Staging[j,mm] ± reconstruction. If sentinel lymph node biopsy performed prechemotherapy and negative findings, may omit axillary lymph node staging

Lumpectomy with surgical axillary staging.[ee] If sentinel lymph node biopsy performed prechemotherapy and negative findings, may omit axillary lymph node staging

ADJUVANT TREATMENT

• Complete planned chemotherapy regimen course if not completed preoperatively plus endocrine treatment if ER-positive and/or PR-positive (sequential chemotherapy followed by endocrine therapy).

· Adjuvant radiation therapy[p] post-mastectomy is based on prechemotherapy tumor characteristics as per **BINV-3**

and

· Endocrine therapy if ER-positive and/or PR positive[x] (category 1)[t]

· Complete up to one year of trastuzumab therapy if HER2-positive (category 1)~~(If T stage ≧ T1c).~~ May be administered concurrent with radiation therapy[p] and with endocrine therapy if indicated. **See Adjuvant Endocrine Therapy (BINV-J)**

• Complete planned chemotherapy regimen course if not completed preoperatively plus endocrine treatment if ER-positive and/or PR-positive (sequential chemotherapy followed by endocrine therapy).

· Adjuvant radiation therapy[p] post-lumpectomy based on prechemotherapy tumor characteristics as per **BINV-2**

and

· Endocrine therapy if ER-positive and/or PR positive[x] (category 1)

· Complete up to one year of trastuzumab therapy if HER2-positive (category 1))(If T stage ≧ T1c). May be administered concurrent with radiation therapy[p] and with endocrine therapy if indicated. **See Adjuvant Endocrine Therapy (BINV-J)**

See Surveillance/ Follow-up (BINV-16)

第BINV-13頁

[j] **See Surgical Axillary Staging (BINV-D)**

[p] **See Principles of Radiation Therapy (BINV-I).**

[x] 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 sequential or concurrent endocrine therapy with radiation therapy is acceptable.

[mm] Axillary staging following preoperative systemic therapy may include sentinel node biopsy or level I/II dissection. Level I/II dissection should be done for patients who were proven node-positive prior to neoadjuvant therapy (category 2B).

Kuehn T, Bauerfeind I, Fehm T, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol 2013;14(7):609-18. Epub 2013/05/21.

Boughey JC, Suman VJ, Mittendorf EA, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA 2013;310(14):1455-61. Epub 2013/10/09.

LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

CLINICAL STAGE → **WORK UP**

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 lllC
Any T, N3, M0

→

- 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]
- Breast MRI[d] (optional), with special consideration for mammographically occult tumors)
- Fertility counseling if premenopausal[e]

Consider systemic staging (particularly if signs and symptoms are present):

- Bone scan or sodium fluoride PET/CT[g] (category 2B)
- Abdominal ± pelvis CT or MRI
- Chest diagnostic CT
- FDG PET/CT[h,i] scan (optional,category 2B) [e]

→ **See Preoperative Systemic Trerapy (BINV-15)**

第BINV-14頁

[a] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org.

[b] See **Principles of HER2 Testing (BINV-A).**

[c] See **NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines**.

[d] See **Principles of Dedicated Breast MRI Testing (BINV-B).**

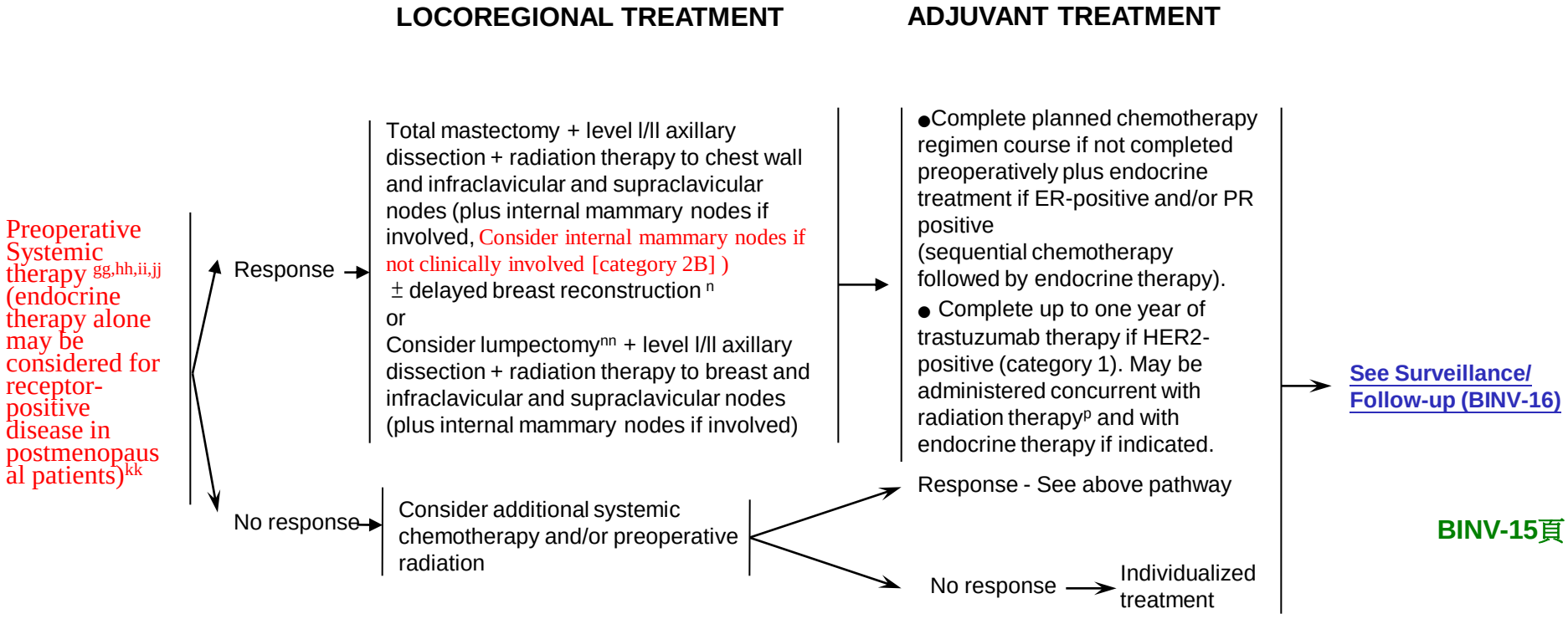
[e] See **Fertility and Birth Control (BINV-C).**

[g] If FDG PET/CT are performed and both clearly indicate bone metastases, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.

[h] FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in LABC when used in addition to standard staging studies.

[i] FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.

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



n See Principles of Reconstruction Following Surgery (BINV-H)

p See Principles of Radiation Therapy (BINV-I).

gg A number of chemotherapy regimens have activity in the preoperative setting. In general, those chemotherapy regimens recommended in the adjuvant setting may be considered in the preoperative setting. See Neoadjuvant/Adjuvant Chemotherapy (BINV-K). If treated with endocrine therapy, an aromatase inhibitor is preferred for postmenopausal women.

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

iiA pertuzumab-containing regimen may be administered preoperatively to patients with greater than or equal to T2 or greater than or equal to N1, HER2-positive breast cancer.

jjAdmistration of all chemotherapy prior to surgery is preferred.

kk See Definition of Menopause (BINV-L).

nn For patients with skin and/or chest wall involvement (T4 non-inflammatory) prior to neoadjuvant therapy, breast conservation may be performed in carefully selected patients based upon a multidisciplinary assessment of local recurrence risk. In addition to standard contraindications to breast conservation (see BINV-G), exclusion criteria for breast conservation include: inflammatory (T4d) disease before neoadjuvant therapy and incomplete resolution of skin involvement after neoadjuvant therapy

SURVEILLANCE/FOLLOW-UP

· History and physical exam 1–4 times per year as clinically appropriate for 5 y, then annually.
• Educate, monitor, and refer for lymphedema management
· Annual mammography
· Women on tamoxifen: annual gynecologic assessment every 12 mo if uterus present
· Women on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter[oo]
· Assess and encourage adherence to adjuvant endocrine therapy.
· Evidence suggests that active lifestyle, achieving and maintaining an ideal body weight (20-25 BMI) may lead to optimal breast cancer outcomes.
• **See NCCN Guidelines for Survivorship**

RECURRENT /STAGE IV DISEASE WORKUP

·History and physical exam
·CBC, platelets
·Liver function tests and alkaline phosphatase
- Chest diagnostic CT
- Brain MRI if suspicious CNS symptoms
- Bone scan or sodium fluoride PET/CT [g] (category 2B)
- FDG PET/CT [i,jj] (optional, category 2B)

·X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan
·Abdominal CT ± pelvic diagnostic CT or MRI
·First recurrence of disease should be Biopsied
·Determination of tumor ER/PR and HER2 status on metastatic site[b,qq,rr]
·Genetic counseling if patient is high risk for hereditary breast cancer [c]

→ **See Systemic Treatment of Recurrent or Stage IV Disease (BINV-18)**

第BINV-16,17頁

oo The use of estrogen, progesterone, or selective estrogen receptor modulators to treat osteoporosis or osteopenia in women with breast cancer is discouraged. The use of a bisphosphonate is generally the preferred intervention to improve bone mineral density. Optimal duration of bisphosphonate therapy has not been established. Factors to consider for duration of anti-osteoporosis therapy include bone mineral density, response to therapy, and risk factors for continued bone loss or fracture. Women treated with a bisphosphonate should undergo a dental examination with preventive dentistry prior to the initiation of therapy, and should take supplemental calcium and vitamin D.

b**See Principles of HER2 Testing (BINV-A)**

c**See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian**

gIf FDG PET/CT is performed and clearly indicates bone metastasis, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.

