振興醫療財團法人振興醫院

乳癌診療指引

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

參考資料：

Breast Cancer Guidelines V3.2014

全民健康保險藥品給付規定 行政院衛生署一百零三年版

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

$\overline{c}$ With

$\overline{s}$ = without

ALP= alkaline phosphatase

PBI = partial breast irradiation

CR = Complete response

PD = Progressive disease

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(2013)。
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(2013)。
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)。

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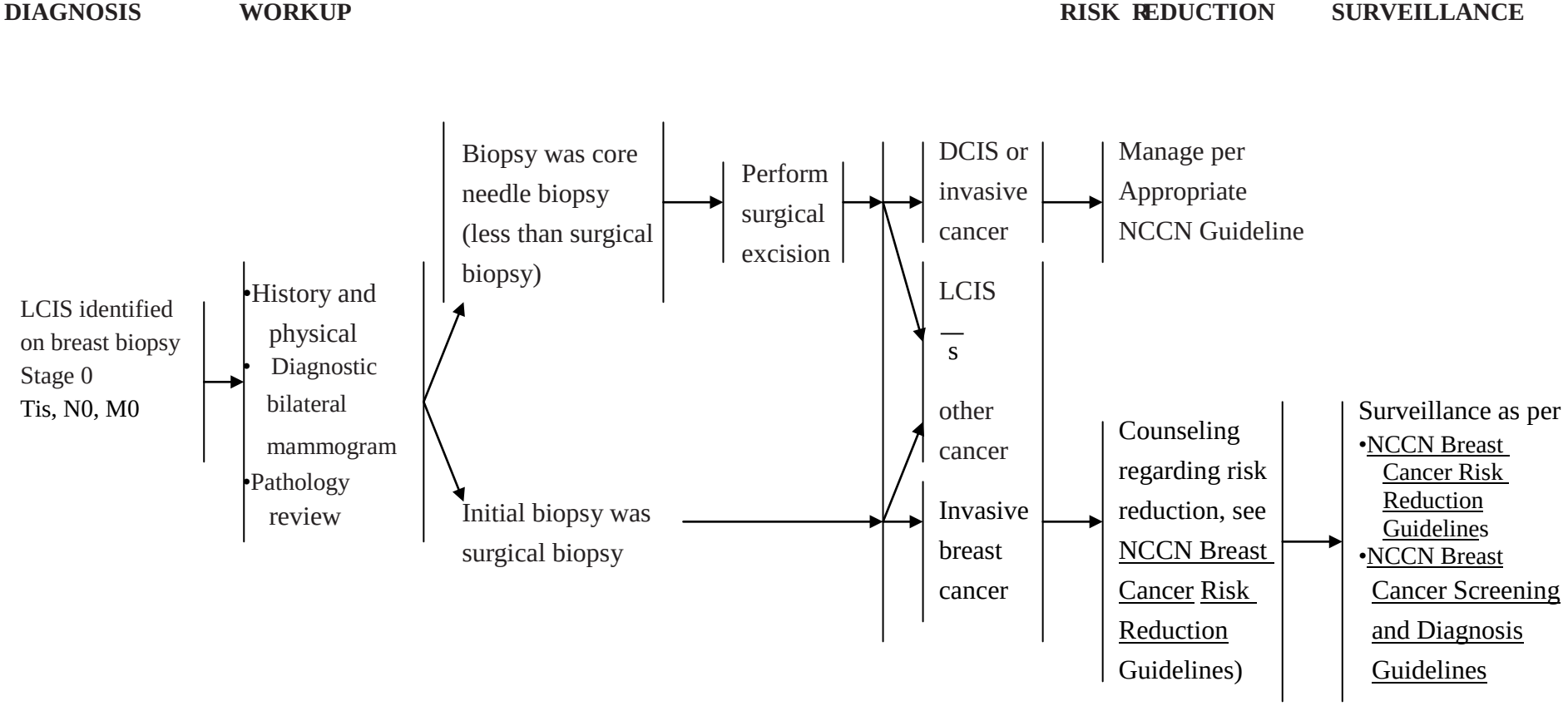


註：1.LCIS 部分，依新版 2013 NCCN 規範，針對多發性 LCIS 之四個末端乳葉侵犯，可被視為高危險浸潤性乳癌。

DIAGNOSIS	WORKUP	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 s lymph node surgery + whole breast R/T or Total mastectomy c or s sentinel node biopsy ± reconstruction or Lumpectomy s LN surgery s R/T

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

CLINICAL STAGE

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

→

WORKUP

- 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)
- Consider fertility counseling if indicated

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:

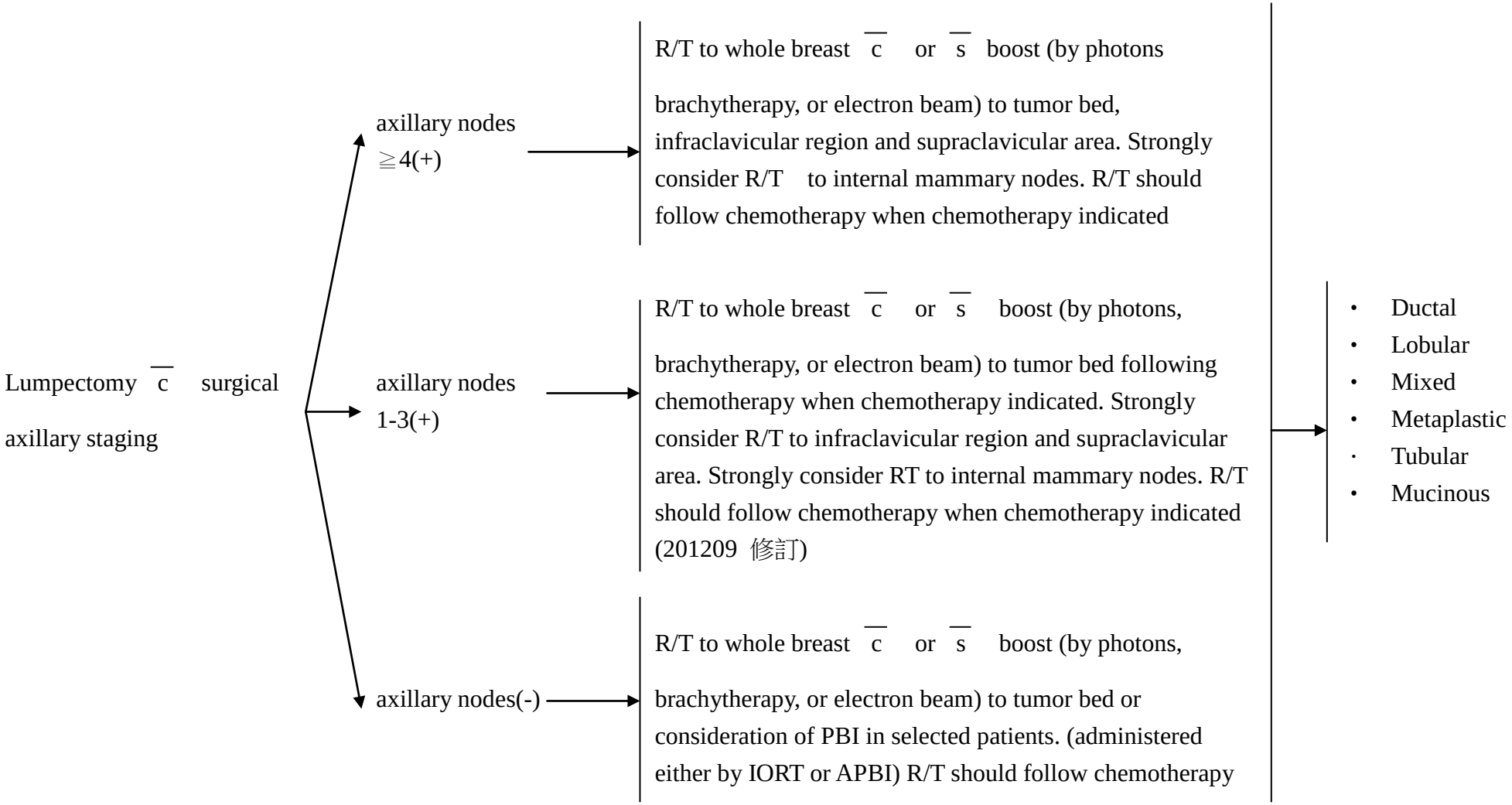
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or fluoride PET/CT
- FDG PET/CT

→

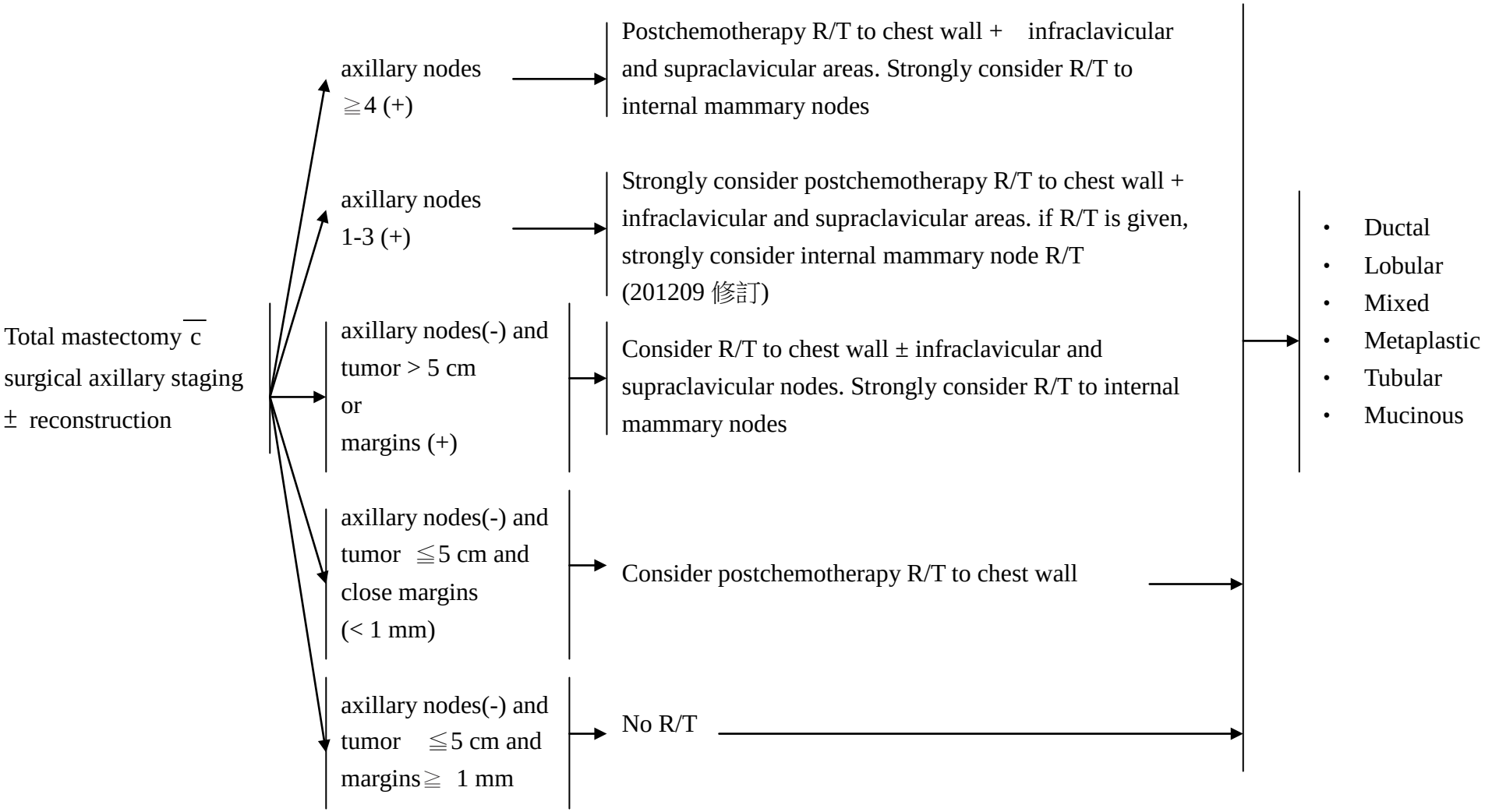
Lumpectomy with surgical axillary staging
or
Total mastectomy with surgical axillary staging ± reconstruction
or
If T2 or T3 and fulfills criteria for breast conserving therapy except for size

