中 山 醫 學 大 學 附 設 醫 院

乳 癌 診 療 指 引

乳癌治療指引制訂日期
2023/11/14 Version16.0
2022/12/27 Version15.0
2021/12/14 Version14.0
2020/12/22 Version13.0
2019/12/31 Version 12.0
2018/11/13 Version 11.0
2017/11/14 Version 10.0
2016/11/15 Version 9.0
2015/12/02 Version 8.0
2014/11/26 Version 7.0
2013/12/25 Version 6.0
2013/05/22 Version 5.1
2012/11/28 Version 5.0
2011/11/17 Version 4.0
2010/12/30 Version 3.0
2009/12/03 Version 2.0
2008/04/02 Version 1.0

本臨床指引參考歐洲腫瘤學會(ESMO)、國家衛生研究院、與美國NCCN版本、台灣乳房醫學會

乳癌多專科醫療團隊編修

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	團隊負責人

修訂內容

<table>
<tr><th>頁數</th><th>原文</th><th>修訂/增修</th></tr>
<tr><td>第 43 頁</td><td>無</td><td>增修
Trodelvy(Sacituzumab govitecan-hziy)

<table><tr><td>Trodelvy(Sacituzumab govitecan-hziy) 10mg/kg iv d1,8</td></tr><tr><td>Q3w</td></tr></table>
for TNBC or HR+/HER 2-
A Bardia, SA Hurvitz, SM Tolaney, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer: ASCENT Clinical Trial Investigators. N Engl J Med 2021;384:1529-41.</td></tr>
<tr><td>第 46 頁</td><td>無</td><td>增修
<u>Accelerated Partial Breast Irradiation (APBI)/Partial Breast Irradiation (PBI)</u>
• APBI/PBI offers comparable local control to WBRT in selected low-risk patients with early-stage breast cancer. However, the optimal external beam-APBI/PBI technique/fractionation for minimizing long-term cosmesis effects has not been determined.
▸ Patients are encouraged to participate in clinical trials.
▸ The NCCN Panel recommends APBI/PBI for any patient who is BRCA negative and meets the 2016 ASTRO criteria. The 2016 ASTRO criteria define patients aged ≥50 years to be considered "suitable" for APBI/PBI if:
◊ Invasive ductal carcinoma measuring ≤2 cm (pT1 disease) with negative margin widths of ≥2 mm, no LVI, and ER-positive
or
◊ Low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.
• RT dosing:
<table><tr><th>Regimen</th><th>Method</th><th>Reference</th></tr><tr><td>30 Gy/5 fractions QOD (preferred)</td><td>External beam RT (EBRT)[e]</td><td>Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. Eur J Cancer 2015;51:451-463.
Meattini I, Marrazzo L, Saieva C, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: Long-term results of the randomized phase III APBI-IMRT-Florence Trial. J Clin Oncol 2020;38:4175-4183.</td></tr></table></td></tr>
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目　　錄

一、何謂乳癌

乳癌是由乳房乳腺管細胞或是腺泡細胞經由不正常分裂、繁殖所形成之惡性腫瘤。這些惡性腫瘤除了侵犯局部器官 (乳房)，更可能轉移到遠處器官如骨骼、肺、肝、腦等，而破壞身體重要器官的功能，造成身體健康之損害，甚至危害生命。

二、乳癌的診斷

整體健康狀況的評估	病史 家族史 停經狀態 理學檢查 全血球記數 肝臟,腎臟,和心臟功能測試(對於計畫使用anthracycline且/或trastuzumab的病人),鹼性磷酸酶和鈣離子,B肝及C肝抗原抗體的檢測
原發腫瘤的評估	理學檢查,乳房攝影 乳房超音波 乳房磁振造影(MRI) 特定族群** 粗針切片以及組織學,分化程度及ER,PgR,HER-2,Ki67 TILs#的檢查
局部淋巴結的評估	理學檢查 超音波 如果懷疑轉移要做超音波指引生檢切片確認
遠處轉移的評估	理學檢查 Stage II以上建議做胸腔電腦斷層檢查 Stage III以上建議做正子造影檢查.骨頭掃描(optional)
MRI,magnetic resonance imaging(磁振造影) ER,oestrogen receptor(雌激素接受器) PgR,progesterone receptor(黃體激素接受器) HER2,human epidermal growth factor 2 receptor(人類表皮生長因子2接受器) **有BRCA家族史；Lobular cancer；Dense breast；懷疑可能多發性的乳癌. #Tumor-infiltrating lymphocytes(分離腫瘤浸潤淋巴細胞)	

*若要施行先導性治療時-腫瘤切片時，建議在腫瘤組織中放置標誌物(以確保切除正確的部位) –optional(自費選項)。

三、乳癌的分期及風險評估(Staging and risk assessment)

1.若臨床檢查和超音波評估懷疑有淋巴轉移，建議用超音波引導的細針抽吸或粗針切片來證實。(IIIA)

2.病患若計畫使用 anthracyclines and trastuzumab 作輔助治療時，建議評估心臟功能。(IA)

3.術後病理應根據 pTMN 系統來評估包括：數目，位置，移除的腫瘤最大直徑，組織形態，腫瘤分級，血管浸潤，生物標識分析，切除邊緣評估，移除總數，淋巴結陽性數目和轉移程度。(IIIA)

4.當傳統的檢查(如 CT, echo)評估有不足時，可以使用 FDG-PET-CT[V,A]。PET-CT 也可用於高風險的病人[V,B]

5.由於 B 肝在台灣盛行率高，建議在化療前做 B 肝抗原抗體檢測，必要時要服用抗病毒藥物，以避免化療時 B 肝被再活化，發生猛爆性肝炎。

6.無症狀的遠端轉移並不常見，不建議術前大規模的實驗性檢查或影像檢查，但若病患有淋巴轉移，腫瘤>5 公分，具侵犯性的生物亞型或實驗性檢查懷疑有移轉現象，則建議 Chest CT,Abdomenal US,Bone scan 的檢查。

7.乳房 MRI 建議使用在下列幾種病人：有 BRCA 家族史；Lobular cancer；Dense breast；懷疑可能多發性的乳癌；傳統影像和身體檢查有落差(例如大小不一)；在前導性治療之前，及前導性治療後的評估；當傳統檢查無法提供完整的資訊時(例如腋下淋巴轉移，但找不到原發乳房腫瘤)；有用植入物時。

8.TIL scoring 有其預測乳癌癒後的價值(尤其在 Her-2 及 TNBC)，可以考慮放到病理報告知中。

9.EBC Systemic treatment: ER(+)Her-2(-)的病人，可考慮利用 OncotypeDx, MammaPrint, PAM50, EndoPredict 等多基因分析工具，來幫助決定病人接受輔助性化療的益處。

四、乳癌的治療與診療指引

乳癌亞型的定義(ESMO臨床指引推薦)

內在亞型	臨床病理分級	註記
管腔A型 Luminal A	**Luminal A-like**: ER(+) HER2(-) Ki67 <20% PR(+) >20% 分子印記檢測為低風險	
管腔B型 Luminal B	**Luminal B-like(HER2-negative):** ER(+) HER2(-) 且Ki67高或PgR低 分子印記檢測為高風險 **Luminal B-like(HER2-positive):** ER(+) HER2(+) 任何Ki67 任何PgR	Ki 67:臨界值為20%(>30%為明顯偏高.<10%為明顯偏低) PR: 臨界值為20%
HER2過度表現	**HER2-positive(non-luminal):** HER2(+) ER(-) PgR(-)	HER2+ 定義為IHC+++或FISH為陽性反應
類基底細胞癌 Basal-like	**三陰性**: ER(-) PgR(-) HER2(-)	大約有80%三陰性和basal-like亞型有重疊，但是三陰性還包含了一些特別的組織學類型，例如:(典型的)髓質(medullary)和腺樣囊性癌(adenoid cystic carcinoma)，其預後較好
ER,oestrogen receptor(雌激素接受器) PgR,progesterone receptor(黃體激素接受器) HER2,human epidermal growth factor 2 receptor(人類表皮生長因子2接受器)		

	Clinical	Pathological
Primary tumor (T)	**Tx** Primary tumor is unable to be assessed. **T0** No evidence of primary tumor. **Tis (DCIS)*** Ductal carcinoma in situ. *Note: Lobular carcinoma in situ (LCIS) is a benign entity and is removed from TNM staging in the AJCC Cancer Staging Manual, 8th Edition. **Tis (Paget)** Paget disease of the nipple not associated with invasive carcinoma and/or DCIS in the underlying breast parenchyma. Carcinoma in the breast parenchyma associated with Paget disease is categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget 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 (round any measurement 1.0 to 1.9 mm to 2 mm). **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 the skin (ulceration or skin nodules). Invasion of the dermis alone does not qualify as T4. **T4a** Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4 **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**Inflammatory carcinoma is restricted to cases with typical skin changes involving one-third or greater 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) **N0** No regional lymph node metastases (by imaging or clinical examination) **N1** Metastases to movable ipsilateral level I, II axillary lymph node(s) **cN1mi****Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm).	**pNX** Regional lymph nodes cannot be assessed (e.g. previously removed or not removed for pathological study) **pN0** No regional lymph node metastasis identified or isolated tumor cells (ITCs) only. **pN0(i+)** ITCs only (malignant cells clusters no larger than 0.2 mm) in regional lymph node(s) **pN0(mol+)** Positive molecular findings by reverse

	N2 Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detectedk ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases **N2a** Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures **N2b** Metastases only in ipsilateral internal mammary nodes and in the absence of-axillary node metastases. **N3** Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in 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. **N3a** Metastases in ipsilateral infraclavicular lymph node(s) **N3b** Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s) **N3c** Metastases in ipsilateral supraclavicular lymph node(s) Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or fine needle aspiration/core needle biopsy respectively. *The cNX category is used sparingly in cases where regional lymph nodes have previously been surgically removed or where there is no documentation of physical examination of the axilla. **cN1mi is rarely used but may be appropriate in cases where sentinel node biopsy is performed before tumor resection, most likely to occur in cases treated with neoadjuvant therapy.	transcriptase polymerase chain reaction (RT-PCR); no ITCs detected **pN1** Micrometastases, or metastases in 1-3 axillary lymph nodes, and/or clinically negative internal mammary nodes with micro- or macrometastases detected by sentinel lymph node biopsy. **pN1mi** Micrometastases (>0.2 mm and/or >200 cells, but none >2.0 mm) **pN1a** Metastases in 1-3 axillary lymph nodes, at least one metastasis >2.0 mm **pN1b** Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs. **pN1c** pN1a and pN1b combined **pN2** Metastases in 4-9 axillary lymph nodes, or positive ipsilateral internal mammary lymph nodes by imaging in the absence of axillary lymph node metastases. **pN2a** Metastases in 4-9 axillary lymph nodes (at least one tumour deposit >2.0 mm) **pN2b** Metastasis only in clinically detected internal mammary nodes with or without microscopic confirmation; with pathologically negative axillary nodes. **pN3** Metastases in≧ 10 axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in ipsilateral internal mammary lymph nodes by imaging in the presence of one or more positive level I, II axillary lymph nodes; or in more than three 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. **pN3a** Metastases in ≧10 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm); or

		metastases to the infraclavicular (level III axillary lymph) nodes. **pN3b** pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b **pN3c** Metastases in ipsilateral supraclavicular lymph nodes * The suffixes (sn) and (f) should be added to the N descriptor to note confirmation by sentinel lymph node biopsy or fine needle aspiration/core needle biopsy, respectively, with no further resection of lymph nodes.
Distant metastasis (M)	**M0** No clinical or radiographic evidence of distant metastases **cM0(i+)** No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumour cells in circulating blood, bone marrow or other non-regional nodal tissue that are not >0.2 mm in a patient without symptoms or signs of metastases **cM1** Distant metastases detected by clinical and radiographic means p**M1** Any histologically proven metastases in distant organs; or if in non-regional nodes, metastases greater than 0.2 mm	

●**Primary tumor (T)** 取消小葉原位癌（LCIS）的pTis定義。LCIS 為良性病变，從TNM 分期中刪除。

Histologic Grade (G)

All invasive breast carcinomas should be assigned a histologic grade. The Nottingham combined histologic grade (Nottingham modification of the SBR grading system) is recommended and is stipulated for use by the College of American Pathologists (see www.cap.org). The grade for a tumor is determined by assessing morphologic features (tubule formation, nuclear pleomorphism, and calibrated mitotic count), assigning a value from 1 (favorable) to 3 (unfavorable) for each feature, and totaling the scores for all three categories. A combined score of 3–5 points is designated as grade 1; a combined score of 6–7 points is grade 2; a combined score of 8–9 points is grade 3. The use of subjective grading alone is discouraged.

Invasive Cancer Histologic Grade (Scarff-Bloom-Richardson [SBR] Grading System, Nottingham Modification)

GX Grade cannot be assessed
G1 Low combined histologic grade (favorable); SBR score of 3-5 points
G2 Intermediate combined histologic grade (moderately favorable); SBR score of 6-7 points
G3 High combined histologic grade (unfavorable); SBR score of 8-9 points

Ductal Carcinoma in situ: Nuclear Grade

GX Grade cannot be assessed G1 Low nuclear grade
G2 Intermediate nuclear grade G3 High nuclear grade

AJCC Anatomic Stage Groups

The Anatomic Stage Group table should only be used in global regions where biomarker tests are not routinely available. Cancer registries in the U.S. must use the Clinical and Pathological Prognostic Stage Group tables for case reporting.