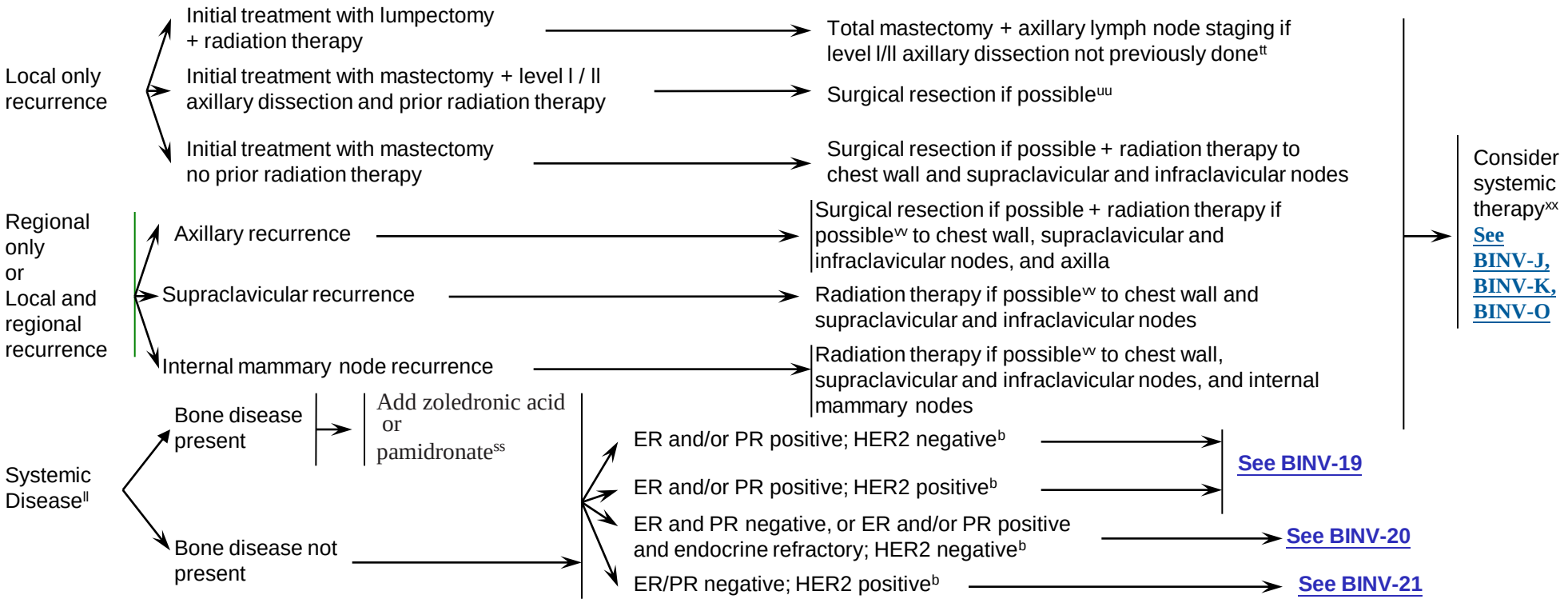
iFDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.

ppFDG PET/CT can be performed at the same time as diagnostic CT. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.

qqFalse-negative ER and/or PR determinations occur, and there may be discordance between the ER and/or PR determination between the primary and metastatic tumor(s). Therefore, endocrine therapy may be considered in patients with non-visceral or asymptomatic visceral tumors, especially in patients with clinical characteristics predicting for a hormone receptor-positive tumor (eg, long disease-free interval, limited sites of recurrence, indolent disease, older age).

rrIn clinical situations where a biopsy cannot safely be obtained but the clinical evidence is strongly supportive of recurrence, treatment may commence based on the ER/PR/HER2 status of the primary tumor.

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE



第BINV-18頁

[b] See Principles of HER2 Testing (BINV-A).

[ss] Denosumab, zoledronic acid, or pamidronate (all with calcium and vitamin D supplementation) should be given (category 1) in addition to chemotherapy or endocrine therapy if bone metastasis is present, expected survival is ≥3 months, and renal function is adequate. Patients should undergo a dental examination with preventive dentistry prior to initiation of this therapy. The optimal schedule for zoledronic acid is monthly x 12, then quarterly.

[tt] In women with a local breast recurrence after breast conserving surgery who had a prior sentinel lymph node biopsy, a repeat SNB may be technically possible. The accuracy of repeat SNB is unproven, and the prognostic significance of repeat SNB after mastectomy is unknown and its use discouraged.

[uu] If not technically resectable, consider systemic therapy to best response, then resect if possible.

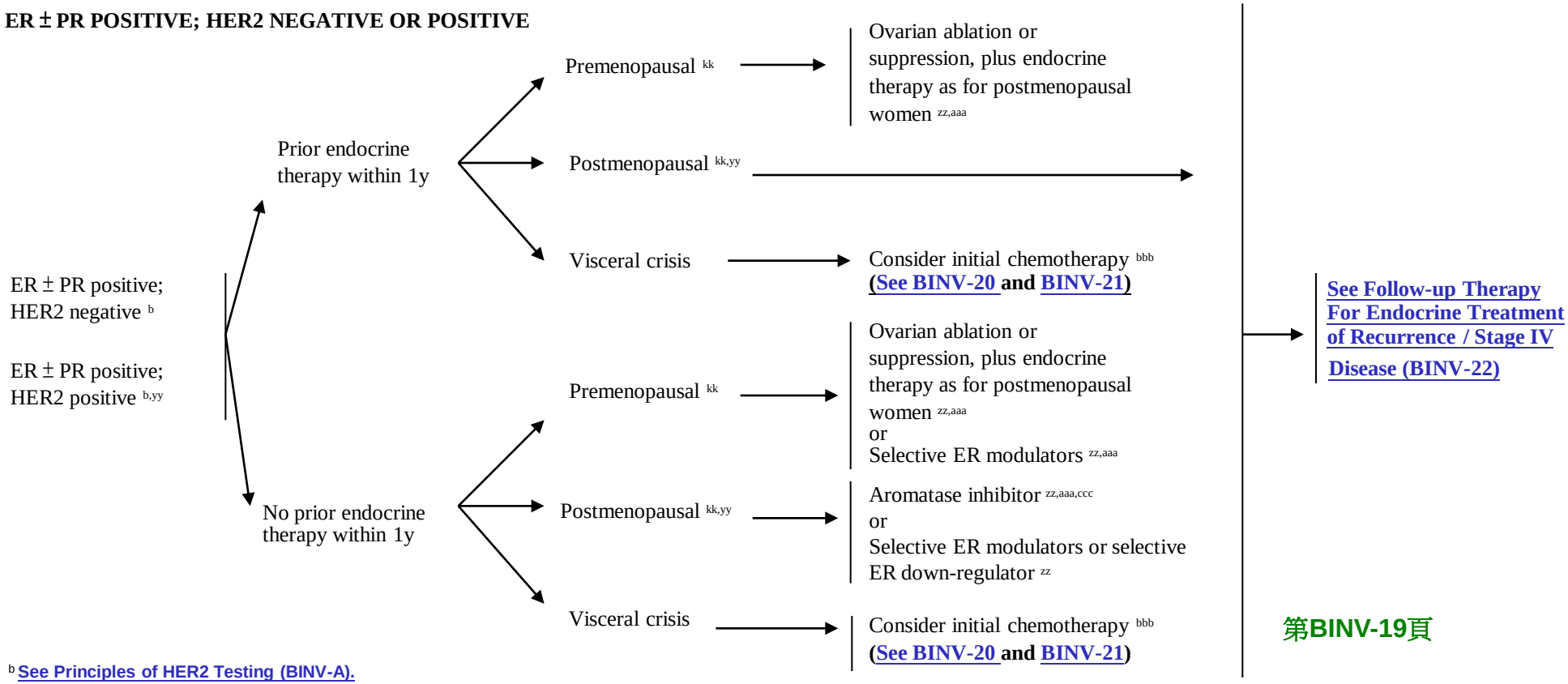
[vv] The decision to use radiation therapy to treat local-regional recurrence must factor in any prior radiation to the area and the risk of late normal tissue toxicity from the sum of the prior and planned radiation courses.

ww The role and timing of surgical removal of the primary in patients presenting with de novo stage IV disease is the subject of ongoing investigations.

xx For additional information see the Discussion section (MS-46).