註 2.：2013 新版 NCCN 規範針對 MRI 使用時機有較多討論，尤其建議於乳房攝影看不到病灶的乳癌患者，針對局部治療之效果評估，MRI 並未有特別優勢。

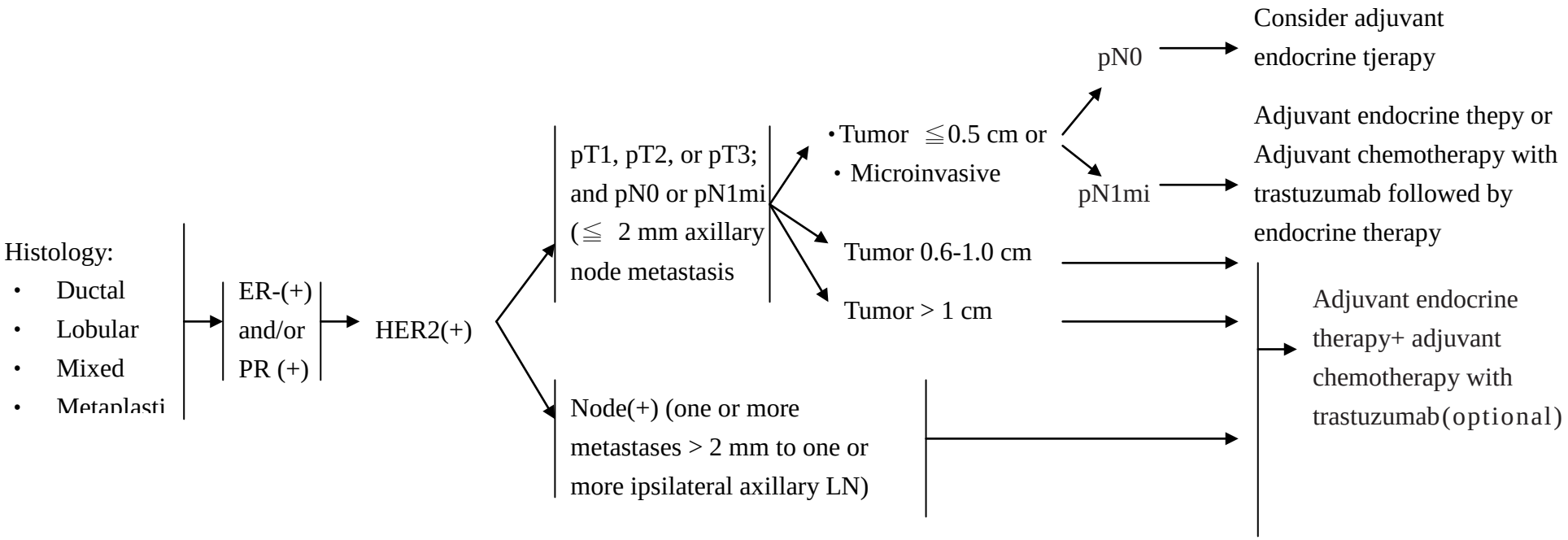
LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



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

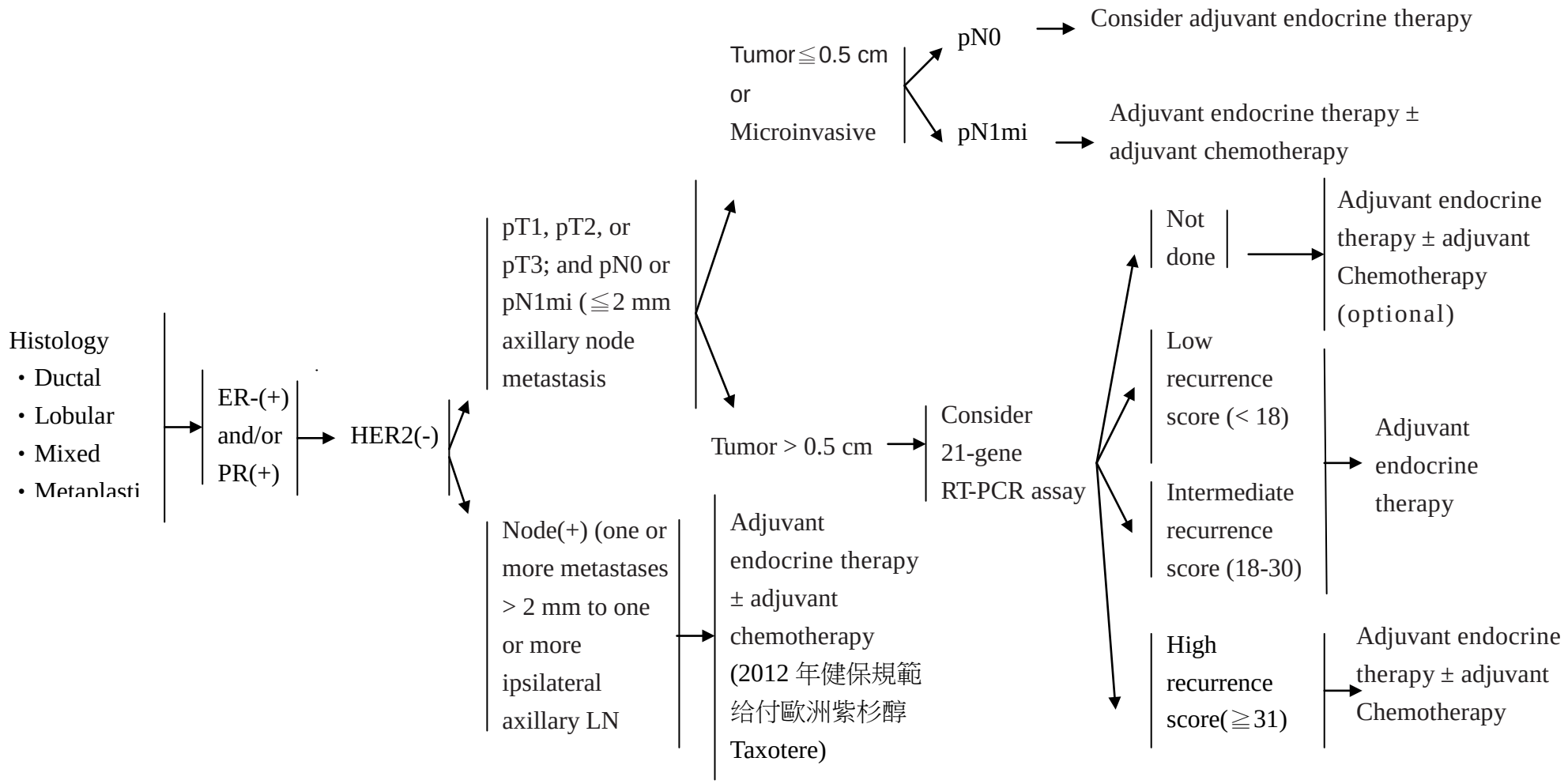


SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR POSITIVE - HER2 POSITIVE DISEASE

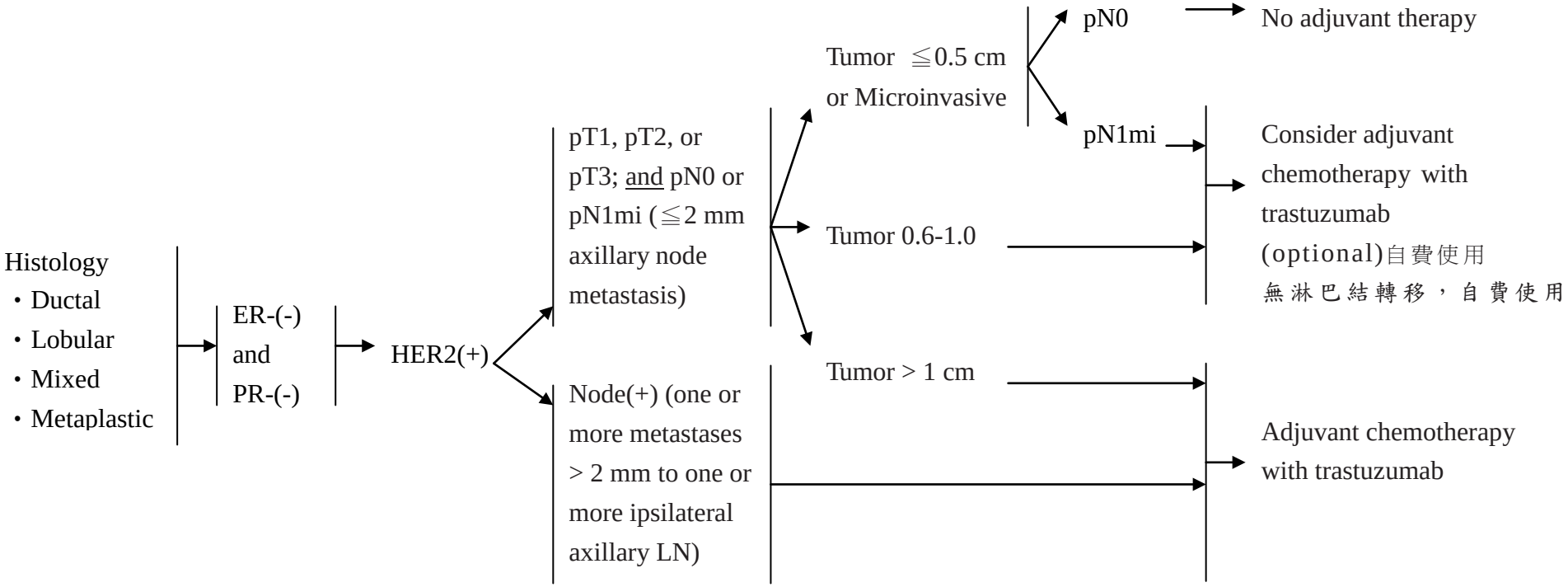


註：1. 針對浸潤性乳癌 ER(+)、Her2(+)部分、淋巴結 pN1mi→可考慮輔助內分泌治療或輔助化療加上賀癌平，再接著加上內分泌治療。
2.針對 ER(+)，Her2(+)，腫瘤>1 公分者，建議內分泌治療加上化學治療合併輔助 Herceptin。