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

Notes:
1.T1 includes T1mi
2.T0 and T1 tumors with nodal micrometastases (N1mi) are staged as Stage IB.
3.T2, T3, and T4 tumors with nodal micrometastases (N1mi) are staged using the N1 category
4.M0 includes M0(i+).
5.The designation pM0 is not valid; any M0 is clinical.
6.If a patient presents with M1 disease prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.
7.Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided the studies are performed within 4 months of diagnosis in the absence of disease progression, and provided the patient has not received neoadjuvant therapy.
8.Staging following neoadjuvant therapy is designated with “yc” or “yp” prefix to the T and N classification. There is no anatomic stage group assigned if there is a complete pathologic response (pCR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

Clinical Prognostic Stage

Clinical Prognostic Stage applies to ALL patients with breast cancer for clinical classification and staging. It uses clinical tumor (T), node (N) and metastases (M) information based on history, physical examination, any imaging performed (not necessary for clinical staging) and relevant biopsies. Genomic profile information is not included in Clinical Prognostic Stage as pathologic information from surgery is necessary to ascertain the prognosis using these tools.

TNM	Grade	HER2	ER	PR	Stage
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	IB
	G2	Positive	Positive	Positive	IA
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	IB
	G3	Positive	Positive	Positive	IA
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	IB
				Negative	

TNM	Grade	HER2	ER	PR	Stage
T0 N1** M0 T1* N1** M0 T2 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	
	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	IIB
	G3	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	IIB
			Negative	Positive	
				Negative	

*T1 Includes T1mi.

**N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status

TNM	Grade	HER2	ER	PR	Stage
T2 N1*** M0 T3 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB

TNM	Grade	HER2	ER	PR	Stage
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G1	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
	G2	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
	G3	Positive	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC

TNM	Grade	HER2	ER	PR	Stage
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G1	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	
				Negative	IIIB
	G2	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	
				Negative	IIIB
	G3	Positive	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	IIIB
			Negative	Positive	
				Negative	IIIC

TNM	Grade	HER2	ER	PR	Stage
Any T Any N M1	Any	Any	Any	Any	IV

Notes:
1.Because N1mi categorization requires evaluation of the entire node, and cannot be assigned on the basis of an FNA or core biopsy, N1mi can only be used with Clinical Prognostic Staging when clinical staging is based on a resected lymph node in the absence of resection of the primary cancer, such as the situation where sentinel node biopsy is performed prior to receipt of neoadjuvant chemotherapy or endocrine therapy.
2.For cases with lymph node involvement with no evidence of primary tumor (e.g. T0 N1, etc.) or with breast ductal carcinoma in situ (e.g. Tis N1, etc.), the grade, HER2, ER, and PR information from the tumor in the lymph node should be used for assigning stage group.
3.For cases where HER2 is determined to be “equivocal” by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, the HER2 “negative” category should be used for staging in the Clinical Prognostic Stage Group.
4.The prognostic value of these Prognostic Stage Groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

***N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1 and T4 N1, respectively.

Pathological Prognostic Stage

Pathological Prognostic Stage applies to patients with breast cancer treated with surgery as the initial treatment. It includes all information used for clinical staging plus findings at surgery and pathological findings from surgical resection. Pathological Prognostic Stage does not apply to patients treated with systemic or radiation prior to surgical resection (neoadjuvant therapy).

TNM	Grade	HER2	ER	PR	Stage
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	
	G2	Positive	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	IB
	G3	Positive	Positive	Positive	IA
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	
			Negative	Positive	
				Negative	IB

TNM	Grade	HER2	ER	PR	Stage
T0 N1** M0 T1* N1** M0 T2 N0 M0	G1	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	
				Negative	IIA
	G2	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	
				Negative	
	G3	Positive	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	

*T1 Includes T1mi.

**N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status

TNM	Grade	HER2	ER	PR	Stage	TNM	Grade	HER2	ER	PR	Stage
T2 N1*** M0 T3 N0 M0	G1	Positive	Positive	Positive	IA	T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G1	Positive	Positive	Positive	IB
				Negative	IIB					Negative	IIIA
			Negative	Positive	IIB				Negative	Positive	IIIA
				Negative						Negative	
		Negative	Positive	Positive	IA			Negative	Positive	Positive	IB
				Negative	IIB					Negative	IIIA
			Negative	Positive					Negative	Positive	
				Negative						Negative	
	G2	Positive	Positive	Positive	IB		G2	Positive	Positive	Positive	IB
				Negative	IIB					Negative	IIIA
			Negative	Positive					Negative	Positive	
				Negative						Negative	
		Negative	Positive	Positive	IB			Negative	Positive	Positive	IB
				Negative	IIB					Negative	IIIA
			Negative	Positive					Negative	Positive	
				Negative						Negative	IIIB
	G3	Positive	Positive	Positive	IB		G3	Positive	Positive	Positive	IIA
				Negative	IIB					Negative	IIIA
			Negative	Positive					Negative	Positive	
				Negative						Negative	
		Negative	Positive	Positive	IIA			Negative	Positive	Positive	IIB
				Negative	IIB					Negative	IIIA
			Negative	Positive					Negative	Positive	
				Negative	IIIA					Negative	IIIC

TNM	Grade	HER2	ER	PR	Stage
T4 N0 M0 T4 N1*** M0 T4 N2 M0 Any T N3 M0	G1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	
				Negative	
	G2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	
				Negative	IIIC
	G3	Positive	Positive	Positive	IIIB
				Negative	
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	IIIC
			Negative	Positive	
				Negative	
Any T Any N M1	Any	Any	Any	Any	IV

Notes:
1.For cases with lymph node involvement with no evidence of primary tumor (e.g. T0 N1, etc.) or with breast ductal carcinoma in situ (e.g. Tis N1, etc.), the grade, HER2, ER and PR information from the tumor in the lymph node should be used for assigning stage group.
2.For cases where HER2 is determined to be “equivocal” by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, HER2 “negative” category should be used for staging in the Pathological Prognostic Stage Group.
3.The prognostic value of these Prognostic Stage Groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy including. anti-HER2 therapy).

Genomic Profile for Pathologic Prognostic Staging When Oncotype DX Score is Less than 11...

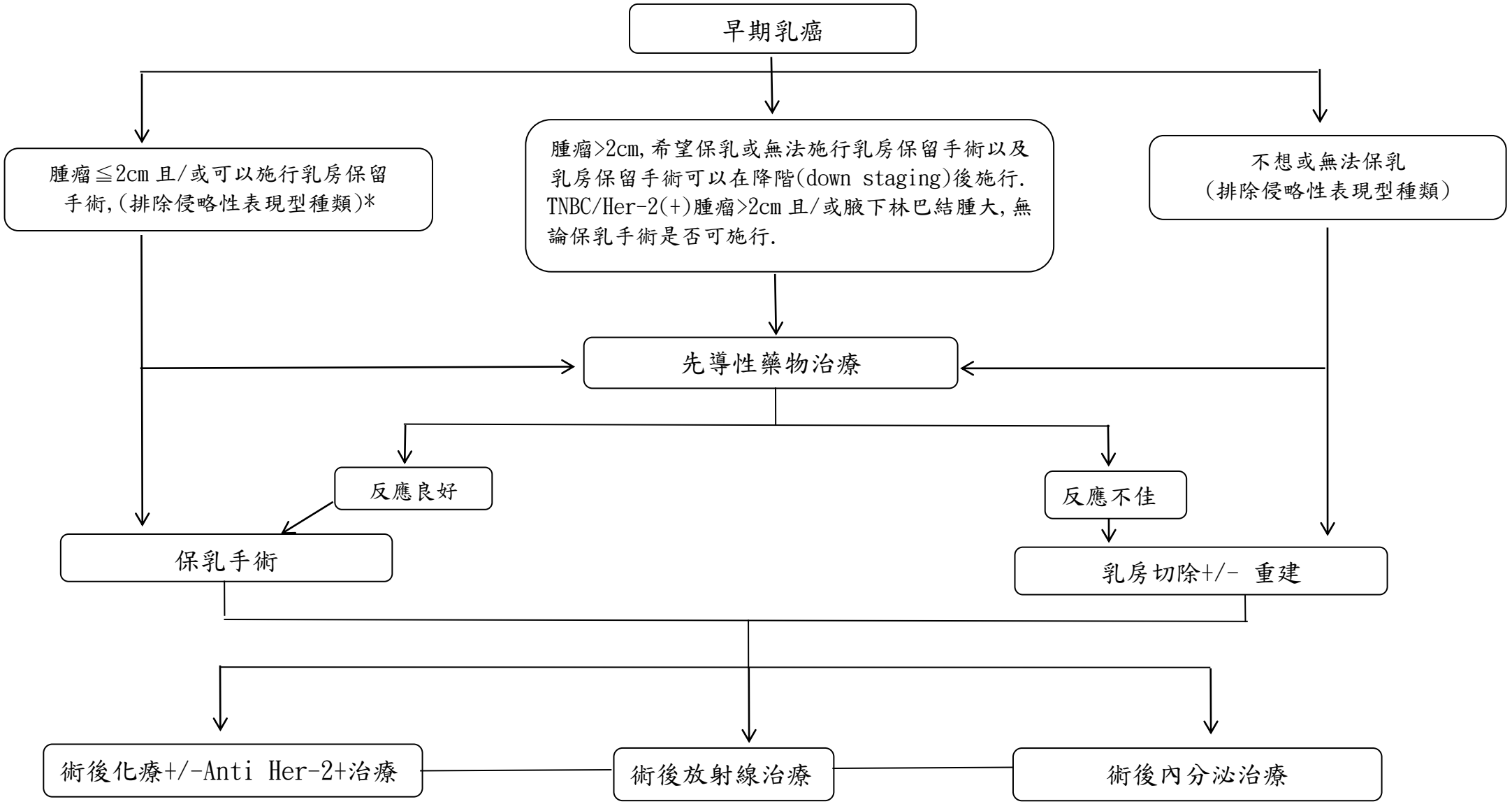
TNM	Grade	HER2	ER	PR	Stage
T1 N0 M0 T2 N0 M0	Any	Negative	Positive	Any	IA

Notes:

1.Obtaining genomic profiles is NOT required for assigning Pathological Prognostic Stage. However genomic profiles may be performed for use in determining appropriate treatment. If the OncotypeDx® test is performed in cases with a T1N0M0 or T2N0M0 cancer that is HER2-negative and ER- positive, and the recurrence score is less than 11, the case should be assigned Pathological Prognostic Stage Group IA.

2.If OncotypeDx® is not performed, or if it is performed and the OncotypeDx® score is not available, or is 11 or greater for patients with T1–2 N0 M0 HER2– negative, ER-positive cancer, then the Prognostic Stage Group is assigned based on the anatomic and biomarker categories shown above.

3.OncotypeDx® is the only multigene panel included to classify Pathologic Prognostic Stage because prospective Level I data supports this use for patients with a score less than 11. Future updates to the staging system may include results from other multigene panels to assign cohorts of patients to Prognostic Stage Groups based on the then available evidence. Inclusion or exclusion in this staging table of a genomic profile assay is not an endorsement of any specific assay and should not limit appropriate clinical use of any genomic profile assay based on evidence available at the time of treatment.

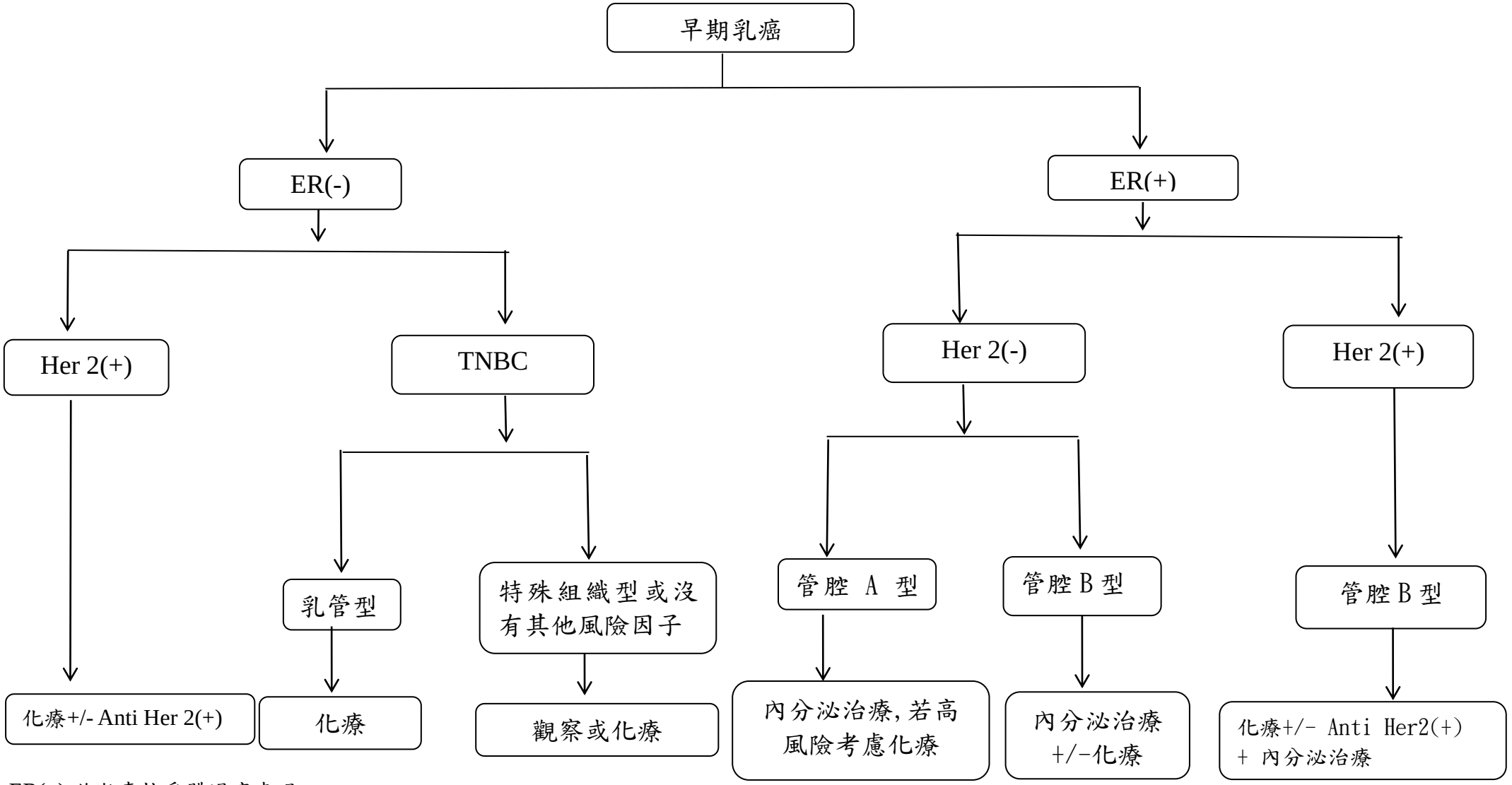


早期乳癌:Early breast cancer is defined as tumours of not more than 5 cm diameter, with either impalpable or palpable but not fixed lymph nodes and no evidence of distant metastases.