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

ER ± PR POSITIVE; HER2 NEGATIVE OR POSITIVE



第BINV-19頁

b See Principles of HER2 Testing (BINV-A).

kk Definition of Menopause (BINV-L)

yy Limited studies document a progression free survival advantage of adding trastuzumab or lapatinib to aromatase inhibition in postmenopausal patients with ER-positive, HER2-positive disease. However, no overall survival advantage has been demonstrated.

zz See Subsequent Endocrine Therapy (BINV-M).

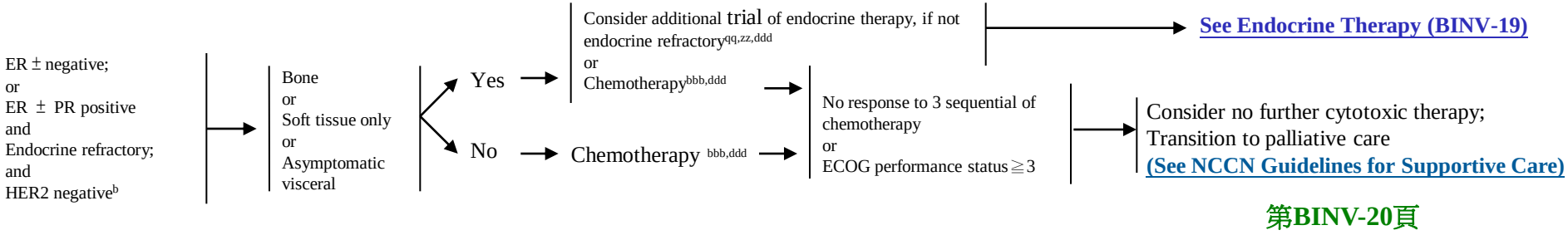
aaa It is unclear that women presenting at time of initial diagnosis with metastatic disease will benefit from the performance of palliative local breast surgery and/or radiation therapy. Generally this palliative local ther response to initial systemic therapy.

bbb See Preferred Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer (BINV-O).

ccc A single study (S0226) in women with hormone receptor-positive breast cancer and no prior chemotherapy, biological therapy, or endocrine therapy for metastatic disease demonstrated that the addition of resulted in prolongation of time to progression. Subset analysis suggested that patients without prior adjuvant tamoxifen and more than 10 years since diagnosis experienced the greatest benefit. Two studies w (FACT and SOFEA) demonstrated no advantage in time to progression with the addition of fulvestrant to anastrozole.

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

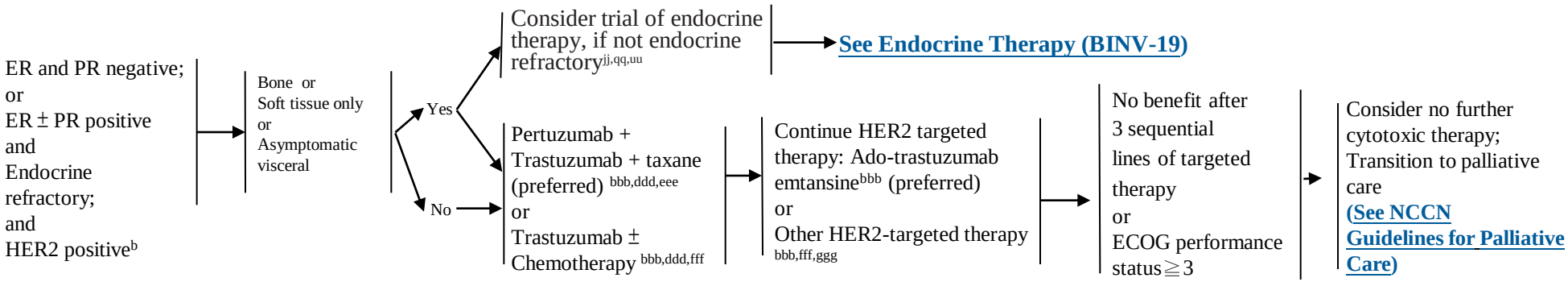
《ER and PR NEGATIVE; or ER ± PR POSITIVE and ENDOCRINE REFRACTORY; HER2 NEGATIVE》



第BINV-20頁

《ER and PR NEGATIVE; or ER ± PR POSITIVE and ENDOCRINE REFRACTORY; and HER2 POSITIVE》

第BINV-21頁



[b] See Principles of HER2 Testing (BINV-A).

[qq] False negative ER and/or PR determinations occur, and there may be discordance between the ER and/or PR determination between the primary and metastatic tumor(s). Therefore, endocrine therapy with its low attendant toxicity may be considered in patients with non-visceral or asymptomatic visceral tumors, especially in patients with clinical characteristics predicting for a hormone receptor positive tumor (eg, long disease free interval, limited sites of recurrence, indolent disease, or older age).

[zz] **See Endocrine Therapy for Recurrent or Stage IV Disease (BINV-M).**

[bbb] **See Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer (BINV-N).**

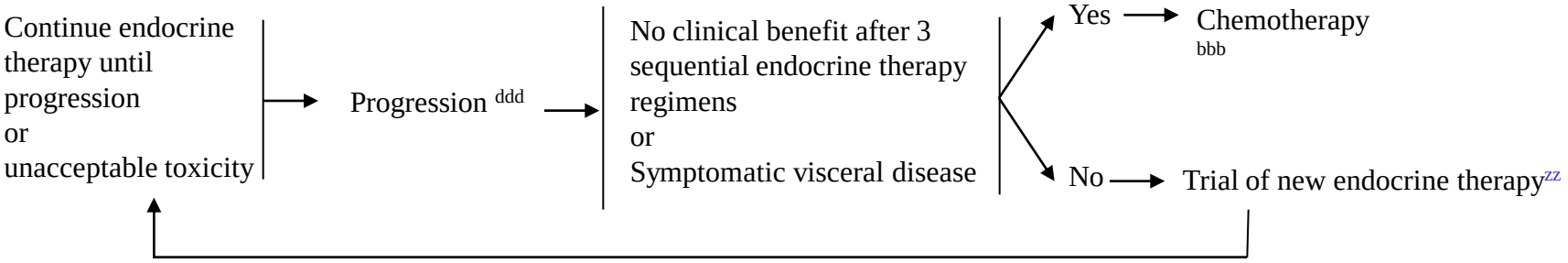
[ddd] **See Principles of Monitoring Metastatic Disease (BINV-O).**

[eee] Continue trastuzumab following progression on first-line trastuzumab-containing chemotherapy for metastatic breast cancer. The optimal duration of trastuzumab in patients with long-term control of disease is unknown.

[fff] Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided.

[ggg] Patients previously treated with chemotherapy plus trastuzumab in the absence of pertuzumab may be considered for one line of therapy including both trastuzumab plus pertuzumab in combination with or without cytotoxic therapy (such as vinorelbine or taxane). Further research is needed to determine the ideal sequencing strategy for anti-HER2 therapy.