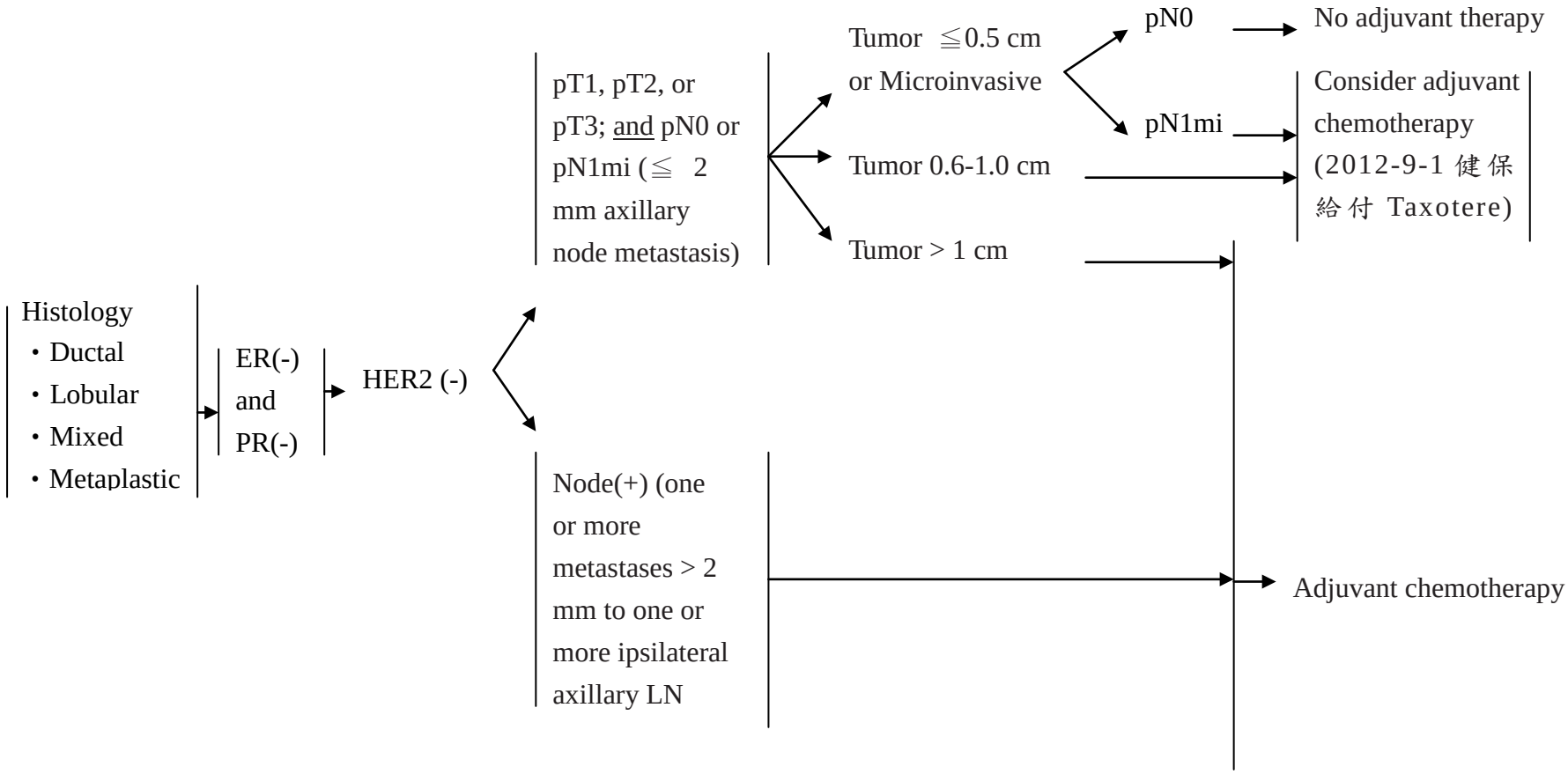
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR POSITIVE - HER2 NEGATIVE DISEASE



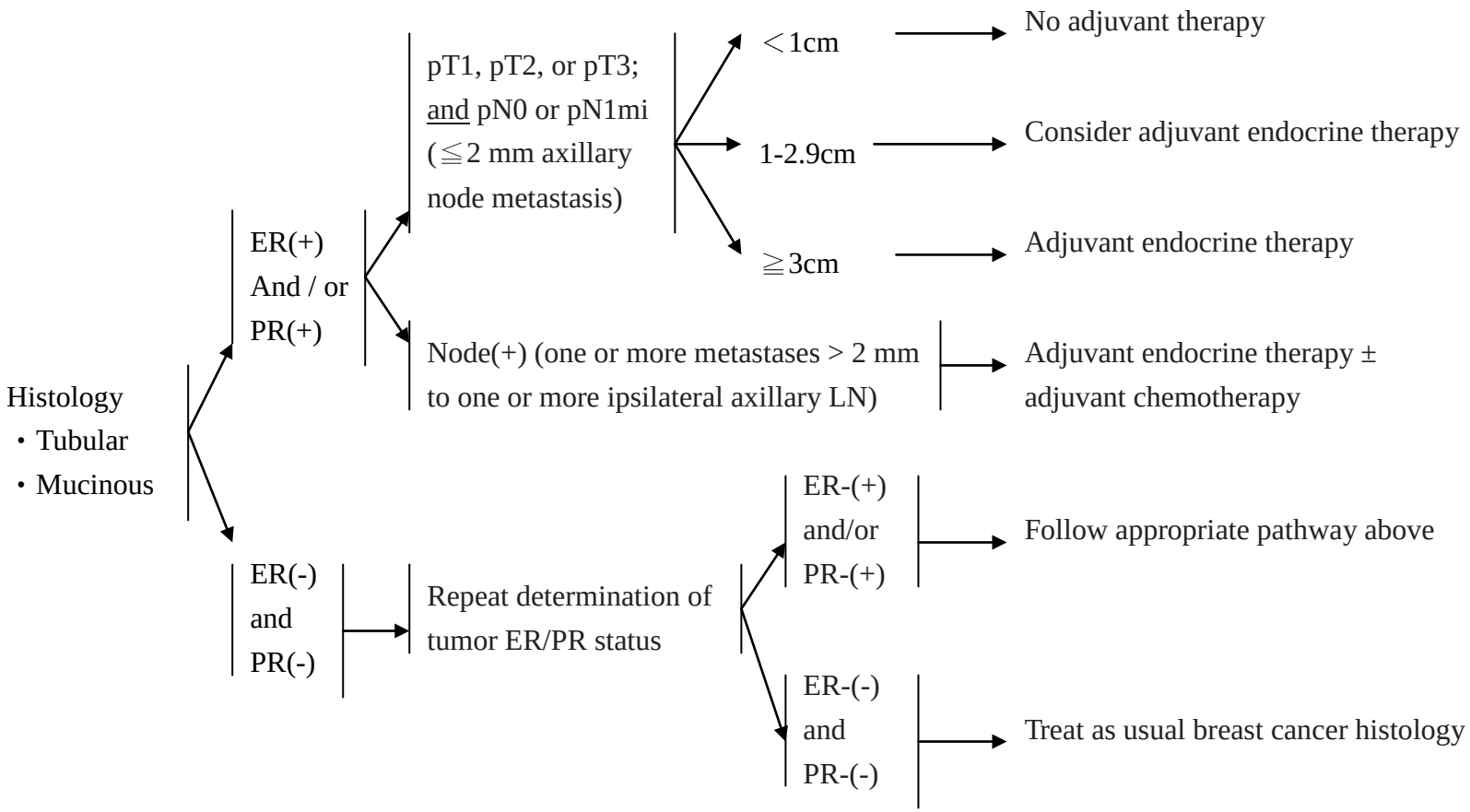
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR NEGATIVE - HER2 POSITIVE DISEASE

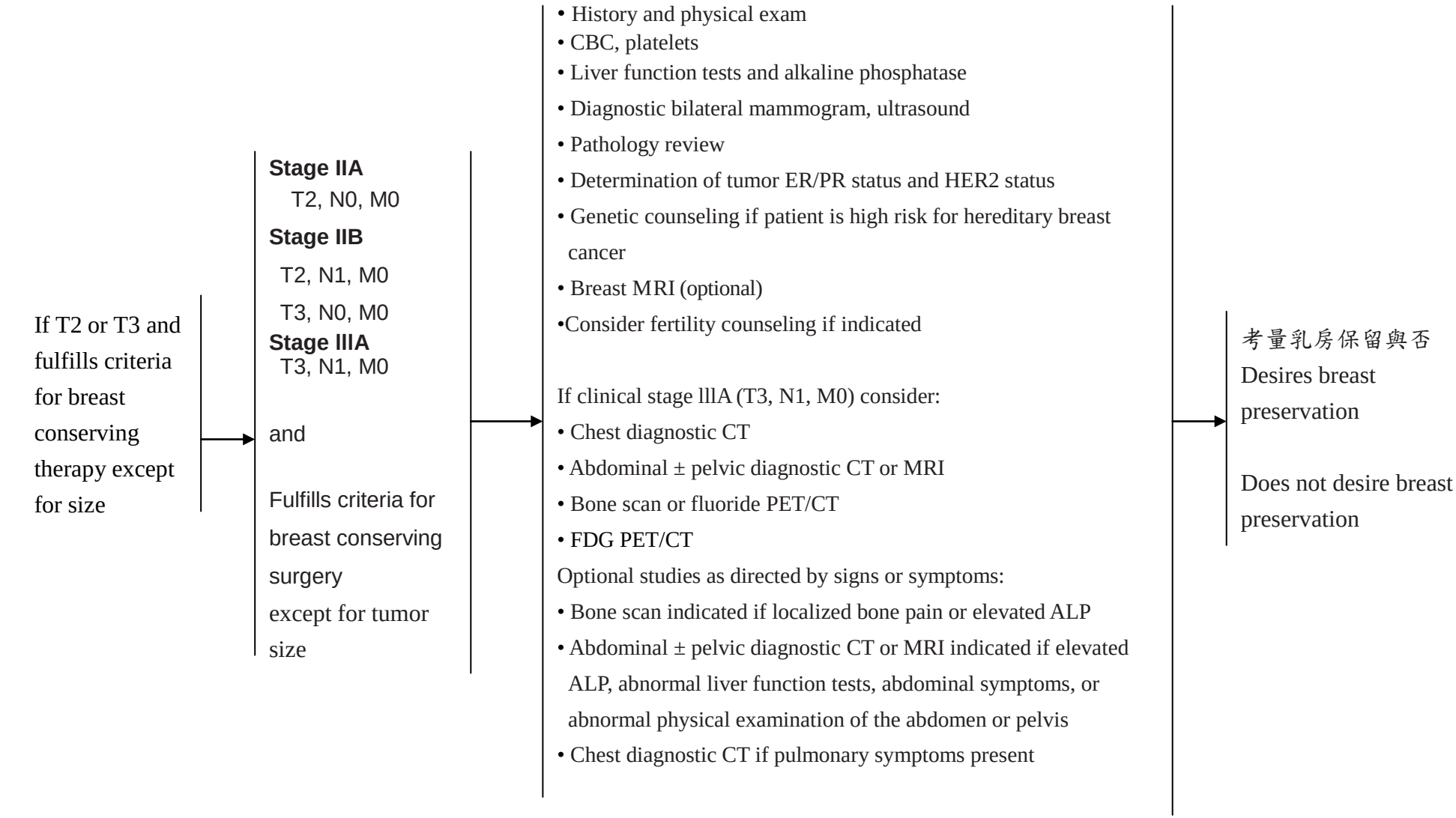


SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR NEGATIVE - HER2 NEGATIVE DISEASE