TNBC:三陰性乳癌

Her2(+):第二型類上皮生長因子過度表現型

侵略性表現種類三陰性及 Her2(+)腫瘤

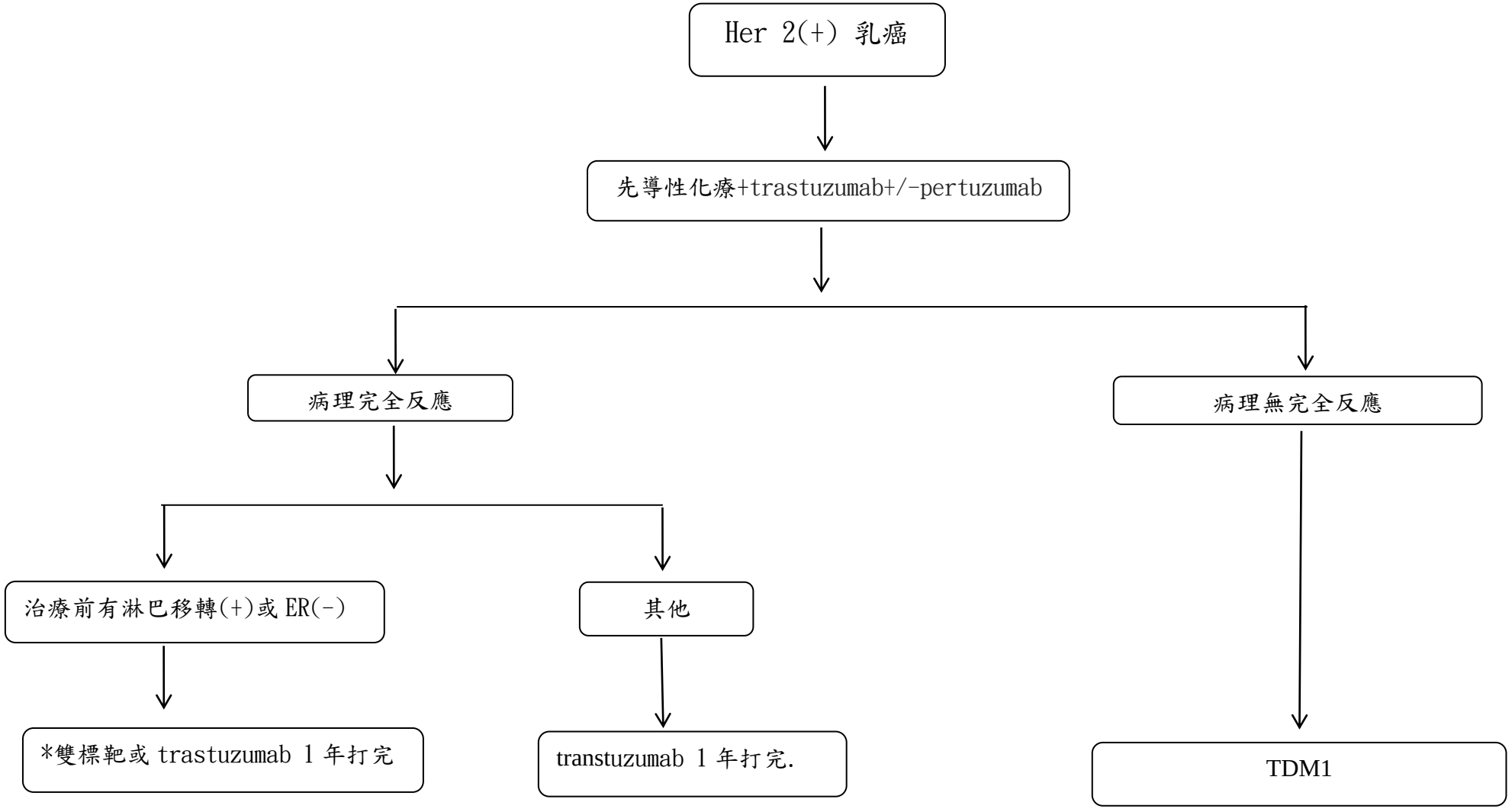


ER(+):雌激素接受體過度表現

TNBC:三陰性乳癌 Her 2(+):第二型類上皮生長因子過度表現型

Anti Her 2(+):指 transtuzumab+/-pertuzumab

特殊組織型態:(Adenoid cystic or apocrine secretory juvenile carcinoma/low grade metastatic cinoma)



*.Pertuzumab+transtuzumab

乳癌的治療依生物標誌來決定

Biomarker	Prognostic	Predictive	Technical validation	Clinical validation	Test and scoring recommendations	Patient selection
ER	++	+++	證據等級 IB	yes	免疫組織(IHC) (≥1%為陽性)	內分泌治療
PgR	+++	+	證據等級 IB	No	免疫組織(IHC) (≥1%為陽性)	若 PgR（-），多數需要化療
HER2	++	+++	證據等級 IB	Yes	見表一	抗 HER2 標靶藥物
Ki67	++	+	No	no	>20%高	>20%則建議化療
Intrinsic subtypes	++	++	Yes	yes	當 IHC 無法準確預測預後時可考慮 Gene expression profile(oncotype 或 mammaprint)	新輔助化療對於每種亞型的反應會有所不同

•對於乳癌亞型的系統性治療建議

Subtype	建議療法	Comments
Luminal A-like	內分泌治療為主	若淋巴結≥4 顆腫瘤≥5 公分，考慮化療
Luminal B-like(HER2-negative)	內分泌治療+化學藥物治療	
Luminal B-like(HER2-positive)	化學藥物治療＋抗 HER2 標靶藥物治療+內分泌治療	若不適合化學藥物治療，可考慮內分泌治療+抗 HER2 標靶藥物治療
HER2-positive(non-luminal)	化學藥物治療+抗 HER2 標靶藥物治療	
Triple-negative(ductal)	化學藥物治療	

(對於特殊的組織學型態,依照 ST GALLEN 2013 建議。)

(一)區域性局部治療(Local-regional):

- 治療策略應基於腫瘤亞型以及期別和患者年齡，喜好和總體的身體健康狀況來評估。
- 高風險的遺傳性癌症(BRCA1/BRCA2 基因突變或以前胸腔因為淋巴瘤接受放射線治療的婦女)手術前需要應預先討論諮詢。(III A)
- 在年輕停經前的病患，需要與她們討論生育的議題並提供保留生育方式的資訊。並且在開始任何治療前先與病患進行討論。[V, A]
- 保乳手術可用於原位癌(DCIS)的治療，但須有安全的切緣(>2mm)，全乳切除也是 DCIS 治療的選項。
- 對於 DCIS，BCS 後進行全乳照射治療(WBRT)或全乳切除可降低局部復發的風險。(I A)
- 乳房原位癌術後服用 Tamoxifen 可降低病患對側乳房發生惡性腫瘤的機會。(II B)
- 乳房保留手術是大部分早期乳癌治療的選擇。在某些情況下乳房全切除仍是必要選項，應考慮腫瘤大小(相對於乳房大小)，多病灶的腫瘤，先前已進行過胸部或乳房的放射線治療或切除邊界持續發現腫瘤細胞，不適合保乳手術或病人自己的選擇。
- 乳房整形腫瘤切除手術(oncoplasty)可以有比較美的外觀。
- 乳房全切除後立即重建是可行的但發炎性乳癌不能做術後立即重建。[V, A]
- 矽膠的植入對於乳房重建是安全且可接受的[III,A]
- 在完成前導性治療後，腫瘤切除是必須的。手術的方式需要考慮初診時的腫瘤型態、分期還有治療後的效果。
- 若計畫於前導性治療後行保乳手術，需要在開始治療前先標記腫瘤位置[V, A]。前導藥物治療前後的乳房 MRI 也需要考慮。[II, A]
- 對於乳房未發現乳房腫瘤，但有淋巴結轉移的病人，治療方式為全乳房放射治療加腋下淋巴廓清術。[IV, B]
- 前哨淋巴結切除為目前治療早期乳癌的標準,除非腋下淋巴結證實有被侵犯到才考慮全腋下淋巴結切除。[II,A]
- 手術前評估若沒有淋巴轉移,即使前哨淋巴切除後病理證實且≤2 顆少數淋巴轉移，若病患接受術後的放射線治療，則可考慮不需要更進一步的腋下手術。[II,B]
- 在接受先導性化療的病患中，若治療前評估腋下淋巴為陰性，則前哨淋巴切除可在治療後再實施。
- 在接受先導性化療的病患中,若治療前臨床評估有腋下淋巴轉移,在治療後臨床評估轉為陰性, 仍可考慮手術前哨淋巴結切除手術。但必須符合下列條件:1.前哨淋巴必須切除至少 3 顆以上, 2. 必須用 dual mapping(blue dye and radioactivity material)，否則建議施行腋下淋巴全切除術。 [V,B]

●乳房保留手術後強烈建議術後進行放射治療[I,A]。 但≧70 歲低風險復發的病患(腫瘤<2 公分,淋巴無轉移, ER(+)),同時接受內分泌治療的病患則可考慮追蹤,不需要術後放射治療。

●保乳手術後，強烈建議實施全乳房放射線治療(WBRT)。[I, A]

●在局部復發風險較高的病人(<50 歲，grade III，血管侵犯，延乳管內轉移或腫瘤邊界不夠)，做 Boost RT 可以降低局部復發率。[I, A]

●加速局部乳房放射治療(APBI)可用於低局部復發率之病人。[III, C]

●乳房切除後輔助性的放射線治療建議用於有侵犯到腋下淋巴結且/或>5cm 的腫瘤，特別是有額外危險因子的病患(HER 2 陽性,ER 陰性)。[I,A]

●術中放射線治療之選擇(IORT)：

Table 1 Comparison of patient groups in original and updated consensus statements

Patient group	Risk factor	Original	Update
Suitability	Age	≥60 y	≥50 y
	Margins	Negative by at least 2 mm	No change
	T stage	T1	Tis or T1
	DCIS	Not allowed	If all of the below: • Screen-detected • Low to intermediate nuclear grade • Size ≤2.5 cm • Resected with margins negative at ≥3 mm
Cautionary	Age	50-59 y	• 40-49 y if all other criteria for "suitable" are met • ≥50 y if patient has at least 1 of the pathologic factors below and does not have any "unsuitable" factors *Pathologic factors:* • Size 2.1-3.0 cm [a] • T2 • Close margins (<2 mm) • Limited/focal LVSI • ER(-) • Clinically unifocal with total size 2.1-3.0 cm [b] • Invasive lobular histology • Pure DCIS ≤3 cm if criteria for "suitable" not fully met • EIC ≤3 cm
	Margins	Close (<2 mm)	No change
	DCIS	≤3 cm	≤3 cm and does not meet criteria for "suitable"
Unsuitable	Age	<50 years	• <40 y • 40-49 y and do not meet the criteria for cautionary
	Margins	Positive	No change
	DCIS	>3 cm	No change

[a] The size of the invasive tumor component.
[b] Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

●乳房切除後輔助性的放射線治療建議用於有侵犯到腋下淋巴結且/或>5cm 的腫瘤，特別是有額外危險因子的病患(HER 2 陽性,ER 陰性)。[I,A]

●乳房切除後輔助性的放射線治療，建議用於腫瘤大於 5 公分，特別是有額外危險因子的病患(HER-2 陽性，ER 陰性)。在有 1~3 顆淋巴轉移的病人，也須考慮使用。[I, A]