FOLLOW-UP THERAPY FOR ENDOCRINE TREATMENT OF RECURRENT OR STAGE IV DISEASE



第BINV-22頁

zz See Endocrine Therapy for Recurrent or Stage IV Disease (BINV-M).

bbb See Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer

ddd See Principles of Monitoring Metastatic Disease (BINV-O)

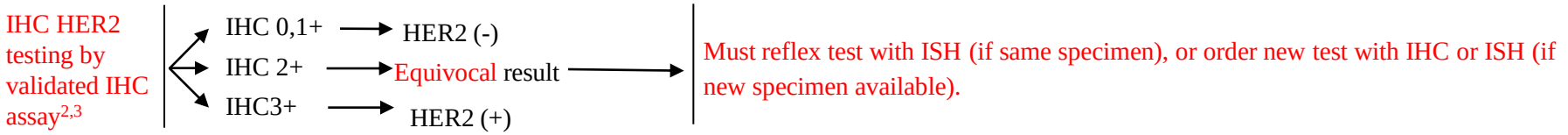
[1] See also, Carlson RW, Moench SJ, Hammond, MEH, et al. HER2 testing in breast cancer: NCCN task force report and recommendations. JNCCN 4:S-1-S-24, 2006.

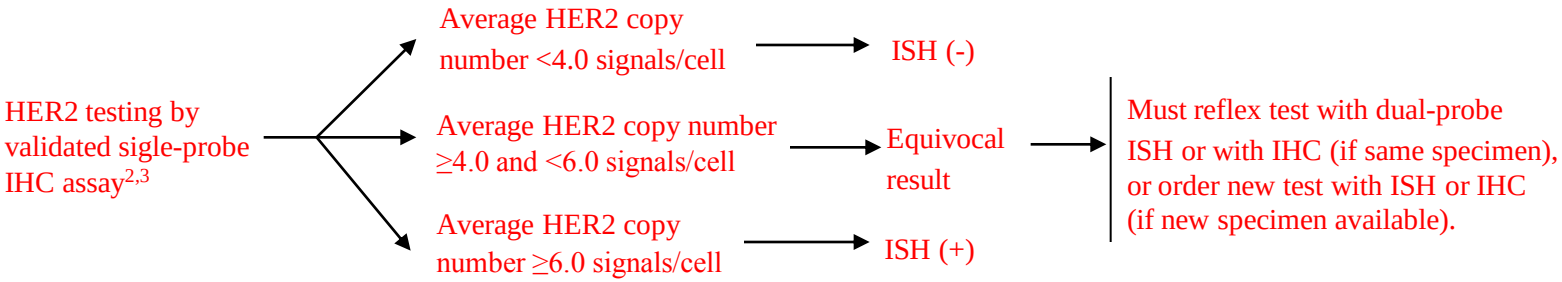
[2] HER2 testing should be done only in laboratories accredited to perform such testing. Ongoing proficiency testing and full reporting of HER2 assay methods and results are required. A laboratory may perform only those tests which have been demonstrated to conform to these quality assurance standards. All other HER2 testing should be sent to a qualified reference laboratory.

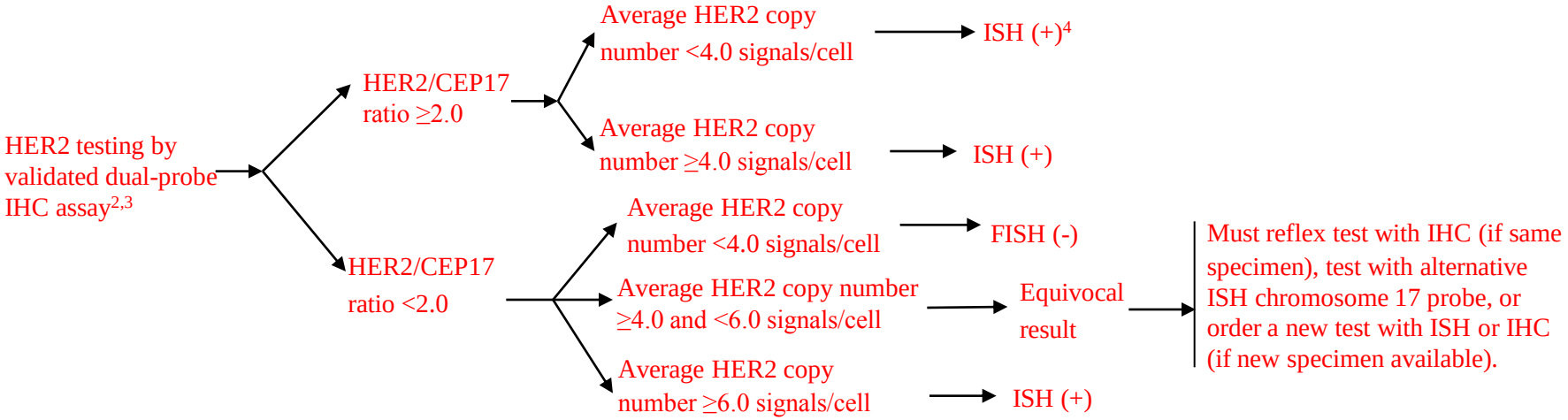
[3] Eithe an immunohistochemistry (IHC) assay or a fluorescence in situ hybridization (FISH) assay can be used to make an initial assessment of HER2 tumor status. All HER2 assays, whether FDA-approved or not, mu be validated. Validation of a HER2 test is defined as at least 95% concordance when the testing method performed in a laboratory is compared with one of the following: a validated HER2 testing method performed in the same laboratory; a validated HER2 testing method performed in another laboratory; or validated reference lab results. Borderline samples should not be included in the validation study. These algorithms are based on the assumption that all validated HER2 tests have been shown to be at least 95% concordant with the complementary form of the HER2 test, either bydirect testing or association with the levels of concordance between complementary testing achieved by the validating laboratory.

[4] Borderline IHC samples (eg, IHC 2+) are subjected to reflex testing by a validated complementary (eg, FISH) method that has shown at least 95% concordance between IHC 0, 1+ results and FISH non-amplified results, and IHC 3+ results and FISH amplified results. Borderline FISH samples (eg, an average HER2 gene/chromosome 17 ratio of 1.8-2.2 or an average HER2 gene copy number of > 4 - < 6) should undergo: counting of additional cells; retesting by FISH; or reflex testing by a valid ted IHC method which is at least 95% concordant with FISH as described above.

PRINCIPLES OF HER2 TESTING[1,2]







[1] NCCN endorses the ASCO/CAP HER2 testing guideline. For additional information, see http://bit.ly/ASCO-HER2GuidelineResources.

[2] Laboratory must participate in a quality assurance accreditation program for HER2 testing. Otherwise, tissue specimen should be sent to an accredited laboratory for testing. Health care systems and providers must cooperate to ensure the highest quality testing.

[3] Evidence from trastuzumab adjuvant trials show that HER2 testing by ISH or IHC have similar utility to predict clinical benefit from HER2-targeted therapy.

[4] See ASCO/CAP HER2 Guideline Data Supplement 2E (available at http://www.asco.org/sites/www.asco.org/files/final_her2_testing_ds_10-3-13.pdf) for more information on these rare scenarios.

PRINCIPLES OF DEDICATED BREAST MRI TESTING

《See NCCN Guidelines for Breast Cancer Screening and Diagnosis for indications for screening MRI in women at increased breast cancer risk. 》

Personnel, Facility, and Equipment

- Breast MRI examinations should be performed and interpreted by an expert breast imaging team working in concert with the multidisciplinary treatment team.
- Breast MRI examinations require a dedicated breast coil and breast imaging radiologists familiar with the optimal timing sequences and other technical details for image interpretation. The imaging center should have the ability to perform MRI-guided needle sampling and/or wire localization of MRI-detected findings.

Clinical Indications and Applications

- May be used for staging evaluation to define extent of cancer or presence of multifocal or multicentric cancer in the ipsilateral breast, or as screening of the contralateral breast cancer at time of initial diagnosis (category 2B). There are no high-level data to demonstrate that the use of MRI to facilitate local therapy decision-making improves local recurrence or survival.[1]
- May be helpful for breast cancer evaluation before and after neoadjuvant therapy to define extent of disease, response to treatment, and potential for breast-conserving therapy.
- May be useful for identifying primary cancer in women with axillary nodal adenocarcinoma or with Paget's disease of the nipple with breast primary not identified on mammography, ultrasound, or physical examination.
- False-positive findings on breast MRI are common. Surgical decisions should not be based solely on the MRI findings. Additional tissue sampling of areas of concern identified by breast MRI is recommended.
- The utility of MRI in follow-up screening of women with prior breast cancer is undefined. It should generally be considered only in those whose lifetime risk of a second primary breast cancer is greater than 20% based on models largely dependent on family history, such as in those with the risk associated with inherited susceptibility to breast cancer.