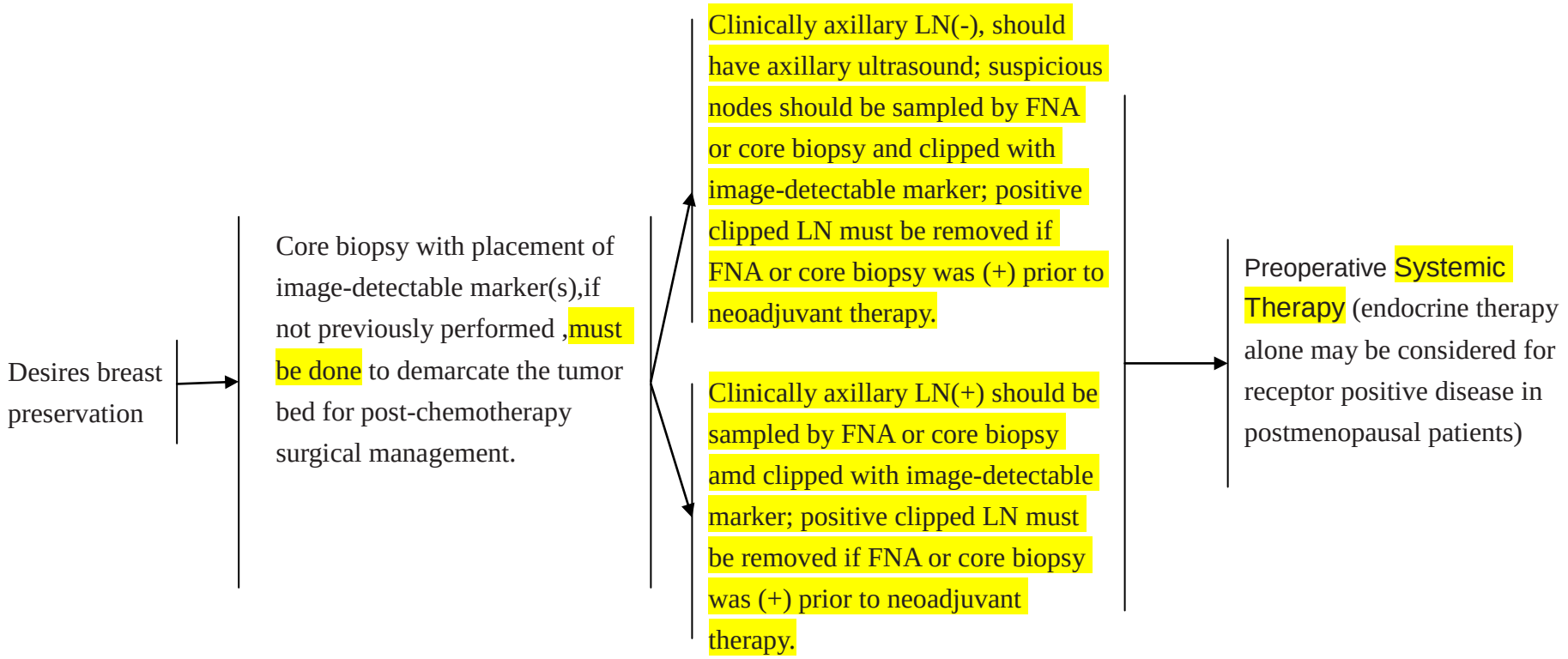


SYSTEMIC ADJUVANT TREATMENT - FAVORABLE HISTOLOGIES



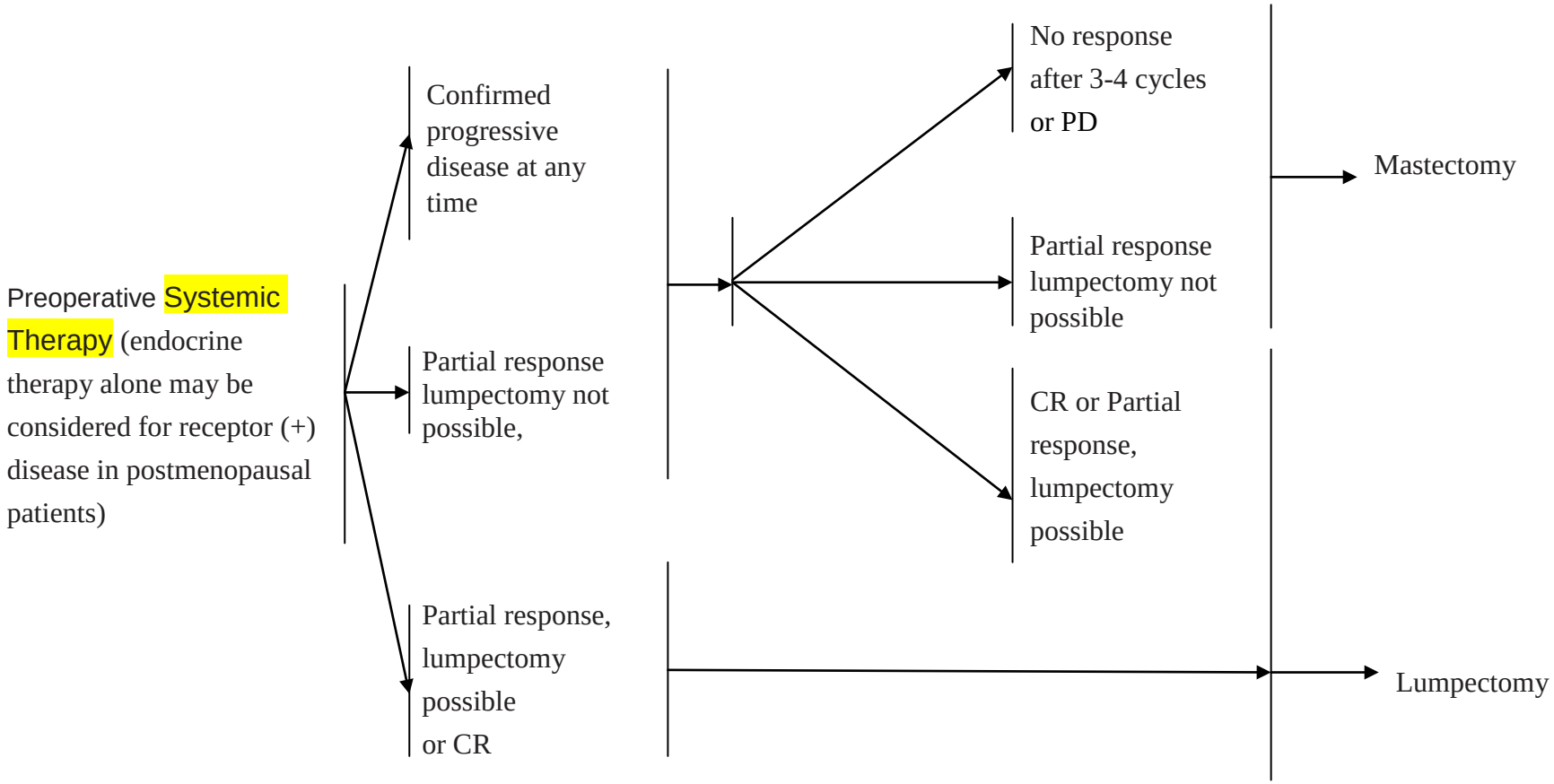

CLINICAL STAGE
WORKUP
If T2 or T3 and fulfills criteria for breast conserving therapy except for size
Stage IIA
T2, N0, M0
Stage IIB
T2, N1, M0
T3, N0, M0
Stage IIIA
T3, N1, M0
and
Fulfills criteria for breast conserving surgery except for tumor size
• History and physical exam
• CBC, platelets
• Liver function tests and alkaline phosphatase
• Diagnostic bilateral mammogram, ultrasound
• 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)
•Consider fertility counseling if indicated
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
Desires breast preservation
Does not desire breast preservation