●在 SLND 後，有前哨淋巴轉移，但沒有做腋下淋巴廓清術(ALND)的病人，建議行腋下放射線治療。(I, B)

●做過 ALND 的病人，不建議常態性的腋下放射線治療。除非有殘存之腫瘤細胞或者淋巴轉移。[I, E]

●在乳房重建的病人，若需要，也要在手術過後進行乳房放射線治療。且此類病人可以考慮先用暫時的組織擴張器。[III, A]

●在 DCIS 的病人，若行保乳手術，建議術後放射線治療。[I, A]

●在低風險的病人，可以考慮不行放射線治療。[V, B]

●在高風險的病人，要考慮 Boost RT。[III, B]

●在 DCIS 行全乳房切除的病人，不考慮術後放射線治療。[I, E]

(二)全身性治療(Systemic-treatment):

●ER 表現為陽性的病人(>=1%)，應該接受雌激素療法[I,A]。在停經前的婦女，Tamoxifen 為標準[I,A]，接受化療後的停經前婦女,卵巢抑制劑可以改善存活率。儘管缺乏長期追蹤和存活率的數據，對於部分停經前的婦女，芳香環轉化酶抑制劑以及卵巢抑制的合併療法是一項選擇。對於停經後的婦女，芳香環轉化酶抑制劑(類固醇和非類固醇)和 Tamoxifen 是有效的治療選擇[I,B]

● ER 陽性的停經前病人，建議使用停經針（GNRH agonist）3-5 年。

●使用 Tamoxifen 的病人建議避免使用高強度以及中等的 CYP2D6 的抑制劑。如果此類藥物無法被替換，應該考慮使用芳香酶抑制劑(在停經前婦女合併使用卵巢抑制劑)[IV,B]

●對於高風險荷爾蒙受體陽性病患(淋巴結陽性)建議延長內分泌治療時間到十年，但需和病患討論治療藥物的副作用及帶來的好處。

●使用卵巢抑制劑的病人以及使用芳香酶抑制劑的病人有較高風險的骨質流失且建議服用適量鈣離子以及維他命 D3。此外，定期評估骨頭礦物質密度是必要的[I,A]

●三陰性、HER2(+)的乳癌以及高風險的 luminal HER2(-)腫瘤建議化療。[I,A]

●docetaxel 和 cyclophosphamide 4 次，對於某些病人(例如處於心臟併發症的危險的患者)可以當作 anthracycline-

based 4 次的替代療法。[I,A]

- 大部分 luminal A 的病人不須化療除非復發風險高(廣泛侵犯的淋巴結>4 顆)的病患。[I,A]
- luminal B HER2(+)應使用化學藥物，抗雌激素和 Trastuzumab 來治療[I,A]。
- HER2(+)(非 luminal)應該使用化療及 trastuzumab 治療。[I,A]
- 除了低風險的特殊組織學亞型，例如分泌型早期型(secretory juvenile)，頂漿分泌型或腺樣囊性癌(apocrine or adenoid cystic carcinoma)，三陰性乳癌建議接受輔助性化療[I,A]
- Chemotherapy 通常為四到八個 cycle-以 anthracycline 或 taxane 為主。建議可以接替(sequential)使用而不要同時使用 anthracycline 與 taxane。(IB)

Primary (neoadjuvant) systemic therapy-PST

- PST 應該用於減少局部晚期和腫瘤大但可手術切除病患的手術範圍，尤其是需要進行乳房切除術的病患・在腫瘤> 2cm、必須要做化學治療的三陰性患者和 HER2 陽性亞型的患者，都應列入考量・[I, B].
- 術前使用的藥物應該與術後使用的藥物相對應・建議大部分的患者使用接序性的 anthracyclines 和 taxanes・[I, B].
- 在三陰性腫瘤和/或具有 BRCA1 / 2 突變的患者中可考慮添加鉑金化合物[I, C].
- 若要使用 PST，則必須在術前完成化學治療的療程・[I, B].
- 對於完成先導性化學治療而未達到 pCR 的高危險群、三陰性患者，可考慮在術後加上 6-8 週次的 capecitabine[I, C].
- 在 ER 陽性/ HER2 陰性且需要 PST 但無明確化學治療適應症的停經後患者，可以考慮術前內分泌治療(4-8 個月或直到最大緩解)並在術後持續使用・[I, A].
- 高度分化性的惡性腫瘤可以考慮使用劑量密集（dose dense)的化療(加上白血球生成劑)。 (I ,B)
- 有 HER2 過度表現的患者,併用 Trastuzumab+ chemotherapy 與單純化療相比可以減少復發機率至一半，並提高總存活率。（I,A)
- 乳癌病患若有 HER2 過度表現,若淋巴結有轉移或淋巴無轉移但腫瘤大於>1cm 建議使用 Trastuzumab 合併 pertuzumab，而<1cm 沒有淋巴轉移，若 ER 為(-)，也可考慮 Trastuzumab 的使用。
- 在 HER2 過度表現的病患，新輔助治療可以考慮雙標靶藥物及化療藥物使用(trastuzumab + pertuzumab)，因可提高 PCR 的比例。
- 由於 Trastuzumab 有心臟毒性,不應同時與 Anthracycline 使用, 與 Taxanes 類藥物合併使用是安全的並已被證實

比交替使用效果更好。（I,A)

- 在開始 trastuzumab 治療前和治療期間都必須定期進行心臟監測，[I, A].
- trastuzumab/lapatinib 雙標靶治並未改善長期結果，因此不建議使用[I, E].
- 在高危險族群(定義為淋巴陽性或 ER 陰性)，可以考慮給予 trastuzumab/pertuzumab 雙標靶治療，從術前或術後開始為期 1 年[I, A].
- 如果先導性化學治療與 anti-HER2 治療完成後仍有殘留浸潤性疾病，儘可能將輔助性 trastuzumab 換成為輔助性 T-DM1[I, A].
- 在特定的高危險族群患者中，先前未使用雙標靶治療的病患 ，可以考慮使用 neratinib 來延長 anti-HER2 治療，治療時需有適當預防和治療腹瀉的對策. [I, B].

- 尤其是在復發風險較高、低雌激素狀態接受卵巢抑制治療的病患或停經後婦女可以預防性給予 Bisphosphonate 或 Denasumab,減少治療相關的骨質流失及降低骨骼併發症的風險。（I,A)
- 即使在年老患者,在允許的情況下還是應該給予 full dose 的藥物。適用 standard chemotherapy 的患者, 應遵循 multidrug regimen 的方案進行治療。(II, D)
- 早期乳腺癌的老年患者之治療應根據生物學(而非實際年齡）年齡，對於較虛弱病患可考慮使用較保守的治療，而對於可進行標準化學治療的老年患者，則應使用標準的多重化學藥物治療，[II, B].
- 在做治療決定之前應進行老年醫學評估[II, A].
- 對局部晚期的病患,或是腫瘤較大但尚可進行全乳切除的病患，在開刀前先給予 primary systemic therapy 可以增加手術的可能性與減少手術難度。(I,A)
- 若使用新輔助化療,建議都應打完計劃的療程，再進行手術。(V,B)
- 化療前應先確認病患肝功能狀況及 B 肝,C 肝病毒檢測。

＊後續追蹤與存活率:後續追蹤的目的是希望能發現早期局部復發或對側乳癌,評估與治療相關產生的併發症,並提供心理支持與專業知識以便讓病人能夠盡快恢復正常的生活。

- 建議前兩年每 3-6 個月(低危險群和 DCIS 患者每 6 個月進行一次回診)，追蹤一次,第三到五年後可改為每 6-8 個月追蹤一次,，第 6 年開始每年回診一次。（V,A)
- 行乳房保留手術（BCS)後建議每年追蹤同側與對側的乳房攝影與超音波和乳房核磁共振檢查(II,A)。 在無症狀的患者中目前沒有其他研究顯示這兩者之外的 image 或 lab 檢查（例如血液計數檢驗，常規化學檢驗，胸部 X

光，骨骼掃描，肝臟超音波，電腦斷層，FDG-PET-CT）或任何腫瘤標誌物檢驗，例如 CA15-3 或 CEA[I, D].對存活率有影響。

●Lobular invasive carcinoma 患者可使用超音波做後續追蹤。(III,B)

●接受內分泌治療（ET)的病人應定期做血液檢查因此類藥物對血脂方面副作用較大。(V,A)

●使用 Tamoxifen 的患者,建議每年行婦科檢查包括腹部超音波(V,B)。

●使用 AIs 的患者建議定期追蹤骨質密度。(I,A)

●應鼓勵病患在治療乳癌後採取健康的生活方式，包括飲食調整、養成定期運動的習慣及控制體重。 應鼓勵病患戒菸或戒酒。(II,B)

●通常不應使用荷爾蒙補充療法[I, D].

●患者應有方便且無限制使用特殊復健的設施和服務[V, A].

●應解決長期生存問題，包括心理需求以及與工作，家庭和性相關的問題[V, A].

晚期乳癌準則

通論

●一但被診斷出有轉移性乳癌，應視情況納入或啟動”全人照顧” 之通報，將相關醫療人員，病患及家屬，集合於一隱密空間，討論治療方向，並做成記錄。

所有病人都應該能接受到最高標準的癌症治療團隊照顧

●和治療團隊完整且清楚的討論

●衛教病人治療策略和其他的支持照護。

●鼓勵病人對於治療策略多表達想法，並共同參與決定。

●讓病人了解，自己提供給醫療團隊的意見，能夠改善治療中可能的不適，且改善生活品質。

●治療團隊要考量病人的個人喜好，經濟能力，價值觀等等。

●給病人最好的治療策略，包含新的治療方式，新的研究證據等等。

●在治療初期，要考慮在適當時機提出可能的存活時間，還有安寧緩和的議題等。

評估

- 雖然例行性的腦部影像檢查並不需要，但檢查的閾值應降低，一但有任何頭部的症狀或不適建議施行腦部的影像檢查。
- 約 2-4 個月要評估內分泌治療反應，2-4 cycle 化療後也要評估療效。
- 腫瘤指數的變化，僅有參考價值。若病患全身狀況穩定，只有腫瘤指數上升，並不需要改變現有的治療。
- 儘可能在移轉的腫瘤進行生檢(biopsy) ，確定組織型態，並檢驗 ER, PR, Her2 及 Ki67。
- 若生物標記與原發腫瘤不同，只要任何一次生檢之 ER 或 Her2 為陽性，則可考慮相對應的標的來治療。

治療通則

- 對於原發腫瘤完整的轉移性乳腺癌女性患者，初始治療建議為全身治療，對於需要緩解症狀或減輕即將發生併發症(如皮膚潰瘍、 出血、真菌感染和疼痛)的女性患者，可考慮在初始全身治療後行手術治療。可考慮將放療作為手術的一種替代選擇。對於某些轉移性乳腺癌患者，完全切除乳腺內腫瘤可能會有潛在生存獲益，但需與病人共同討論治療選擇。

化學治療通則

- 在沒有藥物禁忌或病人因素之下，若之前未使用過 anthracycline 或 taxane 為主的配方時，此兩種藥物可做為 HER-2 陰性 MBC 的第一線治療,但建議單處方使用(monotherapy)。其它如 capecitabine 和 vinorelbine 在擔心掉髮病人身上可考慮。
- 在未使用過 taxane 及對 anthracycline 有抗性之 MBC 或者是考慮到 anthracycline 累積劑量及心毒性的病人要化療時，單一處方的 taxane 首選。其它如 capecitabine 和 vinorelbine 在擔心掉髮病人身上可考慮。
- 在輔助化學治療時，若已使用 taxane,可以再使用於轉移之病患，尤其是已有一年以上的無病存活期的病人。
- 處方期間及種類應量身訂做。
- 通常每一配方(anthracyclines 除外)應使用至疾病進展或"毒性無法接受"。而"毒性無法接受"之決定應和病患共同討論。
- 節拍式(metronoic)化療(指低劑量、較高頻率投藥的方式)可以用在不需要快速降低癌症體積的病人。低劑量口服的(cyclophosphamide和methotrexate)。其他藥物包含capecitabine, vinorelbine。
- Bevacizumab 結合化療作為 MBC 第一或第二線治療有些許 PFS 的好處，但 OS 無差別。Bevacizumab 建議用於篩

選過之病人使用，不建議使用於第一/第二線後的治療。

ER+/HER-2 negative ABC

- 內分泌治療是賀爾蒙受體陽性乳癌的首要選項，即使是有內臟轉移，除非證明有內分泌治療抗性或需要快速控制病情時。
- 對停經前女性來說，抑制卵巢功能或摘除,結合其他的內分泌治療是首選。Tamoxifen 應被考慮的藥物,除非證明對它有藥物抗性。AI 也是選擇之一，但應配合卵巢抑制或卵巢摘除。Fulvestrant 在停經前女性臨床研究尚不足。
- AI 治療過後的選擇目前尚無定論。可選擇 Tamoxifen，CDK4.6 抑制劑(abemaciclib, palbociclib, or ribociclib) ，其它不同作用機轉之 AI，高劑量的(HD)Fulvestrant，megestrol acetate 及 everolimus+AI。
- 針對新診斷未治療過(De novo)第四期的病人，或內分泌治療停藥一年以上的病患，應優先使用 AI + CDK4.6 抑制劑 (第一線)
- 在內分泌治療中, 病程仍進展, 要考慮 Fulvestrant + CDK4.6 抑制劑 (第二線)

