振興醫療財團法人振興醫院

乳癌診療指引

每年修訂兩次，4 月及 10 月修訂

乳癌多專科團隊

2005 年 05 月制定　2009 年 07 月修訂

2010 年 08 月修訂　2011 年 12 月修訂

2012 年 09 月修訂　2012 年 11 月修訂

2013 年 03 月修定　2013 年 08 月修訂

2013 年 10 月修訂　2014 年 12 月修訂

2015 年 12 月修訂

參考資料：

NCCN Guidelines V3.2015

全民健康保險藥品給付規定 行政院衛生署一百零四年版

Physicians' Cancer Chemotherapy Drug Manual 2010

LCIS = Lobular carcinoma in situ

DCIS = Ductal carcinoma in situ

ER = estrogen receptor

PR = progesterone receptor

(+) = positive

(-) = Negative

LN = lymph node

R/T = radiation therapy

c With

s = without

ALP= alkaline phosphatase

PBI = partial breast irradiation

CR = Complete response

PD = Progressive disease

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一、診療指引修訂共識

1. 依據乳癌多專科團隊會議討論決定(2015)。
2. 乳癌之期別，TNM 臨床檢查，超音波、乳房攝影、乳房核磁共振、骨骼掃描、正子檢查、電腦斷層，各不同檢查上註明所看見之臨床期別，於團隊會議中統一臨床或病理期別(2015)。
3. 考慮於慎選 T1，T2 乳癌施行乳房保留手術後，立即施行術中放射治療(唯屬於自費項目)(2013)。
4. 年齡超過 75-79 歲，T1N0、ER(+)，low-grade，partial mastectomy，可不需做 R/T(2012)。
5. 年齡超過 70 歲以上，依照個別情形治療，依 NCCN，並未有明確詳細規範(2012)。

二、化療處方修定共識

1. 依癌症評鑑委員之建議，刪去不用之術前，術後化療處方(2013)。
2. 依癌症預評檢討會議 20130413，僅列出化療處方，依病情修飾劑量，並不需特別註明，不算另一處方(2013)。
3. 依據新版 2013 NCCN 規範刪去 TAC 、FAC、AC 之術前化療處方；加上 TC 術前化療處方(2013)。
4. 依據 2014.V3 版修訂於 Her2(+)，術前、術後、轉移使用標靶藥物考慮同時 Pertuzumab + Trastuzumab 使用(2014)。
5. 依據 2014.V3 版修訂於第一期低危險性族群 Her2(+)可選擇祇用 Paclitaxel + Trastuzumab 使用(2014)。
6. **化療藥物修改如下:(2015/12/21)**

Her2 - Neoadjuvant

1.Dose-dense AC followed by paclitaxel :目前無使用此處方，待刪除診療指引此治療處方。

2.AC followed by paclitaxel l :刪除診療指引此治療處方。

3.TC:待標註自費及規範使用頻率為四次。

4.Modified CMF :目前已較少人使用此第一代的處方，待刪除診療指引此治療處方。
5.AC followed by docetaxel : 目前無使用此處方，待刪除診療指引此治療處方。
6.FEC followed by docetaxel : Docetaxel 標註自費。
7.FEC :為不需自費的治療處方,暫決定予以保留,待找文獻佐證確認使用頻率次數。

Her2 + Neoadjuvant

1.AC followed by T chemotherapy with Trastuzumab: 2015/12/23 刪除此化療處方。
2.TCH :討論 TCH 中的的“C”改成 Cisplatin 是否能被接受，待標註 Carboplatin 需自費及若腋下淋巴結(-)T 也須自費。12/23 已與蘇正熙主任討論，待刪除 Carboplatin 改 Cisplatin 並找出文獻佐證此治療處方。
3.T followed by FEC chemotherapy with trastuzumab: 刪除診療指引此治療處方。
4.Docetaxel + trastuzumab followed by FEC :保留此治療處方。
5.Chemotherapy followed by trastuzumab:保留此治療處方。
6.AC followed by docetaxel with trastuzumab:刪除診療指引此治療處方。
7.Pertuzumab + trastuzumab + docetaxel:NCCN 有此項處方,但 Docetaxel 劑量 75-100mg/m2 IV，後續待找到能佐證之文獻佐證並將劑量修改為 75 mg/m2 IV。
8.Pertuzumab + trastuzumab + paclitaxel : 刪除診療指引此治療處方。
9.Paclitaxel/carboplatin +trastuzumab : 刪除診療指引此治療處方。

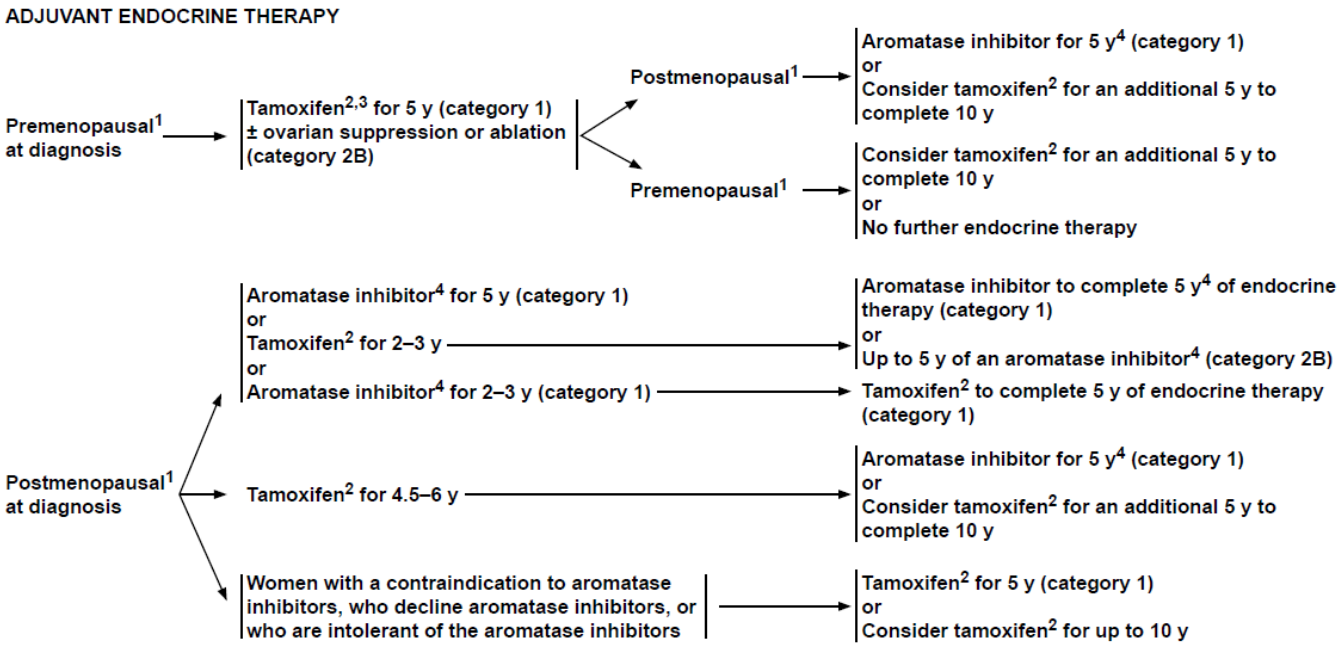
Her2 - adjuvant

1.FAC :刪除診療指引此治療處方。
2.AC followed by paclitaxel : 刪除診療指引此治療處方。
3.TC :保留此治療處方，並標註適用的個案族群，如心臟功能不佳、年長。
4.Modified CMF: 刪除診療指引此治療處方。
5.AC followed by docetaxel: 刪除診療指引此治療處方。
6.FEC followed by docetaxel :保留此治療處方。
7.FEC :待補上使用 6cycle。

Her2 + adjuvant

1. AC followed by T chemotherapy with Trastuzumab-1: 刪除診療指引此治療處方。
2. TCH : Carboplatin 需標註自費、Trastuzumab 註明視淋巴結轉移與否決定是否自費。
3. Docetaxel + trastuzumab followed by FEC : 刪除診療指引此治療處方。
4. Chemotherapy followed by trastuzumab : 刪除診療指引此治療處方。
5. AC followed by docetaxel with trastuzumab :保留此治療處方。
6. Paclitaxel + trastuzumab:待標註 Node(-)Low Risk 自費使用。
7. Pertuzumab + trastuzumab + docetaxel followed by FEC chemotherapy: 刪除診療指引此治療處方。
8. Pertuzumab + trastuzumab + Paclitaxel followed by FEC chemotherapy: 刪除診療指引此治療處方。

內分泌治療增加 NCCN 最新的資料如下:



Metastatic 待將目前院內診療指引列出的項目核對院內常用的處方予以保留。

Table of Contents

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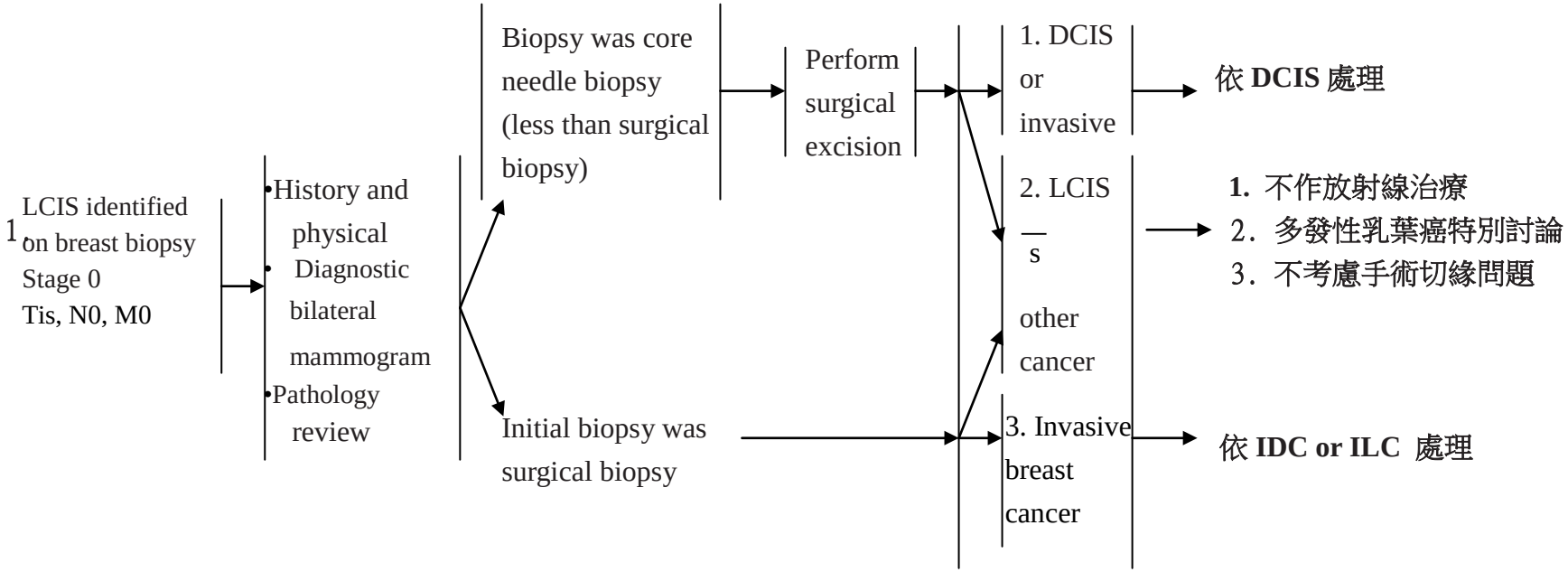
(原位癌)Lobular Carcinoma in Situ(LCIS)
乳葉原位癌

診斷　　診斷檢察　　RISK REDUCTION　　SURVEILLANCE



註：1. LCIS 部分，依新版 2013 NCCN 規範，針對多發性 LCIS 之四個末端乳葉侵犯，可被視為高危險浸潤性乳癌。
2. 2015/12/21 修正

(原位癌)Ductal Carcinoma in Situ(DCIS)
乳腺管內癌

診斷	診斷檢察	PRIMARY TREATMENT
DCIS Stage 0 Tis, N0, M0 →	• History and physical exam • Diagnostic bilateral mammogram • Pathology review • Determination of tumor ER status • Genetic counseling if patient is high risk for hereditary breast cancer →	Lumpectomy $\overline{s}$ lymph node surgery + whole breast R/T or Total mastectomy $\overline{c}$ or $\overline{s}$ sentinel node biopsy ± reconstruction or Lumpectomy $\overline{s}$ LN surgery $\overline{s}$ R/T

(原位癌)Ductal Carcinoma in Situ(DCIS)
乳腺管內癌

DCIS POSTSURGICAL TREATMENT

Risk reduction therapy for ipsilateral breast following breast conserving surgery:
Consider tamoxifen for 5 years for:
- Patients treated c breast-conserving therapy(lumpectomy) and R/T, especially for those with ER-positive DCIS.
- The benefit of tamoxifen for ER-negative DCIS is uncertain
- Patients treated c excision alone

Risk reduction therapy for contralateral breast
- Counseling regarding 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
- If treated with tamoxifen, monitor per NCCN Breast Cancer Risk Reduction Guidelines

Margin status in DCIS

Substantial controversy exists regarding the definition of negative pathologic margin in DCIS. Controversy arises out of the heterogeneity of the disease, difficulities in distingquishing the spectrum of hyperplastic conditions, anatomic considerations of the location of yhe margin, and inadequate prospective data on prognostic factors in DCIS.