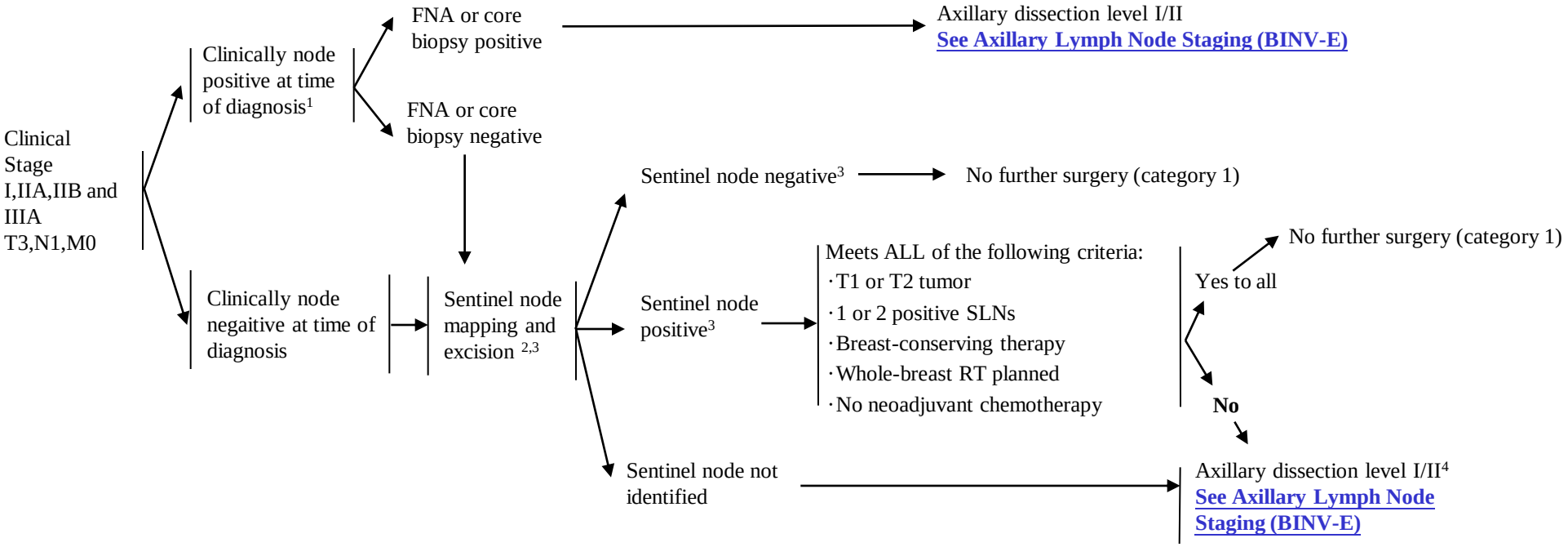
[1] Houssami N, Ciatto S, Macaskill P, Lord SJ, Warren RM, Dixon JM, Irwig L. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008;26:3248-3258.

FERTILITY AND BIRTH CONTROL

See NCCN Guidelines for Adolescent and Young Adult Oncology

- All premenopausal patients should be informed about the potential impact of chemotherapy on fertility and asked about their desire for potential future pregnancies. Patients who may desire future pregnancies should be referred to fertility specialists before chemotherapy.
- Although amenorrhea frequently occurs during or after chemotherapy, it appears that the majority of women younger than 35 y resume menses within 2 y of finishing adjuvant chemotherapy.
- Menses and fertility are not necessarily linked. Absence of regular menses, particularly if the patient is taking tamoxifen, does not necessarily imply lack of fertility. Conversely, the presence of menses does not guarantee fertility. There are limited data regarding continued fertility after chemotherapy.
- Patients should not become pregnant during treatment with radiation therapy, chemotherapy, or endocrine therapy.
- Although data are limited, hormone-based birth control is discouraged regardless of the hormone receptor status of the patient's cancer.
- Alternative methods of birth control include intrauterine devices (IUDs), barrier methods, or, for patients with no intent of future pregnancies, tubal ligation or vasectomy for the partner.
- Randomized trials have shown that ovarian suppression with GnRH agonist therapy administered during adjuvant chemotherapy in premenopausal women with ER-negative tumors may preserve ovarian function and diminish the likelihood of chemotherapy-induced amenorrhea.
- Breast feeding following breast-conserving cancer treatment is not contraindicated. However, the quantity and quality of breast milk produced by the breast conserved may not be sufficient or may be lacking some of the nutrients needed. Breast feeding during active treatment with chemotherapy and endocrine therapy is not recommended.
- Smaller historical experiences in patients with ER-positive disease have reported conflicting results with regard to the protective effect of GnRH agonist therapy on fertility.

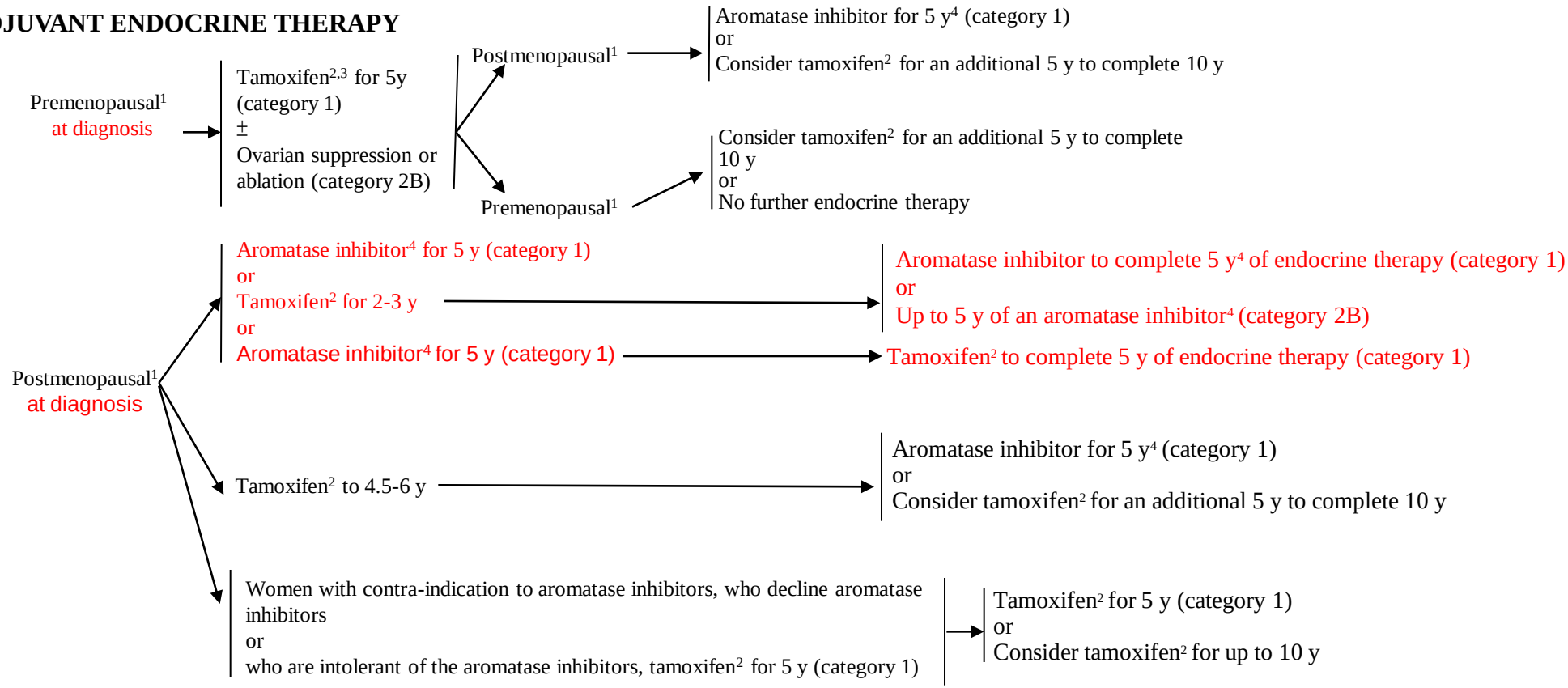
SURGICAL AXILLARY STAGING - STAGE I, IIA, AND IIB and IIIA T3,N1,M0



第BINV-D頁

[1] Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound-guided FNA or core biopsy in determining if a patient needs axillary lymph node dissection.
[2] Sentinel lymph node mapping injections may be peritumoral, subareolar, or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).
[3] Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.
[4] For patients with clinically negative axillae who are undergoing mastectomy and for whom radiation therapy is planned, axillary radiation may replace axillary dissection level I/II for regional control of disease.