目前健保規範 CDK4/6 抑制劑 (如 ribociclib；palbociclib)：(108/10/1、108/12/1、109/4/1、109/10/1、110/5/1、110/10/1)

1.做為停經後乳癌婦女發生遠端轉移後須完全符合以下條件：(1)荷爾蒙接受體為強陽性：ER 或 PR >30%。(2)HER-2 檢測為陰性。(3)經完整疾病評估後未出現器官轉移危急症狀 (visceral crisis)。

2.經事前審查核准後使用，核准後每 24 週須檢附療效評估資料再次申請，若疾病惡化即不得再次申請。

3.若為 ribociclib 每日最多處方 3 粒，palbociclib 每日最多處方 1 粒，本類藥品僅得擇一使用，唯有在耐受不良時方可轉換使用。本類藥品使用總療程合併計算，以每人給付 24 個月為上限。

1.做為停經後乳癌婦女發生遠端轉移後之全身性藥物治療，須完全符合以下條件：(109/10/1、110/5/1、110/10/1)

(1)荷爾蒙接受體為強陽性：ER 或 PR >30%。

(2)HER-2 檢測為陰性。

(3)經完整疾病評估後未出現器官轉移危急症狀(visceral crisis)且無中樞神經系統(CNS)轉移。（110/10/1）

(4)骨轉移不可為唯一轉移部位。（110/10/1）

(5)病患目前未接受卵巢功能抑制治療(包含 GnRH analogue 等) 且滿足下列條件之一：（110/5/1）

I.年齡滿 55 歲。

II.曾接受雙側卵巢切除術。

III.FSH 及 estradiol 血液檢測值在停經後數值範圍內。

2.經事前審查核准後使用，核准後每 24 週須檢附療效評估資料再次申請，若疾病惡化即必須停止使用，且後續不得再申請使用本類藥品。（110/10/1）

3.使用限制：

(1)ribociclib 每日最多處方 3 粒。

(2)palbociclib 每日最多處方 1 粒。

(3)本類藥品僅得擇一使用，唯有在耐受不良時方可轉換使用，使用總療程合併計算，以每人終生給付 24 個月為上限，惟 110 年 9 月 30 日以前已核定用藥之病人，得經事前審查核准後，使用至疾病惡化或總療程達 24 個月為止，且後續不得再申請使用本類藥品。（110/10/1）

4.若先前使用 everolimus 無效後，不得再申請本類藥品。(109/4/1)

●化療後的維持性的內分泌治療是合理的,但仍需隨機試驗的研究。

●同時給予化療及內分泌治療沒有增加存活期的好處，最好不要同時使用。

HER-2-positive ABC

●除非有禁忌，抗 HER-2 療法應及早使用於轉移性乳癌病人。

●對 ER+/HER-2+的 MBC 病患，優先選擇內分泌治療(ET)而非化療，抗 HER-2 療法加內分泌治療應在治療之初即開始使用，因為相對單獨內分泌治療(ET)有較佳的 PFS 好處。加上抗 HER-2 療法沒有增加總體存活期。

●在抗 HER-2 療法結合化療或內分泌治療期間有疾病進展時，應考慮加上另一種標靶治療，因為可以抑制另一 HER-2 路徑。

●標靶治療 MBC 的時間長短目前尚無定論。

●若使用 trastuzumab 時疾病有進展，使用 trastuzumab +lapatinib 也是合理的選擇。

●Her-2 陽性之轉移性病患，第一線藥物治療應考慮雙標靶加上化療(trastuzumab + pertuzumab + Doxetaxel),第二線則考慮 TDM1 來治療。(I.A)

三陰性晚期乳癌 (Advanced TNBC)

●對於非BRCA mutation的病人，目前尚未有明確的臨床試驗證據，證明哪種化療藥物最適合。因此，所有Her-2 negative可以使用的化學治療，都能用在TNBC。

●對於advanced TNBC(無論有無BRCA mutation)，病人或使用過anthracycline +/- taxane的狀況下，Carboplatin有比

docetaxol更好的效果和較少的毒性。因此carboplatin在此類的病人是很重要的治療選項。

●對於HER-2 negative and germline BRCA1/2 mutation的病患可考慮使用PARP inhibitors (如Olaparib, Talazaparib)

健保申請規範 Olaparib (如 Lynparza)：(109/11/1)

(1)單獨使用於曾接受前導性、術後輔助性或轉移性化療，且具生殖細胞 BRCA1/2 致病性或疑似致病性突變之三陰性(荷爾蒙接受體及 HER2 受體皆為陰性)轉移性乳癌病人。

(2)須經事前審查核准後使用：

I.每次申請之療程以 3 個月為限。

II.初次申請時需檢附 ER、PR、HER2 皆為陰性之檢測報告，以及 germline BRCA 1/2 突變之檢測報告。BRCA 1/2 檢測需由該項目符合以下認證之實驗室執行，檢測報告上應註明方法學與檢測平台，若為病理檢體由病理專科醫師簽發報告，若非病理檢體由相關領域專科醫師簽發報告，且於檢測報告上加註專科醫師證書字號。(111/6/1、111/8/1)

i.衛生福利部食品藥物管理署精準醫療分子檢驗實驗室列冊登錄。

ii.美國病理學會(The College of American Pathologists，CAP)實驗室認證。

iii.財團法人全國認證基金會(Taiwan Accreditation Foundation，TAF)實驗室認證(ISO15189)。

iv.台灣病理學會分子病理實驗室認證。

Ⅲ. 再次申請必須提出客觀證據（如：影像學）證實無惡化，才可繼續使用。

(3)Olaparib 與 talazoparib 僅得擇一使用，除因耐受性不良，不得互換。（111/8/1)

(4)每日最多使用 4 粒。

Talazoparib (如 Talzenna)：(110/3/1) 1.限用於治療同時符合下列條件之18歲以上局部晚期或轉移性乳癌病患： (1)曾接受前導性、術後輔助性或轉移性化療者，或是無法接受化療者。 (2) germline BRCA 1/2突變。 (3)第二型人類表皮生長因子接受體(HER2)、雌激素受體(ER)以及黃體素受體(PR) 均呈現陰性。

2.須經事前審查核准後使用:(1)每次申請之療程以3個月為限。(2)初次申請時需檢附ER、PR、HER2皆為陰性之檢測報告，以及germline BRCA 1/2突變之檢測報告。BRCA 1/2檢測需由該項目符合以下認證之實驗室執行，檢測報告上應註明方法學與檢測平台，若為病理檢體由病理專科醫師簽發報告，若非病理檢體由相關領域專科醫師簽發報告，且於檢測報告上加註專科醫師證書字號。(111/6/1、111/8/1)

I.衛生福利部食品藥物管理署精準醫療分子檢驗實驗室列冊登錄。

II.美國病理學會(The College of American Pathologists，CAP)實驗室認證。
III.財團法人全國認證基金會(Taiwan Accreditation Foundation，TAF)實驗室認證(ISO15189)。
VI. 台灣病理學會分子病理實驗室認證。
3.Talazoparib與olaparib僅得擇一使用，除因耐受性不良，不得互換。（111/8/1)
4.Next Generation Sequencing associated biomarker testing for medicine therapies(optional)
●三陰性晚期乳癌, 要檢驗腫瘤PD-L1的濃度(無論原發或移轉處), 以決定是否使用免疫檢查點抑制劑.

對於骨頭,腦轉移的治療建議:

●已確診有轉移,特別是侵犯到骨頭的乳癌病人,針對骨轉移的藥物(bisphosphonate or denosumab)應常規性的與其他全身性治療合併使用。(1A)
●有骨轉移並持續有局部疼痛的病人應該安排影像評估,以確定是否有病理性骨折。如果懷疑或已發現有長骨骨折,則需請骨科醫師評估是否需要手術固定,以及術後做局部 RT。如果沒有明顯的骨折風險,RT 為首選治療。(1A)
●有神經系統症狀且懷疑有脊髓壓迫的病人必須盡快安排相關的影像學檢查, MRI 為首選,照射部位應包括懷疑的脊椎以及鄰近部位。盡快照會神經外科醫師或骨科醫師來評估是否需要手術減壓,或是放射性治療 RT。(1B)
●單顆或數顆小型但仍可切除的腦轉移腫瘤應該予以手術切除或立體定位放射手術(radiosurgery)治療. 如果無法切除則建議用 Radiosurgery 來治療。(1B)

支持性療法與安寧緩和治療

●支持性療法應該被納入為乳癌治療計劃的一部分,讓乳癌患者可以安全地且更容易接受其他支持性的治療。(1A)
●治療初期就應該與緩和醫療的專家合作,給病人最有效的疼痛控制及舒緩其他副作用。(1A)
●需要緩解疼痛的病人應該要給予有效的疼痛控制(包括 morphine)。(1A)
●在理想狀況下,應該在轉移性乳癌早期診斷出來的時候就與病人討論臨終的意願。當積極治療已經無法控制疾病的進展,或是治療的副作用大於益處,醫師及醫療團隊應該主動與病人和家屬討論安寧治療。 (expert opinion)

懷孕中發生的乳癌

●對疑似乳腺癌的孕婦的評估應包括乳房和腋下淋巴結超音波，帶屏蔽的乳房 X 光，乳房和可疑淋巴結 CNB，CXR。另可考慮腹部超音波，胸部及腹部的 MRI 以排除轉移的可能性。
●懷孕早期任何時間均不應給予化療。
●懷孕中晚期接受化學治療的畸胎率與一般產婦無異。

●化療以 anthracycline 對胎兒較為安全，5-FU 及 cyclophosphamide 也有資料顯示對胎兒是安全的。

●紫杉醇類化療較無明顯數據，若疾病有需要可以考慮 weekly paclitaxol。

●妊娠期間禁止內分泌治療和放療，因此內分泌治療和放療應在產後期開始。

●在每次回診以及做出每個治療決定時，腫瘤科醫師和母嬰醫學專科醫師之間的溝通都必不可少。姚忠瑾醫師提供

轉移性男性乳癌

● ER+的男性轉移性乳癌可以使用 endocrine therapy 治療,除非乳癌表現有 endocrine resistance 或是進展快速需要用到化療時。(expert opinion)

● ER+的男性轉移性乳癌,建議使用 Tamoxifen。(expert opinion)

●如果因為禁忌症而無法使用 Tamoxifen，則可以考慮併用 AI 和促黃體激素釋放激素（LHRH) 的促效型抑制劑，但必須與患者討論其高毒性，以避免順從性問題。[IV, B].

●男性乳腺癌患者不應該單獨使用 AI 作為荷爾蒙輔助治療[IV, E].

●化學治療和 anti-HER2 治療的適應症和配方應遵循與女性乳腺癌患者相同的建議[IV, A].

名詞解釋 EBC:Early breast cancer ABC:Advanced breast cancer MBC:Metatitis breast cancer

證據等級

Level I：有顯著意義的隨機對照研究（Randomized controlled trials, RCT）報告。包括大型且low bias的RCT, 此類RCT延伸出來的meta-analyses。

Level II：小型的RCT或是大型但懷疑有bias的RCT,此類RCT延伸出來的meta-analysis。

Level III：前瞻性世代研究報告prospective cohort。

Level IV：回顧性世代研究（retrospective cohort)及病例對照組研究（Case-control study）。

Level V：無對照組的研究, 個案報告, 專家意見（Expert opinion）

建議等級

Group A：有強烈證據顯示有顯著的臨床益處，強烈建議。

Group B：較無強烈的研究證據顯示, 尚有臨床益處，一般建議。

Group C：證據不足功效或利益不大,風險或缺點大於臨床益處。（副作用，費用等）。無特別推薦。

Group D：有適度的證據顯示無臨床益處或療效不佳，一般不推薦使用。

Group E: 有強烈的證據顯示療效不佳或無臨床益處，不建議。

乳癌病人若有以下條件可以考慮做基因檢測

- 年齡<45 歲乳癌病人
- 年齡介於 46~60 歲 乳癌病人
  1.任何年齡得到第二次乳癌
  2.大於 1 位家族成員有乳癌，胰臟癌，卵巢癌或者攝護腺癌（任何年齡）
- 年齡<60 歲：三陰性乳癌
- 大於兩位家族成員有乳癌病史（任何年齡）
- 男性乳癌
- 為了相關用藥（例如 PARPi）

五、化學治療原則

Neoadjuvant /Adjuvant chemotherapy

AC

Doxorubicin	60 mg/m^2	iv	d1
Cyclophosphamide	600 mg/m^2	iv	d1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)			

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients agec 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507 .

Fisher, B et al. Treatment of axillary lymph node-negative, estrogen receptor-negative breast cancer: updated findings from National Surgical Adjuvant Breast and Bowel Project clinical trials. J Natl Cancer Inst 2004; 96:1823 .

EC

Epirubicin	75 - 100 mg/m^2	iv	d1
Cyclophosphamide	600 mg/m^2	iv	d1
Q3w x 4 cycles or Q2W x 4-6 cycles (with GCSF support)			

Piccart MJ et al. Phase III trial comparing two dose levels of epirubicin combined with cyclophosphamide with cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer. . J Clin Oncol 2001; 19:3103.