Margins greater than 10mm are widely accepted as negative (but may be excessive and may lead to a less optimal cosmetic outcome)

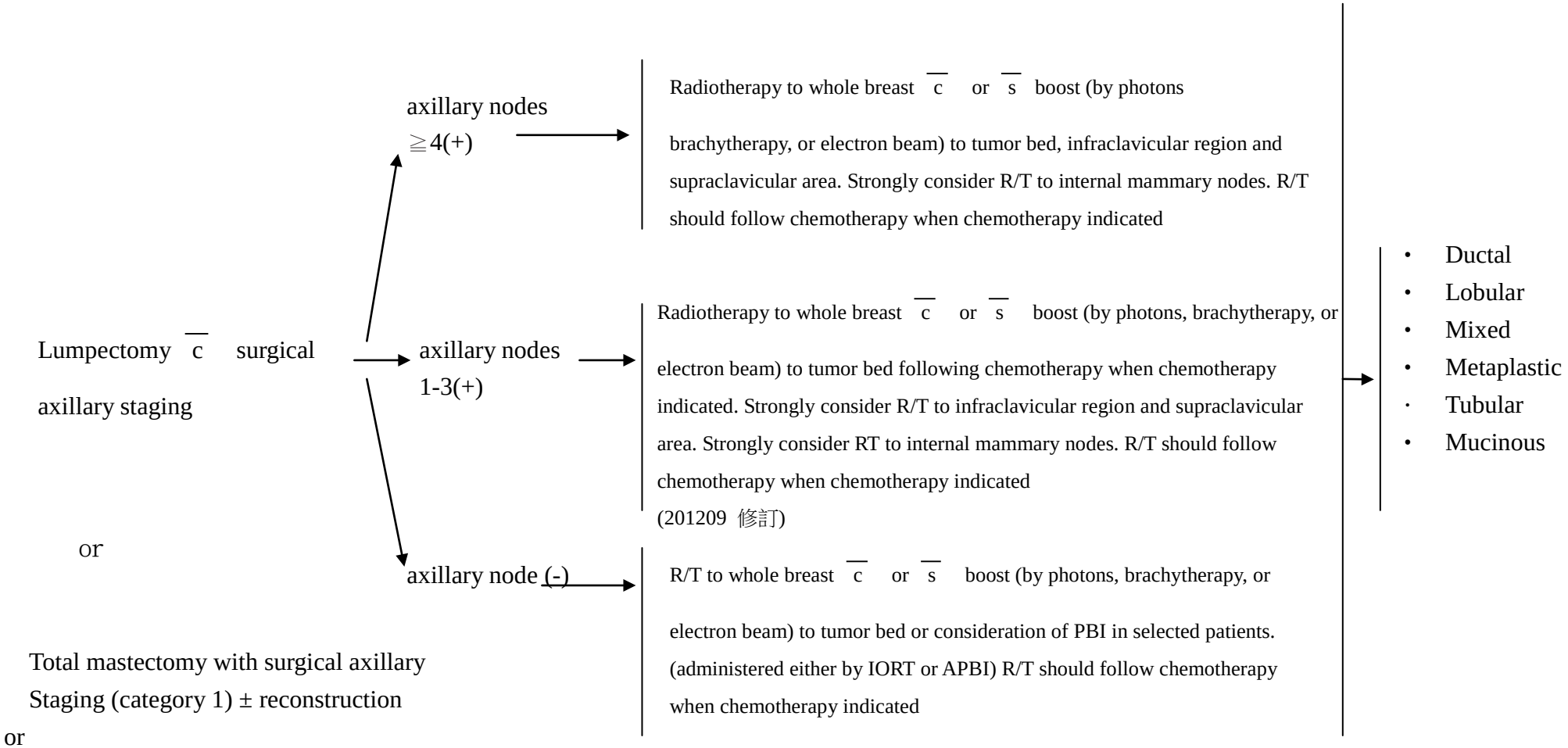
Margins less than 1mm are considered inadequate.

With pathologic margins between 1-10mm , wider margins are generally associated with lower local recurrence rates. However, close surgical margins (<1mm) at the fibroglandular boundary of the breast (chest 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)

2015/12/21 增訂

臨床期別	診斷檢察	
Stage IA T1, N0, M0 or **Stage IIA** T0, N1, M0 T1, N1, M0 T2, N0, M0 or **Stage IIB** T2, N1, M0 T3, N0, M0 or **Stage IIIA** T3 N1, M0	• History and physical exam • CBC, platelets • Liver function tests and ALP • Diagnostic bilateral mammogram, ultrasound as necessary • Pathology review • Determination of tumor ER/PR status and HER2 status • Genetic counseling if patient is high risk for hereditary breast cancer • Breast MRI (optional) 針對乳房攝影難以察覺(occult) 病灶 (2015/12/21 修訂) • Consider fertility counseling if premenopausal (2015/12/21 修訂) For clinical stage I-IIB, consider additional studies only if directed by signs or symptoms • 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 lllA (T3, N1, M0) consider: • Chest diagnostic CT • Abdominal ± pelvic diagnostic CT or MRI • Bone scan or sodium fluoride PET/CT • FDG PET/CT	Lumpectomy with surgical axillary staging or Total mastectomy with surgical axillary staging ± reconstruction or If T2 or T3 and fulfills criteria for breast conserving therapy except for size

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



or

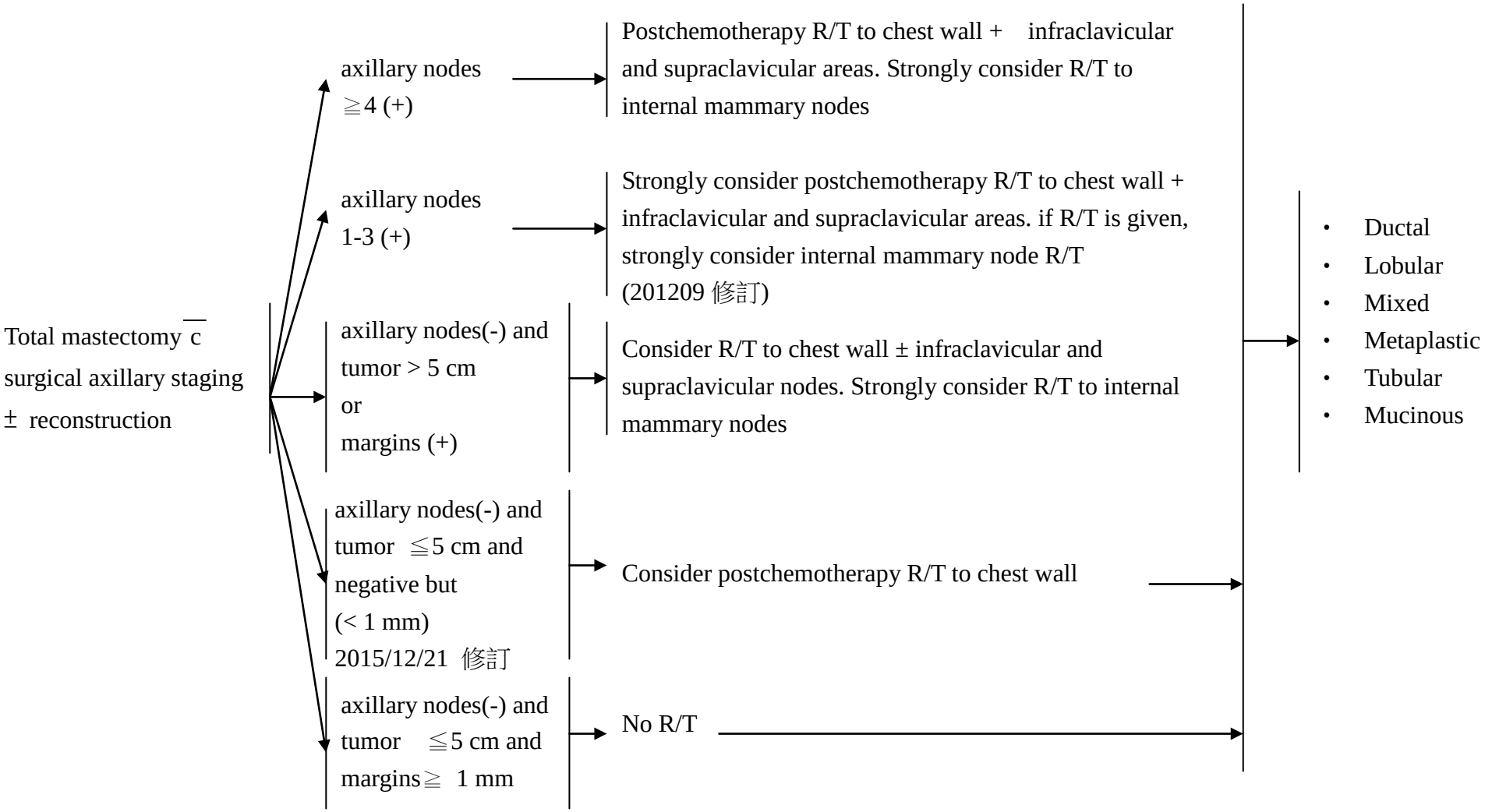
Total mastectomy with surgical axillary Staging (category 1) ± reconstruction

or

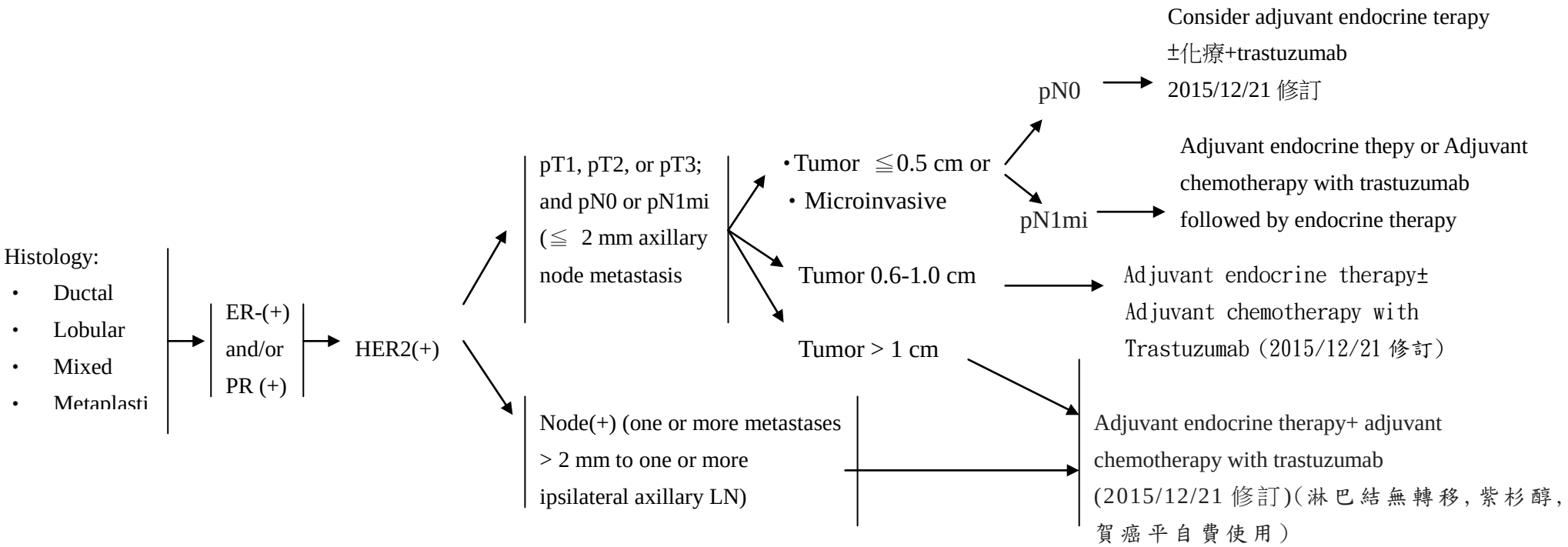
If T2 or T3 and fulfills criteria for breast Conserving therapy except for size

(2015/12/21 增訂)

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



SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR 陽性 - HER2 陽性



＊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 mwtaplastic or mixed component does not alter prognosis.

＊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.

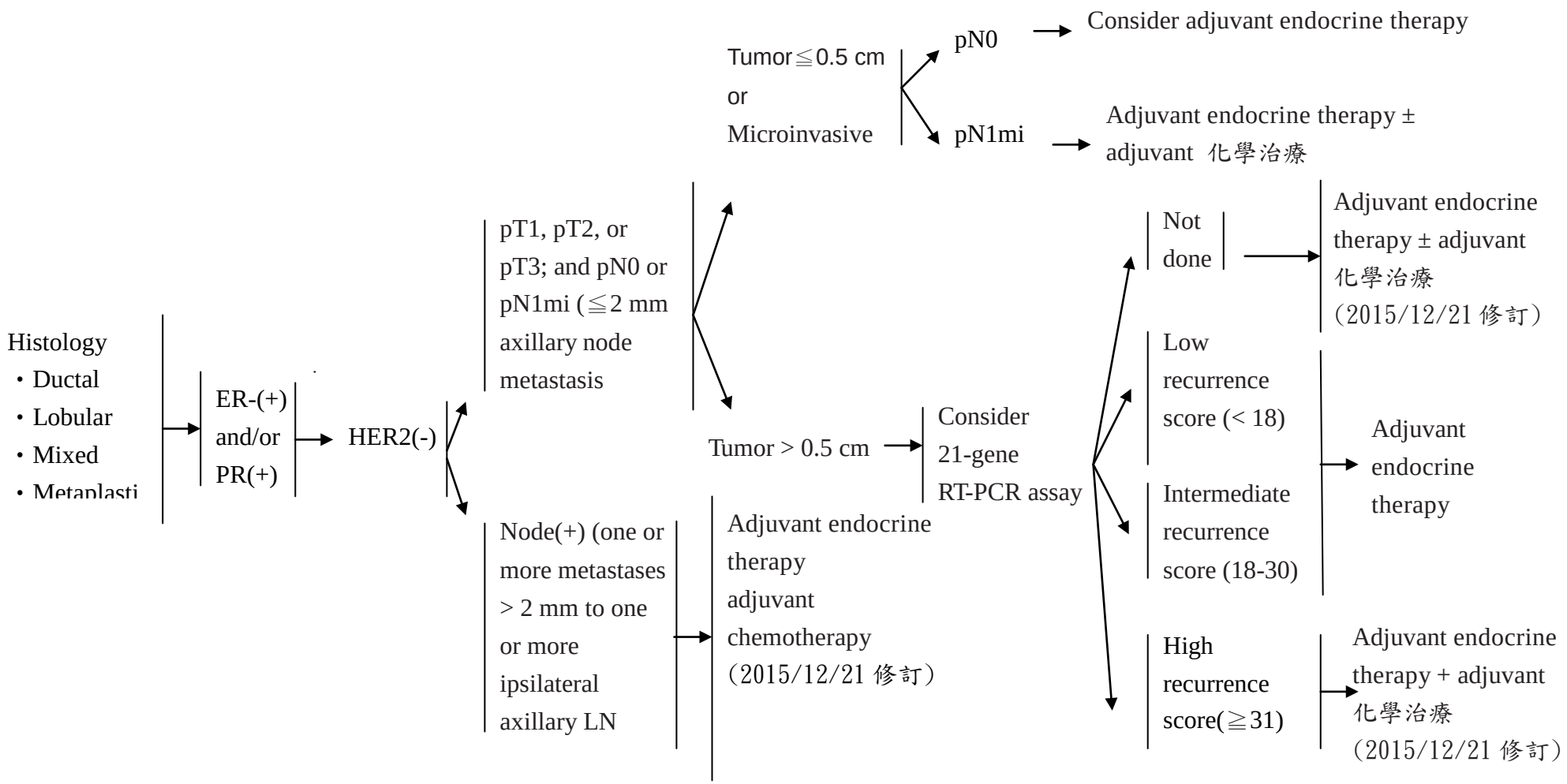
＊Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with radiation therapy is acceptable