ADJUVANT ENDOCRINE THERAPY



第BINV-J頁

[1] See Definition of Menopause (BINV-L).
[2] Some SSRIs like fluoxetine and paroxetine decrease the formation of endoxifen, 4-OH tamoxifen, and active metabolites of tamoxifen, and may impact its efficacy.Caution is advised about coadministration of these drugs with tamoxifen. However, citalopram and venlafaxine appear to have minimal impact on tamoxifen metabolism. At this time, based on current data the panel recommends against CYP2D6 testing for women being considered for tamoxifen therapy. Coadministration of strong inhibitors of CYP2D6 should be used with caution.

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≧60 y
- Age < 60 y and amenorrheic for 12 or more months in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression and follicle-stimulating hormone (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 beginning of adjuvant chemotherapy, amenorrhea is not a reliable indicator of menopausal status as ovarian function may still be intact or resume despite anovulation/ amenorrhea after chemotherapy. For these women with therapy-induced amenorrhea, oophorectomy or serial measurement of FSH and/or estradiol are needed to ensure postmenopausal status if the use of aromatase inhibitors is considered as a component of endocrine therapy.

ENDOCRINE THERAPY FOR RECURRENT OR STAGE IV

第BINV-L頁

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

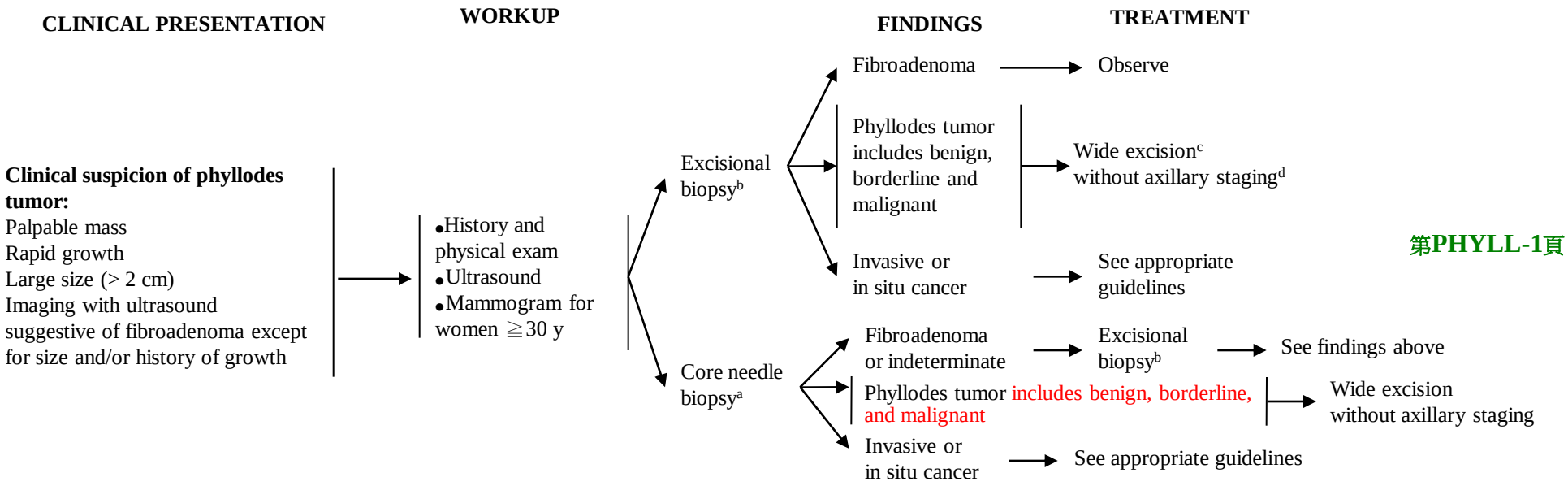
Postmenopausal Patients

- Non-steroidal aromatase inhibitor (anastrozole, letrozole)
- Steroidal aromatase inactivator (exemestane)
- Fulvestrant
- Tamoxifen or Toremifene
- Exemestane + everolimus[1]
- Palbociclib + letrozole[2]
- Megestrol acetate
- Fluoxymesterone
- Ethinyl estradiol

第BINV-M頁

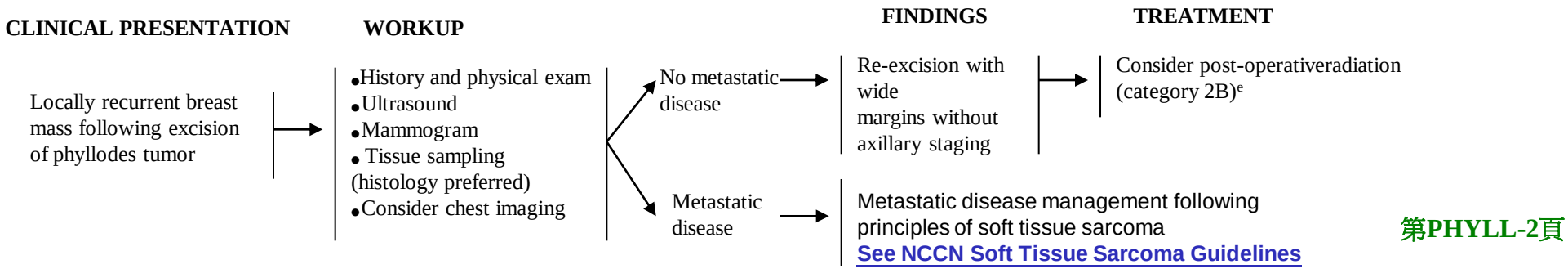
1 A combination of exemestane with everolimus can be considered for patients who meet the eligibility criteria for BOLERO-2 (progressed within 12 mo or on non-steroidal AI, or any time on tamoxifen).

2 Palbociclib in combination with letrozole may be considered as a treatment option for first-line therapy for postmenopausal patients with ER-positive, HER2-negative metastatic breast cancer.



第PHYLL-1頁

PHYLLODES TUMOR RECURRENCE



第PHYLL-2頁

[a] FNA will not, and core biopsy may not distinguish fibroadenoma from phyllodes tumor in most cases.
[b] Excisional biopsy includes complete mass removal, but without the intent of obtaining surgical margins.
[C] Wide excision means excision with the intention of obtaining surgical margins 1 cm. Narrow surgical margins are associated with heightened local recurrence risk, but are not an absolute indication for mastectomy when partial mastectomy fails to achieve margin width 1 cm.
[d] There are no prospective randomized data supporting the use of radiation treatment with phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (eg, chest wall recurrence following mastectomy), radiation therapy may be considered following.the same principles that are applied to the treatment of soft tissue sarcoma.
e There are no prospective randomized data supporting the use of radiation treatment with phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (eg, chest wall recurrence following mastectomy), radiation therapy may be considered following the same principles that are applied to the treatment of soft tissue sarcoma.

乳癌臨床指引
(Cancer of the Breast)

CLINICAL PRESENTATION

Clinical suspicion of Paget's disease[a]

WORKUP

Clinical breast exam
Diagnostic bilateral mammogram, ultrasound as necessary

- Examination or imaging positive for breast lesion → See PAGET-2
- Examination and imaging negative for breast lesion

第PAGET-1頁

WORKUP

Examination or imaging positive for breast lesion → Core biopsy of breast lesion and full- thickness skin biopsy of involved nipple-aeola complex (NAC)

TREATMENT

- Breast and NAC biopsy negative → Clinical follow-up Re-biopsy if not healing
- Breast DCIS [b] and NAC Paget's → See NCCN Guidelines for Noninvasive Breast Cancer for DCIS (DCIS-1)
- Breast invasive cancer and NAC Paget's [b] → See NCCN Guidelines for Invasive Breast Cancer (BINV-1)
- Breast negative for cancer and positive NAC Paget's [b] → Consider MRI and tissue sampling → Central lumpectomy including NAC with whole breast radiation therapy
  or
  Total mastectomy[c] ± sentinel node biopsy with or without breast reconstruction
  or
  Central lumpectomy including NAC± sentinel node biopsy without radiation therapy (category 2B)

Examination or imaging Negative for breast lesion → Full- thickness skin biopsy of involved NAC

- NAC biopsy positive for Paget's[b] → Consider MRI and tissue sampling → Central lumpectomy including NAC with whole breast radiation therapy
  or
  Total mastectomy[c] ± sentinel node biopsy with or without breast reconstruction
  or
  Central lumpectomy including NAC± sentinel node biopsy without radiation therapy (category 2B)
- NAC biopsy Negative for Paget's → Clinical follow-up Re-biopsy if not healing