LC(Liposomal doxorubicin-optional)

Liposmal doxorubicin	35- 50 mg/m^2	iv	d1
Cyclophosphamide	600 mg/m^2	iv	d1
Q3w x 4 cycles or Q4w x 4 cycles			

Pegylated Liposomal Doxorubicin as Adjuvant Therapy for Stage I-III Operable Breast Cancer.Lu YC, Ou-Yang FU, Hsieh CM, Chang KJ,

Chen DR, Tu CW, Wang HC, Hou MF.In Vivo. 2016 Mar-Apr;30(2):159-63.

健保規範:Doxorubicin hydrochloride liposome injection(如 Lipo-Dox、Caelyx)：用於單一治療有心臟疾病風險考量之轉移性乳癌患者。(93/11/1)

TC

Docetaxel	60 - 100 mg/m^2 iv	d1
Cyclophosphamide	600 mg/m^2 iv	d1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)		

Jones SE et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006; 24:5381.

健保規範: Docetaxel 1.局部晚期或轉移性乳癌。2.與 anthracycline 合併使用於腋下淋巴結轉移之早期乳癌之術後輔助性化學治療。(99/6/1)3.早期乳癌手術後，經診斷為三陰性反應且無淋巴轉移的病人，得作為與 cyclophosphamide 併用 doxorubicin 的化學輔助療法 4.除以上條件，其餘皆自費。

Docetaxel+ Cisplatin

Docetaxel	60 - 75mg/m^2 iv	day1
Cisplatin	60- 75 mg/m^2 iv	day1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)		

A randomized phase II trial of platinum salts in basal-like breast cancer patients in the neoadjuvant setting. Results from the GEICAM/2006-03, multicenter study. (Abstract in PubMed)Breast Cancer Res Treat (2012) 136:487–493

CMF po

Cyclophosphamide	100 mg/m^2 /d po	day1-14
Methotrexate	40 mg/m^2 iv	day1, 8
5- FU	600 mg/m^2 iv	day1, 8
Q4w x 6 cycles		

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients agec 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507.

CMF IV

Cyclophosphamide	600 mg/m^2 iv	day1
Methotrexate	40 mg/m^2 iv	day1
5-FU	600 mg/m^2 iv	day1
Q3w x 6 cycles		

Weiss RB et al. Adjuvant chemotherapy after conservative surgery plus irradiation versus modified radical mastectomy. Analysis of drug dosing and toxicity. Am J Med 1987; 83:455.

FAC

5-FU	500 mg/m^2 iv	day1
Doxorubicin	50 mg/m^2 iv	day1
Cyclophosphamide	500 mg/m^2 iv	day1
Q3w x 6 cycles		

Martin M et al. Doxorubicin in combination with fluorouracil and cyclophosphamide (i.v. FAC regimen d1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.v. CMF regimen d1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. Ann Oncol 2003; 14:833.

FEC

5-FU	500 - 600 mg/m^2 iv	day1
Epirubicin	50 - 100 mg/m^2 iv	day1
Cyclophosphamide	500 - 600 mg/m^2 iv	day1
Q3w x 6 cycles or Q2W x 4-6 cycles (with GCSF support)		

Bonneterre J et al. Epirubicin increase long term survival in adjuvant chemotherapy of patients with poor prognosis, node positive, early breast cancer: 10 years follow up results of the French Adjuvant Study Group 05 randomized trial. J Clin Oncol 2005; 23:2686.

FLC

5-FU	500 - 600 mg/m^2 iv	day1
*Lipodox	35mg/m^2 iv	day1
Cyclophosphamide	500 - 600 mg/m^2 iv	day1
Q3w x 6 cycles or Q2W x 4-6 cycles (with GCSF support)		

Rayson D, Suter T.M, Jackisch C,et al:Cardiac Safety of Adjuvant Pegylated Liposomal Doxorubicin With Concurrent Trastuzumab:A Randomized Phase II Trial Annals of Oncology 2012;23:1780-1788.

Juan Lao, Julia Madani, Teresa Puértolas,et al. Liposomal Doxorubicin in the Treatment of Breast Cancer Patients: A Review Journal of Drug Delivery. 2013, Article ID 456409, 12 pages

*Epirubicin 替換自費使用 Liposomal doxorubicin(optional-需與醫師討論)

AC/EC→Paclitaxel Qw (or Paclitaxel→AC/EC)

Paclitaxel	80 mg/m^2 iv	day1
Qw x 12 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

健保規範:Paclitaxel 腋下淋巴轉移之乳癌且動情素受體為陰性之患者，paclitaxel 可作為接續含 doxorubicin 在內之輔助化學治療。（91/4/1、94/1/1、98/8/1）

AC/EC→Docetaxel Q3w (or Docetaxel→AC/EC)

Docetaxel	60-100 mg/m^2 iv	day1
Q3w x 4 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

健保規範: Docetaxel 1.局部晚期或轉移性乳癌。2.與 anthracycline 合併使用於腋下淋巴結轉移之早期乳癌之術後輔助性化學治療。(99/6/1)3.早期乳癌手術後，經診斷為三陰性反應且無淋巴轉移的病人，得作為與 cyclophosphamide 併用 doxorubicin 的化學輔助療法 4.除以上條件，其餘皆自費。

TAC

Docetaxel	50 - 75 mg/m^2	iv	day1
Doxorubicin	50 mg/m^2	iv	day1
Cyclophosphamide	500 mg/m^2	iv	day1
Q3w x 6 cycles			

Martin M et al. Adjuvant docetaxel for node-positive breast cancer. N Eng J Med 2005; 352:2302 .

TEC

Docetaxel	50-75 mg/m^2	iv	day1
Epirubicin	50-75 mg/m^2	iv	day1
Cyclophosphamide	500 mg/m^2	iv	day1
Q3w x 6 cycles			

P Piedbois et al. Dose-dense adjuvant chemotherapy in node-positive breast cancer: docetaxel followed by epirubicin/cyclophosphamide (T/EC), or the reverse sequence (EC/T), every 2 weeks, versus docetaxel, epirubicin and cyclophosphamide (TEC) every 3 weeks. AERO B03 randomized phase II study. Ann Oncol. 2007; 18: 52.

Cisplatin

Cisplatin	75 mg/m^2	iv	day1
Q3w			

Carboplantin

Carboplantin	6 mg, AUC	iv	day1
Q3w			

Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.

Docetaxel+ Carboplantin

Docetaxel	60 - 75mg/m^2	iv	day1
Carboplantin	6 mg, AUC	iv	day1
Cycled every 21 days for 6 cycles			

von Minckwitz G, Schneeweiss A, Loibl S, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial Lancet Oncol 2014;15:747-756.

Paclitaxel(Weekly) + carboplatin

Paclitaxel	80mg/m^2 iv	day 1 8 15
Carboplantin	AUC 6 iv(q3w)/AUC2 iv(q1w)	day 1
Cycled every 21 days for4 cycles		

Loibl S, O'Shaughnessy J, Untch M, et al. Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial. Lancet Oncol 2018;19(4):497-509.

Adjuvant Targeted therapy

Trastuzumab IV/SC +/- Chemotherapy

Trastuzumab can be given after completion of chemotherapy as well，loading dose 8 mg/kg，followed by 6 mg/kg，iv q3w for a total of 1 year.
Trastuzumab 4 mg/kg loading dose followed by 2 mg/kg iv qw during chemotherapy，then 6 mg/kg iv q3w，for a total of 1 year
Trastuzumab 600mg ， for a total of 1 year

Smith I et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomized controlled trial. Lancet 2007; 369:29.

Romond EH et al. Trastuzumab plus adjuvant chemotherapy for operable Her2-positive breast cancer. N Eng J Med 2005; 353:1673

健保申請條件如下~

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(IHC 3+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。

An FDA-approved biosimilar is an appropriate substitute for trastuzumab

Pertuzumab -optional

loading dose 840 mg IV day 1 followed by 420 mg IV Cycled every 21 days to complete 1y of therapy q3w

Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Ann Oncol 2013;24:2278-2284.

Swain S, Kim S-B, Cortes J, et al. Confirmatory overall survival(OS) analysis of CLEOPATRA: a randomized, double-blind, placebocontrolled Phase III study with pertuzumab (P), trastuzumab (T), anddocetaxel (D) in patients (pts) with HER2-positive first-line (1L)metastatic breast cancer (MBC). Cancer Research 2012;72:P5-18-26.

Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012;366:109-119.

Datko F, D'Andrea G, Dickler M, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with metastatic HER2-overexpressing metastatic breastcancer [abstract]. Cancer Research 2012;72:Abstract P5-18-20.

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

Chemotherapy for Metastatic breast cancer

Doxorubicin

Doxorubicin	60-75 mg/m^2 iv	day1
Q3w		

or

Doxorubicin	20 mg/m^2 iv	day1
Qw		

Chan S et al. Prospective randomized trial of docotaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999;17:2341.
Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinial trial. Am J Clin Oncol 1991;14:38.

Epirubicin

Epirubicin	60-90 mg/m^2 iv	day1
Q3w		

or

Epirubicin	20 mg/m^2 iv	day1
Qw		

Bastholt L et al. Dose-response relationship of epirubicin in the treatment of postmenopausal patients with metastatic breast cancer: a randomized study of epirubicin at four different dose levels performed by the Danish Breast Cancer Cooperative Group. J Clin Oncol 1996;14:1146.
Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinial trial. Am J Clin Oncol 1991;14:38.

Liposomal doxorubicin

Liposmal doxorubicin	35- 50 mg/m^2 iv	day1
Q3-4w		

O'Brien ME et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCL versus conventional doxorubicin for first line treatment of metastatic breast cancer. Ann Oncol 2004;15:440.
健保申請條件:1.用於單一治療有心臟疾病風險考量之轉移性乳癌患者。2.除以上條件，其餘皆自費。

Cisplatin

Cisplatin	75 mg/m^2 iv	day1
Q3w		

Carboplantin

Carboplantin	6 mg, AUC iv	day1
Q3w		

Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.

Docetaxel

Docetaxel	60-100 mg/m^2 iv	day1
Q3w		

or

Docetaxel	25 -40 mg/m^2 iv	day1
Qw		

Harvey V et al. Phase III trial of comparing three doses of docetaxel for second-line treatment of advanced breast cancer. J Clin Oncol 2006; 24:4963.

Burstein, HJ et al. Docetaxel administered on a weekly basis for metastatic breast cancer. J Clin Oncol 2000; 18:1212.

Paclitaxel

Paclitaxel	80 mg/m^2 iv	day1
Qw		

Bishop, JF et al. Initial paclitaxel improves outcome compared with CMFP combination chemotherapy as front-line therapy in untreated metastatic breast cancer. J Clin Oncol 1999; 17:2355.

Seidman AD et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all Her-2 overexpressors and random assignment to trastuzumab or not in Her-2 nonoverexpressors: Final results of Cancer and Leukemia Group B Protocol 9840. J Clin Oncol 2008; 26:1642.

健保規範;Paclitaxel

限用於已使用合併療法(除非有禁忌症、至少應包括使用 anthracycline)失敗的轉移性乳癌患者。(91/4/1、94/1/1)

Gemcitabine

Gemcitabine	800-1200 mg/m^2 iv	day1, 8, 15
Q4w		

Carmichael, J et al. Advanced breast cancer: a phase II trial with gemcitabine. J Clin Oncol 1995; 13:2731.

健保規範;Gemcitabine (如 Gemzar)

限用於 Gemcitabine 與 paclitaxel 併用，可使用於曾經使用過 anthracycline 之局部復發且無法手術切除或轉移性之乳癌病患。(94/10/1)

GP

Gemcitabine	800-1200 mg/m^2 iv	day1, 8,
Paclitaxel	175 mg/m^2 iv	day1
following paclitaxel on day 1	Cycled every 21 days.	

GP

Gemcitabine	800 mg/m^2 iv	day1, 8,15
Paclitaxel	80 mg/m^2 iv	day1, 8,15
Q4w		

Kun-Ming Rau et al.Weekly Paclitaxel Combining with Gemcitabine is an Effective and Safe Treatment for Advanced Breast Cancer Patients Jpn J Clin Oncol 2011;41(4)455–461

Vinorelbine

Vinorelbine	20 - 25 mg/m^2 iv、50-80 mg/m^2 po	day1,8
Q3w		

Gasparini, G et al. Vinorelbine is an active antiproliferative agent in pretreated advanced breast cancer patients: a phase II study. J Clin Oncol 1994; 12:2094.

健保規範;**Vinorelbine**

晚期或無法手術切除之非小細胞肺癌及轉移性乳癌病患。本成分之口服劑型與注射劑型不得併用

Capecitabine

Capecitabine	800 - 1250 mg/m^2 po bid	day1-14
Q3w		

Fumoleau, P et al. Multicentre, phase II study evaluating capecitabine monotherapy in patients with anthracycline- and taxane-pretreated metastatic breast cancer. Eur J Cancer 2004; 40:536.

1. capecitabine 與 docetaxel 併用於治療對 anthracycline 化學治療無效之局部晚期或轉移性乳癌病患。
2. 單獨用於對 taxanes 及 anthracycline 化學治療無效，或無法使用 anthracycline 治療之局部晚期或轉移性乳癌病患。

UFT po

Uracil/Tegafur	270 mg/m^2 /day po
7 days/week	

Y Park. Uracil-tegafur and tamoxifen vs cyclophosphamide, methotrexate, fluorouracil, and tamoxifen in post-operative adjuvant therapy for stage I, II, or IIIA lymph node-positive breast cancer: a comparative study. British Journal of Cancer (2009), 1 – 7

健保規範:Uracil-Tegafur

限轉移性胃癌、轉移性直腸癌、轉移性結腸癌、轉移性乳癌之病患使用（89/10/1、97/12/1）。

AC

Doxorubicin	60 mg/m^2 iv	day1
Cyclophosphamide	600 mg/m^2 iv	day1
Q3w		

Nabholtz JM et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: results of a randomized, multicenter, phase III trial. J Clin Oncol 2003;21:968.