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

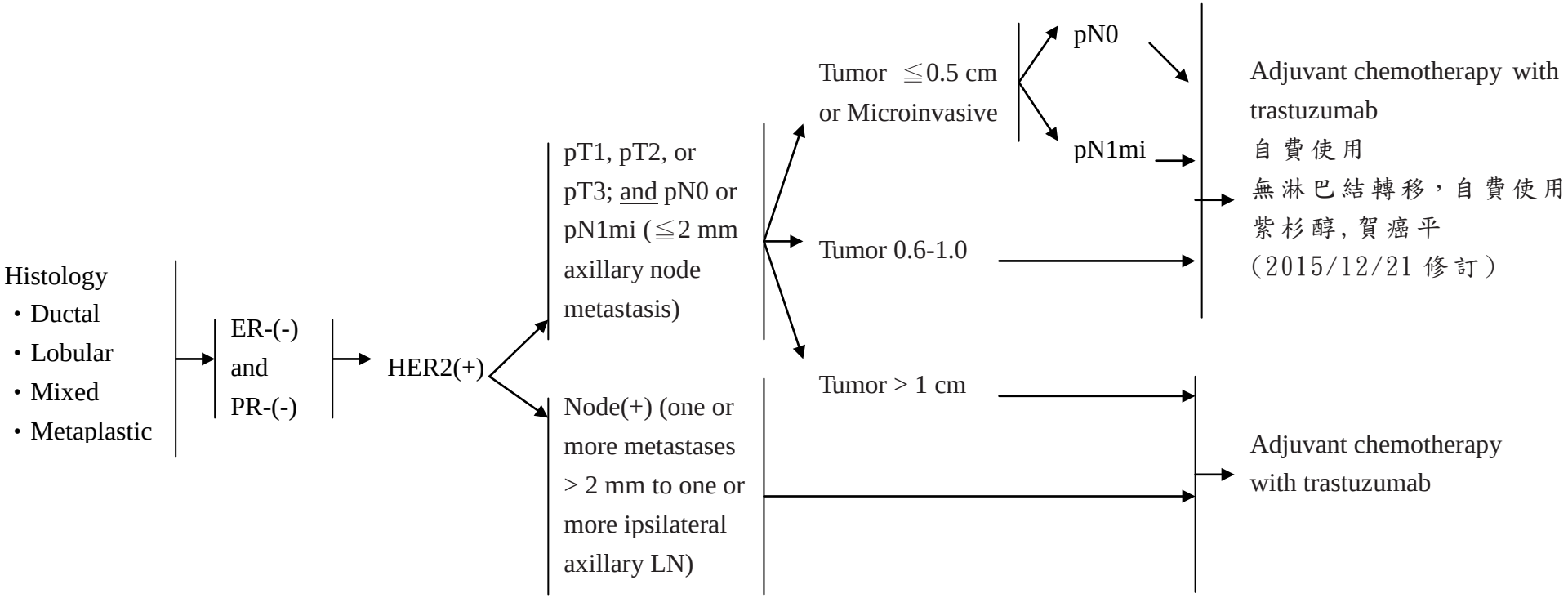
＊The prognosis of patients with T1a and T1b tumors that are node negative is uncertain even when HER2 is amplified or over-expressed. This is a population of breast cancer patients that was not studied in the available randomized trials. The decision for use of trastuzmab therapy in this cohort of patients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

＊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.

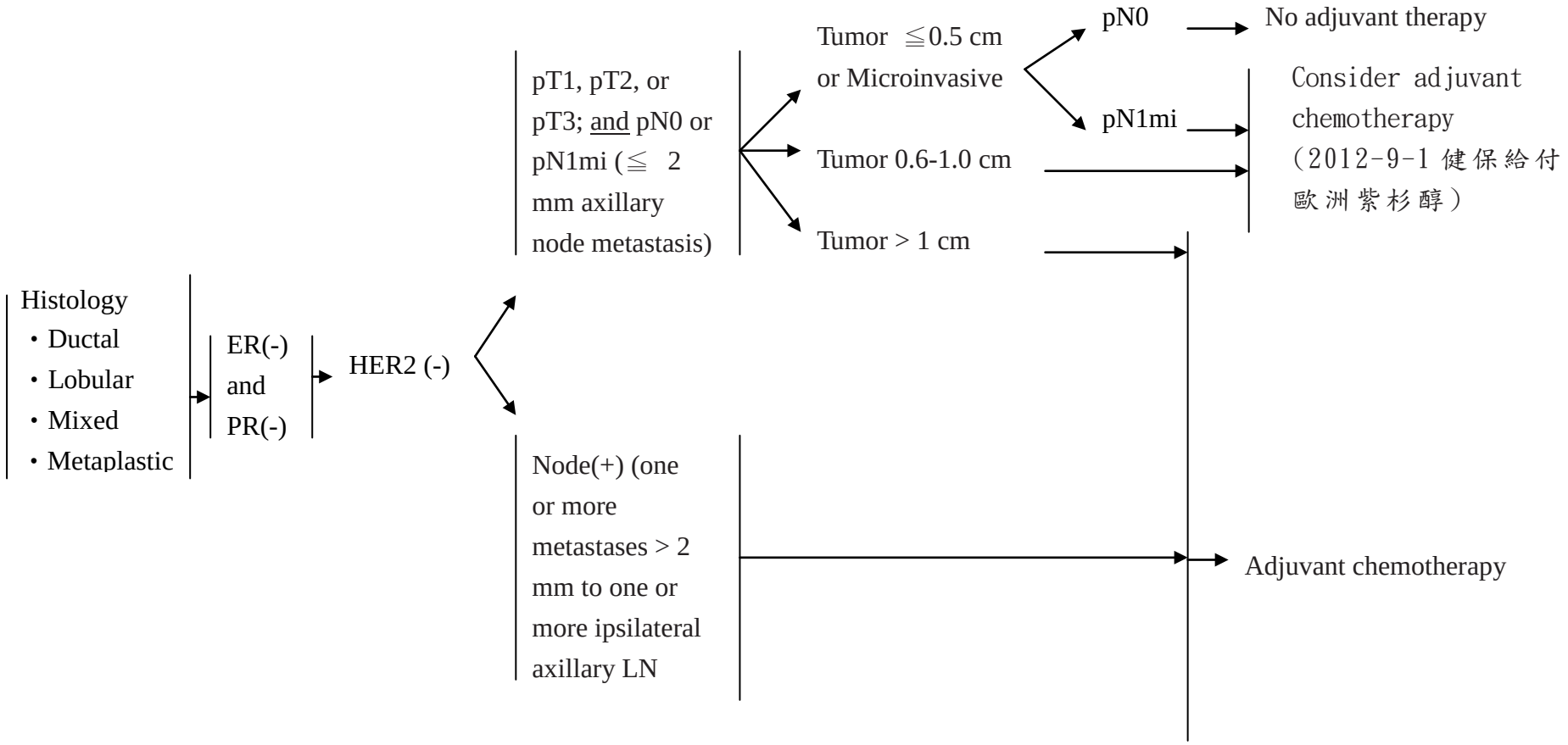
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR 陽性 - HER2 陰性 Disease



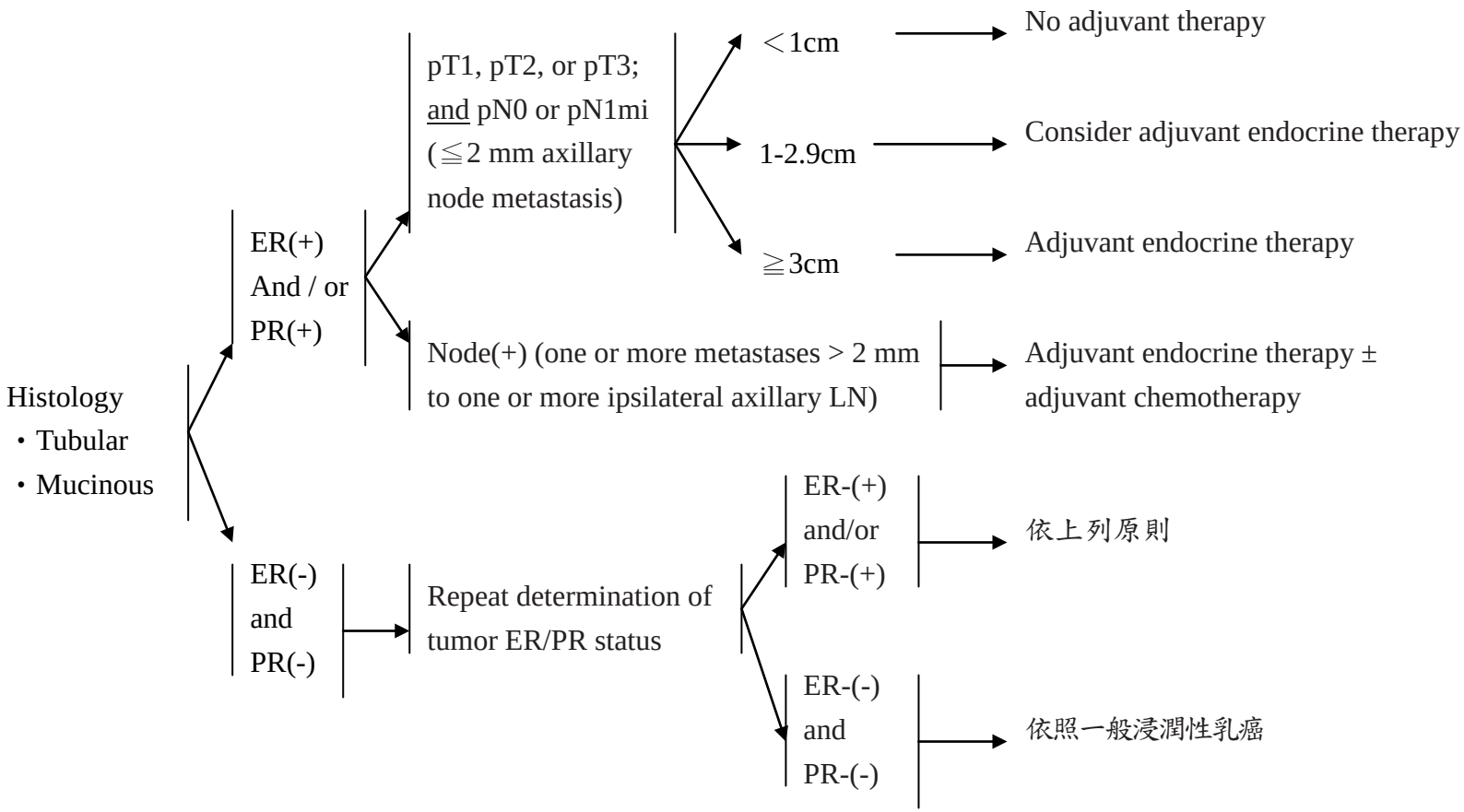
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR 陰性 - HER2 陽性 Disease



SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR 陰性 - HER2 陰性 DISEASE



SYSTEMIC ADJUVANT TREATMENT - FAVORABLE HISTOLOGIES



CLINICAL STAGE

Stage IIA
T2, N0, M0

Stage IIB
T2, N1, M0

T3, N0, M0

Stage IIIA
T3, N1, M0

and
考慮保留乳房手術者

→

WORKUP

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound
- Pathology review
- ER/PR status and HER2 status
- Genetic counseling if patient is high risk for hereditary breast cancer
- Breast MRI (optional)
- Consider fertility counseling if premenopause

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

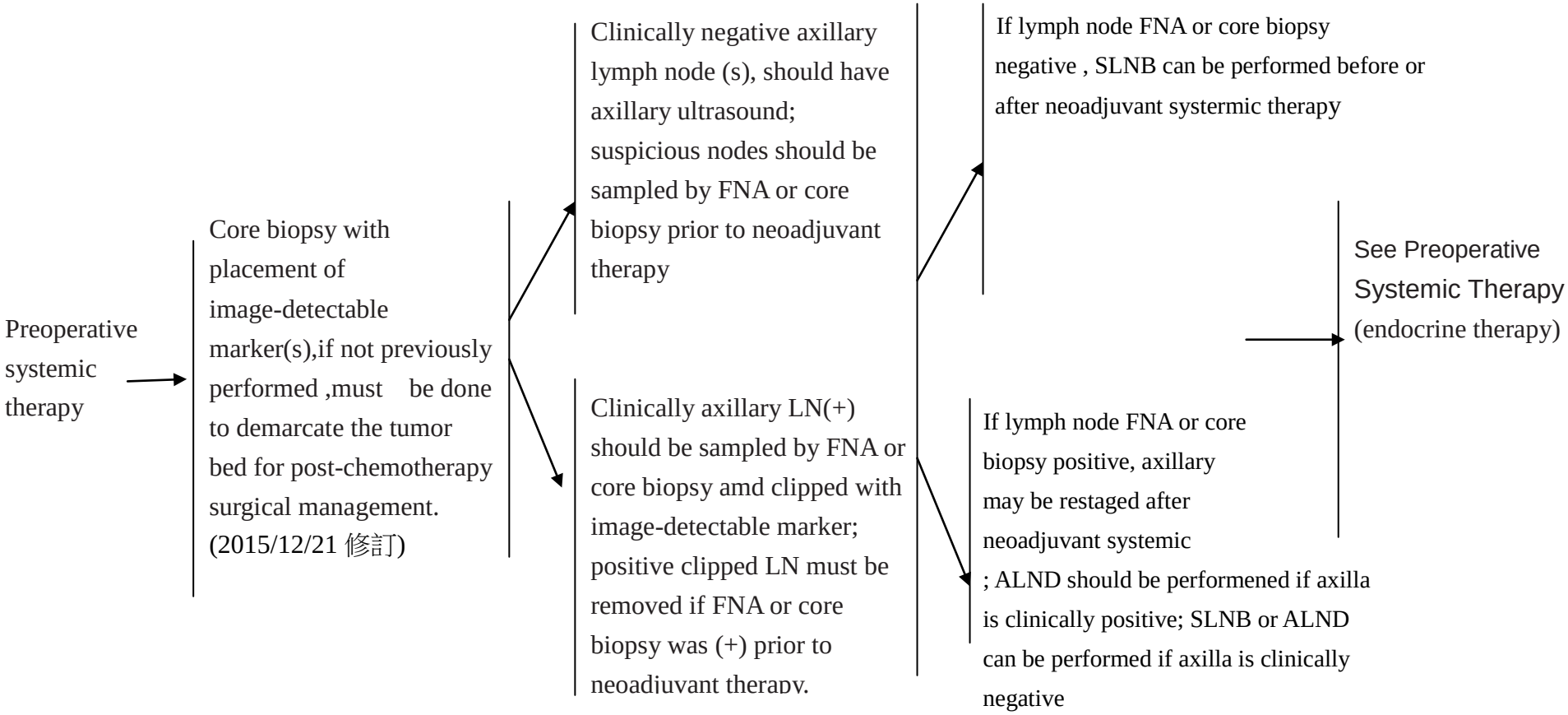
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or fluoride PET/CT
- FDG PET/CT