Preoperative Systemic Therapy Breast And Axillary Evaluation



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)**



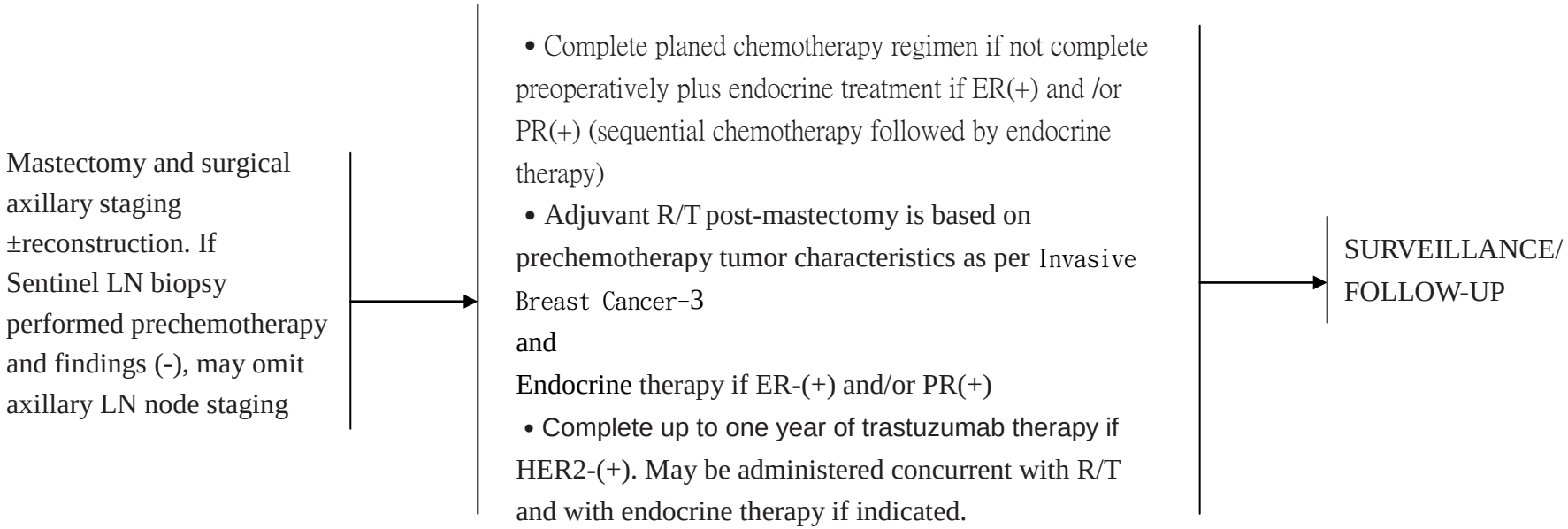
註：術前化學治療規範

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

2.≧T2,≧N1,Her2(+)，考慮加上 Pertuzumab + Trastuzumab

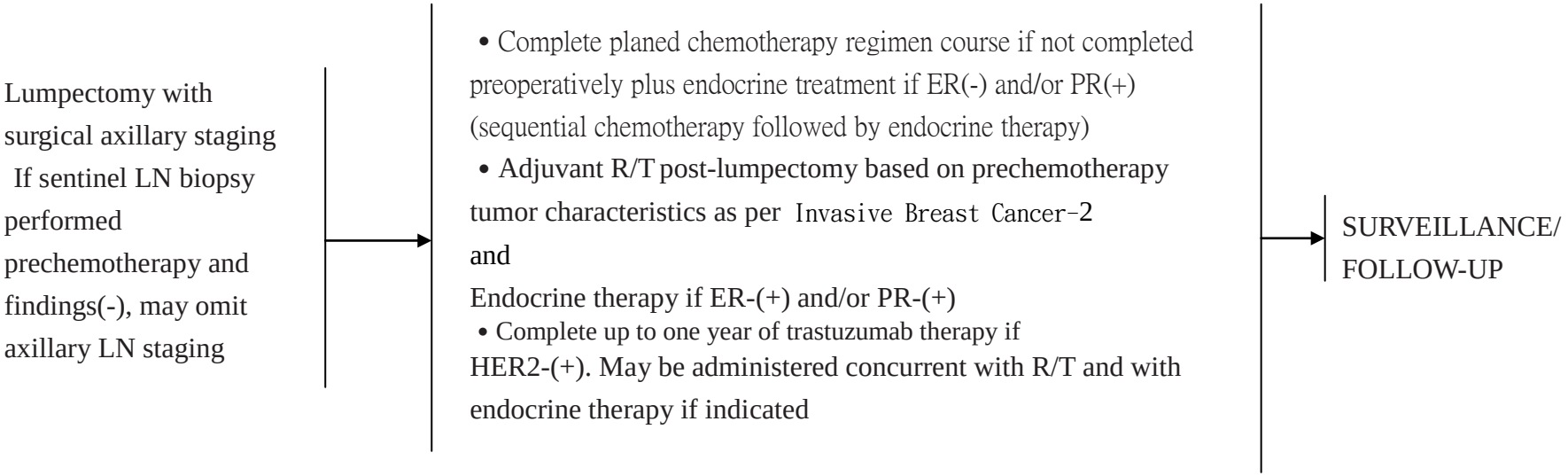
LOCAL TREATMENT

ADJUVANT TREATMENT



LOCAL TREATMENT

ADJUVANT TREATMENT



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。

CLINICAL STAGE

WORKUP

StageIII

T0, N2,M0
T1, N2, M0
T2, N2, M0
T3, N2, M0

Stage IIIA patients with T3, N1, M0 disease

See Invasive Breast Cancer-2

Stage IIIB

T4, N0, 0
T4, N1, M0
T4, N2, M0

Stage lllC

Any T, N3, M0

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- 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)
- 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

Optional studies as 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

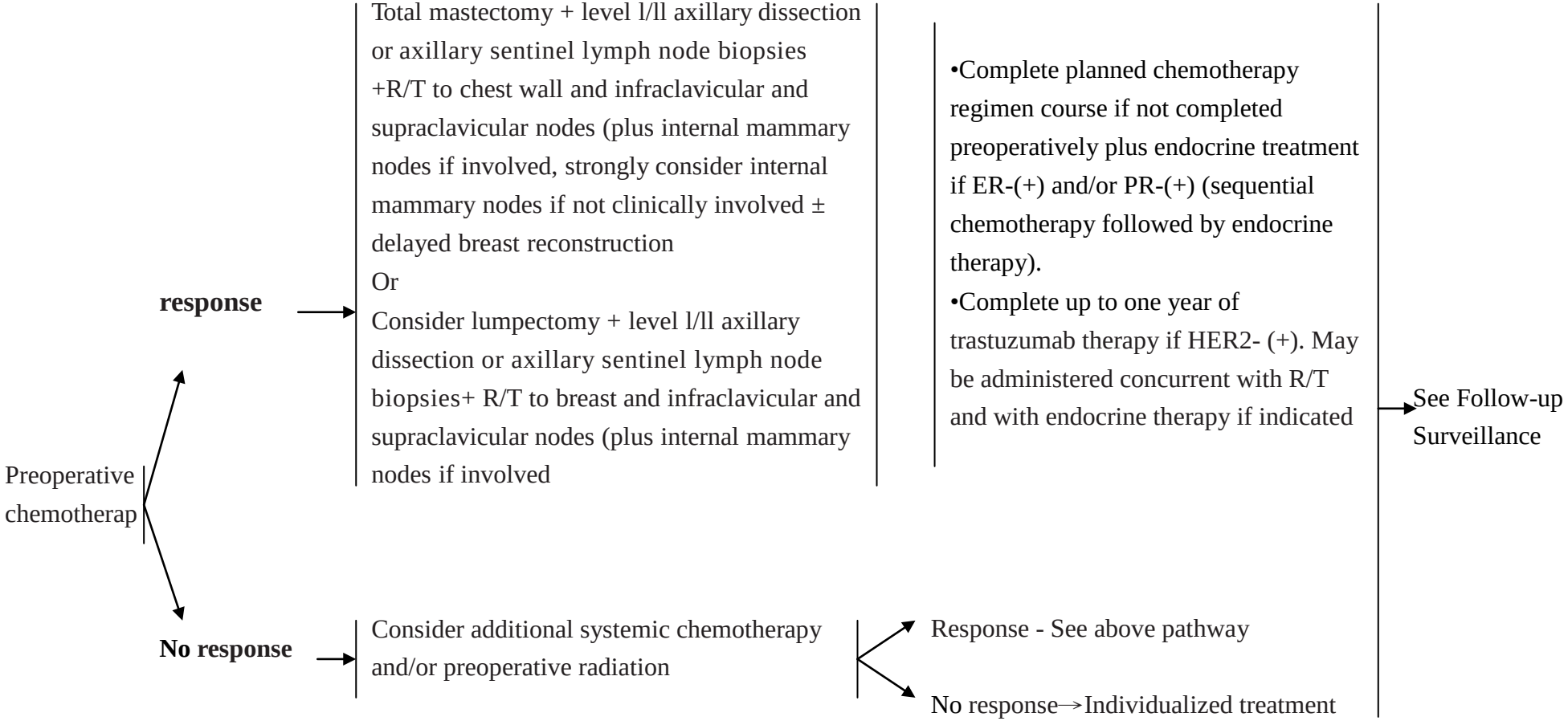
See Preoperative Chemotherapy

Stage IV

Any T, AnyN, M1

See Initial Workup for Stage IV Disease

PREOPERATIVE CHEMOTHERAPY FOR LOCALLY ADVANCY | **LOCOREGIONAL TREATMENT** | **ADJUVANT TREATMENT**



SURVEILLANCE/FOLLOW-UP

- History and physical exam every 4-6 mo for 5 y, then every 12 mo
- 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
- 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

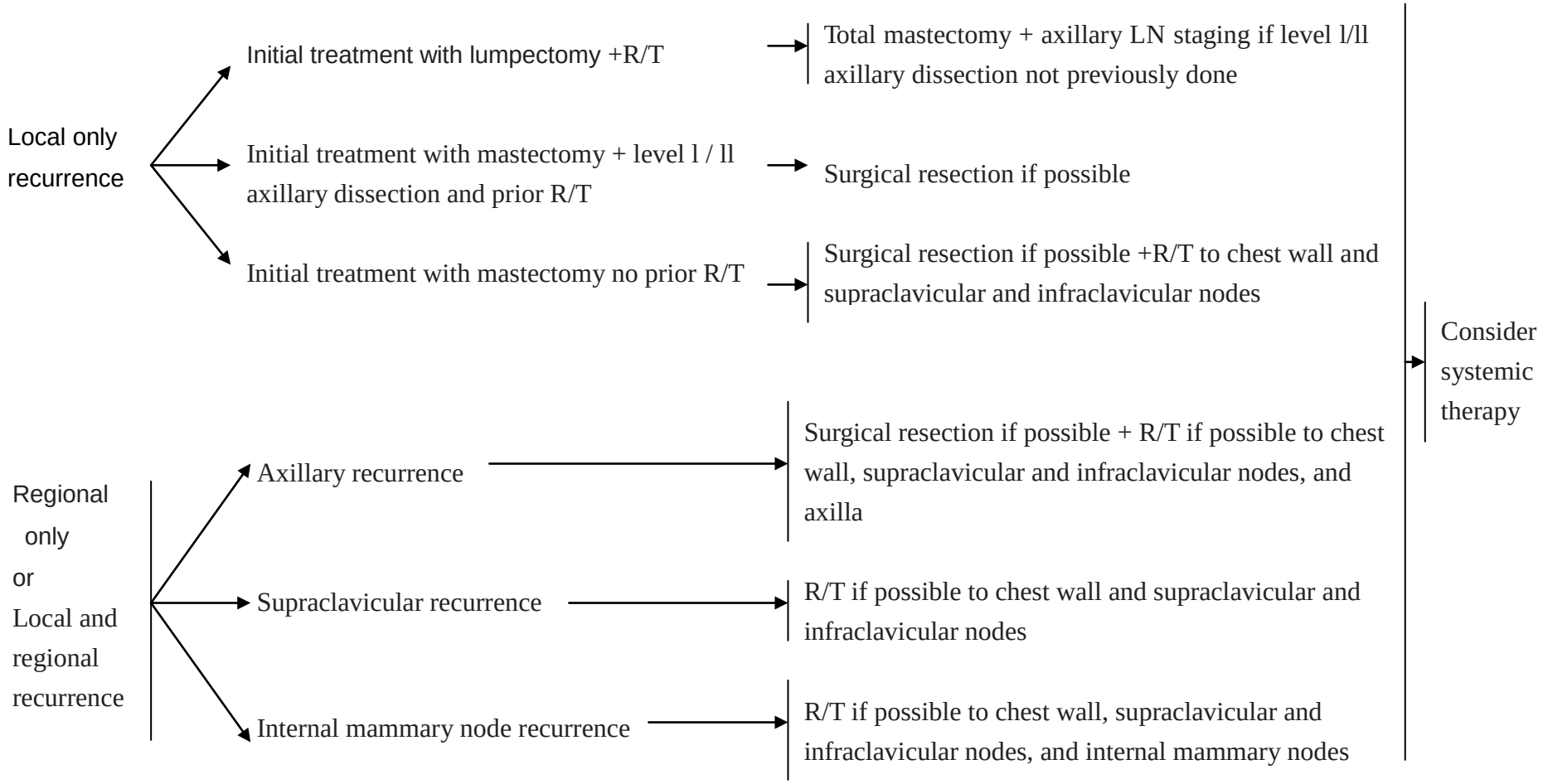
RECURRENT WORKUP or INITIAL WORKUP FOR STAGE IV DISEASE