EC

Epirubicin	75 mg/m^2	iv	day1
Cyclophosphamide	600 mg/m^2	iv	day1
Q3w , or Q2W(and GCSF support)			

Langley RE et al. Phase III trial of epirubicin plus paclitaxel compared with epirubicin plus cyclophosphamide as first-line chemotherapy for metastatic breast cancer: United Kingdom National Cancer Research Institute Trial AB01. J Clin Oncol 2005; 23:8322.

Eribulin

Eribulim	1.4mg/m^2	iv	day1,8
Q3w			

Pooled analyses of eribulin in metastatic breast cancer patients with at least one prior chemotherapy.
Pivot X1, Marmé F2, Koenigsberg R3, Guo M4, Berrak E5, Wolfer A6. 2016 Aug;27(8):1525-31. doi: 10.1093/annonc/mdw203. Epub 2016 May 13.

健保規範:(如 Halaven):(103/12/1、106/11/1)1. 用於治療轉移性乳癌患者且先前曾接受過 anthracycline 和 taxane 兩種針對轉移性乳癌之化學治療輔助性治療。2. 每 3 個療程需進行療效評估，病歷應留存評估紀錄，無疾病惡化方可繼續使用。(106/11/1)

Ixabepilone

Ixabepilone	40mg/m^2	iv	day1
Capecitabine	2000mg/m^2	po	day1
Q3w			

1. Li J, Ren J, Sun W. Systematic review of ixabepilone for treating metastatic breast cancer. Breast Cancer. 2017 Mar;24(2):171-179. doi: 10.1007/s12282-016-0717-0. Epub 2016 Aug 4. Review. PubMed PMID: 27491426.

2.Puhalla, S., & Brufsky, A. (2008). Ixabepilone: a new chemotherapeutic option for refractory metastatic breast cancer. Biologics : Targets & Therapy, 2(3), 505–515.

3.Sparano, J. A., Vrdoljak, E., Rixe, O., Xu, B., Manikhas, A., Medina, C., … Conte, P. (2010). Randomized Phase III Trial of Ixabepilone Plus Capecitabine Versus Capecitabine in Patients With Metastatic Breast Cancer Previously Treated With an Anthracycline and a Taxane. Journal of Clinical Oncology, 28(20), 3256–3263. http://doi.org/10.1200/JCO.2009.24.4244

健保規範:Ixabepilone (如 Ixempra):(110/2/1) 1. 限 Ixabepilone 合併 capecitabine 用於局部晚期或轉移性乳癌患者，需符合以下 條件之一： (1)對 taxane 有抗藥性且無法接受 anthracycline 治療者。 (2)對 taxane 及 anthracycline 治療無效者。 2. 每 3 個療程需進行療效評估，病歷應留存評估紀錄，無疾病惡化方可繼續使用。 3. Ixabepilone 與 eribulin 用於治療上述之轉移性乳癌患者時，僅得擇一使用，且不得互換(ixabepilone 限用於未曾使用過 eribulin 之病患)。

Target therapy for Metastatic breast cancer

Trastuzumab IV/SC +/- Chemotherapy

Trastuzumab 8mg/kg iv over 90 min first wk followed by 6 mg/kg iv over 30 min	q3w
Trastuzumab 4 mg/kg loading dose followed by 2 mg/kg iv	qw
Trastuzumab 600mg for a total of 1 year	

Cobleigh, MA et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. J Clin Oncol 1999; 17:2639.

健保規範: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。(91/4/1、99/1/1)(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(93/8/1、95/2/1、99/1/1)

(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；但與 pertuzumab 及 docetaxel 併用時，不在此限。(99/1/1、108/5/1)

經事前審查核准後使用，核准後每 24 週須檢附療效評估資料再次申請，若疾病有惡化情形即不應再行申請(105/11/1)。

An FDA-approved biosimilar is an appropriate substitute for trastuzumab

Pertuzumab +/- Chemotherapy

840 mg IV day 1 followed by 420 mg IV Cycled every 21 days to complete 1 y of therapy	q3w

Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Ann Oncol 2013;24:2278-2284.

Swain S, Kim S-B, Cortes J, et al. Confirmatory overall survival(OS) analysis of CLEOPATRA: a randomized, double-blind, placebocontrolled Phase III study with pertuzumab (P), trastuzumab (T), anddocetaxel (D) in patients (pts) with HER2-positive first-line (1L)metastatic breast cancer (MBC). Cancer Research 2012;72:P5-18-26.

Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012;366:109-119.

Datko F, D'Andrea G, Dickler M, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with metastatic HER2-overexpressing metastatic breastcancer [abstract]. Cancer Research 2012;72:Abstract P5-18-20.

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

健保規範:(108/05/01)

1. Pertuzumab 與 trastuzumab 及 docetaxel 併用於治療轉移後未曾以抗 HER2 或化學療 法治療之 HER2 過度表現(IHC3+或 FISH+)轉移性乳癌病患。 2.須經事前審查核准後使用，核准後每 18 週須檢附療效評估資料再次申請，若疾病有惡化情形即不應再行申請，每位病人至多給付 18 個月為限。

Ado-trastuzumab emtansine(TDM1)

ado-trastuzumab emtansine	3.6 mg/kg IV	day 1
Cycled every 21 days.		

Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer [supplementary appendix available online]. N Engl J Med 2012;367:1783-1791.
Ellis PA, Barrios CH, Eiermann W, et al. Phase III, randomized study of trastuzumab emtansine (T-DM1) {+/-} pertuzumab (P) vs trastuzumab + taxane (HT) for first-line treatment of HER2-positiveMBC: Primary results from the MARIANNE study. ASCO Meeting Abstracts 2015;33:507.

健保規範(110/2/1):限單獨使用於 HER2 過度表現 (IHC3+或 FISH+)之轉移性乳癌患者作為二線治療，且同時符合下列情形： (1)之前分別接受過 trastuzumab 與一種 taxane 藥物治療，或其合併療法，或 pertuzumab 與 trastuzumab 與一種 taxane 藥物治療。 (2)之前已經接受過轉移性癌症治療，或在輔助療法治療期間或完成治療後 6 個月內 癌症復發。 (3)合併有主要臟器(不包含骨及軟組織)轉移。 2.經事前審查核准後使用，核准後每 12 週須檢附療效評估資料再次申請，若疾病有惡化情形即不應再行申請，每位病人至多給付 10 個月(13 個療程為上限)。3.Trastuzumab emtansine 和 lapatinib 僅能擇一使用，不得互換。

Bevacizumab(自費) + Chemotherapy

Bevacizumab	10 mg/kg iv	d1
Q2w		

or

Bevacizumab	15 mg/kg iv	d1
Q3w		

Miller KD et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Eng J Med 2007; 357:2666.
Miles D et al. Randomized, double-blind, placebo-controlled, phase III study of bevacizumab (BV) with docetaxel (D) or docetaxel with placebo (PL) as first-line therapy for patients with locally recurrent or metastatic breast cancer (mBC): AVADO. 2008 ASCO annual meeting. LBA1011.

An FDA-approved biosimilar is an appropriate substitute for Bevacizumab

Lapatinib + Xeloda

Lapatinib	1250mg po	
Xeloda	2000mg/m^2 po	d1-14

Lancet Oncol 2013 Jan;14(1):64-71.doi:10.1016/S1470-2045(12)70432-1.Epub 2012 Nov.

健保規範:lapatinib（如 Tykerb）

1.與 capecitabine 併用，使用於曾接受 anthracycline, taxane 以及 trastuzumab 治療後病況惡化之轉移性乳癌併有腦部轉移，且為 HER2 過度表現(IHC3+或 FISH+)患者。

2.每 3 個月需進行療效評估，病歷應留存評估紀錄，無疾病惡化方可繼續使用。(106/11/1)

Capecitabine（如 Xeloda）

1.Capecitabine 與 docetaxel 併用於治療對 anthracycline 化學治療無效之局部晚期或轉移性乳癌病患。

2. 單獨用於對 taxanes 及 anthracycline 化學治療無效，或無法使用 anthracycline 治療之局部晚期或轉移性乳癌病患。

BEEP

Bevacizumab	15 mg/kg iv	d1
Etoposide	70 mg/m^2/d	d2, 3, 4
Cisplatin	70 mg/m^2	d2
Q3w		

Lu YS, et al. Bevacizumab preconditioning followed by etoposide and cisplatin (BEEP) is a highly effective treatment for brain metastases of breast cancer progressing from radiotherapy — result of a multi-center phase II study. ECC 2013:1878.

Everolimus

Everolimus	10mg po

健保規範::Everolimus 5mg 及 10mg(如 Afinitor 5mg 及 10mg)：

與 exemestane 併用，作為先前已使用過非類固醇類之芳香環酶抑制劑治療無效，而未曾使用 exemestane 之荷爾蒙接受體陽性、HER2 受體陰性且尚未出現器官轉移危急症狀 (visceral crisis)之轉移性乳癌病人的治療，且使用本品無效後，不得申請 CDK4/6 抑制劑藥品（104/9/1、109/4/1）。限每日最大劑量為 10㎎。（108/10/1）

Bachelot T, Bourgier c, Cropet C, et al. TAMRAD: A GINECO randomized phase II trial of everolimus in combination with tamoxifenversus tamoxifen alone in patients (pts) with hormone-receptor positive, HER2 negative metastatic breast Cancer (MBC) with prior exposure to aromatase inhibitors (AI) [abstract]. Cancer Res 2010;70(24 Supplement):

Yardley DA, Noguchi S, Pritchard KI, et al. Everolimus plusexemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis. Adv Ther2013;30:870-884.

Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. N Engl J Med 2012;366:520-529.

Enhertu(Fam trastuzumab deruxtecan -nxki)

Enhertu(trastuzumab deruxtecan)	5.4 mg/kg iv	d1
Q3w		

for HER2 IHC 1+ or 2+/ISH negative)

Modi S, Jacot W, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-lowadvanced breast cancer [article and supplementary appendix published online ahead of print June 5, 2022]. N Engl J Med 2022.

Modi S, Saura C, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. N Engl J Med 2020;382:610-621.

Trodelvy(Sacituzumab govitecan-hziy)

Trodelvy(Sacituzumab govitecan-hziy)	10mg/kg iv	d1,8
Q3w		

for TNBC or HR+/HER 2-

A Bardia, SA Hurvitz, SM Tolaney, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer: ASCENT Clinical Trial Investigators. N Engl J Med 2021;384:1529-41.

六、免疫藥物治療

Immune therapy

Pembrolizumab

Pembrolizumab	200mg IV	day 1/q3wks
Weekly paclitaxel	80mg/m^2 IV	day 1/q1w
carboplatin	AUC 5 (q3w)/1.5(q1w)IV day 1	
Cycled every 21days x 4cycle(cycles1-4)		
followed by		
Pembrolizumab	200mg IV	day 1
Doxorubicin	60mg/m^2 IV or Epirubicin 90mg/m^2 IV	day 1
Cyclophosphamide	600mg/m^2 IV	day 1
Cycled every 21days x 4cycle(cycles5-8)		
followed by		
Pembrolizumab	200mg IV	day 1/q3wks
Cycled every 21days x 9cycles		

Preoperative/Adjuvant therapy regimens NCCN p.66

High-risk triple-negative breast cancer (TNBC): Preoperative pembrolizumab + carboplatin + paclitaxel, followed by preoperative pembrolizumab + cyclophosphamide + doxorubicin or epirubicin, followed by adjuvant pembrolizumab

七、放射線治療原則

術前全身性系統治療

在接受術前治療時，放射治療和治療範圍的適應症應基於治療前臨床分期，病理分期和腫瘤型態。

全乳房放射治療

*目標為整個乳房組織。

*放射治療劑量:

整個乳房應以 25－28 放射次數接受 45－50.4 Gy 的劑量，或以 15－16 放射次數接受 40－42.5 Gy 的劑量（低分次放射治療）。

對於復發風險較高的患者，建議加強腫瘤手術切除後之範圍。典型的加強劑量為以 4-8 放射次數接受 10-16 Gy 的劑量。

*所有劑量排程 1 週 5 天

胸壁放射治療(含乳房重建)

*目標為含當同側胸壁，乳房切除手術範圍和引流部位。

*根據患者是否進行乳房重建，使用光子或電子射束技術是合適的。

*電腦斷層影像以識別肺和心臟的體積，並最大程度地減少這些器官的暴露。

*應特別考慮使用推注材料，以確保皮膚劑量足夠。

* 放射治療劑量以 25－28 放射次數接受 45－50.4 Gy 的劑量於胸壁±加強劑量於疤痕範圍，以每次 1.8-2 Gy 的劑量總劑量為 60 Gy

*所有劑量排程 1 週 5 天

局部淋巴結放射治療

*放射治療劑量以 25－28 放射次數接受 45－50.4 Gy 的劑量於局部淋巴結範圍.