Optional studies as directed by signs or symptoms:

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

→ 考量乳房保留與否

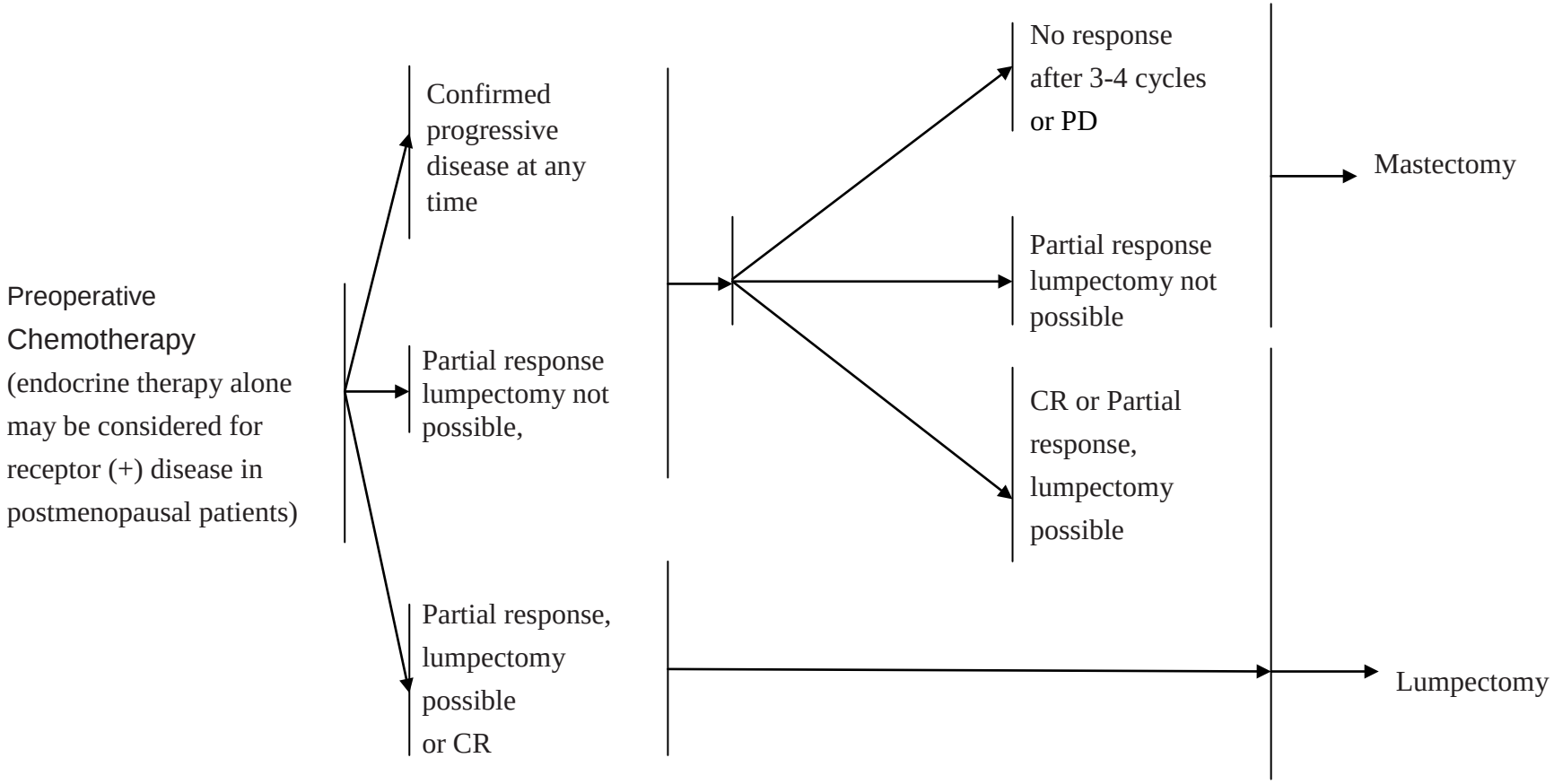
內分泌或化學治療，乳房及腋下評估



註:術前化療部份(乳房腫瘤評估)，考慮乳房保留手術，術前切片放置可監測到之記號

PRIMARY TREATMENT **RESPONSE(評估化療反應)**

(針對IIA-IIIA)



註：術前化學治療或內分泌治療規範

修改：1.如確定為復發進展(progressive disease,PD)→考慮直接乳房切除

2.不再作第二線化療

局部治療

術後治療

Mastectomy and surgical axillary staging ±reconstruction. If Sentinel LN biopsy performed prechemotherapy and findings (-), may omit axillary LN node staging

- Complete planed chemotherapy regimen if not complete preoperatively plus endocrine treatment if ER(+) and /or PR(+) (sequential chemotherapy followed by endocrine therapy)
- Adjuvant R/T post-mastectomy is based on prechemotherapy tumor characteristics and Endocrine therapy if ER-(+) and/or PR(+)
- Complete up to one year of trastuzumab therapy if HER2-(+). May be administered concurrent with R/T and with endocrine therapy if indicated.

局部治療

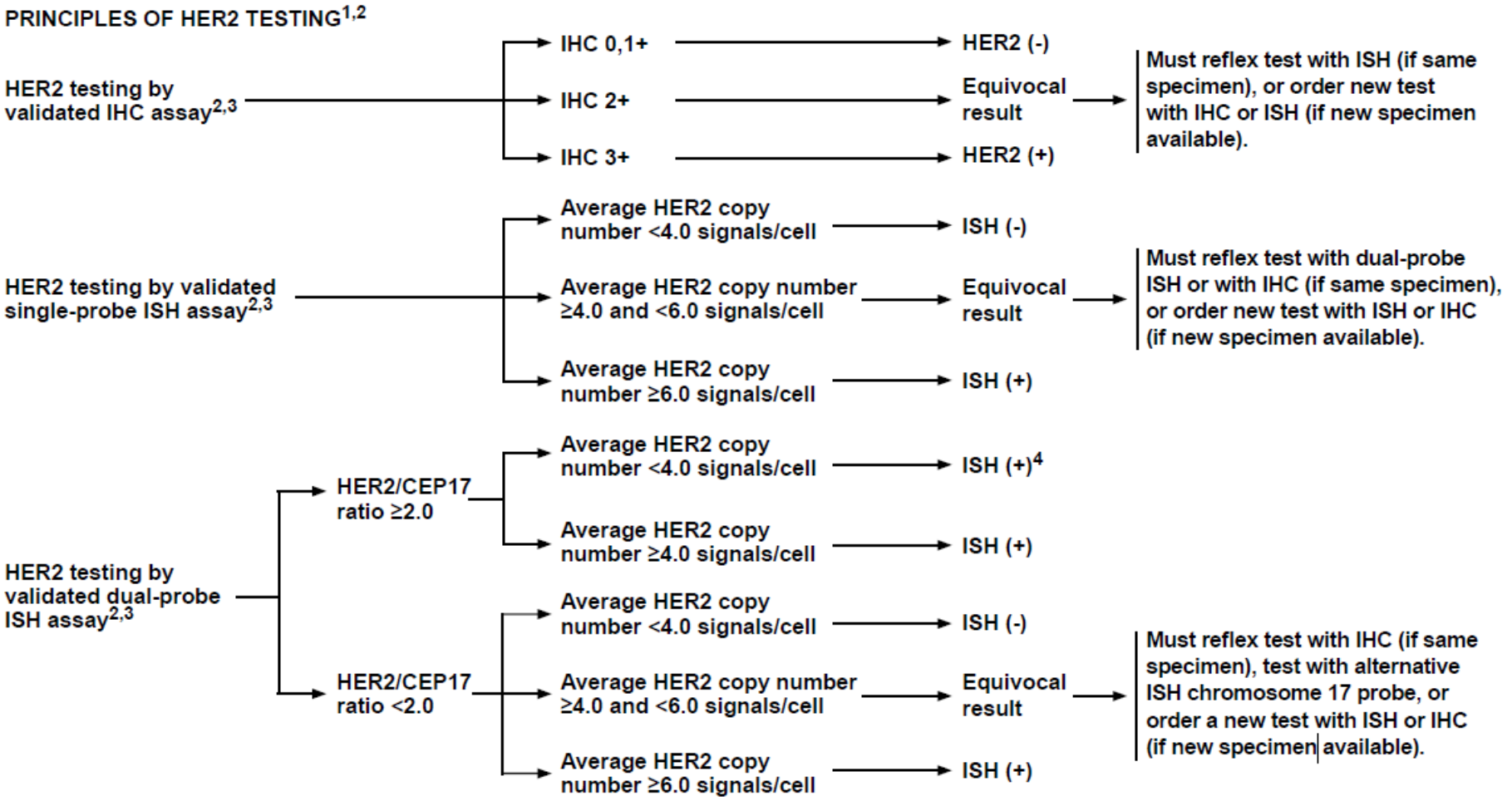
術後治療

Lumpectomy with surgical axillary staging
If sentinel LN biopsy performed prechemotherapy and findings(-), may omit axillary LN staging

→

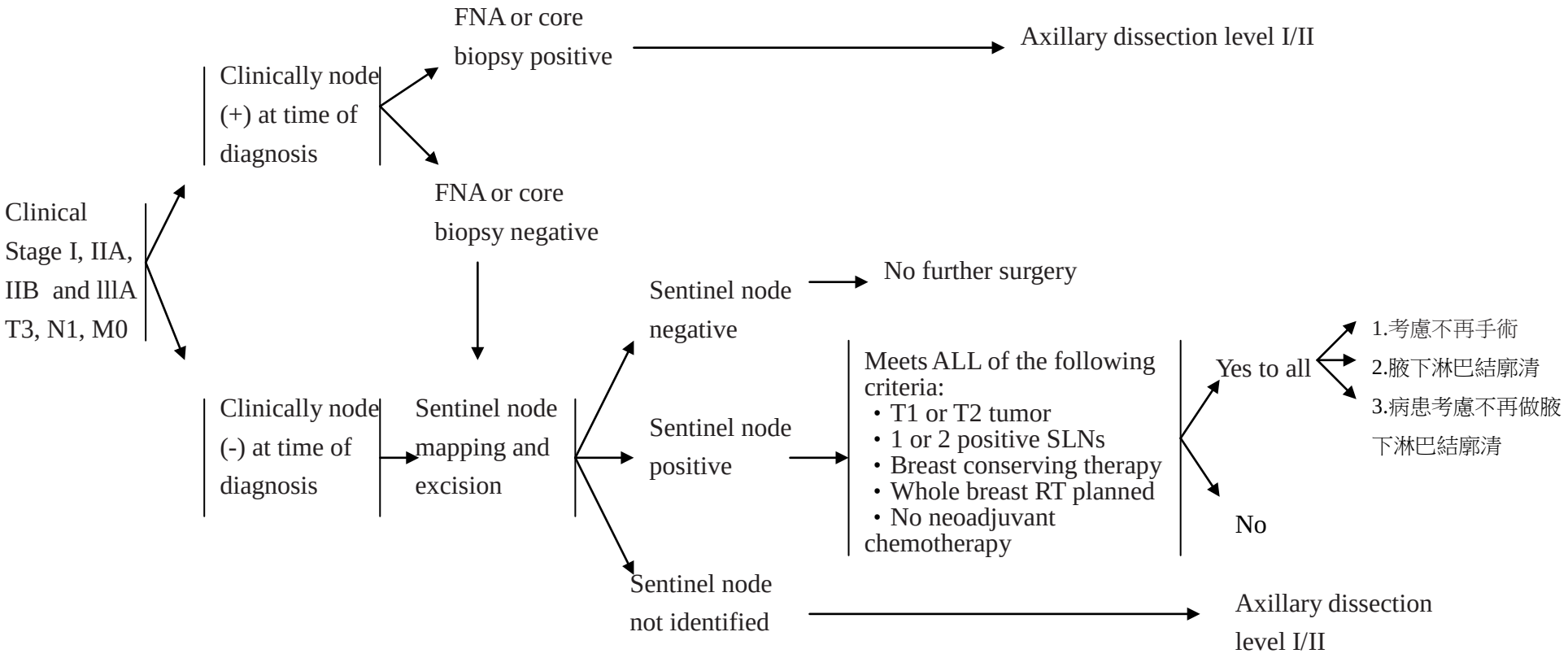
- Complete planed chemotherapy regimen course if not completed preoperatively plus endocrine treatment if ER(-) and/or PR(+) (sequential chemotherapy followed by endocrine therapy)
- Adjuvant R/T post-lumpectomy based on prechemotherapy tumor characteristics and Endocrine therapy if ER-(+) and/or PR-(+)
- Complete up to one year of trastuzumab therapy if HER2-(+). May be administered concurrent with R/T and with endocrine therapy if indicated

註：術前化學治療後，無論全切除或部分切除，術後應完全術前計劃之化學治療，不再進入臨床試驗做術後化療。


PRINCIPLES OF HER2 TESTING[1,2]
HER2 testing by validated IHC assay[2,3]
IHC 0,1+
HER2 (-)
IHC 2+
Equivocal result
IHC 3+
HER2 (+)
Must reflex test with ISH (if same specimen), or order new test with IHC or ISH (if new specimen available).
HER2 testing by validated single-probe ISH assay[2,3]
Average HER2 copy number <4.0 signals/cell
ISH (-)
Average HER2 copy number ≥4.0 and <6.0 signals/cell
Equivocal result
Average HER2 copy number ≥6.0 signals/cell
ISH (+)
Must reflex test with dual-probe ISH or with IHC (if same specimen), or order new test with ISH or IHC (if new specimen available).
HER2 testing by validated dual-probe ISH assay[2,3]
HER2/CEP17 ratio ≥2.0
Average HER2 copy number <4.0 signals/cell
ISH (+)[4]
Average HER2 copy number ≥4.0 signals/cell
ISH (+)
HER2/CEP17 ratio <2.0
Average HER2 copy number <4.0 signals/cell
ISH (-)
Average HER2 copy number ≥4.0 and <6.0 signals/cell
Equivocal result
Average HER2 copy number ≥6.0 signals/cell
ISH (+)
Must reflex test with IHC (if same specimen), test with alternative ISH chromosome 17 probe, or order a new test with ISH or IHC (if new specimen available).