- History and physical exam
- CBC, platelets
- Liver function tests
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Brain MRI if suspicious CNS symptoms
- Bone scan or fluoride PET/CT
- X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan
- First recurrence of disease should be biopsied
- Determination of tumor ER/PR and HER2 status if unknown, originally (-) or not over- expressed
- Genetic counseling if patient is high risk for hereditary breast cancer

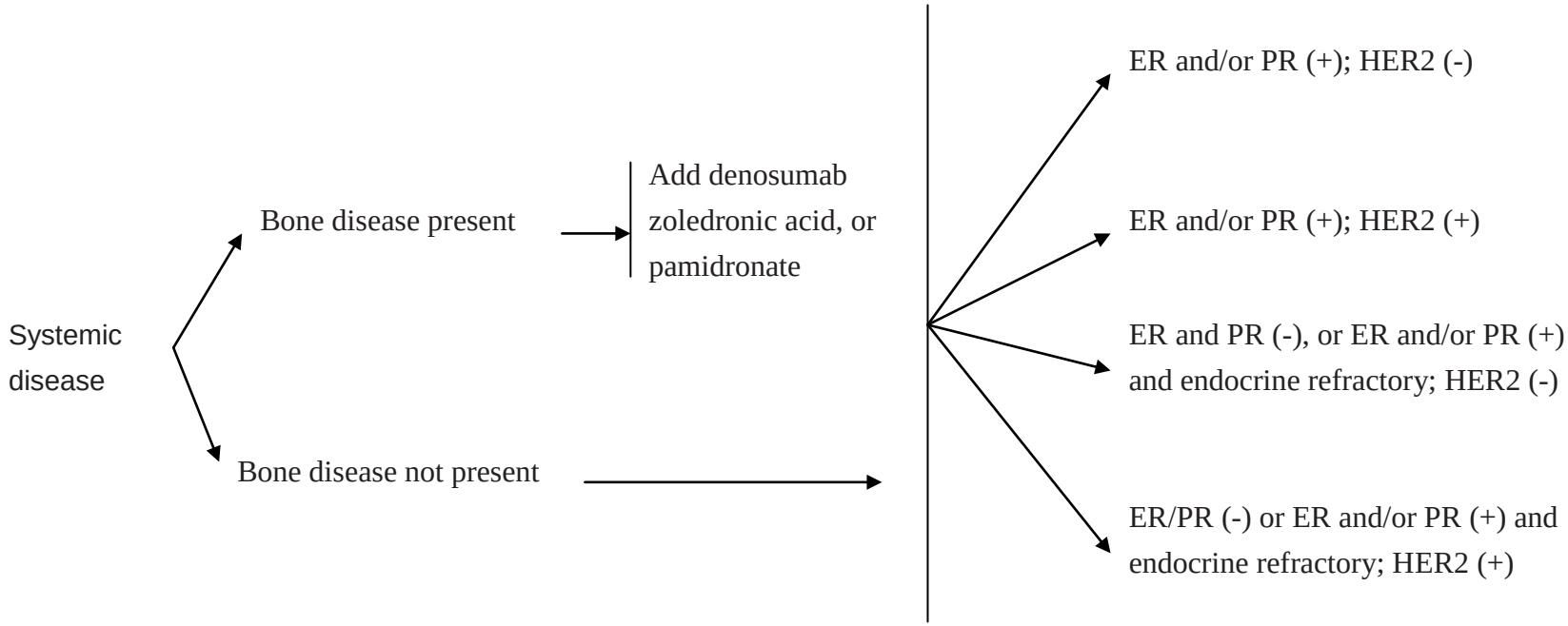
→ Locoregional disease

→ Systemic disease

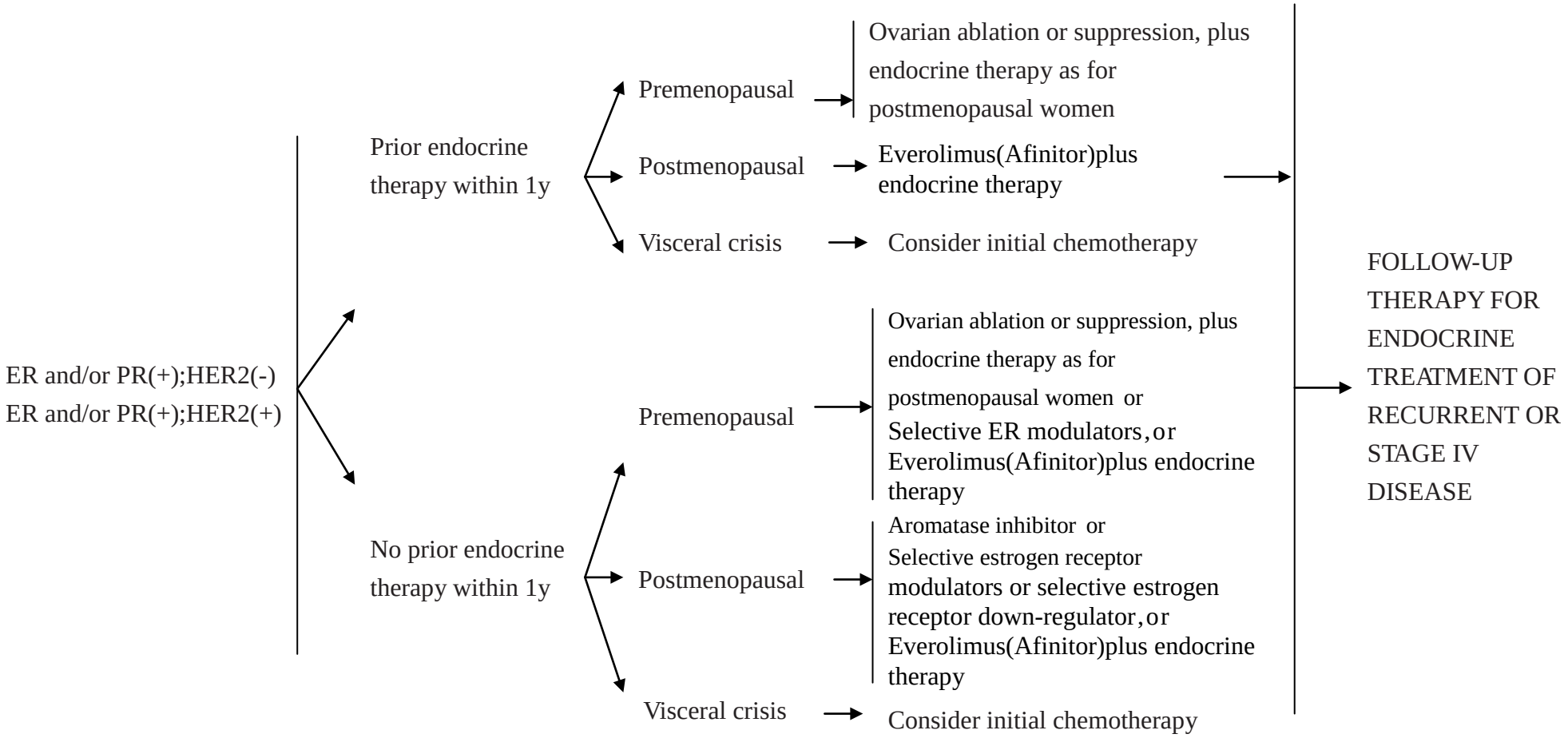
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE



SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

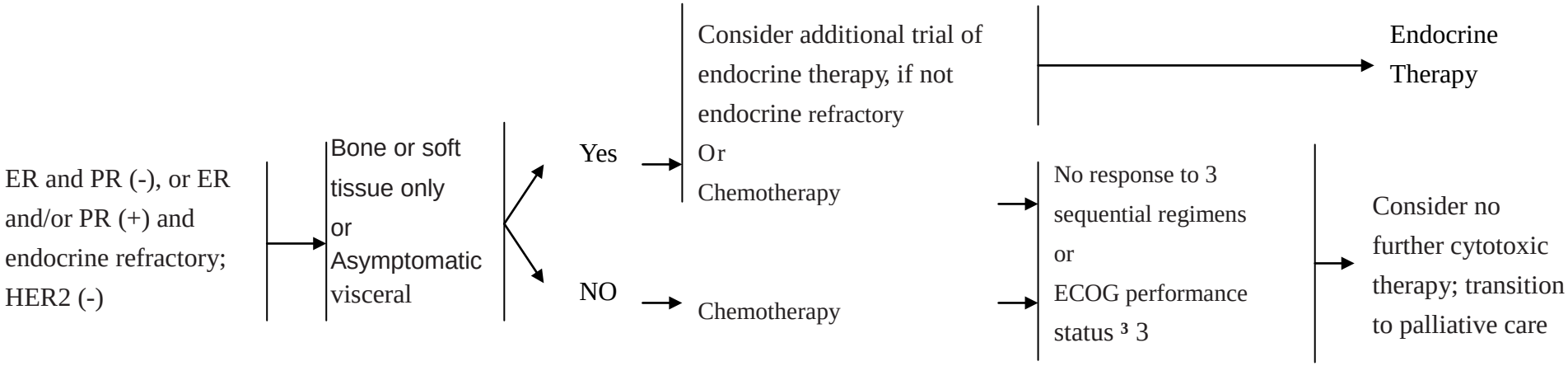


SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE ER and/or PR POSITIVE; HER2 NEGATIVE OR POSITIVE