*所有劑量排程 1 週 5 天

Accelerated Partial Breast Irradiation (APBI)/Partial Breast Irradiation (PBI)

• APBI/PBI offers comparable local control to WBRT in selected low-risk patients with early-stage breast cancer. However, the optimalexternal beam-APBI/PBI technique/fractionation for minimizing long-term cosmesis effects has not been determined.

►Patients are encouraged to participate in clinical trials.

►The NCCN Panel recommends APBI/PBI for any patient who is *BRCA* negative and meets the 2016 ASTRO criteria. The 2016 ASTRO criteria define patients aged ≥50 years to be considered "suitable" for APBI/PBI if:

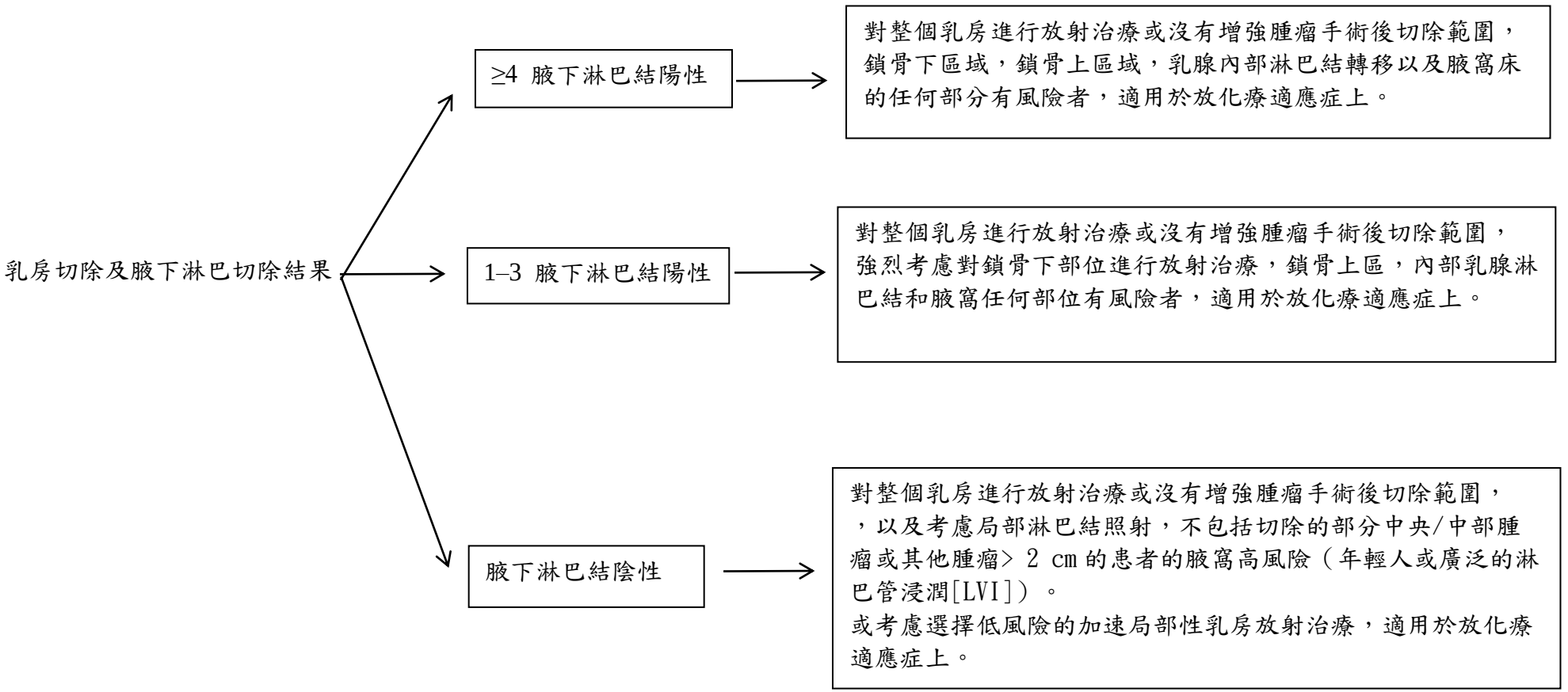
◊ Invasive ductal carcinoma measuring ≤2 cm (pT1 disease) with negative margin widths of ≥2 mm, no LVI, and ER-positive or

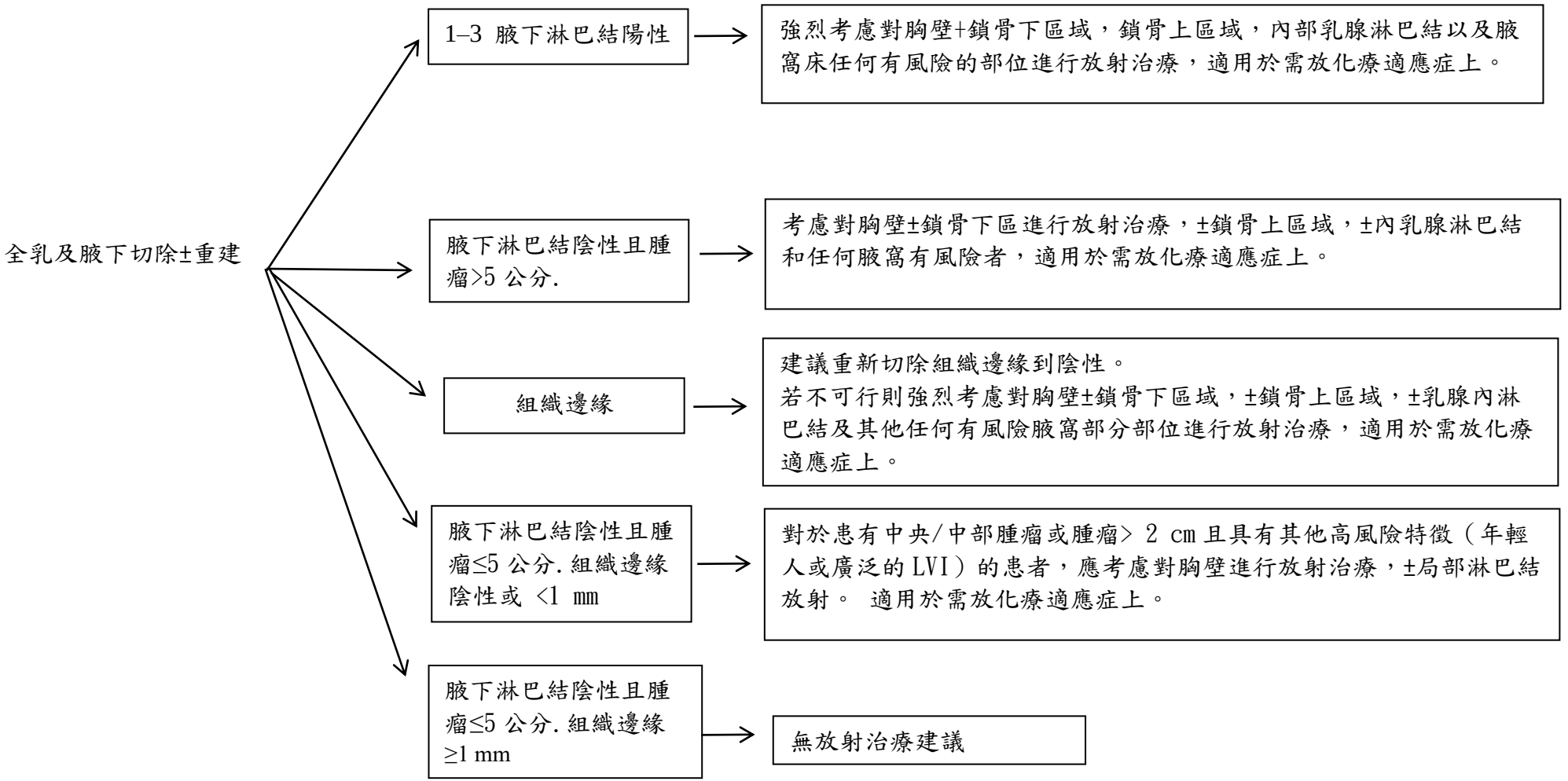
◊ Low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.

• **RT dosing**:

Regimen	Method	Reference
30 Gy/5 fractions QOD(preferred)	External beam RT (EBRT)	Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. Eur J Cancer2015;51:451-463. Meattini I, Marrazzo L, Saieva C, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: Long-term results of the randomized phase III APBI-IMRT-Florence Trial. JClin Oncol 2020;38:4175-4183.

LOCOREGIONAL TREATMENT OF T1-3,N0-1,M0 DISEASE




全乳及腋下切除±重建
1–3 腋下淋巴結陽性
強烈考慮對胸壁+鎖骨下區域，鎖骨上區域，內部乳腺淋巴結以及腋窩床任何有風險的部位進行放射治療，適用於需放化療適應症上。
腋下淋巴結陰性且腫瘤>5 公分.
考慮對胸壁±鎖骨下區進行放射治療，±鎖骨上區域，±內乳腺淋巴結和任何腋窩有風險者，適用於需放化療適應症上。
組織邊緣
建議重新切除組織邊緣到陰性。
若不可行則強烈考慮對胸壁±鎖骨下區域，±鎖骨上區域，±乳腺內淋巴結及其他任何有風險腋窩部分部位進行放射治療，適用於需放化療適應症上。
腋下淋巴結陰性且腫瘤≤5 公分. 組織邊緣陰性或 <1 mm
對於患有中央/中部腫瘤或腫瘤> 2 cm 且具有其他高風險特徵（年輕人或廣泛的 LVI）的患者，應考慮對胸壁進行放射治療，±局部淋巴結放射。 適用於需放化療適應症上。
腋下淋巴結陰性且腫瘤≤5 公分. 組織邊緣≥1 mm
無放射治療建議

術中放射線治療(IORT):

Table 1 Comparison of patient groups in original and updated consensus statements

Patient group	Risk factor	Original	Update
Suitability	Age	≥60 y	≥50 y
	Margins	Negative by at least 2 mm	No change
	T stage	T1	Tis or T1
	DCIS	Not allowed	If all of the below: • Screen-detected • Low to intermediate nuclear grade • Size ≤2.5 cm • Resected with margins negative at ≥3 mm
Cautionary	Age	50-59 y	• 40-49 y if all other criteria for "suitable" are met • ≥50 y if patient has at least 1 of the pathologic factors below and does not have any "unsuitable" factors *Pathologic factors:* • Size 2.1-3.0 cm [a] • T2 • Close margins (<2 mm) • Limited/focal LVSI • ER(-) • Clinically unifocal with total size 2.1-3.0 cm [b] • Invasive lobular histology • Pure DCIS ≤3 cm if criteria for "suitable" not fully met • EIC ≤3 cm
	Margins	Close (<2 mm)	No change
	DCIS	≤3 cm	≤3 cm and does not meet criteria for "suitable"
Unsuitable	Age	<50 years	• <40 y • 40-49 y and do not meet the criteria for cautionary
	Margins	Positive	No change
	DCIS	>3 cm	No change

[a] The size of the invasive tumor component.

[b] Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

名詞解釋：

- **Early stage breast cancer**：Stage I, II
- **Locally advanced breast cancer**：Stage III, IV
- **DCIS** s/p lumpectomy with moderate risk：New Van Nuys Prognostic Index Scoring System≧7
- **DCIS**：Ductal carcinoma in situ
- **BCS**：Breast-conservative surgery
- **SCN**：supra-clavicular lymph nodes
- **IMN**：internal mammary lymph nodes
- **IORT**: Intra-operative Radiotherapy

表一 HER2 判讀結果

判讀結果	HER2/cep17 比值	腫瘤細胞平均 HER2 基因數目	HER2 免疫組織染色結果
HER2 陽性(基因擴增)	HER2/CEP17 ratio ≧2.0	average HER2 copy number ≧4.0 signals/cell	N/A
	HER2/CEP17 ratio ≧2.0	average HER2 copy number <4.0 signals/cell	3
	HER2/CEP17 ratio <2.0	average HER2 copy number ≧6.0 signals/cell	2+/3+
	HER2/CEP17 ratio <2.0	verage HER2 copy number≧4.0 and <6.0 signals/cell	3
HER2 陰性(無基因擴增)	HER2/CEP17 ratio <2.0	average HER2 copy number <4.0 signals/cell	N/A
	HER2/CEP17 ratio ≧2.0	average HER2 copy number <4.0 signals/cell	0/1+/2+
	HER2/CEP17 ratio <2.0	average HER2 copy number ≧6.0 signals/cell	0/1+
	HER2/CEP17 ratio <2.0	average HER2 copy number≧4.0 and <6.0 signals/cell	0/1+/2+

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乳癌各期別完成治療率定義

癌別	期別	治療方式	完治率定義
乳癌	0	手術±放療±賀爾蒙治療	完成乳房切除手術為完治日
	I II III	手術±化療±放療 ±賀爾蒙治療±標靶	1. 完成部分乳房切除手術+局部放射治療療程結束為完治日 2. 完成全乳房切除手術為完治日 3.完成乳房切除手術+化療療程至少 4cycle 為完治日 4.執行前導性化療+乳房切除手術為完治日 5.若拒絕手術治療而執行賀爾蒙藥物治療至少使用 1 年為完治日
	IV	化療±標靶±手術 ±賀爾蒙治療	1.化療(含口服)至少 6 個月為完治日 2.賀爾蒙藥物治療至少使用 1 年為完治日 3.治療中轉安寧照護為完治日

自 110.1.1 起適用