(2015/12/21 增訂)

SURGICAL AXILLARY STAGINGI,IIA,IIB,and IIIA T3,N1,M0



註：針對第Ⅰ，2A 期乳癌施行前哨淋巴結陰性，則不再施行淋巴結廓清，前哨淋巴結陽性患者考慮 1. 不再作腋下淋巴結廓清，2. 腋下淋巴結廓清，3. 病患意願，要求不再作腋下淋巴結廓清。

NON-TRASTUZUMAB CONTAINING COMBINATIONS

NEOADJUVANT REGIMENS

TC

- Docetaxel 75 mg/m^2 IV day 1
- Cyclophosphamide 600 mg/m^2 IV day 1

Cycled every 3weeks for 4 cycles

Reference:

Jones S, Holmes F, O'Shaughnessey J, et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US Oncology Research trial 9735. J Clin Oncol 2009;27:1177-1183.

FEC followed by docetaxel

- 5-Fluorouracil 500 mg/m^2 IV day 1
- Epirubicin 100 mg/m^2 IV day 1
- Cyclophosphamide 500 mg/m^2 day

Cycled every 21 days for 3 cycles.

Followed by

- Docetaxel 75 mg/m^2 day 1

Cycled every 21 days for 3 cycles.

Reference:

Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCCPACS 001 trial. J Clin Oncol 2006; 24:5664-5671.

FEC

- 5-fluorouracil 500 mg/m^2 IV day 1
- Epirubicin 100 mg/m^2 IV day 1
- Cyclophosphamide 500 mg/m^2 IV day 1

Repeat cycle every 21 days

Reference:

Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCCPACS 001 trial. J Clin Oncol 2006; 24:5664-5671.

TRASTUZUMAB CONTAINING COMBINATIONS
NEO ADJUVANT REGIMENS

TCH

- Docetaxel 75 mg/m^2 IV day 1
- Carboplatin AUC 6 IV day 1

Cycled every 21 days for 6 cycles With

- Trastuzumab 4 mg/kg wk 1

Followed by

- Trastuzumab 2 mg/kg for 17 wks Followed by

·Trastuzumab 6 mg/kg IV every 3 wks to complete 1 year of trastuzumab therapy. Cardiac monitoring at baseline, 3, 6, and 9 mo註：TCH原用藥組合為Docetaxel+ Carboplatin+ Trastuzumab

根據文獻，TCH中的的“C”亦可使用Cisplatin 60 mg/m^2 IVD day 1

Reference:
Judith Hurley, Philomena Doliny, Isildinha Reis, Orlando Silva, Carmen Gomez-Fernandez, Pedro Velez,Giovanni Pauletti, Jodeen E. Powell, Mark D. Pegram, and Dennis J. Slamon. Docetaxel, Cisplatin, and Trastuzumab As Primary Systemic Therapy for Human Epidermal Growth Factor Receptor 2–Positive Locally Advanced Breast Cancer. JOURNAL OF CLINICAL ONCOLOGY.2006;24;1831-1839.

TRASTUZUMAB CONTAINING COMBINATIONS

NEOADJUVANT REGIMENS

T followed by FEC chemotherapy with trastuzumab

• Trastuzumab 4 mg/kg IV for one dose beginning just prior to first dose of paclitaxel

Followed by

• Trastuzumab 2 mg/kg IV weekly for 23 wks

• Paclitaxel 225 mg/m^2 by 24 h IV infusion every 21 days for 4 cycles

(alternatively paclitaxel may be administered as paclitaxel 80 mg/m^2 by 1 h IV infusion weekly for 12 wks)

Followed by

• 5-Fluorouracil 500 mg/m^2 on days 1 and 4

• Epirubicin 75 mg/m^2 IV on day 1

• Cyclophosphamide 500 mg/m^2 on day 1

Cycled every 21 days for 4 cycles.

※ Trastuzumab健保给付規定:

1. 早期乳癌
   (1)外科手術前後，化學療法(術前輔助治療或輔助治療)治療後，具HER2過度表現(IHC3+或FISH+)，且具腋下淋巴結轉移但無遠處臟器轉移之早期乳癌患者，作為輔助性治療用藥。
   (2)使用至多以一年為限
2. 轉移性乳癌
   (1)單獨使用於治療腫瘤細胞上有HER2過度表現(IHC3+或FISH+)，曾接受過一次以上化學治療之轉移性乳癌病人。
   (2)與paclitaxel或docetaxel併用，使用於未曾接受過化學治療之轉移性乳癌病患，且為HER2過度表現(IHC3+或FISH+)者。
   (3)轉移性乳癌且HER2過度表現之病人，僅限先前未使用過本藥品者方可使用。
3. 經事前審查核準後使用。

Reference:
Buzdar A, Ibrahim N, Francis D, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: Results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. J Clin Oncol 2005;23:3676-3685.

TRASTUZUMAB CONTAINING COMBINATIONS
NEOADJUVANT REGIMENS

Docetaxel + trastuzumab followed by FEC

- Docetaxel 100 mg/m^2 by 1 h IV day 1

Cycled every 21 days for 3 cycles , With

- Trastuzumab 4 mg/kg IV with first dose of docetaxel day 1.Followed by
- Trastuzumab 2 mg/kg IV weekly to complete 9 wks of trastuzumab. Followed by
- 5-Fluorouracil 600 mg/m^2 IV day 1
- Epirubicin 60 mg/m^2 day 1
- Cyclophosphamide 600 mg/m^2 day 1

Cycled every 21 days for 3 cycles

Cardiac monitoring at baseline, after last FEC cycle, at 12 and 36 mo after chemotherapy.

Reference:
Joensuu H, Kellokumpu-Lehtinen P-L, Bono P, et al: Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. N Engl J Med 2006;354:809-20.

Chemotherapy followed by trastuzumab

Approved adjuvant chemotherapy regimen for at least 4 cycles ,

Followed by

- Trastuzumab 8 mg/kg IV times 1 dose , Followed by
- Trastuzumab 6 mg/kg IV every 21 days for 1 y

Cardiac monitoring at baseline, 3, 6,and 9 mo

Reference:
Martine J,Piccart-Gebhart,M.D, et al. Trastuzumab after Adjuvant chemotherapy in Her2-positive Breast Cancer,The New England Journal of Medicine 2005;353(16)1659-1672.

TRASTUZUMAB CONTAINING COMBINATIONS

NEOADJUVANT REGIMENS

Pertuzumab + trastuzumab + docetaxel

•Pertuzumab 840 mg IV day 1 Followed by 420 mg IV

• Trastuzumab 8 mg/kg IV day 1 Followed by 6 mg/kg IV

• Docetaxel 75 mg/m^2 IV day 1

Cycled every 21 days (2015/12/21 修訂)

Reference:
Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol 2012;13:25-32.

術後化療

NON-TRASTUZUMAB CONTAINING COMBINATIONS

ADJUVANT REGIMENS

TC

˙Docetaxel 75 mg/m^2 IV day 1

˙Cyclophosphamide 600 mg/m^2 IV day 1

Cycled every 3weeks for 4 cycles

註:須評估年紀大,心臟功能 (2015/12/21 修訂)

Reference:

Jones S, Holmes F, O'Shaughnessey J, et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US Oncology Research trial 9735. J Clin Oncol 2009;27:1177-1183.

NON-TRASTUZUMAB CONTAINING COMBINATIONS
ADJUVANT REGIMENS

FEC followed by docetaxel

- 5-Fluorouracil 500 mg/m^2 IV day 1
- Epirubicin 100 mg/m^2 IV day 1
- Cyclophosphamide 500 mg/m^2 day

Cycled every 21 days for 3 cycles.

Followed by

- Docetaxel 75 mg/m^2 day 1

Cycled every 21 days for 3 cycles.

Reference:

Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCCPACS 001 trial. J Clin Oncol 2006; 24:5664-5671.

NON-TRASTUZUMAB CONTAINING COMBINATIONS
ADJUVANT REGIMENS

FEC 【for node (-)】

- 5-fluorouracil 500 mg/m^2 IV day 1
- Epirubicin 100 mg/m^2 IV day 1
- Cyclophosphamide 500 mg/m^2 IV day 1

Repeat cycle every 21 day for 6 cycles

Reference:

Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCCPACS 001 trial. J Clin Oncol 2006; 24:5664-5671.

TRASTUZUMAB CONTAINING COMBINATIONS

PREFERRED ADJUVANT REGIMENS

TCH

- Docetaxel 75 mg/m^2 IV day 1
- Carboplatin AUC 6 IV day 1

Cycled every 21 days for 6 cycles With

- Trastuzumab 4 mg/kg wk 1

Followed by

- Trastuzumab 2 mg/kg for 17 wks Followed by

Trastuzumab 6 mg/kg IV every 3 wks to complete 1 year of trastuzumab therapy. Cardiac monitoring at baseline, 3, 6, and 9 mo.

註：TCH原用藥組合為Docetaxel+ Carboplatin+ Trastuzumab

根據文獻，TCH中的的“C”亦可使用Cisplatin 60 mg/m^2 IVD day 1

Reference:

Judith Hurley, Philomena Doliny, Isildinha Reis, Orlando Silva, Carmen Gomez-Fernandez, Pedro Velez,Giovanni Pauletti, Jodeen E. Powell, Mark D. Pegram, and Dennis J. Slamon. Docetaxel, Cisplatin, and Trastuzumab As Primary Systemic Therapy for Human Epidermal Growth Factor Receptor 2–Positive Locally Advanced Breast Cancer. JOURNAL OF CLINICAL ONCOLOGY.2006;24;1831-1839.

TRASTUZUMAB CONTAINING COMBINATIONS

OTHER ADJUVANT REGIMENS:

AC followed by docetaxel with trastuzumab

- Doxorubicin 60 mg/m^2 IV day 1
- Cyclophosphamide 600 mg/m^2 day 1

Cycled every 21 days for 4 cycles Followed by

- Docetaxel 75 mg/m^2

Cycled every 21 days for 4 cycles With

- Trastuzumab 4 mg/kg IV wk one Followed by
- Trastuzumab 2 mg/kg IV weekly for 11 wks Followed by
- Trastuzumab 6 mg/kg every 21 days to complete 1 y of trastuzumab therapy

Cardiac monitoring at baseline, 3, 6, and 9 mo. (2015/12/21 修訂)

Reference:

Slamon D, Eiermann W, Robert N, et al. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med 2011;365:1273-1283.

Paclitaxel + trastuzumab (node (-) ; low risk) 自費使用 (2015/12/21 NEJM 修訂)

- Paclitaxel 80 mg/m^2 IV weekly for 12 weeks

With

- Trastuzumab 4 mg/kg IV with first dose of paclitaxel

Followed by

- Trastuzumab 2 mg/kg IV weekly to complete 1 y of treatment. As an alternative, trastuzumab 6 mg/kg IV every 21 days may be used following the completion of paclitaxel, and given to complete 1 y trastuzumab treatment.

Cardiac monitoring at baseline, 3, 6, and 9 mo.

Reference:

Tolaney S, Barry W, Dang C, et al. Adjuvant paclitaxel and trastuzumab for node-negative HER2-positive breast cancer. N Engl J Med 2015;372:134-141.

◆ **停經前**
- Tamoxifen(Nolvadex)

◆ **停經後**
- Tamoxifen(Nolvadex)
- Arimidex(Anastrozole)
- Femara(Letrozole)
- Aromasin

健保給付條文:

9.1.3.Letrozole：(88/11/1、90/10/1、92/3/1、97/11/1、98/11/1、99/9/1、102/8/1)

1.接受抗動情激素治療失敗的自然或人工停經後之末期乳癌病人之治療、停經後之局部晚期或轉移性乳癌婦女患者之第一線治療用藥。

2.停經後且荷爾蒙接受體呈陽性，有淋巴結轉移之乳癌病人，作為 tamoxifen 治療五年後的延伸治療，且不得與其他 aromatase inhibitor 併用。使用時需同時符合下列規定：(97/11/1)

(1)手術後大於等於 11 年且無復發者不得使用。

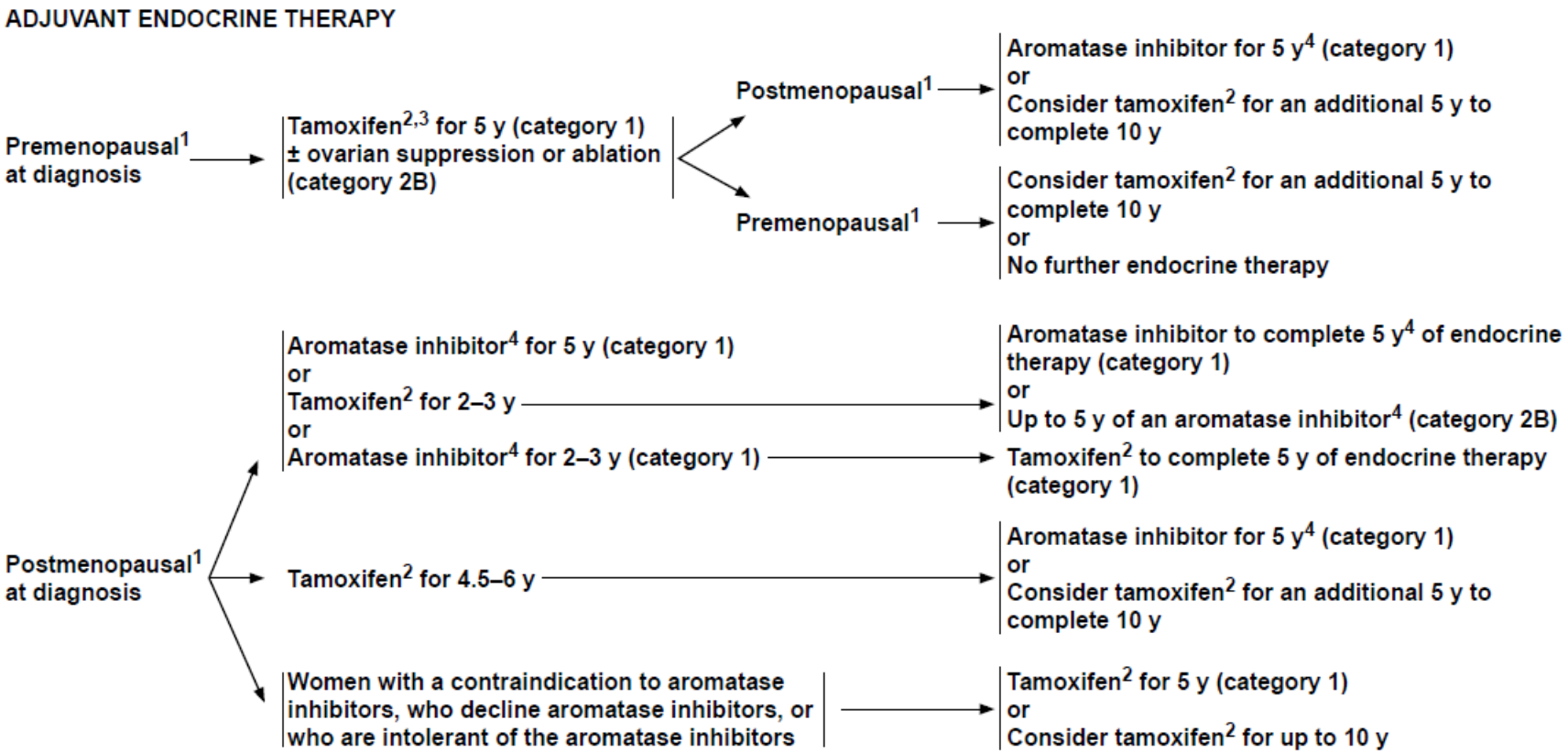
(2)每日最大劑量 2.5mg，使用不得超過四年。

3.**停經後且荷爾蒙接受體呈陽性之早期乳癌病人，經外科手術切除後之輔助治療，且不得與 tamoxifen 或其他 aromatase inhibitor 併用。使用時需同時符合下列規定**：(98/11/1、99/9/1、102/8/1)