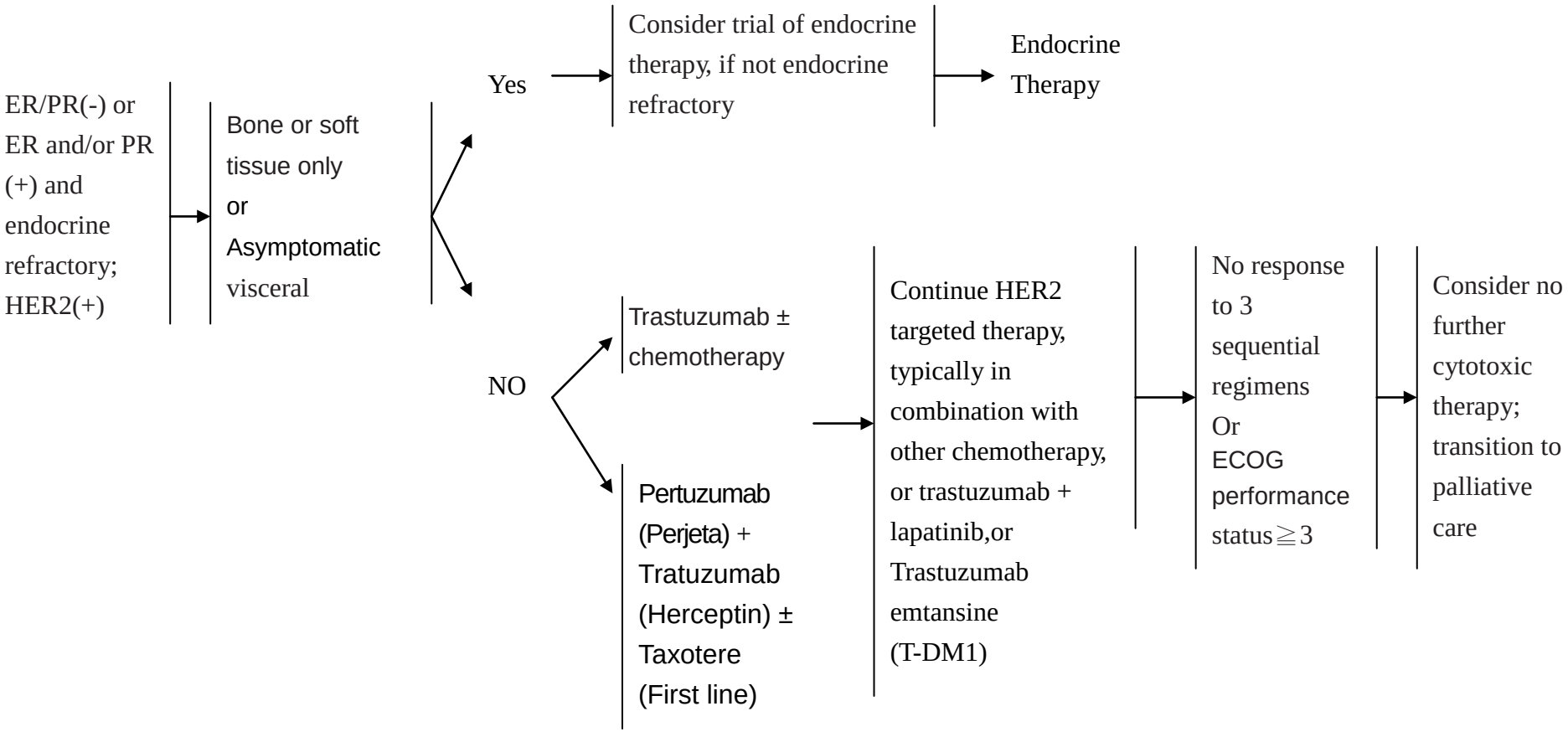
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

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

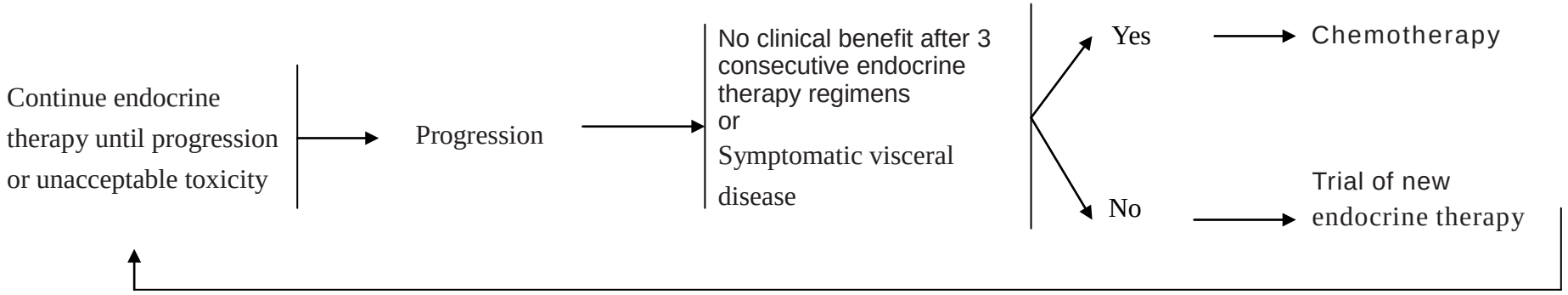


SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

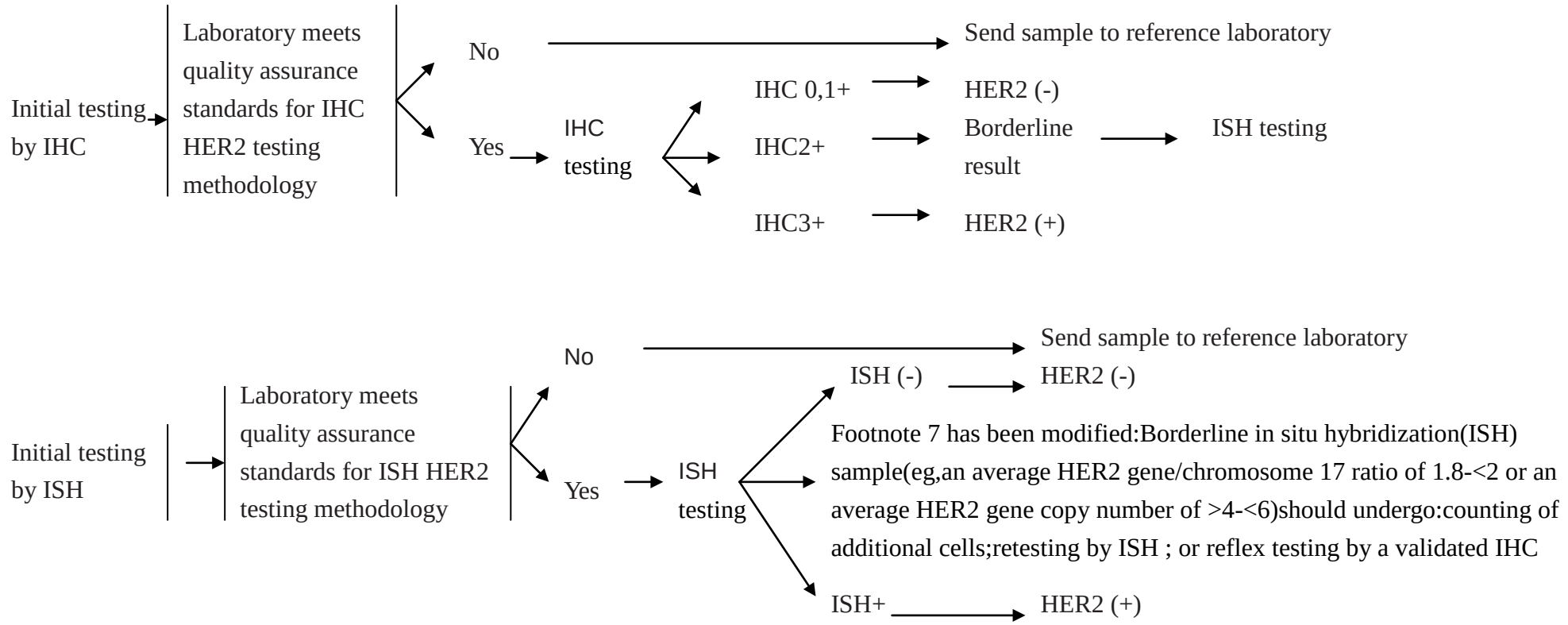
ER and PR NEGATIVE; or ER and/or PR POSITIVE and ENDOCRINE REFRACTORY; and HER2 POSITIVE