Appropriate systemic adjuvant Therapy **as clinically indicated**

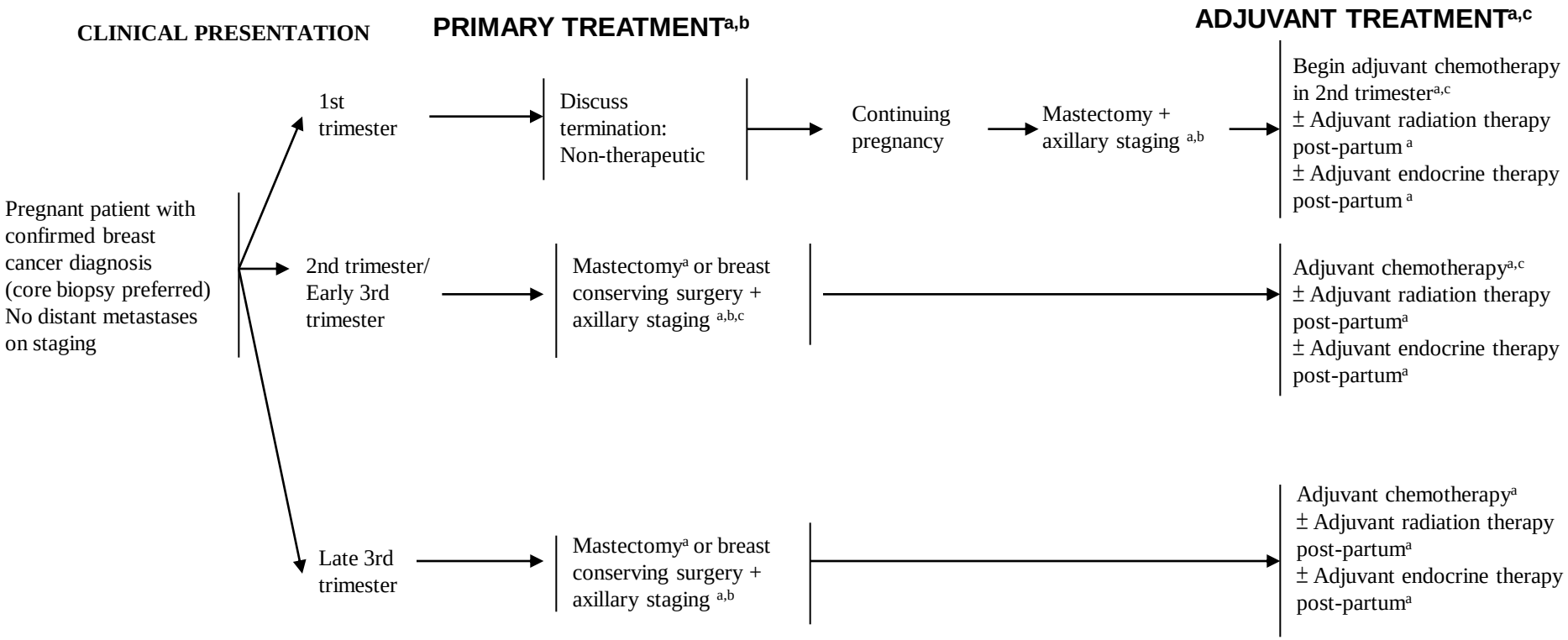
See NCCN Guidelines for DCIS or Invasive Breast Cancer

[a] Nipple or areolar eczema, ulceration, bleeding, itching.

[b] To assess the extent of disease or to confirm additional disease, consider MRI. See Principles of Dedicates

[c] Mastectomy is always an option with any manifestation of Paget's disease (See Discussion section).

第PAGET-2頁



第PREG-1頁

a Considerations and selection of optimal local therapy and systemic therapy are similar to that recommended in non-pregnancy-associated breast cancer; see other sections of this guideline. However, the selection and timing of chemotherapy, endocrine therapy, and radiation therapy is different in the pregnant versus non-pregnant patient (**See Discussion section**). Chemotherapy should not be administered during the first trimester of pregnancy, and radiation therapy should not be administered during any trimester of pregnancy. Most experience with chemotherapy during pregnancy for breast cancer is from regimens that utilize various combinations of doxorubicin, cyclophosphamide, and fluorouracil. Considerations for postpartum chemotherapy are the same as for non-pregnancy-associated breast cancer.

b Use of blue dye is contraindicated in pregnancy; radiolabeled sulfur colloid appears to be safe for sentinel node biopsy in pregnancy.**See Surgical Axillary Staging (BINV-D)**.

c There are insufficient safety data to recommend general use of taxanes during pregnancy. However, the use of paclitaxel weekly administration after the first trimester is acceptable if clinically indicated by disease status. The use of anti-HER2 therapy is contraindicated during pregnancy.

乳癌臨床指引
(Cancer of the Breast)

CLINICAL PRESENTATION [a]

Clinical pathologic Diagnosis of IBC
Stage T4d, N0-N3, M0

WORKUP

- History and physical exam
- CBC, platelets
- Liver function tests
- Pathology review[b]
- Determination of tumor ER/PR status and HER2 status[c]
- Bilateral diagnostic mammogram, ultrasound as necessary
- Breast MRI (optional)
- Fertility counseling if premenopausald (optional)
- Bone scan or sodium fluoride PET/CT(category 2B)[e]
- CT scan chest/abd/pelvis (category 2B)
- Chest CT (if pulmonary symptoms are present)
- Genetic counseling if patient is high risk for hereditary breast cancer[f]
- FDG PET/CT scan[g,h] (category 2B) [f]

TREATMENT

Preoperative chemotherapy,[i] anthracycline + taxane (preferred)[i] If tumor HER2 positive.HER2-targeted therapy[j]

Response → Total mastectomy + level I/II axillary dissection + radiation therapy to chest wall and supraclavicular nodes (plus internal mammary nodes if involved, consider internal mammary nodes if not clinically involved [category 3]) ± delayed breast reconstruction[l]

→ Complete planned chemotherapy regimen course if not completed preoperatively plus endocrine treatment if ER-positive and/or PR-positive (sequential chemotherapy followed by endocrine therapy). Complete up to 1 year of trastuzumab if tumor HER2-positive (category 1) . May be administered concurrently with radiation therapyn and with endocrine therapy if indicated.

No response → Consider additional systemic chemotherapy [m] ± preoperative radiation

Response → See above pathway

No response → Individualized treatment

第IBC-1頁

第IBC-2頁

a Inflammatory breast cancer is a clinical syndrome in women with invasive breast cancer that is characterized by erythema and edema (peau d'orange) of a third or more of the skin of the breast. The differential diagnosis includes cellulitis of the breast or mastitis. Pathologically, a tumor is typically present in the dermal lymphatics of the involved skin, but dermal lymphatic involvement is neither required, nor sufficient by itself for a diagnosis of inflammatory breast cancer.

b The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and noninvasive carcinomas of the breast. http://www.cap.org.

c **See Principles of HER2 Testing (BINV-A).**

d **See Fertility and Birth Control (BINV-C).**

e If FDG PET/CT is performed and clearly indicates bone metastasis on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.

f **See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian**

g FDG PET/CT can be performed at the same time as diagnostic CT. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.

h FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.

i **See Neoadjuvant/Adjuvant Chemotherapy (BINV-K).**

j A pertuzumab-containing regimen may be administered preoperatively to patients with HER2-positive IBC.

k Patients with stage IV or recurrent IBC should be treated according to the guideline for

l **See Principles of Breast Reconstruction Following Surgery (BINV-H).**

m **See Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer (BINV-N).**

n **See Principles of Radiation Therapy (BINV-I).**

Staging

American Joint Committee on Cancer (AJCC 7th)

Primary Tumor(T)

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 is NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underling breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted .
T1		Tumor ≦20 mm in greatest dimension
	T1mic	Tumor ≦1 mm in greatest dimension
	T1a	Tumor < 1mm but≦5 mm in greatest dimension
	T1b	Tumor > 5mm but≦10 mm in greatest dimension
	T1c	Tumor > 10mm but≦20 mm in greatest dimension
T2		Tumor > 20mm but≦50 mm in greatest dimension
T3		Tumor > 50mm in greatest dimension
T4		Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)*
	T4a	Extension to chest wall, not including only pectoralis muscle adherence/ invasion.
T4b		Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin of which do not meet the criteria for inflammatory carcinoma
T4c		Both T4a and T4b
T4d		Inflammatory carcinoma**