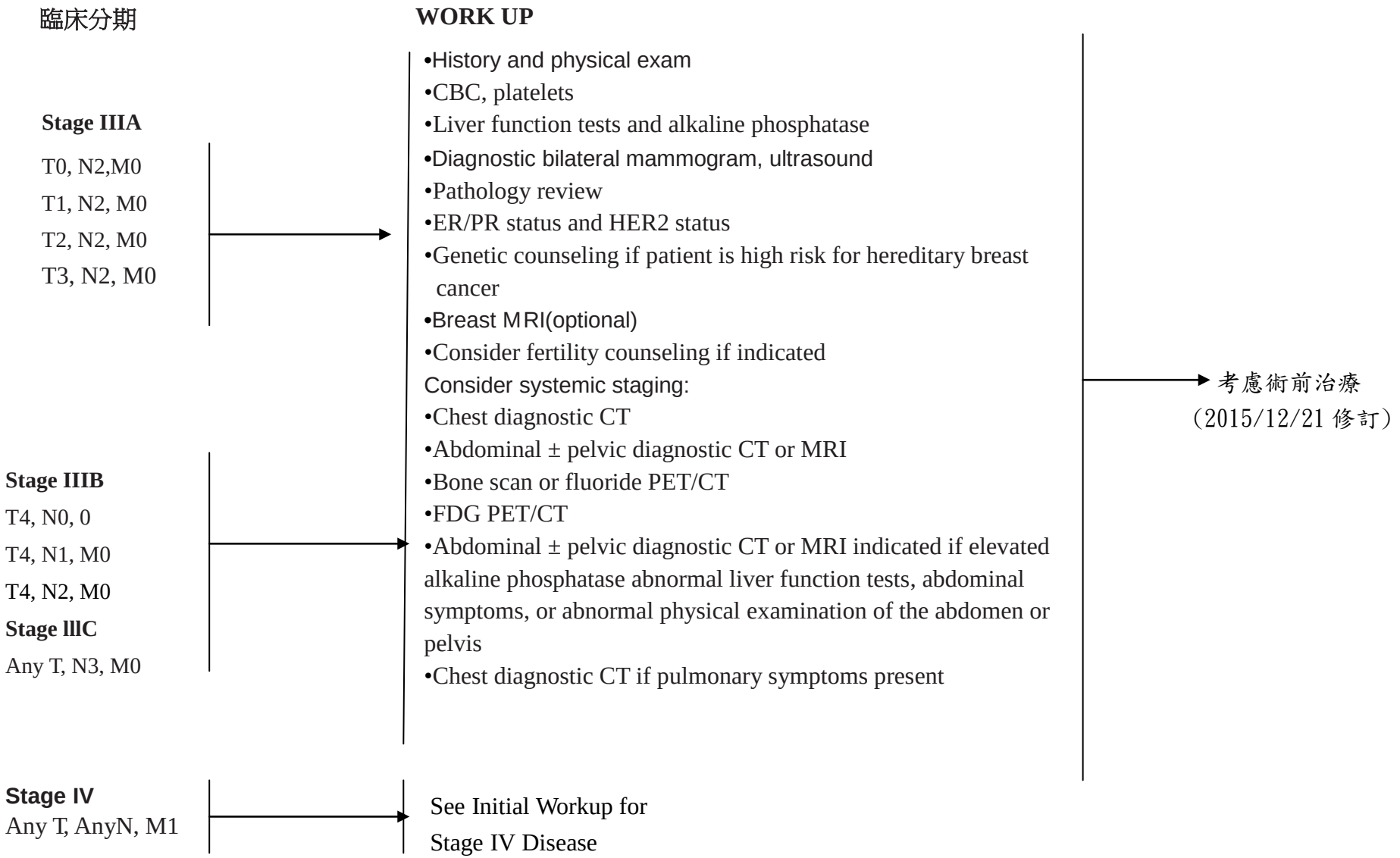
(1)每日最大劑量 2.5mg，使用不得超過五年；

(2)若由 tamoxifen 轉換使用本品，則使用期限合計不得超過 5 年。

4.病歷上應詳細記載手術資料、病理報告(應包含 ER、PR 之檢測結果且無復發現象)及用藥紀錄(如 tamoxifen 使用五年證明)。(2015/12/21 修訂)


ADJUVANT ENDOCRINE THERAPY
Premenopausal[1] at diagnosis
Tamoxifen[2,3] for 5 y (category 1) ± ovarian suppression or ablation (category 2B)
Postmenopausal[1]
Aromatase inhibitor for 5 y[4] (category 1) or Consider tamoxifen[2] for an additional 5 y to complete 10 y
Premenopausal[1]
Consider tamoxifen[2] for an additional 5 y to complete 10 y or No further endocrine therapy
Postmenopausal[1] at diagnosis
Aromatase inhibitor[4] for 5 y (category 1) or Tamoxifen[2] for 2–3 y or Aromatase inhibitor[4] for 2–3 y (category 1)
Aromatase inhibitor to complete 5 y[4] of endocrine therapy (category 1) or Up to 5 y of an aromatase inhibitor[4] (category 2B)
Tamoxifen[2] to complete 5 y of endocrine therapy (category 1)
Tamoxifen[2] for 4.5–6 y
Aromatase inhibitor for 5 y[4] (category 1) or Consider tamoxifen[2] for an additional 5 y to complete 10 y
Women with a contraindication to aromatase inhibitors, who decline aromatase inhibitors, or who are intolerant of the aromatase inhibitors
Tamoxifen[2] for 5 y (category 1) or Consider tamoxifen[2] for up to 10 y

2015/12/21 增訂


臨床分期
WORK UP
Stage IIIA
T0, N2,M0
T1, N2, M0
T2, N2, M0
T3, N2, M0
•History and physical exam
•CBC, platelets
•Liver function tests and alkaline phosphatase
•Diagnostic bilateral mammogram, ultrasound
•Pathology review
•ER/PR status and HER2 status
•Genetic counseling if patient is high risk for hereditary breast cancer
•Breast MRI(optional)
•Consider fertility counseling if indicated
Consider systemic staging:
•Chest diagnostic CT
•Abdominal ± pelvic diagnostic CT or MRI
•Bone scan or fluoride PET/CT
•FDG PET/CT
•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
考慮術前治療
(2015/12/21 修訂)
Stage IIIB
T4, N0, 0
T4, N1, M0
T4, N2, M0
Stage lllC
Any T, N3, M0
Stage IV
Any T, AnyN, M1
See Initial Workup for Stage IV Disease

術前治療
FOR LOCALLY ADVANCY

LOCOREGIONAL TREATMENT

ADJUVANT TREATMENT

術前內分泌
或化學治療

response →

Total mastectomy + level l/ll axillary dissection or axillary sentinel lymph node biopsies +R/T to chest wall and infraclavicular and supraclavicular nodes (plus internal mammary nodes if involved, strongly consider internal mammary nodes if not clinically involved ± delayed breast reconstruction

Or

Consider lumpectomy + level l/ll axillary dissection or axillary sentinel lymph node biopsies+ R/T to breast and infraclavicular and supraclavicular nodes (plus internal mammary nodes if involved

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

•Complete up to one year of trastuzumab therapy if HER2- (+). May be administered concurrent with R/T and with endocrine therapy if indicated

No response → Consider additional systemic chemotherapy and/or preoperative radiation