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

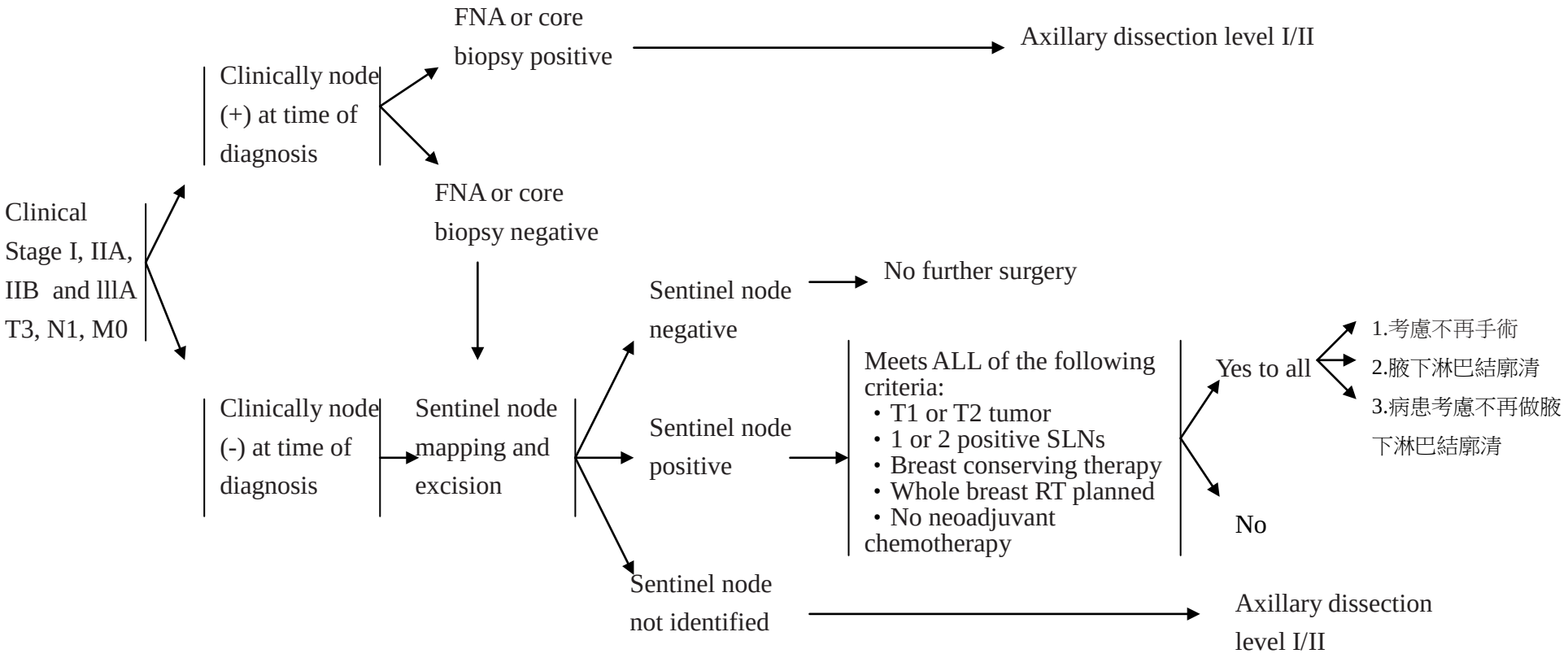


PRINCIPLES OF HER2 TESTING



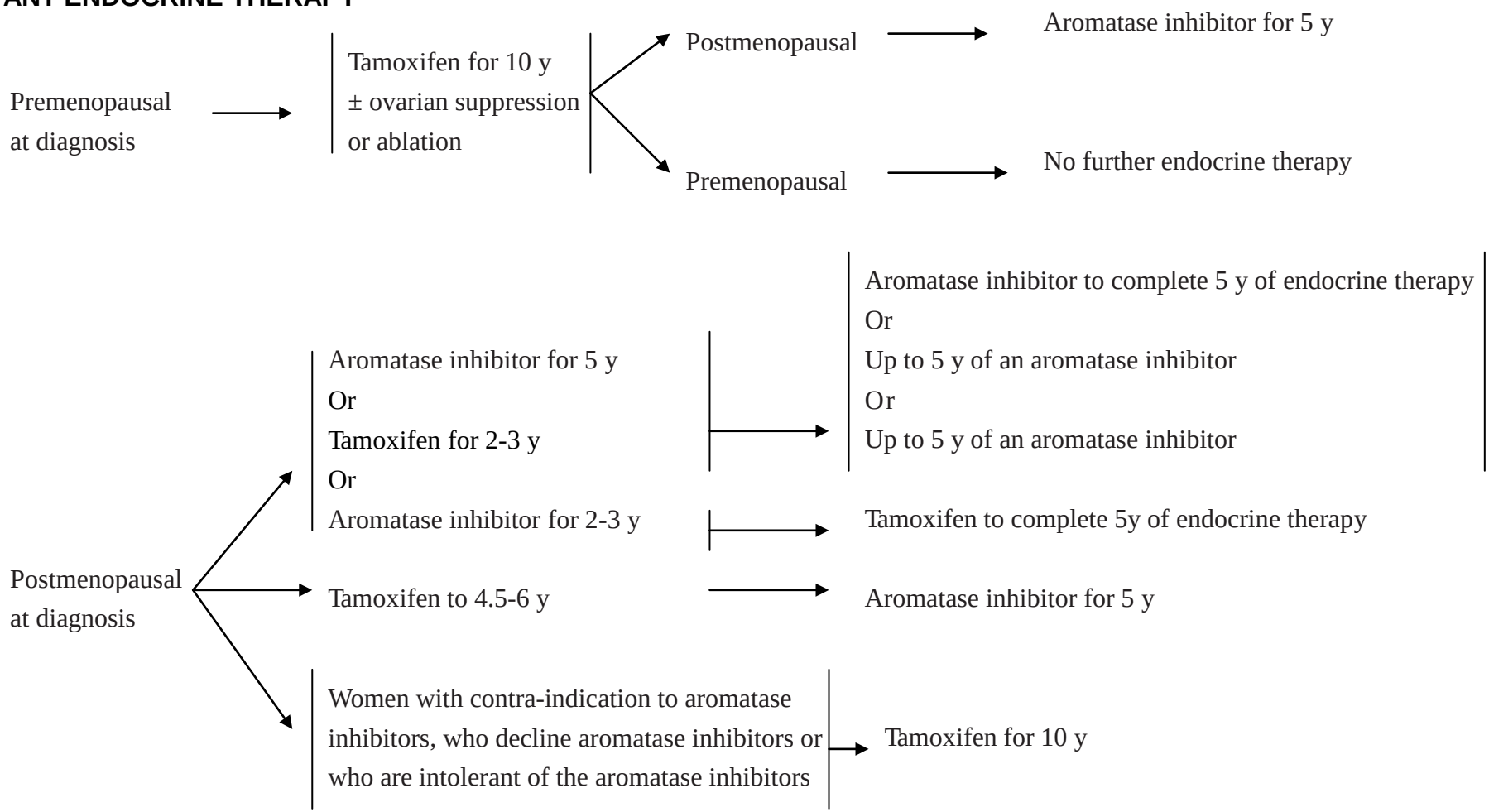
註 1.：針對 Her2 test 刪去 FISH testing borderline 部份之後的評估，可 為 Her2/neu IHC 或 Her2/neu FISH 兩者均為陽性，或任一為陽性，則視為 Her2/neu 陽性。

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。

ADJUVANT ENDOCRINE THERAPY



NON-TRASTUZUMAB CONTAINING COMBINATIONS
NEOADJUVANT REGIMENS

Dose-dense AC followed by paclitaxel

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

Cycled every 14 days for 4 cycles.
Followed by

- Paclitaxel 80 mg/m^2 by 3 h IV infusion

Cycled every 7 days for 12 weeks. (All cycles are with filgrastim support).

AC followed by paclitaxel

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

Cycled every 21 days for 4 cycles.
Followed by

- Paclitaxel 80 mg/m^2 by 1 h IV infusion weekly for 12 wks.

TC

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

Cycled every 3weeks for 4 cycles

Modified CMF

- Cyclophosphamide 600 mg/m^2 IV days 1
- Methotrexate 40 mg/m^2 IV days 1
- 5-Fluorouracil 600 mg/m^2 IV days 1

Repeat cycle every 21 days for 4 cycles

AC followed by docetaxel

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

Cycled every 21 days for 4 cycles.

Followed by

- Docetaxel 75 mg/m^2 IV on day 1

Cycled every 21 days for 4 cycles

NON-TRASTUZUMAB CONTAINING COMBINATIONS

NEO 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 1

Cycled every 21 days for 3 cycles.

Followed by

- Docetaxel 75 mg/m^2 day 1

Cycled every 21 days for 3 cycles.

NON-TRASTUZUMAB CONTAINING COMBINATIONS

NEO ADJUVANT REGIMENS

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

TRASTUZUMAB CONTAINING COMBINATIONS

NEOADJUVANT REGIMENS

AC followed by T chemotherapy with Trastuzumab

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

Cycled every 21 days for 4 cycles.

Followed by

- Paclitaxel 80 mg/m^2 by 1 h IV weekly for 12 wks 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 3 wk may be used following the completion of paclitaxel, and given to complete 1 y of trastuzumab treatment.Cardiac monitoring at baseline, 3, 6, and 9 mo.

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

Cycled every 21 days for 4 cycles. Followed by

- Paclitaxel 175 mg/m^2 by 3 h IV day 1

Cycled every 21 days for 4 cycles 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 3 wk may be used following the completion of paclitaxel, and given to complete 1y of trastuzumab treatment.Cardiac monitoring at baseline, 3, 6, and 9 mo

TRASTUZUMAB CONTAINING COMBINATIONS
NEO ADJUVANT REGIMENS

TCH

- Docetaxel 75 mg/m^2 IV day 1
- Carboplatin AUC 5 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：ACH原用藥組合為Docetaxel+ Carboplatin+ Trastuzumab

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

Reference

1 Che Lin · Dar-Ren Chen · King-Jen Chang ·Tsai-Wang Chang · Hwei-Chung Wang .A phase II study of neoadjuvant chemotherapy with docetaxel, cisplatin and trastuzumab for T2 breast cancers. ORIGINAL ARTICLE.2012; 69:1363–1368.
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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。

經事前審查核準後使用。

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.

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

TRASTUZUMAB CONTAINING COMBINATIONS

NEOADJUVANT 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 100 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.

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 75-100 mg/m^2 IV day 1

Cycled every 21 days

Pertuzumab + trastuzumab + paclitaxel

•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

•paclitaxel 80 mg/m^2 IV day 1 weekly

or

•paclitaxel 175 mg/m^2 day 1 Cycled every 21 days

Other first-line agents for Her2-positive disease:

Paclitaxel/carboplatin + trastuzumab

•Carboplatin AUC 6 IV day 1

•Paclitaxel 175 mg/m^2 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 Cycled every 21 days

術後化療

NON-TRASTUZUMAB CONTAINING COMBINATIONS

ADJUVANT REGIMENS

FAC

- 5-Fluorouracil 500 mg/m2 IV days 1 & 8 or days 1 & 4
- Doxorubicin 50 mg/m^2 IV day 1(or by 72 h continuous infusion)
- Cyclophosphamide 500 mg/m^2 IV day 1

Cycled every 21 days for 6 cycles.

AC followed by paclitaxel

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

Cycled every 21 days for 4 cycles.

Followed by

- Paclitaxel 80 mg/m^2 by 1 h IV infusion weekly for 12 wks.

TC

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

Cycled every 3weeks for 4 cycles

Modified CMF

- Cyclophosphamide 600 mg/m^2 IV days 1
- Methotrexate 40 mg/m^2 IV days 1
- 5-Fluorouracil 600 mg/m^2 IV days 1

Repeat cycle every 21 days for 4 cycles

AC followed by docetaxel

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

Cycled every 21 days for 4 cycles.

Followed by

- Docetaxel 75 mg/m^2 IV on day 1

Cycled every 21 days for 4 cycles

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 1

Cycled every 21 days for 3 cycles.

Followed by

- Docetaxel 75 mg/m^2 day 1

Cycled every 21 days for 3 cycles.

NON-TRASTUZUMAB CONTAINING COMBINATIONS

ADJUVANT REGIMENS

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 day

TRASTUZUMAB CONTAINING COMBINATIONS
PREFERRED ADJUVANT REGIMENS

AC followed by T chemotherapy with Trastuzumab-1

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

Cycled every 21 days for 4 cycles.

Followed by

- Paclitaxel 80 mg/m^2 by 1 h IV weekly for 12 wks 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 3 wk may be used following the completion of paclitaxel, and given to complete 1 y of trastuzumab treatment.Cardiac monitoring at baseline, 3, 6, and 9 mo.

TRASTUZUMAB CONTAINING COMBINATIONS

PREFERRED ADJUVANT REGIMENS

TCH

- Docetaxel 75 mg/m^2 IV day 1
- Carboplatin AUC 5 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：ACH原用藥組合為Docetaxel+ Carboplatin+ Trastuzumab

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

Reference

1 Che Lin · Dar-Ren Chen · King-Jen Chang ·Tsai-Wang Chang · Hwei-Chung Wang .A phase II study of neoadjuvant chemotherapy with docetaxel, cisplatin and trastuzumab for T2 breast cancers. ORIGINAL ARTICLE.2012; 69:1363–1368.

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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.

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

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 100 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.

Paclitaxel + trastuzumab

- 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.

Pertuzumab + trastuzumab + docetaxel followed by FEC chemotherapy

Neoadjuvant therapy:

•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/m^2 IV day 1

Cycled every 21 days for 4 cycles

Followed by adjuvant therapy

•Fluorouracil 600 mg/m^2 IV day 1

•Epirubicin 90 mg/m^2 IV day 1

•Cyclophosphamide 600 mg/m^2 day 1

Cycled every 21 days for 3 cycles

Followed by

• Trastuzumab 6 mg/kg IV every 21 days to complete 1 y of trastuzumab treatment.

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

Pertuzumab + trastuzumab + Paclitaxel followed by FEC chemotherapy

Neoadjuvant therapy:

- Pertuzumab 840 mg IV day 1 Followed by 420 mg IV
- Trastuzumab 8 mg/kg IV day 1 Followed by 6 mg/kg IV
- Paclitaxel 80 mg/m^2 IV days 1,8, and 15

Cycled every 21 days for 4 cycles

Followed by adjuvant therapy

- Fluorouracil 600 mg/m^2 IV day 1
- Epirubicin 90 mg/m^2 IV day 1
- Cyclophosphamide 600 mg/m^2 day 1

Cycled every 21 days for 3 cycles

Followed by

- Trastuzumab 6 mg/kg IV every 21 days to complete 1 y of trastuzumab treatment.

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

◆ **停經前**
- Tamoxifen(Nolvadex)

◆ **停經後**
- Arimidex(Anastrozole)
- Femara(Letrozole)

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)。

- **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

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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

.

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