***Note: Invasion of the dermis alone does not qualify as T4.**

****Note: Inflammatory carcinoma is restricted to cases with typical skin changes involving a third or more of the skin of the breast. While the histologic presence of invasive carcinoma invading dermal lymphatics is supportive of the diagnosis, it is not required, nor is dermal lymphatic invasion without typical clinical findings sufficient for a diagnosis of inflammatory breast cancer.**

Regional Lymph Nodes (N)

NX		Regional lymph nodes cannot be assessed (e.g., previously)
pNX		Regional lymph nodes cannot be assessed (e.g., removed, or not removed for pathologic study)
N0		No regional lymph node metastasis
pN0		No regional lymph node metastasis identified histologically
pN0(i-)		No regional lymph node metastasis histologically, negative IHC
pN0(i+)		Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
pN0(mol-)		No regional lymph node metastasis identified histologically, negative molecular findings (RT-PCR)
pN0(mol+)		Positive molecular findings (RT-PCR), but no regional lymph node metastases detected by histology or IHC
N1		Metastases to movable ipsilateral level I,II axillary lymph node (s)
	pN1	Metastases: or metastases in 1 to 3 axillary lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lympho node biopsy but not clinically detected**
	pN1mi	Micrometastasis (greater than 0.2mm and/or more 200 cells, but none greater than 2.0mm)
	pN1a	Metastases in 1 to 3 axillary lymph nodes, at least one metastases greater than 2.0 mm
	pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lympho node biopsy but not clinically detected**
	pN1	Metastases: or metastases in 1 to 3 axillary lymph nodes; and in internal mammary nodes with micrometastases or macrometastases detected by sentinel lympho node biopsy but not clinically detected**
N2		Metastases in ipsilateral level I,II axillary lymph nodes that are clinically fixed or matted; or in clinically evident axillary lymph nodes metastases
	pN2	Metastases in 4 to 9 axillary lymph nodes; or in clinically evident axillary lymph nodes metastases

Regional Lymph Nodes (N)

N2a		Metastases in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
	pN2a	Metastasis in 4 to 9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)
N2b		Metastasis only in clinically detected***ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastases
	pN2b	Metastasis in clinically detected*** internal mammary lymph nodes in the absence of axillary lymph node metastases
N3		Metastasis in ipsilateral infraclavicular(level III axillary) lymph node (s) with or without level I,II axillary lymph node involvement, or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node(s) metastases; or metastases in ipsilateral supraclavicular lymph node (s) with or without axillary or internal mammary lymph node involvement
	pN3	Metastasis in 10 or more axillary lymph nodes, or in infraclavicular (level III axillary) lymph nodes, or in clinically detected*** ipsilateral internal mammary lymph nodes in the presence of 1 or more positive level I,II axillary lymph nodes; or in more than 3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases or in ipsilateral supraclavicular lymph nodes
N3a		Metastasis in ipsilateral infraclavicular lymph node (s)
	pN3a	Metastasis in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm); or metastasis to the infraclavicular (level III axillary) lymph node (s)
N3b		Metastasis in ipsilateral internal mammary lymph node (s) and axillary sentinel lymph node(s)
	pN3b	Metastasis in clinically detected*** ipsilateral internal mammary nodes in the presence of 1 or more postitive axillary lymph nodes; or in more than 3 axillary sentinel lymph nodes and in internal mammary lymph nodes with micrometastasis or macroscopic detected by sentinel lymph node biopsy but not clinically detected**
N3c		Metastasis in ipsilateral supraclavicular lymph node (s)
	pN3c	Metastasis in ipsilateral supraclavicular lymph nodes

*Classification is based on axillary lymph nodes dissection with or without axillary lymph nodes biopsy. Classification is based solely lymph nodes biopsy without subsequent axillary lymph nodes dissection is designated(sn) for “sentinal node,”for example, pN0(sn).

**Note: Not clinically detected is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected is by clinical examination.
***Note: Clinically detected is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristic highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with an (f) suffix, for example, cN3a(f). Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, for example, cN1. Information regarding the confirmation of the nodal status will be designated in sitespecific factors as clinical, fine needle aspiration, core biopsy, or sentinel lymph node biopsy. Pathologic classification (pN) is used for excision or sentinel lymph node biopsy only in conj unction with a pathologic T assignment.

Note: Isolated tumor cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immonohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

DISTANT METASTASIS (M)

M0	No clinical or radiographic evidence of distant metastases (no pathologic M0; use clinical M to complete stage group)
cM0(i)	No clinical or radiographic evidence of distant metastases (no pathologic M0; use clinical M to complete stage group)
M1	Distant detectable metastases metastasese as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

CLINICAL

GROUP	T	N	M
0	Tis	N0	M0
IA	T1*	N0	M0
IB	T0	N1mi	M0
	T1*	N1mi	M0
IIA	T0	N1**	M0
	T1*	N1*	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

***T1 includes T1mi**
****T0 and T1 tumor with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB**

HISTOLOGIC GRADE (NOTTINGHAM COMBINED HISTOLOGIC GRADE IS RECOMMENDED)

GX Grade cannot be assessed
G1 Low combined histologic grade (favorable)
G2 Intermediate combined histologic grade (moderately favorable)
G3 High combined histologic grade (unfavorable)

PATHOLOGIC

GROUP	T	N	M
0	Tis	N0	M0
IA	T1*	N0	M0
IB	T0	N1mi	M0
	T1*	N1mi	M0
IIA	T0	N1**	M0
	T1*	N1*	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

***T1 includes T1mi**
****T0 and T1 tumor with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.**

六、Updated on 2015/04/09、2015/8/13

內容:

【LCIS-1頁】:[WORKUP]處維持本院2014版本，因本院原位癌治療較符合台灣醫院治療方式。
【LCIS-1頁】:[RISK REDUCTION]處維持本院2014版本，因本院無基因檢測。
【LCIS-1頁】:[Surveillance]處修改成NCCN2015 V2版本，分類。
【DCIS-1頁】:維持不變。
【DCIS-2頁】:維持不變。
【BINV-1頁】:[WORKUP]處維持本院2014版本，因本院無”壓力評估”措施。
【BINV-2頁】:修改成NCCN2015 V2版本，放射線治療將”Strongly”刪除，因台灣治療方式為”Consider…”。
【BINV-3頁】:維持不變，放射線治療將”Strongly”刪除，因台灣治療方式為”Consider…”。
【BINV-4頁】:維持不變。
【BINV-5頁】:同意NCCN2015 V2版本。
【BINV-6頁】:維持不變。
【BINV-7頁】:同意NCCN2015 V2版本。
【BINV-8頁】:維持不變。
【BINV-9頁】:維持不變。
【BINV-10頁】:同意NCCN2015 V2版本。WORKUP]處修改成NCCN2015 V2版本，簡單化。
【BINV-11頁】:同意NCCN2015 V2版本。
【BINV-12頁】:維持不變。
【BINV-13頁】:同意NCCN2015 V2版本。
【BINV-14頁】:同意NCCN2015 V2版本。
【BINV-15頁】:修改成NCCN2015 V2版本，放射線治療將”Strongly”刪除，因台灣治療方式為”Consider…”。
【BINV-16、17頁】:修改成NCCN2015 V2版本，[SURVEILLANCE/FOLLOW-UP]將” In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening”刪除，因本院還是會為病人擔心害怕復發，而協助安排做影像方面檢查。

六、Updated on 2015/04/09、2015/8/13

內容:

【BINV-18頁】:維持不變。
【BINV-19頁】:維持不變。
【BINV-20頁】:維持不變。
【BINV-21頁】:維持不變。
【BINV-22頁】:維持不變。
【BINV-A頁】:修改成NCCN2015 V2版本。
【BINV-B頁】:修改成NCCN2015 V2版本。
【BINV-C頁】:修改成NCCN2015 V2版本。
【BINV-D頁】:維持不變。
【BINV-J頁】:修改成NCCN2015 V2版本。
【BINV-M頁】:修改成NCCN2015 V2版本。
【BINV-O頁】:建議刪除，因為臨床醫師依據癌症個案當時身體狀況，再加上健保補助項目來安排追蹤檢查。
【PHYLL-1頁】:修改成NCCN2015 V2版本。
【PHYLL-2】:維持不變。
【PAGET-1】:維持不變。
【PAGET-2】:修改成NCCN2015 V2版本。
【PREG-1】:維持不變。
【IBC-1、2】:[WORKUP]處修改成NCCN2015 V2版本。