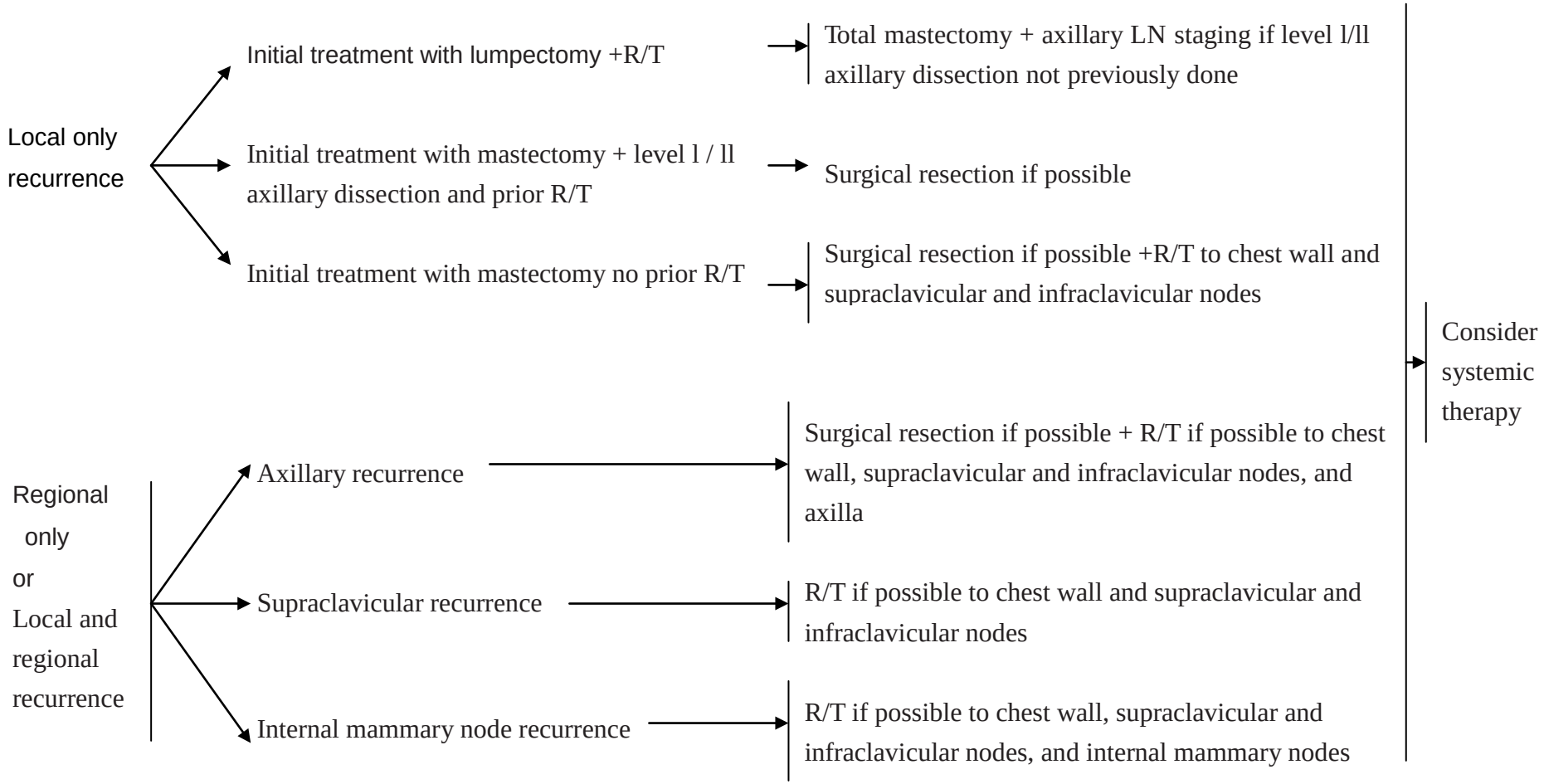
Response – 依上述原則

No response→個別考慮

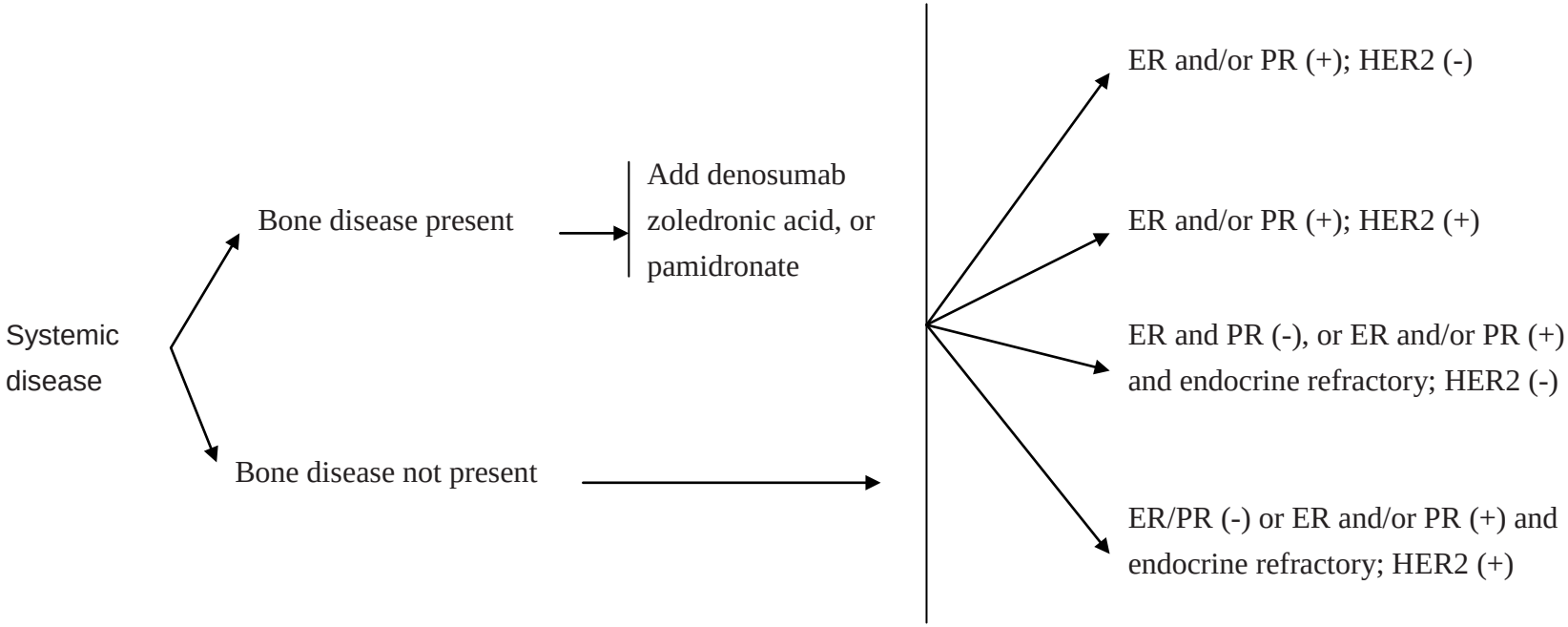
RECURRENT/STAGE IV DISEASE

CLINICAL STADE	WORKUP
Recurrent or stage IV disease →	• History and physical exam • CBC, platelets • Liver function tests and ALP • Chest diagnostic CT (if pulmonary symptoms present) • Abdominal±pelvic diagnostic CT or MRI • Brain MRI if suspicious CNS symptoms • Bone scan or sodium fluoride PET/CT (category B2) • FDG PET/CT • X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan • First recurrence of disease should be biopsies • Determination of tumor ER/PR and HER2 status on metastatic site • Genetic counseling if patient is high risk for hereditary breast cancer

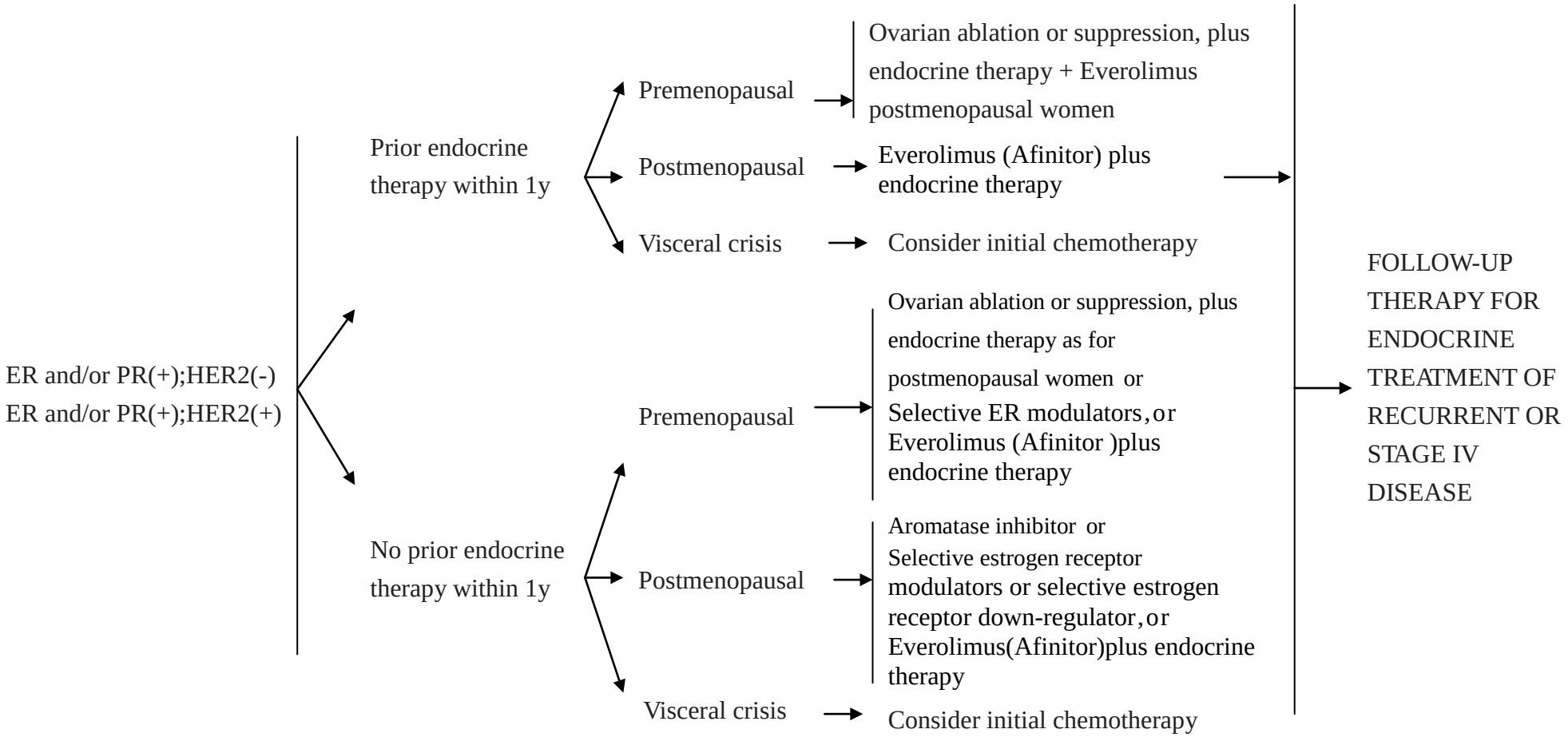
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE



全身性治療

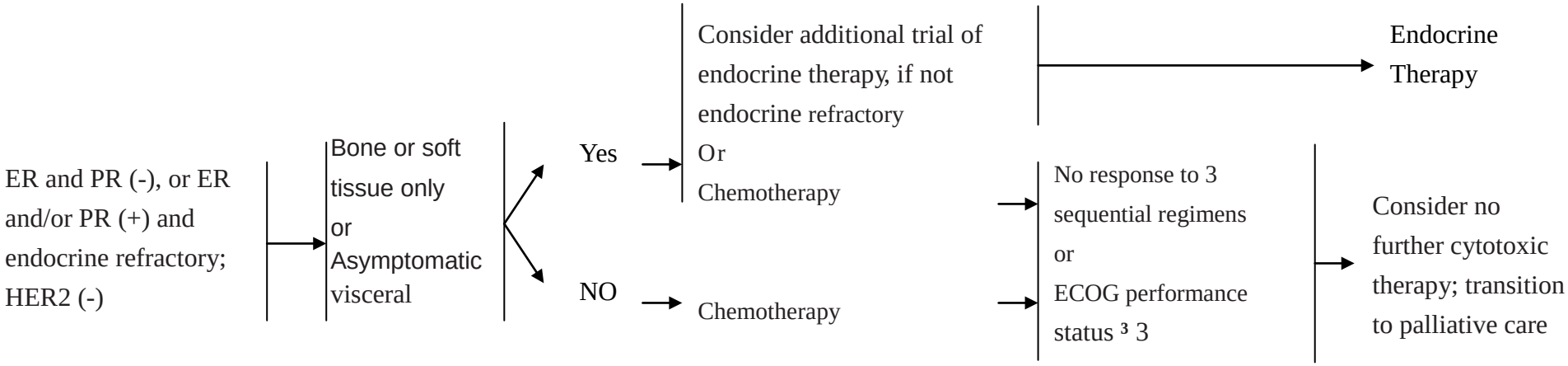


SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE ER and/or PR 陽性 ; HER2 陰性 OR 陽性


ER and/or PR(+);HER2(-)
ER and/or PR(+);HER2(+)
Prior endocrine therapy within 1y
Premenopausal
Ovarian ablation or suppression, plus endocrine therapy + Everolimus postmenopausal women
Postmenopausal
Everolimus (Afinitor) plus endocrine therapy
Visceral crisis
Consider initial chemotherapy
No prior endocrine therapy within 1y
Premenopausal
Ovarian ablation or suppression, plus endocrine therapy as for postmenopausal women or Selective ER modulators, or Everolimus (Afinitor)plus endocrine therapy
Postmenopausal
Aromatase inhibitor or Selective estrogen receptor modulators or selective estrogen receptor down-regulator, or Everolimus(Afinitor)plus endocrine therapy
Visceral crisis
Consider initial chemotherapy
FOLLOW-UP THERAPY FOR ENDOCRINE TREATMENT OF RECURRENT OR STAGE IV DISEASE

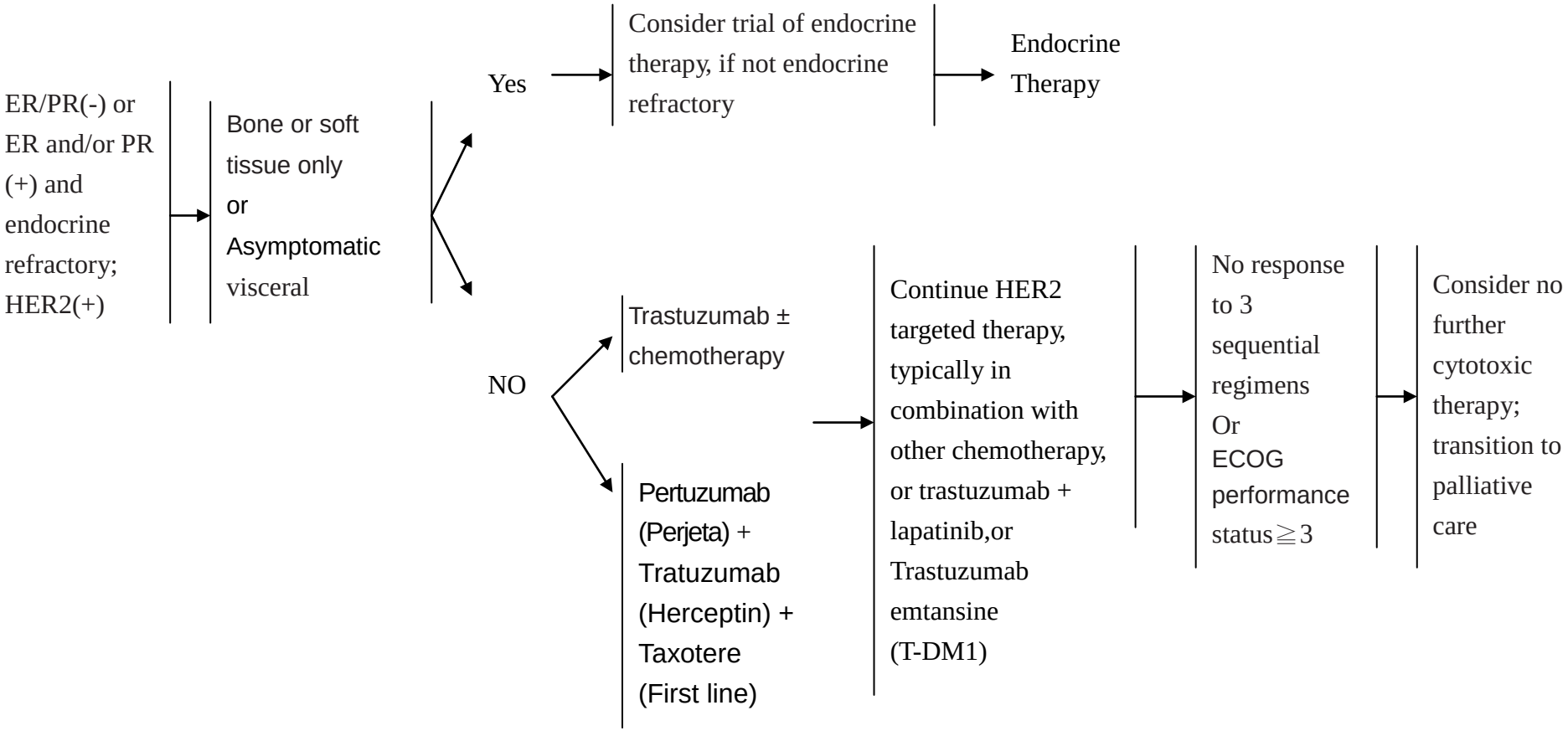
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

ER and PR 陰性; or ER and/or PR 陽性 and ENDOCRINE REFRACTORY; HER2 陰性

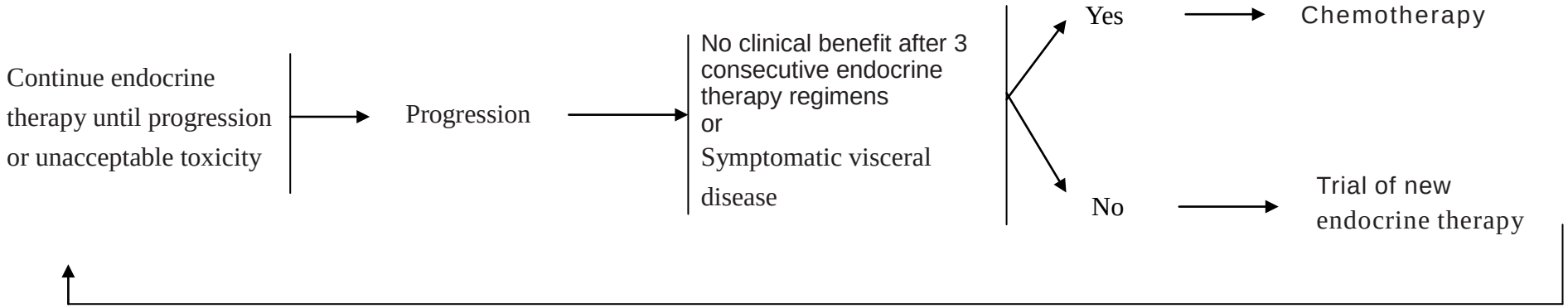


SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

ER and PR NEGATIVE; or ER and/or PR POSITIVE and ENDOCRINE REFRACTORY; and HER2 POSITIVE



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



- **Chemotherapy**
  - **First-line**

    1.Pertuzumab(PERJETA)+Herceptin+Taxotere ---For HER2(+)
  - **Second-line**

    1. **Trastuzumab emtansine (T-DM1) ---For HER2(+)**

- **Hormone Therapy**

  1.Everolimus(Afinitor)+H/T(for MBC)

  2.Faslodex

CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER[1]

Preferred single agents:

Anthracyclines
- Doxorubicin
- Pegylated liposomal doxorubicin

Taxanes
- Paclitaxel

Anti-metabolites
- Capecitabine
- Gemcitabine

Other microtubule inhibitors
- Vinorelbine
- Eribulin

Other single agents:
- Cyclophosphamide
- Carboplatin
- Docetaxel
- Albumin-bound paclitaxel
- Cisplatin
- Epirubicin
- Ixabepilone

Chemotherapy combinations:
- CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)
- FEC (fluorouracil/epirubicin/cyclophosphamide)
- AC (doxorubicin/cyclophosphamide)
- EC (epirubicin/cyclophosphamide)
- CMF (cyclophosphamide/methotrexate/fluorouracil)
- Docetaxel/capecitabine
- GT (gemcitabine/paclitaxel)
- Gemcitabine/carboplatin
- Paclitaxel/bevacizumab[2]

Preferred first-line agents for HER2-positive disease:
- Pertuzumab + trastuzumab + docetaxel (category 1)[4]
- Pertuzumab + trastuzumab + paclitaxel[4]

Other first-line agents for HER2-positive disease:

Trastuzumab alone or with:
- Paclitaxel ± carboplatin
- Docetaxel
- Vinorelbine
- Capecitabine

Preferred agents for trastuzumab-exposed HER2-positive disease:
- Ado-trastuzumab emtansine (T-DM1)

Other agents for trastuzumab-exposed HER2-positive disease:
- Lapatinib + capecitabine
- Trastuzumab + capecitabine

- Trastuzumab + lapatinib (without cytotoxic therapy)
- Trastuzumab + other agents[3,4]

DOSING SCHEDULES FOR CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

Preferred single agents:

Anthracyclines:

Doxorubicin
- 60–75 mg/m² IV day 1, cycled every 21 days[1]

or
- 20 mg/m² IV day 1 weekly[2]

Pegylated liposomal encapsulated doxorubicin[3]
- 50 mg/m² IV day 1

Cycled every 28 days.

Taxanes:

Paclitaxel
- 175 mg/m² IV day 1

Cycled every 21 days.[4]
or
- 80 mg/m² IV day 1 weekly[5]

Antimetabolites:

Capecitabine[6]
- 1000–1250 mg/m² PO twice daily days 1–14

Cycled every 21 days.

Gemcitabine[7]
- 800–1200 mg/m² IV days 1, 8, and 15

Cycled every 28 days.

Other microtubule inhibitors:

Vinorelbine[8]
- 25 mg/m² IV day 1 weekly

Eribulin[9]
- 1.4 mg/m² IV days 1 and 8

Cycled every 21 days.

Other single agents:

Cyclophosphamide[10]
- 50 mg PO daily on days 1–21

Cycled every 28 days.

Carboplatin[11]
- AUC 6 IV on day 1

Cycled every 21–28 days.

Docetaxel[12,13]
- 60-100 mg/m² IV day 1

Cycled every 21 days.
or
- 35 mg/m² IV weekly for 6 wks followed by a 2-week rest, then repeat[14]

Albumin-bound paclitaxel
- 100 mg/m² or 150 mg/m² IV days 1, 8, and 15

Cycled every 28 days.[15,16]
or
- 260 mg/m² IV

Cycled every 21 days.[15]

Cisplatin[17]
- 75 mg/m² IV on day 1

Cycled every 21 days.

Epirubicin[18]
- 60–90 mg/m² IV day 1

Cycled every 21 days.

Ixabepilone[19]
- 40 mg/m² IV day 1

Cycled every 21 days.

DOSING SCHEDULES FOR CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

Chemotherapy combinations:

CAF chemotherapy[20]
- Cyclophosphamide 100 mg/m² PO days 1–14
- Doxorubicin 30 mg/m² IV days 1 & 8
- 5-fluorouracil 500 mg/m² IV days 1 & 8

Cycled every 28 days.

FAC chemotherapy[21]
- 5-fluorouracil 500 mg/m² IV days 1 & 8 or days 1 & 4
- Doxorubicin 50 mg/m² IV day 1 (or by 72-h continuous infusion)
- Cyclophosphamide 500 mg/m² IV day 1

Cycled every 21 days.

FEC chemotherapy[22]
- Cyclophosphamide 400 mg/m² IV days 1 & 8
- Epirubicin 50 mg/m² IV days 1 & 8
- 5-fluorouracil 500 mg/m² IV days 1 & 8

Cycled every 28 days.

AC chemotherapy[23]
- Doxorubicin 60 mg/m² IV day 1
- Cyclophosphamide 600 mg/m² IV day 1

Cycled every 21 days.

EC chemotherapy[24]
- Epirubicin 75 mg/m² IV day 1
- Cyclophosphamide 600 mg/m² IV day 1

Cycled every 21 days.

CMF chemotherapy[25]
- Cyclophosphamide 100 mg/m² PO days 1–14
- Methotrexate 40 mg/m² IV days 1 & 8
- 5-fluorouracil 600 mg/m² IV days 1 & 8

Cycled every 28 days.

Docetaxel/capecitabine chemotherapy[26]
- Docetaxel 75 mg/m² IV day 1
- Capecitabine 950 mg/m² PO twice daily days 1–14

Cycled every 21 days.

GT chemotherapy[27]
- Paclitaxel 175 mg/m² IV day 1
- Gemcitabine 1250 mg/m² IV days 1 & 8 (following paclitaxel on day 1)

Cycled every 21 days.

Gemcitabine/carboplatin[28]
- Gemcitabine 1000 mg/m² on days 1 & 8
- Carboplatin AUC 2 IV on days 1 & 8

Cycled every 21 days.

Paclitaxel plus bevacizumab[29]
- Paclitaxel 90 mg/m² by 1 h IV days 1, 8, & 15
- Bevacizumab 10 mg/kg IV days 1 & 15

Cycled every 28 days.

DOSING SCHEDULES FOR CHEMOTHERAPY REGIMENS FOR HER-2 POSITIVE RECURRENT OR METASTATIC BREAST CANCER

Preferred first-line agents for HER2-positive disease:

Pertuzumab + trastuzumab + docetaxel[30]
- Pertuzumab 840 mg IV day 1 followed by 420 mg IV
- Trastuzumab 8 mg/kg IV day 1 followed by 6 mg/kg IV
- Docetaxel 75–100 mg/m² IV day 1

Cycled every 21 days.

Pertuzumab + trastuzumab + paclitaxel[31]
- Pertuzumab 840 mg IV day 1 followed by 420 mg IV cycled every 21 days
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV cycled every 21 days[33]
- Paclitaxel 80 mg/m² IV day 1 weekly[31]
  or
- Paclitaxel 175 mg/m² day 1 cycled every 21 days

Other first-line agents for HER2-positive disease:

Paclitaxel/carboplatin + trastuzumab[32]
- Carboplatin AUC 6 IV day 1
- Paclitaxel 175 mg/m² IV day 1

Cycled every 21 days.
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Weekly paclitaxel/carboplatin + trastuzumab[34]
- Paclitaxel 80 mg/m² IV days 1, 8, & 15
- Carboplatin AUC 2 IV days 1, 8, & 15

Cycled every 28 days.
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Trastuzumab + paclitaxel
- Paclitaxel
  - 175 mg/m² IV day 1 cycled every 21 days[35]
    or
  - 80–90 mg/m² IV day 1 weekly[36]
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Trastuzumab + docetaxel
- Docetaxel
  - 80–100 mg/m² IV day 1 cycled every 21 days[37]
    or
  - 35 mg/m² IV days 1, 8, and 15 weekly[38]
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Trastuzumab + vinorelbine[39]
- Vinorelbine
  - 25 mg/m² IV day 1 weekly
    or
  - 30–35 mg/m² IV days 1 and 8

Cycled every 21 days.
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

DOSING SCHEDULES FOR CHEMOTHERAPY REGIMENS FOR HER-2 POSITIVE RECURRENT OR METASTATIC BREAST CANCER

Trastuzumab + capecitabine[41]
- Capecitabine 1000–1250 mg/m² PO twice daily days 1–14 cycled every 21 days
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly[35,42]
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Preferred agents for trastuzumab-exposed HER2-positive disease:

Ado-trastuzumab emtansine (T-DM1)[43]
- 3.6 mg/kg IV day 1

Cycled every 21 days.

Other agents for trastuzumab-exposed HER2-positive disease:

Lapatinib + capecitabine[44]
- Lapatinib 1250 mg PO daily days 1–21
- Capecitabine 1000 mg/m² PO twice daily days 1–14

Cycled every 21 days.

Trastuzumab + capecitabine[45]
- Capecitabine 1000–1250 mg/m² PO twice daily days 1–14

Cycled every 21 days.
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly[35,42]
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

Trastuzumab + lapatinib[46]
- Lapatinib 1000 mg PO daily
- Trastuzumab
  - 4 mg/kg IV day 1 followed by 2 mg/kg IV weekly
    or
  - 8 mg/kg IV day 1 followed by 6 mg/kg IV every 21 days[33]

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一、放射治療政策

DCIS

BCT with lumpectomy followed by adjuvant radiotherapy (NSAPB B-17 Level I, EORTC 108-53, Level I), Selected group may not need adjuvant RT, Old age with adjuvant hormone therapy, low grade, small tumor side (6mm) free surgical margin (5-10mm) (ECOG 5194, Level II)

Alternative treatment: Total mastectomy

For IORT

PTV: The surgical cavity,

20Gy , prescribed to 1cm beyond the wall of surgical cavity, delivered in single fraction.

For APBI

PTV: The surgical cavity

34 Gy, prescribed to 1cm beyond the wall of surgical cavity, in 10 fractions delivered twice per day.

APBI may be administered prior to chemotherapy

For Whole Breast Irradiation

CTV: the whole breast

PTV: Expansion 5-7 mm from CTV.

Dose: 45-50Gy in 1.8-2 Gy fractions. An additional 10-16Gy dose maybe delivered to the surgical bed.

I-IIB (T1-2N0-1)

BCT with lumpectomy & surgical axillary staging, followed by adjuvant RT (Grade A)

Alternative treatment: Total mastectomy

CTV: the whole breast . RT to LN is indicated for patient with more than 4 nodes or inadequately dissected regional LN. For patient with 1-3 positive nodes, RT to LN maybe considered if high risk features present (risk of SCV failure = 20% based on retrospective data): ECE, LVSI, less than 10 LN removed, >20% of dissected nodes +, largest + node >2 cm (Strom et al. 2005)

PTV: Expansion 5-7 mm from CTV.

Dose 50Gy in 1.8-2 Gy fractions. An additional 10-16Gy dose is delivered to the surgical bed.

IIB (T3N0) - IIIC

Post mastectomy radiotherapy is indicated (GradeA, EBCTCG RT Level I)

Neoadjuvant C/T followed by surgery and surgical axillary staging, Adjuvant RT as indicated

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CTV: The ipsilateral chest wall RT to LN is indicated for patient with more than 4 nodes or inadequately dissected regional LN. For patient with 1-3 positive nodes, RT to LN maybe considered if high risk features present (risk of SCV failure = 20% based on retrospective data): ECE, LVSI, less than 10 LN removed, >20% of dissected nodes +, largest + node >2 cm (Strom et al. 2005).

PTV: Expansion 5-7 mm from CTV.

Dose: 45-50Gy in 1.8-2 Gy fractions , An additional 10-16Gy dose is delivered to the surgical bed maybe considered

IV

Systemic therapy, Palliative RT may be needed`

二、執行程序(procedures)：

Simulation

CT simulation is needed, MRI maybe required to reduce hotspot in target volume (Level I)

Patients usually treated in supine position with customized
immobilization device

Bilateral arms abducted and externally rotated
Wire all surgical scars

Mark estimated medial, lateral, cranial, and caudal field borders

Normal Tissue Constraints

Iipsilateral lung V20 is limited to <30%, V30 <20%

Left ventricle and combined bilateral ventricle limits: V5<10% and V25<5%.

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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 underlying 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
T1mi	Tumor ≦ 1 mm in greatest dimension
T1a	Tumor >1 mm but ≦ 5 mm in greatest dimension
T1b	Tumor >5 mm but ≦ 10 mm in greatest dimension
T1c	Tumor >10 mm but ≦ 20 mm in greatest dimension
T2	Tumor >20 mm but ≦ 50 mm in greatest dimension
T3	Tumor >50 mm 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 the 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 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 removed)
pNX	Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)
N0	No regional lymph node metastases
pN0	No regional lymph node metastasis identified histologically
pN0(i-)	No regional lymph node metastases 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 metastases 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	Micrometastases; or metastases in 1 to 3 axillary lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected**
pN1mi	Micrometastases (greater than 0.2 mm and/or more than 200 cells, but none greater than 2.0 mm)
pN1a	Metastases in 1 to 3 axillary lymph nodes, at least one metastasis greater than 2.0 mm
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected**
pN1c	Metastases in 1 to 3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected**

REGIONAL LYMPH NODES (N)	
pN2	Metastases in 4 to 9 axillary lymph nodes; or in clinically detected*** internal mammary lymph nodes in the absence of axillary lymph node metastases
N2a	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases
pN2a	Metastases in 4 to 9 axillary lymph nodes; or in clinically detected*** internal mammary lymph nodes in the absence of axillary lymph node metastases
N2b	Metastases in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
pN2b	Metastases in 4 to 9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)
N3	Metastases 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 metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
pN3	Metastases 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 detected by sentinel lymph node biopsy but not clinically detected**; or in ipsilateral supraclavicular lymph nodes
N3a	Metastases in ipsilateral infraclavicular lymph node(s)
pN3a	Metastases in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm); or metastases to the nfraclavicular (level III axillary lymph) nodes

REGIONAL LYMPH NODES (N)	
N3c	Metastases in clinically detected*** ipsilateral internal mammary lymph nodes in the presence of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected**
pN3b	Metastases in ipsilateral supraclavicular lymph node(s)
pN3c	Metastases in ipsilateral supraclavicular lymph nodes *Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for “sentinel node,” for example, pN0(sn).
	**Note: Not clinically detected is defined as not detected by imaging studies(excluding lymphoscintigraphy) or not detected by clinical examination. ***Note: Clinically detected is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics 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 conjunction 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 single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by mmunohistochemical (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, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow or other non-regional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm