中山醫學大學附設醫院
乳癌診療指引

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

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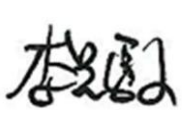
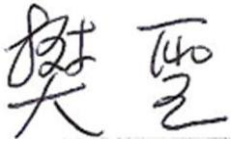
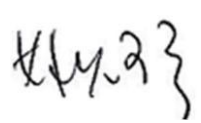
乳癌多專科醫療團隊編修

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	抗癌藥物安全小組	團隊負責人
				

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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),
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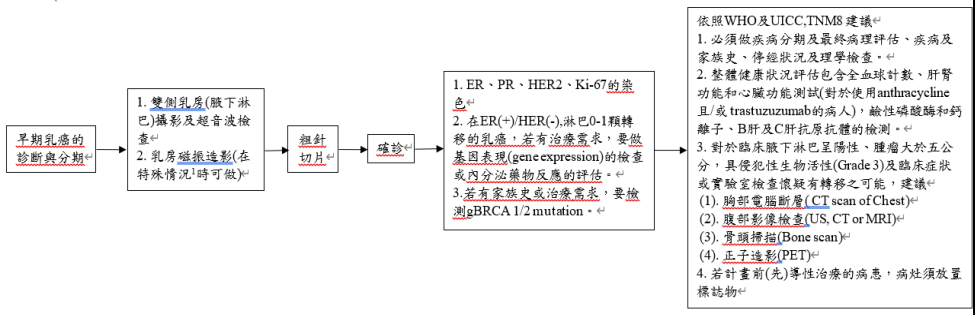
<tr><td colspan="2">MRI, magnetic resonance imaging(磁振造影)
ER, oestrogen receptor(雌激素接受器) PgR, progesterone receptor(黃體激素接受器)
HER2, human epidermal growth factor 2 receptor(人類表皮生長因子2接受器)
**有BRCA家族史；Lobular cancer；Dense breast；懷疑可能多發性的乳癌.
#Tumor-infiltrating lymphocytes(分離腫瘤浸潤淋巴細胞)</td></tr>
</table></td><td>二、乳癌的診斷
 
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<tr><td>第７２頁</td><td>無</td><td><table>
<tr><td colspan="2">PIK3CA activating mutation
HR-positive, HER2-negative</td></tr>
<tr><td>Regimen</td><td>Inavolisib 9mg PO QD + palbociclib 125mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W</td></tr>
<tr><td>藥名</td><td>Inavolisib 9mg PO QD + palbociclib 125mg PO QD+ Fulvestrant INJ 250MG/5ML Q1.Q15 Q4W</td></tr>
<tr><td>Ref.</td><td>Turner NC, Im SA, Saura C, et al. Inavolisib-based therapy in PIK3CA-mutated advanced breast cancer. N Engl J Med 2024;391:1584-1596.</td></tr>
<tr><td>健保給付</td><td>self-pay</td></tr>
</table>
<table>
<tr><td colspan="2">PIK3CA activating mutation
HR-positive, HER2-negative</td></tr>
<tr><td>Regimen</td><td>Alpelisib 300mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W</td></tr>
<tr><td>藥名</td><td>Alpelisib 300mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W</td></tr>
<tr><td>Ref.</td><td>Andre F, Ciruelos E, Rubovszky G, et al. Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. N Engl J Med 2019;380:1929-1940.</td></tr>
<tr><td>健保給付</td><td>預計 2026 年 01 月 01 日開始給付，
1.與 fulvestrant 併用於曾接受 CDK4/6 抑制劑治療但疾病惡化的停經後轉移性乳癌病人，且須完全符合下列條件：
(1)待測腫瘤為：ER 或 PR＞30%。
(2)HER-2 檢測為陰性。
(3)具有 PIK3CA 基因突變。
2.需經事前審查核准後使用：
(1)初次申請需檢附 PIK3CA 基因突變檢測報告，且需符合全民健康保險藥品給付規定之通則十二。
(2)核准後每 12 週需檢附療效評估資料再次申請，若疾病惡化是必須停止使用。
3.每日最多處方 2 粒。</td></tr>
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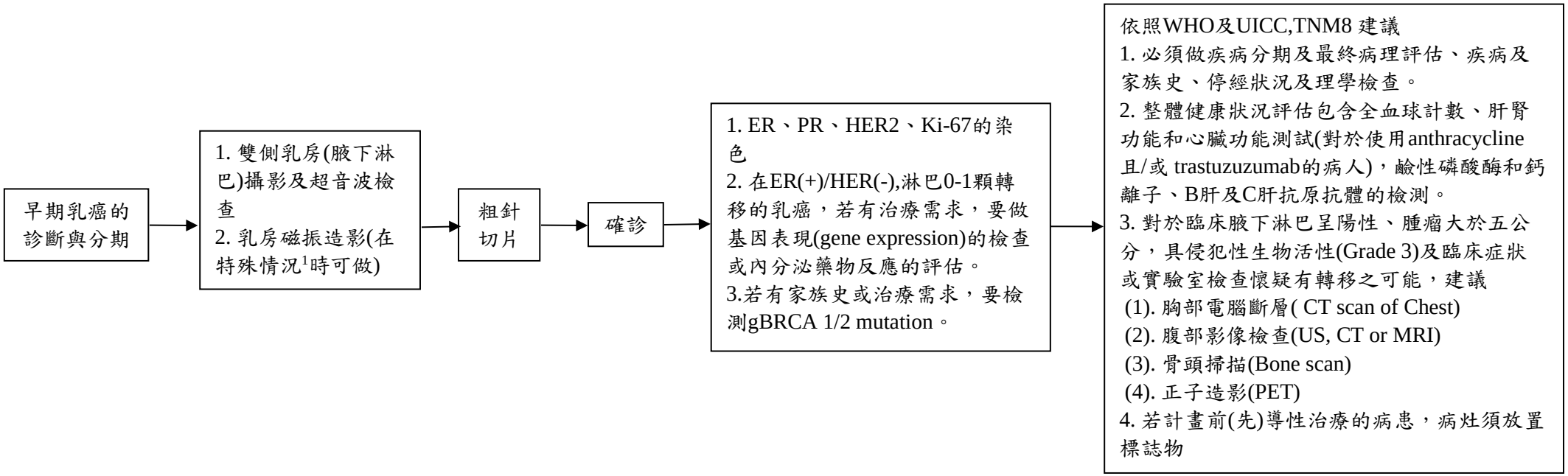
目　　錄

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



備註: [1] Magnetic resonance imaging (MRI) of the breasts is recommended in case of uncertainties following standard imaging and in special clinical situations [e.g. familial breast cancer associated with germline BRCA1/2 mutation (gBRCA1/2m) and other high-risk PVs, lobular cancers,suspicion of multifocality and/or multicentricity,presence of breast implants.

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, Sono)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 **pM1** 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	IB
			Negative	Positive	
				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

*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	
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	
				Negative	
	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	
				Negative	IIIB
	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	
				Negative	
		Negative	Positive	Positive	
				Negative	IIIA
			Negative	Positive	
				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	
				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
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	IIIB
				Negative	
			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:

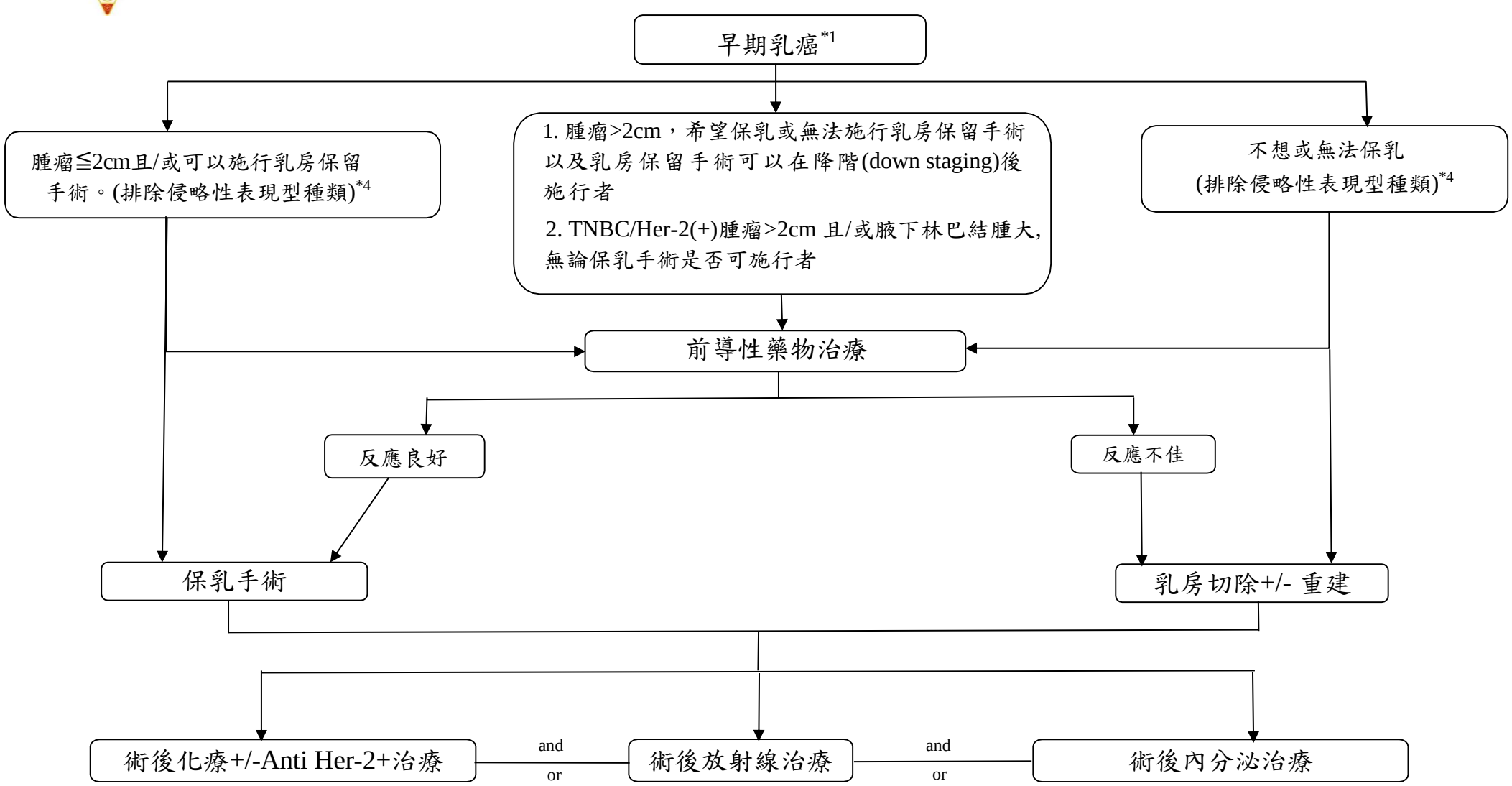
1. For cases with lymph node involvement with no evidence of primary tumor (e.g. T0 N1, etc.) or with breast ductal carcinoma in situ (e.g. Tis N1, etc.), the grade, HER2, ER and PR information from the tumor in the lymph node should be used for assigning stage group.
2. For cases where HER2 is determined 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.

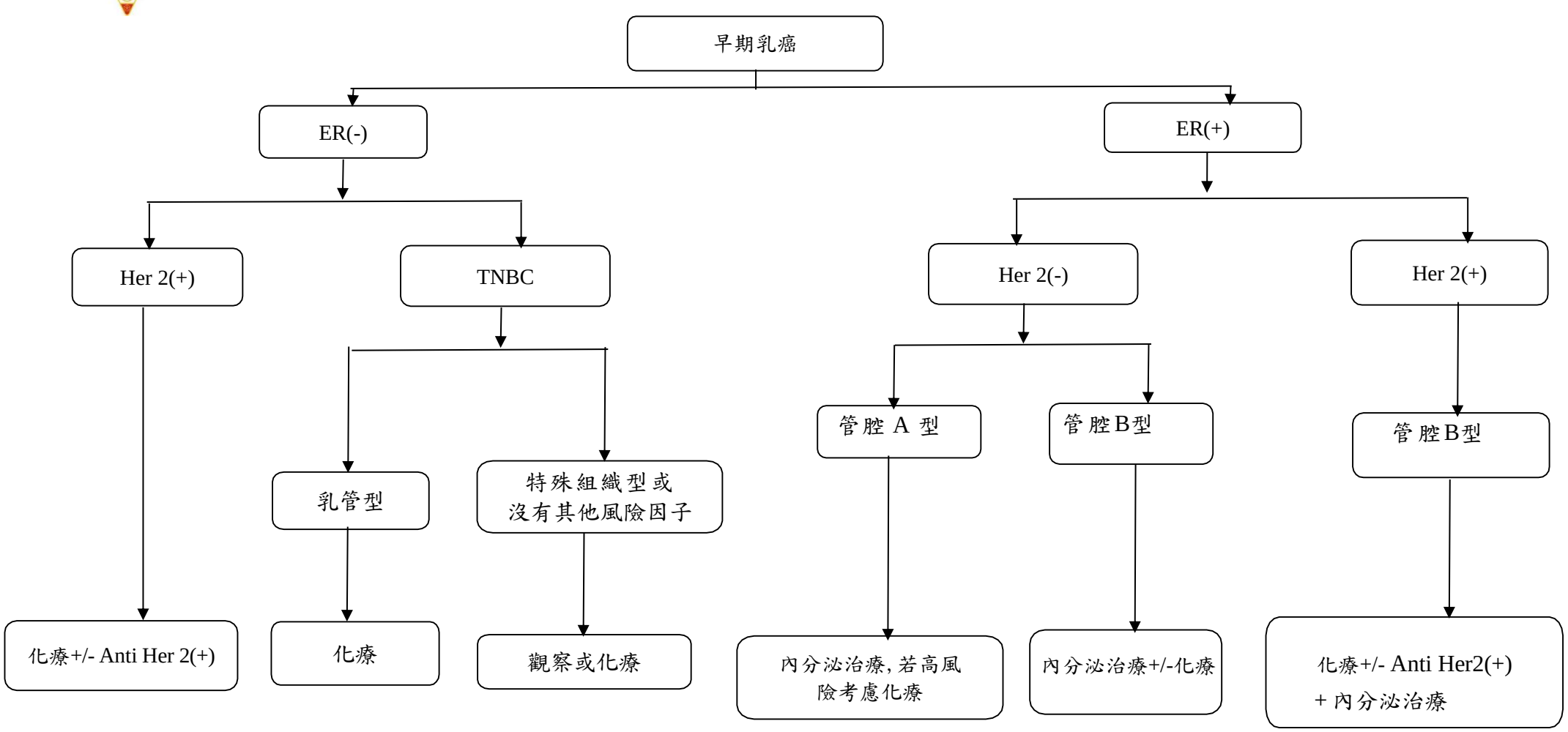


*1早期乳癌：Early breast cancer is defined as tumours of not more than 5 cm diameter, with either impalpable or palpable but not fixed lymph nodes and no evidence of distant metastases. 通常是指0-IIIA期。

*2TNBC：三陰性乳癌

*3Her2(+)：第二型類上皮生長因子過度表現型

*4侵略性表現種類：三陰性及 Her2(+)腫瘤

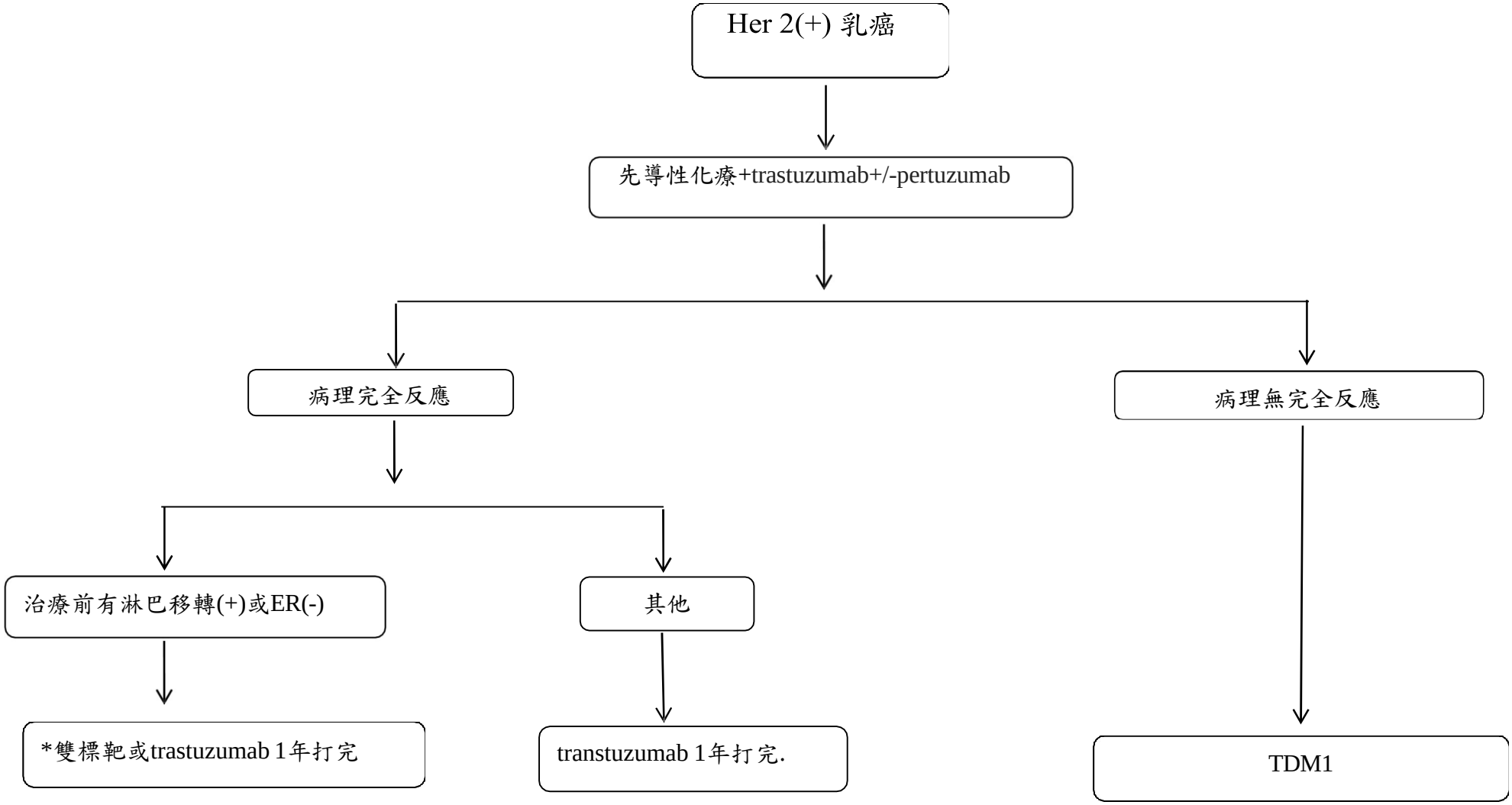


ER(+):雌激素接受體過度表現

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。

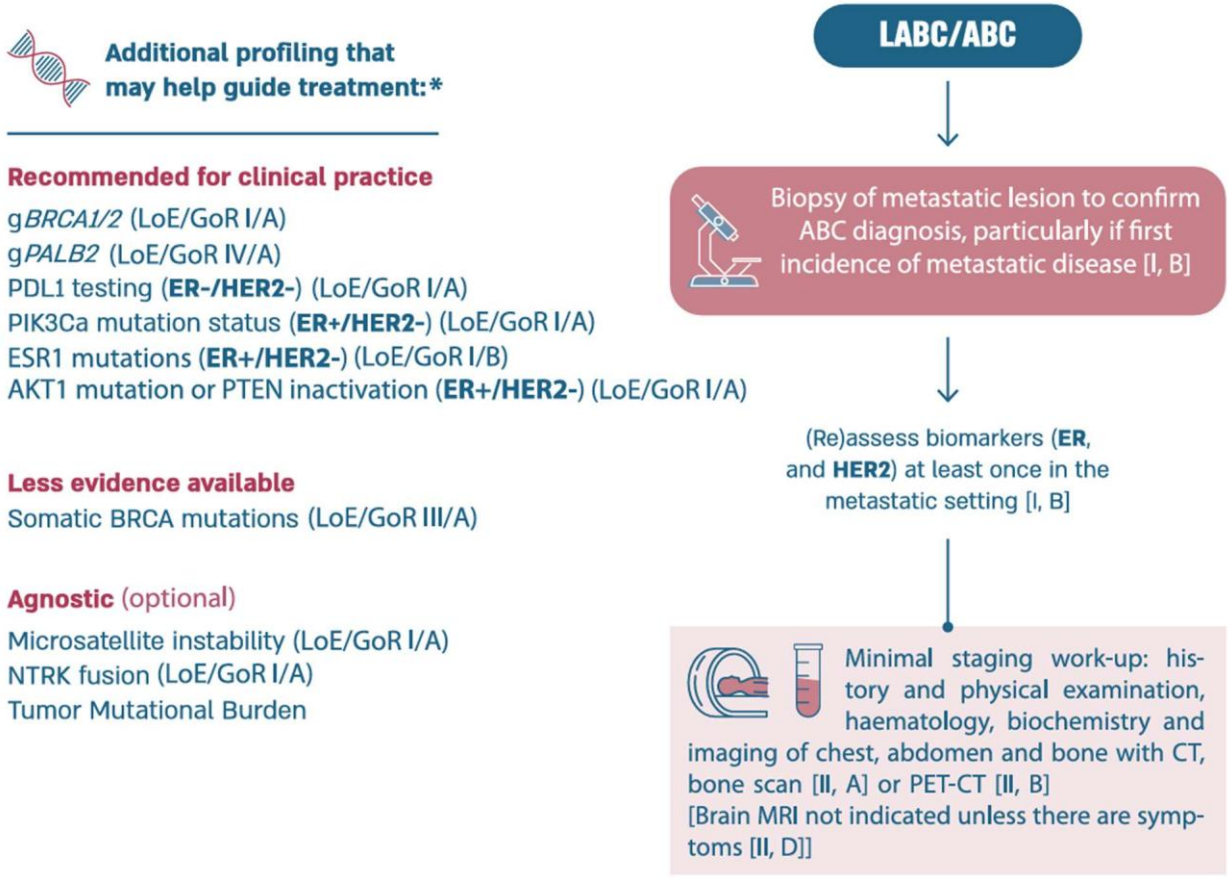
所有病人都應該能接受到最高標準的癌症治療團隊照顧

- 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。
- PR在轉移表現下的意義不大，主要是用來作為三陰性乳癌的評估。

治療選擇至少必須考慮以下因素：ER/Her2、先前做過的治療與毒性、無病間隔期、腫瘤負荷量、生理年齡、共病、經期狀況、社經與心理狀況、患者對於治療的偏若可以使用標靶藥物，則需知道HER2陰性患者中的BRCA表現、ER陽性患者中PIK3CA變異表現、三陰性患者中PD-L1表現。



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。
- 對於新診斷的第四期病人，切除原發腫瘤並不會增加存活，但在以下情況可以執行
  - ➢ 有症狀的原發腫瘤，以控制症狀
  - ➢ 遠端轉移已受控制，原發腫瘤仍在惡化

➢ 除原發腫瘤外，沒有其他症狀

- 年齡不應作為影響治療選擇的單一因子。
- 治療假期：在謹慎地監控下，預先計畫治療的休息期，以面對長期的治療
- 若疾病有長期的完全緩解，可考慮暫停治療。

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 (luminal-like) negative ABC

- 內分泌治療(ET)

✓ 即使在有內臟轉移狀況下仍為首選，除非證明有內分泌治療抗性或因內臟危機需要快速控制病情時。

✓ 對停經前女性而言，卵巢功能抑制或卵巢摘除，再結合其他的內分泌治療是首選。若患者拒絕卵巢功能抑制或卵巢摘除，Tamoxifen是唯一可考慮的藥物

✓ 一線內分泌藥物的選擇取決於adjuvant ET的類型/持續時間以及結束後的時間；可選擇AI、Tamoxifen或Fulvestrant，適用

於停經前女性+ OFS/OFA，男性（+LHRH agonist）和停經後女性。

- CDK4/6 inhibitor

√ 搭配ET使用，為治療首選。目前有顯著的PFS、OS益處，同時有良好的生活品質。

√ 可搭配AI及Fulvestrant使用

√ Tamoxifen不可與Ribociclib一同使用。

√ 與化療做為第一線治療而言，有相似的療效，但有較佳的生活品質。

√ 對於特定患者(較低的疾病負荷、無病間隔期、患者偏好、可及性限制)，單獨使用ET作為一線治療，CDK4/6 inhibitor + ET作為二線治療，也是一個選擇。(SONIA trial)

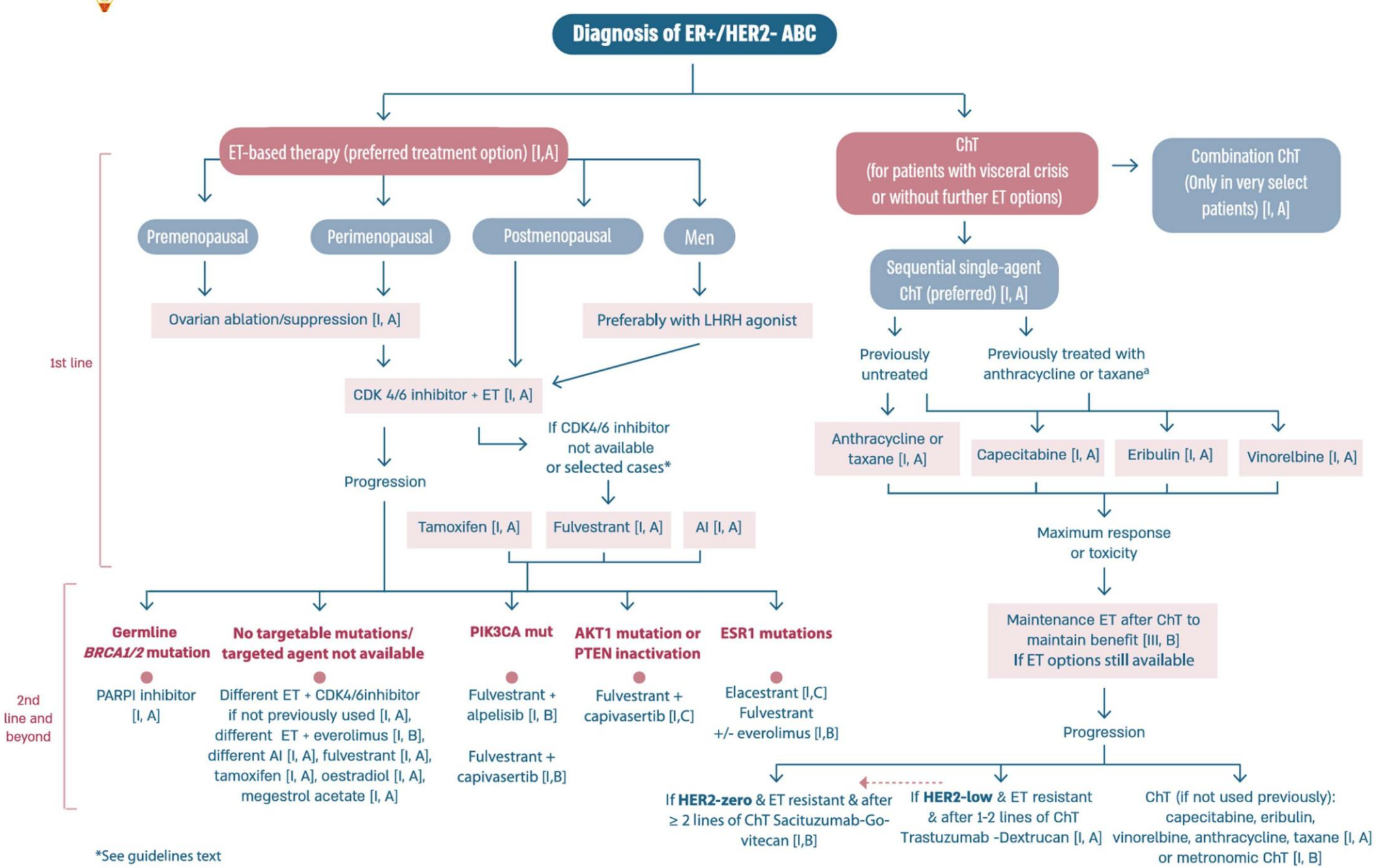
√ 在部分研究中，於具侵襲性的疾病表現的患者中，也具有優良的效果。(RIGHT Choice trial)

- 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、113/1/1、113/3/1)
- 1. 用於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、113/1/1)
- (1)荷爾蒙接受體為：ER或PR >30%。（109/10/1、113/1/1)
- (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.用於停經前/正在停經乳癌婦女發生遠端轉移後之全身性藥物治療，須與芳香環轉化酶抑制劑及GnRH analogue併用。（113/1/1）
- (1)荷爾蒙接受體為：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。
- (4)骨轉移不可為唯一轉移部位。
- 3.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）
- 4.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。
- 5.110年9月30日以前已核定用藥之病人，得經事前審查核准後，使用至總療程(即終生24個月)或總療程期間疾病惡化為止，且後續不得再申請使用本類藥品。（110/10/1、113/1/1）
- 6.若先前使用everolimus無效後，不得再申請本類藥品。(109/4/1)
- 7.若先前於早期乳癌使用abemaciclib無效後，不得再申請本類藥品。(113/3/1)

- Everolimus
  - √ 合併AI使用，可獲得PFS的延長，不過沒有OS的益處。
  - √ 也可合併Tamoxifen or fulvestrant使用
  - √ 需使用類固醇漱口水以預防口腔炎
  - √ 疾病進展後不應使用。
- Alpelisib
  - √ PIK3CA-mutant
  - √ 合併fulvestrant使用，可獲得PFS的延長，不過沒有OS的益處。
  - √ 建議用於CDK4/6 inhibitor + ET之後的第二線治療
  - √ 應注意HbA1c以及使用抗組織胺以預防皮疹。
- Elacestrant (口服選擇性雌激素受體降解劑（SERD）)
  - √ 可單獨使用作為具有 ESR1 突變患者的第二或第三線治療。
- Capivasertib (AKT抑制劑)
  - √ 搭配Fulvestrant，可作為內分泌治療抗性患者的治療選項，特別是在具有AKT路徑（PIK3CA/PTEN/AKT1）變異的患者中
- Antibody-drug conjugates (ADCs)
  - √ Sacituzumab govitecan (SG)
    - 於HER2低或HER2零之患者均有些許PFS延長，可作為一個治療選擇。
  - √ Datopotamab Deruxtecan (Dato-DXd)
    - 不建議使用
  - √ Trastuzumab deruxtecan (T-DXd)
    - 於HER2 low患者具有顯著PFS/OS成效。
    - 可能發生間質性肺炎甚至致死，應密切監測預防。
    - 於ER+/Her2 low患者，建議優先使用T-DXd而後SG。
- nonsteroidal Al and fulvestrant
  - √ 可使用於未接受過adjuvant ET且不使用CDK4/6 inhibitor + ET的患者。

√ 沒有跟CDK4/6 inhibitor + ET的比較

- ET-base的治療沒有絕對的優先順序，取決於先前使用的藥物、對這些藥物的反應持續時間、疾病負擔、患者偏好和可用性。
- 二線之後的治療包括之前未使用過的單一藥物(NSAI, SAI,tamoxifen, fulvestrant, megestrol acetate, low-dose estrogen, Single agent abemaciclib)
- 使用曾經用過的藥物也可以列為考慮，但沒有強力證據支持。
- 不應同時使用化學治療+內分泌治療。
- 化療後的內分泌治療(maintenance ET)是一個合理的選項


Diagnosis of ER+/HER2- ABC
ET-based therapy (preferred treatment option) [I,A]
ChT (for patients with visceral crisis or without further ET options)
Combination ChT (Only in very select patients) [I, A]
Premenopausal
Perimenopausal
Postmenopausal
Men
Ovarian ablation/suppression [I, A]
Preferably with LHRH agonist
1st line
CDK 4/6 inhibitor + ET [I, A]
If CDK4/6 inhibitor not available or selected cases*
Progression
Tamoxifen [I, A]
Fulvestrant [I, A]
AI [I, A]
Sequential single-agent ChT (preferred) [I, A]
Previously untreated
Previously treated with anthracycline or taxane[a]
Anthracycline or taxane [I, A]
Capecitabine [I, A]
Eribulin [I, A]
Vinorelbine [I, A]
Maximum response or toxicity
Maintenance ET after ChT to maintain benefit [III, B] If ET options still available
Progression
2nd line and beyond
Germline BRCA1/2 mutation
PARPI inhibitor [I, A]
No targetable mutations/ targeted agent not available
Different ET + CDK4/6inhibitor if not previously used [I, A], different ET + everolimus [I, B], different AI [I, A], fulvestrant [I, A], tamoxifen [I, A], oestradiol [I, A], megestrol acetate [I, A]
PIK3CA mut
Fulvestrant + alpelisib [I, B]
Fulvestrant + capivasertib [I,B]
AKT1 mutation or PTEN inactivation
Fulvestrant + capivasertib [I,C]
ESR1 mutations
Elacestrant [I,C] Fulvestrant +/- everolimus [I,B]
If HER2-zero & ET resistant & after ≥ 2 lines of ChT Sacituzumab-Govitecan [I,B]
If HER2-low & ET resistant & after 1-2 lines of ChT Trastuzumab -Dextrucan [I, A]
ChT (if not used previously): capecitabine, eribulin, vinorelbine, anthracycline, taxane [I, A] or metronomic ChT [I, B]
*See guidelines text

HER-2-positive ABC

• anti-HER2 therapy

- ✓ 除非有禁忌症，抗HER-2療法應及早使用於轉移性乳癌病人。
- ✓ 在接受抗HER2治療並合併使用細胞毒性或內分泌藥物後病情惡化的患者，應在後續治療中提供額外的抗 HER-2 治療，因為持續抑制 HER2 路徑是有益的。
- ✓ 目前不清楚抗HER-2療法的最佳順序。
- ✓ 目前不清楚抗HER-2治療MBC的最佳持續時間。
- ✓ 在腫瘤完全緩解的患者中，最佳的抗HER2維持治療持續時間尚不清楚。持續完全緩解幾年後可以考慮停止抗HER2治療。
- ✓ 對於ER +/HER2+ ABC患者，如果選擇 ET + anti-HER2 治療作為一線治療，則可以使用雙重抗HER2 阻斷（pertuzumab + trastuzumab 或 lapatinib + trastuzumab），因為它能提供PFS益處，但缺乏OS益處
- ✓ 對於選擇化療 + anti-HER2 治療作為一線治療並且提供了益處的 ER +/HER2+ ABC患者，在停止化療後使用 ET + anti-HER2 治療作為維持治療是合理的選擇，儘管這一策略尚未在隨機試驗中進行研究。維持治療的持續時間應該是直到疾病進展、不可接受的毒性或患者要求停止治療。
- ✓ 維持治療需使用ET+單一anti-HER-2藥物或雙標靶藥物沒有相關數據。
- ✓ 對於使用過抗HER-2療法並且有大於一年的無病間斷期或是未使用過抗HER-2療法之患者，化療 +trastuzumab 勝過化療 + lapatinib。
- ✓ 無論有沒有使用過anti-HER-2療法，化療+trastuzumab + pertuzumab 均為第一線建議療法。但是若疾病惡化，則不建議使用。

• Antibody-drug conjugates (ADCs)

- ✓ Trastuzumab Deruxtecan（T-DXd）是經歷過 Trastuzumab 和 Pertuzumab 治療後的二線治療中的首選治療選項之一。比起TDM-1有更好的PFS及24個月存活率。
- ✓ 可能發生間質性肺炎甚至致死，應密切監測預防。
- ✓ 在無法使用TDXd的狀況下，TDM-1仍是建議的第二線治療。
- ✓ 即使使用於第二線之後，TDXd仍是建議的治療，PFS及OS都優於capecitabine + trastuzumab or lapatinib。

• 酪氨酸激酶抑制劑（Tyrosine kinase inhibitor，TKI）

- ✓ 在使用過trastuzumab, pertuzumab and T-DM1的患者，特別是有腦轉移，使用tucatinib + trastuzumab +

capecitabine 比起trastuzumab + capecitabine有更好的PFS及OS。

✓ 以trastuzumab為基底的療法治療過的患者疾病惡化後，trastuzumab + lapatinib是合理的治療選擇。

✓ neratinib + capecitabine並不建議使用。仍需相關研究結果來闡明這個組合在腦轉移的效果。

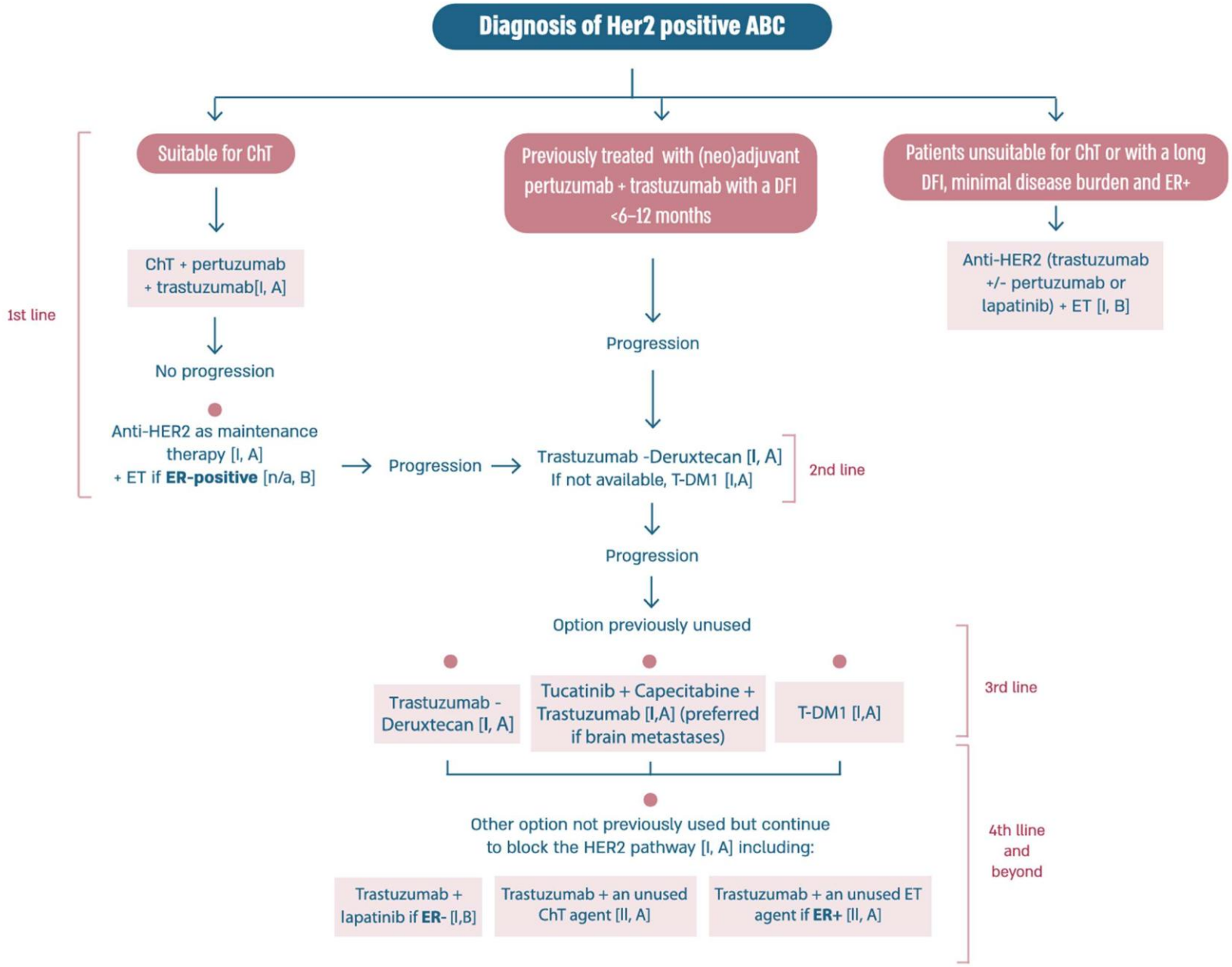
• Margetuximab搭配化療的組合不建議使用，需要進一步的研究結果來闡明CD16A genotype的角色。

• 化學治療

✓ 搭配trastuzumab的第一線首選為vinorelbine 或是 taxane。

✓ 搭配trastuzumab的後線可使用vinorelbine, taxanes, capecitabine, eribulin, liposomal, anthracyclines, platinums, gemcitabine or metronomic CM.

✓ 搭配trastuzumab + pertuzumab 為 docetaxel [I/A] or paclitaxel [I/B], vinorelbine [II/A], nab-paclitaxel [II/B], capecitabine [I/A]，或是使用metronomic 化療於老年人


Diagnosis of Her2 positive ABC
Suitable for ChT
Previously treated with (neo)adjuvant pertuzumab + trastuzumab with a DFI <6–12 months
Patients unsuitable for ChT or with a long DFI, minimal disease burden and ER+
ChT + pertuzumab + trastuzumab[I, A]
Anti-HER2 (trastuzumab +/- pertuzumab or lapatinib) + ET [I, B]
1st line
No progression
Progression
Anti-HER2 as maintenance therapy [I, A] + ET if ER-positive [n/a, B]
Progression
Trastuzumab -Deruxtecan [I, A] If not available, T-DM1 [I,A]
2nd line
Progression
Option previously unused
Trastuzumab - Deruxtecan [I, A]
Tucatinib + Capecitabine + Trastuzumab [I,A] (preferred if brain metastases)
T-DM1 [I,A]
3rd line
Other option not previously used but continue to block the HER2 pathway [I, A] including:
Trastuzumab + lapatinib if ER- [I,B]
Trastuzumab + an unused ChT agent [II, A]
Trastuzumab + an unused ET agent if ER+ [II, A]
4th lline and beyond

三陰性晚期乳癌 **(Advanced TNBC)**

- 化學治療
  - ✓ 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。
  - ✓ androgen receptor (AR)對於TNBC是個有潛力的指標，但AR antagonist agents沒有有力的數據支持，因此並不建議使用
- Checkpoint inhibitors
  - ✓ 搭配化學治療(pembrolizumab + taxane or carboplatin/gemcitabine)是PD-L1+* TNBC的首選第一線治療。
  - ✓ atezolizumab + nab-paclitaxel也可考慮作為第一線治療
  - ✓ 不建議用於後線治療
  - ✓ 目前仍不建議用於其他種類(non-TNBC)的乳癌，仍需更多研究結果支持。
- Antibody-drug conjugates (ADCs)
  - ✓ Sacituzumab govitecan可用於後線治療，有PFS及OS的益處。
  - ✓ Trastuzumab deruxtecan (T-DXd) 使用於Her-2 low，並且接受過1-2線化療患者的後續治療，比起化療有更好的PFS及OS。
  - ✓ 關於ADCs用於TNBC的優先順序沒有明確結果，建議SG優先於T-DXd

Hereditary ABC

- 對於 ABC 患者，生殖系統基因檢測結果具有治療意涵，因此應儘早進行。如果發現致病性生殖系統突變，應向患者及其家屬提供適當的諮詢。
- 目前，只有 BRCA 1/2 的生殖系統突變在臨床應用和治療影響方面有穩健的數據
- 除了germline PALB2 mutation之外，大多數其他中高滲透性基因突變在 ABC 情況下對患者本身沒有直接的臨床意涵。
- BRCA-associated ABC
  - ✓ 對於gBRCA-相關，並且先前使用過anthracycline的advance TNBC 或 endocrine-resistant ABC ，建議使用platinum基底的化學治療。
- PARP inhibitor
  - ■ 對於gBRCA突變的患者，PARP inhibitor (olaparib or talazoparib)是TNBC 或 ER+/HER2- ABC 的首選之一，有PFS跟QoL的益處。
  - ■ 在somatic BRCA1/2 mutation 或是 germline PALB2 mutation，使用olaparib有益處。
  - ■ 目前不清楚單獨使用 olaparib or talazoparib和platinum的療效比較，或是兩者並用的使用方式
  - ■ 在ER+ gBRCA-associated ABC，對於 PARP inhibitor 及CDK4/6 inhibitor + ET的使用順序沒有明確結論。不過因為OS表現，建議先使用CDK4/6 inhibitor + ET
  - ■ 在triple negative PD-L1+ and gBRCA-associated ABC，對於 PARP inhibitor 及化療+ pembrolizumab的使用順序沒有明確結論。不過因為OS表現，建議先使用化療+ pembrolizumab
  - ■ 在BROCADE3 trial中，使用PARP inhibitor (veliparib) in gBRCA-mutated MBC及platinum，作為維持治療有PFS益處，但沒有OS益處

9.85.PARP抑制劑(如olaparib、niraparib、talazoparib)：(109/11/1、111/6/1、111/8/1、112/1/1、112/11/1、113/3/1、113/6/1、113/9/1)

1.卵巢、輸卵管或原發性腹膜癌(olaparib、niraparib)：(109/11/1、 111/6/1、111/8/1、112/1/1、113/3/1、113/6/1、113/9/1)

(1)單獨使用於具下列所有條件的病患做為維持治療，限用兩年：

I.對第一線含鉑化療有治療反應後使用。

II.具germline or somatic BRCA 1/2致病性或疑似致病性突變(109/11/1、111/8/1)

III.FIGO (International Federation of Gynecology and Obstetrics)

Stage III or IV disease。

(2)須經事前審查核准後使用：(109/11/1、111/6/1、111/8/1、113/6/1)

I.每次申請之療程以6個月為限。

II.初次申請時需檢附germline or somatic BRCA 1/2突變檢測報告，且需符合全民健康保險藥品給付規定之通則十二。 (111/6/1、111/8/1、113/6/1)

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niraparib僅能擇一使用，除因耐受不良，不得互換。(112/1/1)

(4) niraparib使用時，體重大於(含)77公斤且基期血小板高於(含)15萬/uL，每日最多使用300mg；體重小於77公斤或基期血小板低於15萬/uL，每日最多使用200mg。(112/1/1)

(5) FIGO Stage IV disease具germline or somatic BRCA 1/2致病性或疑似致病性突變者，若已經申請olaparib、niraparib用於第一線化學治療後維持性治療時不得另外申請bevacizumab併用，除因olaparib、niraparib耐受性不良，在維持性治療可再換成bevacizumab(限使用Avastin、Vegzelma)單獨使用，總申請療程以17個療程為上限。(113/3/1、113/9/1)

2.三陰性乳癌(olaparib、talazoparib)：(109/11/1、111/6/1、111/8/1、112/1/1、113/6/1)

(1) olaparib單獨使用於曾接受前導性、術後輔助性或轉移性化療，且具germline BRCA 1/2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。(109/11/1、111/8/1、112/1/1)

(2) talazoparib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：(110/3/1、111/8/1、112/1/1)

I.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。

II.具germline BRCA 1/2突變(110/3/1、111/8/1)

III.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。

(3)須經事前審查核准後使用：(109/11/1、111/6/1、111/8/1、112/1/1、113/6/1)

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，且需符合全民健康保險藥品給付規定之通則十二。 (111/6/1、111/8/1、113/6/1)

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。

(4)Olaparib與talazoparib僅得擇一使用，除因耐受性不良，不得互換。（111/8/1、112/1/1)

3.去勢療法無效的轉移性攝護腺癌 (mCRPC) (olaparib)：（112/11/1、113/6/1)

(1)用於具germline or somatic BRCA 1/2致病性或疑似致病性突變且先前接受過新荷爾蒙藥物(novel hormonal agents)治療後惡化之成人病人。

(2) 經事前審查核准後使用，每3個月需再次申請：(113/6/1)

I.初次申請時需檢附germline or somatic BRCA 1/2突變檢測報告，且需符合全民健康保險藥品給付規定之通則十二。

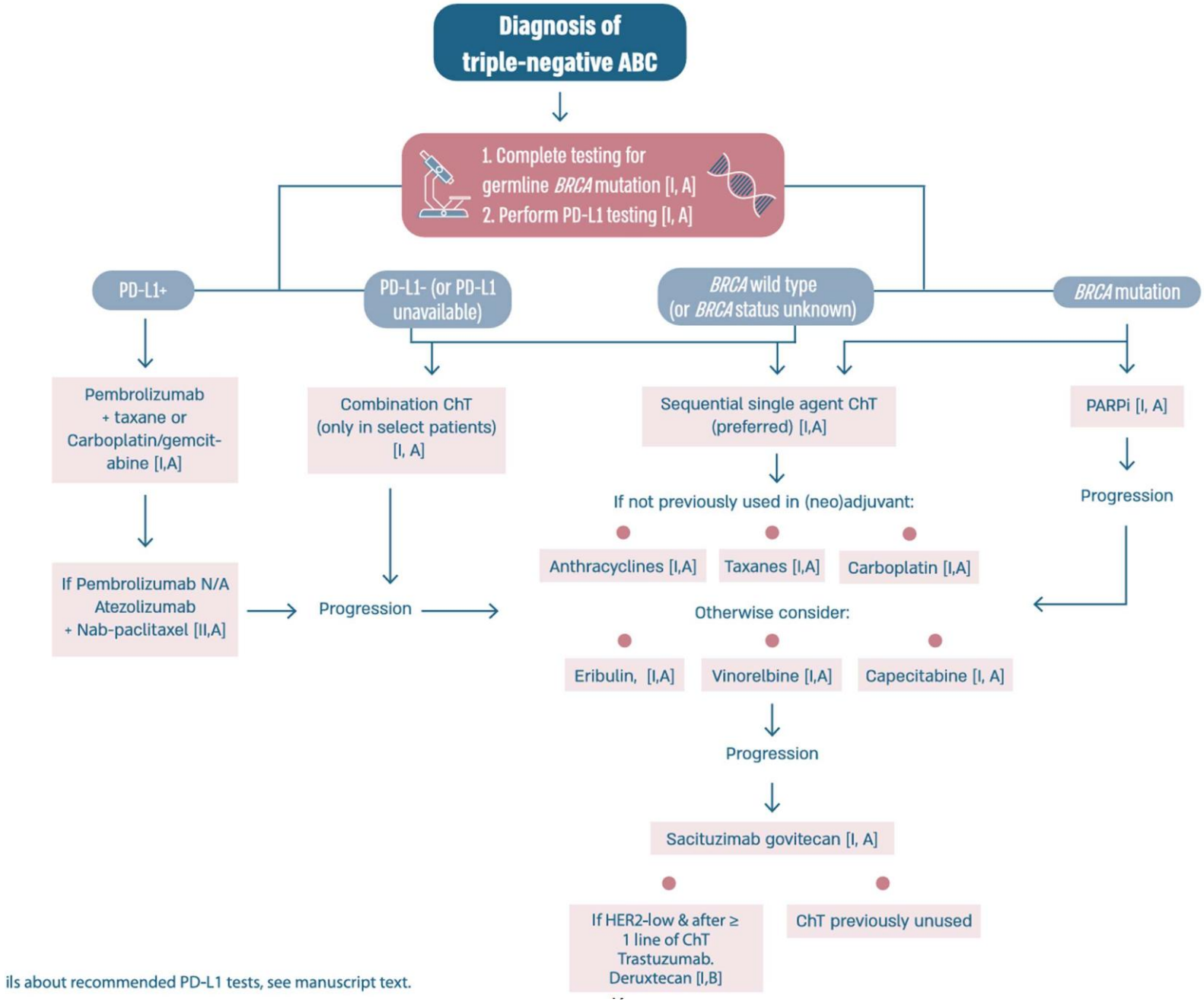
II.申請時需檢附病理報告、使用雄性素去除療法紀錄及系列PSA和睪固酮數據。

III.再申請時若PSA值下降未超過治療前的50%以上，則需停藥。

IV.下降達最低值後之持續追蹤出現PSA較最低值上升50%以上且PSA≧2ng/ml，則需停藥，但影像學證據尚無疾病進展者，可以繼續使用。

(3)不得合併化療使用。

4.Olaparib每日最多使用4粒(112/1/1)


Diagnosis of triple-negative ABC
1. Complete testing for germline BRCA mutation [I, A]
2. Perform PD-L1 testing [I, A]
PD-L1+
PD-L1- (or PD-L1 unavailable)
BRCA wild type (or BRCA status unknown)
BRCA mutation
Pembrolizumab + taxane or Carboplatin/gemcit-abine [I,A]
Combination ChT (only in select patients) [I, A]
Sequential single agent ChT (preferred) [I,A]
PARPi [I, A]
If not previously used in (neo)adjuvant:
Anthracyclines [I,A]
Taxanes [I,A]
Carboplatin [I,A]
Progression
If Pembrolizumab N/A Atezolizumab + Nab-paclitaxel [II,A]
Progression
Otherwise consider:
Eribulin, [I,A]
Vinorelbine [I,A]
Capecitabine [I, A]
Progression
Sacituzimab govitecan [I, A]
If HER2-low & after ≥ 1 line of ChT Trastuzumab. Deruxtecan [I,B]
ChT previously unused
ils about recommended PD-L1 tests, see manuscript text.

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)
- 無症狀患者不需要定期追蹤腦部影像，腦部影像主要適用於Her-2+或是TNBC患者。
- 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。
- 腦部手術或放射手術後，經常需要全腦放射治療。應衡量疾病控制與認知功能影響的風險。
- Her-2+乳癌合併腦部轉移
  - ✓ 有很長的存活期，因此在可以執行的情況下，局部治療優於全腦放射治療。
  - ✓在可以使用立體定位放射治療的情況下，系統性治療不應因此改變。若anti-Her2的治療已經中止，可以重啟。一個可以考慮的治療是tucatinib + Trastuzumab + Capecitabine，但更建議用於局部治療後的復發。
  - ✓ TDM-1及T-DXd對於腦部轉移有益處，可做為治療選項。
  - ✓ 若腦轉移是最嚴重的部分並且無法使用局部治療，tucatinib + Trastuzumab + Capecitabine是最佳選擇。

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

- 所有處於生育年齡的 ABC 患者都應接受關於使用非激素避孕方法的諮詢（無論腫瘤亞型如何），並了解在接受 ABC 治療期間懷孕的風險。
- 對於未接受 OFS/OFA 治療的生育年齡 ABC 患者，應特別注意，因為許多用於 ABC 的治療具有低生殖毒性，不會誘導更年期。
- 管理孕期 ABC 患者是一個複雜且需要多學科討論和有經驗的照護的情況。應向該領域的專家尋求建議。在適當和透明地共享所有管理選擇及其對患者生存、胎兒健康和孩子未來的潛在影響的信息後，必須始終考慮患者和患者希望參與的人的偏好。
- 最適合用來為孕期患者分期的影像檢查是MRI
- 唯一可以適用的全身性治療是在第2.3孕期的化學治療。
- 最棘手的情況是在第1.2孕期診斷的Her-2+ 乳癌，因為anti-Her2治療最為重要，但不可於整個孕期中使用
- 於12週內中止妊娠是可以考慮的一個選項。
- 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。
- 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

- 需要基因諮詢與測試
- ER+ ABC
  - 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。
  - 建議使用Tamoxifen。
  - 若需要使用AI，因合併使用促黃體激素釋放激素（LHRH) 的促效型抑制劑或是睪丸切除術。若要單純使用LHRH agonist也可以，但需要密集注意反應。
  - 與女性相同的治療方式，包括CDK4/6, mTOR and PI3KCA inhibitors.
- 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

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

Regimen	**(AC) Doxorubicin+Cyclophosphamide**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Doxorubicin	60 mg/m^2	IV	drip 60min, day1	Q3w x 4 cycles or Q2W x 4 cycles	with GCSF support
Cyclophosphamide	600 mg/m^2	IV	drip 60min, day1		
Ref.	*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 .*				

Regimen	**(EC) Epirubicin+Cyclophosphamide**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Epirubicin	75 - 100 mg/m^2	IV	drip 60min, day1	Q3w x 4 cycles or Q2W x 4-6 cycles	with GCSF support
Cyclophosphamide	600 mg/m^2	IV	drip 30 mins, days 1		
Ref.	*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.*				

Regimen	**LC(Liposomal doxorubicin-optional)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Liposmal doxorubicin	35- 50 mg/m^2	IV	drip 60min, day1	Q3w x 4 cycles or Q4w x 4 cycles	
Cyclophosphamide	600 mg/m^2	IV	drip 30 mins, days 1		
Ref.	*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.*				
健保給付	*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)*				

Regimen	**TC(Docetaxel +Cyclophosphamide)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	60 - 100 mg/m^2	IV	drip 60min, day1	Q3w x 4-6 cycles or Q2W x 4-6 cycles	
Cyclophosphamide	600 mg/m^2	IV	drip 30 mins, days 1		
Ref.	*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.*				
健保給付	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。				

Regimen	**Docetaxel+ Cisplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	60 - 75 mg/m^2	IV	drip 120min, day1	Q3w x 4-6 cycles or Q2W x 4-6 cycles	with GCSF support
Cisplatin	60 - 75 mg/m^2	IV	drip 120min, day1		

Ref.	*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*				
Regimen	**CMF po (Cyclophosphamide +MTX+Fluorouracil)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Cyclophosphamide	100 mg/m^2	PO	day1-14	Q4w x 6 cycles	
Methotrexate	40 mg/m^2	IV	drip 30 mins, days 1 &8		
5- FU	600 mg/m^2	IV	drip 30 mins, days 1 &8		
Ref.	*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.*				

Regimen	**CMF IV (Cyclophosphamide +MTX+Fluorouracil)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Cyclophosphamide	600 mg/m^2	IV	day1-14	Q4w x 6 cycles	
Methotrexate	40 mg/m^2	IV	drip 30 mins, days 1 &8		
5- FU	600 mg/m^2	IV	drip 30 mins, days 1 &8		
Ref.	*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.*				

Regimen	**AC/EC→Paclitaxel Qw (or Paclitaxel→AC/EC)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Paclitaxel	80 mg/m^2	IV	60min, day1	Qw x 12 cycles	
Ref.	*Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.*				
健保給付	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)*				

Regimen	**AC/EC→Docetaxel Q3w (or Docetaxel→AC/EC)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	60-100 mg/m^2	IV	60min, day1	Q3w x 4 cycles	
Ref.	*Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.*				
健保給付	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。				

Regimen	**TEC (Docetaxel+Epirubicin+Cyclophosphamide)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	50-75 mg/m^2	IV	120min, day1	Q3w x 6 cycles	
Epirubicin	75-100 mg/m^2	IV	30min, day1		
Cyclophosphamide	500 mg/m^2	IV	60min, day1		
Ref.	*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.*				

Regimen	**TAC (Docetaxel+ Doxorubicin +Cyclophosphamide)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	50-75 mg/m^2	IV	120min, day1	Q3w x 6 cycles	
Doxorubicin	50-60 mg/m^2	IV	30min, day1		
Cyclophosphamide	500 mg/m^2	IV	60min, day1		
Ref.	*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.*				

Regimen	**Docetaxel+ Carboplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	60-75 mg/m^2	IV	60min, day1	Cycled every 21 days for 4-6 cycles	
Carboplantin	6 mg, AUC	IV	60min, day1		
Ref.	*von Minckwitz G, Schneeweiss A, Loibl S, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive earlybreast cancer (GeparSixto; GBG 66): a randomised phase 2 trial Lancet Oncol 2014;15:747-756.*				

Regimen	**Paclitaxel(Weekly) + carboplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Paclitaxel	80 mg/m^2	IV	60min,day 1 8 15	Cycled every 21 days for4 cycles	
Carboplantin	AUC 6 (q3w)	IV	60min,day 1		
Ref.	*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.*				

Regimen	**Paclitaxel(Weekly) + carboplatin(Weekly) (wPCb)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Paclitaxel	80 mg/m^2	IV	60min,day 1 8 15	Cycled every 28 days for 6 cycles	
Carboplantin	AUC 2 (q1w)	IV	60min,day 1 8 15		
Ref.	*Yu KD, Ye FG, He M, et al. Effect of adjuvant paclitaxel and carboplatin on survival in women with triple-negative breast cancer: A phase 3 randomized clinical trial. JAMA Oncol 2020;6:1390- 1396.* *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.

Neoadjuvant/Adjuvant combined Target therapy

Regimen	**Trastuzumab(Herceptin;H, Ogivri) +/- Paclitaxel (weekly)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Trastuzumab	loading dose 8 mg/kg followed by 6 mg/kg	IV or SC	90min or 5min	Q3w	than 6 mg/kg iv q3w, for 1 year
Trastuzumab	loading dose 4 mg/kg followed by 2 mg/kg	IV or SC	90min or 5min	Qw	than 6 mg/kg iv q3w, for 1 year
Paclitaxel	80 mg/m^2	IV	60min,day 1 8 15	12 weeks	
Ref.	*Tolaney S, Barry W, Dang C, et al. Adjuvant paclitaxel and trastuzumab for node-negative HER2-positive breast cancer. N Engl J Med 2015;372:134-141.*				
健保給付	健保申請條件如下~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。				

Regimen	**Trastuzumab(Herceptin;H, Ogivri)+/- Docetaxel + Carboplantin (TCPH)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Trastuzumab	loading dose 8 mg/kg followed by 6 mg/kg	IV or SC	90min or 5min	Q3w	than 6 mg/kg iv q3w, for 1 year
Trastuzumab	loading dose 4 mg/kg followed by 2 mg/kg	IV or SC	90min or 5min	Qw	than 6 mg/kg iv q3w, for 1 year
Docetaxel	60-75 mg/m^2	IV	60min, day1	Cycled every 21 days for 4-6 cycles	
Carboplantin	6 mg, AUC	IV	60min, day1		
Ref.	*Slamon D, Eiermann W, Robert N, et al. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med 2011;365:1273-1283.*				
健保給付	健保申請條件如下~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。				

Regimen	**Trastuzumab + Pertuzumab or Phesgo (sc) +/- Docetaxel + Carboplantin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Trastuzumab + Pertuzumab	loading dose 840mg followed by 420mg	IV	90min+120min	Q3w	than 420 mg iv q3w, for 1 year
Docetaxel	60-75 mg/m^2	IV	60min, day1	Cycled every 21 days for 4-6 cycles	
Carboplantin	6 mg, AUC	IV	60min, day1		
Ref.	*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.
健保給付	早期乳癌 *(1)*外科手術前後以本藥品及化學療法*(*術前輔助治療或輔助治療*)*併用作為輔助性治療用藥，用於具*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病人，若使用於外科手術後，須達病理上緩解*(pCR)*。 *(2)*下列Ⅰ*~III*使用於外科手術前後之總療程合併計算，依藥品仿單記載以 *18* 個療程為上限： Ⅰ：本藥品 *II*：*trastuzumab* *III*：*pertuzumab* 與 *trastuzumab* 併用 *(3)*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。

Neoadjuvant Chemotherapy with Immunotherapy

Regimen	**Paclitaxel(Weekly) + carboplatin + Pembrolizumab(keytruda)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Paclitaxel	80 mg/m^2	IV	60 mins, day 1	q1w	any histology
Carboplantin	AUC 5 (q3w) AUC1.5(q1w)	IV	60 mins, day 1		
Pembrolizumab	200mg	IV	30mins, day 1	q3wks	
Ref.	*1. Gupta S, Nair NS, Hawaldar RW, et al. Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A phase III randomized controlled trial. Presented at: 2022 San Antonio Breast Cancer Symposium; December 6-10, 2022; San Antonio, TX. Abstract GS5-01.* *2. Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. N Engl J Med, 2020;382:810-821* *3. Sharma P, Kimler BF, O'Dea A, et al. Randomized phase II trial of anthracycline-free and anthracycline-containing neoadjuvant carboplatin chemotherapy regimens in stage I-III triple-negative breast cancer (NeoSTOP). Clin Cancer Res 2021;27:975-982.*				

健保給付	健保規範*(114.06.01)*早期三陰性乳癌：非轉移性、第*II*期至第*IIIb*期（*cT1c N1-2* 或 *T2-N0-2*） *I.*術前前導性治療： 限*pembrolizumab* 每 *3* 週 *1* 次與*carboplatin* 和*paclitaxel* 併用至多 *4* 個療程，接續*pembrolizumab* 每 *3* 週 *1* 次與*cyclophosphamide* 和*doxorubicin* 或*epirubicin* 併用至多 *4* 個療程，做為初診斷病人前導性治療用藥。 *II.*術後輔助治療：上述病人接受過術前前導性治療後，限手術後未達*pCR* 者，單用*pembrolizumab* 每 *3* 週 *1* 次，做為輔助治療用藥，且至多使用 *9* 個療程。 *III.*上述*pembrolizumab* 用於早期三陰性乳癌依前述療程規定至多使用 *17* 個療程，且用於術後輔助治療，*pembrolizumab* 與*olaparib* 僅能擇一支付。

Adjuvant Immunotherapy regimens

Regimen	**Carboplantin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Pembrolizumab	200mg	IV	30mins, day 1	q3wks	9 cycles
Ref.	*Sharma P, Kimler BF, O'Dea A, et al. Randomized phase II trial of anthracycline-free and anthracycline-containing neoadjuvant carboplatin chemotherapy regimens in stage I-III triple-negative breast cancer (NeoSTOP). Clin Cancer Res 2021;27:975-982.*				

Adjuvant chemotherapy regimens

Regimen	**Cisplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Cisplatin	75 mg/m^2	IV	120min, day1	Q3w	
Ref.	*Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.*				

Regimen	**Carboplantin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes

Carboplantin	6 mg, AUC	IV	60min, day1	Q3w	
Ref.	*Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.*				

Advanced/Metastasis regimens

Regimen	**Doxorubicin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Doxorubicin	60-75 mg/m^2	IV	drip 60min, day1	Q3w	
Doxorubicin	20 mg/m^2	IV	drip 60min, day1	Qw	
Ref.	*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.*				

Regimen	**Epirubicin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Epirubicin	60-90 mg/m^2	IV	drip 60min, day1	Q3w	
Epirubicin	20 mg/m^2	IV	drip 60min, day1	Qw	
Ref.	*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.*				

Regimen	**Liposomal doxorubicin (Lipo-Dox)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Liposomal doxorubicin	35-50 mg/m^2	IV	60min	Q3-4w	
Ref.	*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.*				
健保給付	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。				

Regimen	**Cisplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Cisplatin	75 mg/m^2	IV	60min	Q3w	
Ref.	*Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.*				

Regimen	**Carboplantin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Carboplantin	6 mg, AUC	IV	30min	Q3w	
Ref.	*Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.*				

Regimen	**Docetaxel**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	25-40 mg/m^2	IV	60min	Qw	
Ref.	*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.*				

Regimen	**Paclitaxel Qw**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Paclitaxel	80 mg/m^2	IV	60min	Qw	
Ref.	*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.*				
健保給付	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)*				

Regimen	**Gemcitabine**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Gemcitabine	800-1200 mg/m^2	IV	30min	day 1.8.15 Q4w	
Ref.	*Carmichael, J et al. Advanced breast cancer: a phase II trial with gemcitabine. J Clin Oncol 1995; 13:2731*				
健保給付	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*）				

Regimen	**Gemcitabine + Paclitaxel**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Gemcitabine	800-1200 mg/m^2	IV	30min	day 1.8.Q3w	following paclitaxel on day 1 Cycled every 21 days.
Paclitaxel	175 mg/m^2	IV	60min	day 1 Q3w	
Ref.	*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*				

Regimen	**Gemcitabine +Carboplatin**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Gemcitabine	800-1200 mg/m^2	IV	30min	day 1.8 Q3w	
Carboplatin	AUC 2	IV	60min	day 1.8 Q3w	
Ref.	*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*				

Regimen	**Vinorelbine (Navelbine)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Vinorelbine	50-80 mg/m^2	PO QW(total dose)		tiw	1.3.5day/w
Ref.	*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.*				
健保給付	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				

Regimen	**Capecitabine (Xeloda)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Capecitabine	800-1250 mg/m^2	PO BID		day 1-14 Q3w	
Ref.	*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.*				
健保給付	*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。				

Regimen	**UFT**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Uracil/Tegafur	270 mg/m2 /day po	PO		7 days/week	
Ref.	*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*				
健保給付	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*）。				

Regimen	**Eribulin (Halaven)**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Eribulin	1.4 mg/m^2	IV	60min	day1.8 Q3w	
Ref.	*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.*				
健保給付	*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。健保規範:（如 *Halaven*）：（*103/12/1*、*106/11/1*） *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)*				

Regimen	**Ixabepilone**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Ixabepilone	40 mg/m^2	IV	3hrs	day 1, Q3w	
Capecitabine	2000 mg/m^2	PO QD		day1, Q3w	
Ref.	*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*				
健保給付	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*)*。				

Regimen	**Bevacizumab(自費)(Avastin) + Chemotherapy**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Bevacizumab	10 mg/m^2	IV	90min	day 1, Q2w	
Bevacizumab	15 mg/m^2	IV	90min	day1, Q3w	
Ref.	*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.*				

Regimen	**Lapatinib(Tykerb) + Xeloda**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Lapatinib	1250 mg/m^2	PO QD		day 1-14	
Capecitabine	2000 mg/m^2	PO QD		day 1-14	
Ref.	*Lancet Oncol 2013 Jan;14(1):64-71.doi:10.1016/S1470-2045(12)70432-1.Epub 2012 Nov.*				
健保給付	*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。				

Regimen	**Everolimus(Afinitor) + Endocrine therapy**				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Everolimus	10 mg	PO QD		day 1-14	
Ref.	*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.*				
健保給付	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 *10mg*。（*108/10/1*）				

Target therapy

HER2 過度表現(IHC3+ or FISH+)

First-line therapy

Regimen	**Trastuzumab (Herceptin;H, Ogivri) 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**
藥名(學名)	**Trastuzumab**
Ref.	*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.*
健保給付	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 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)。

HER2 過度表現(IHC3+ or FISH+)	
First-line therapy	
Regimen	**Pertuzumab(Perjeta;P) +/- Chemotherapy** **840 mg IV day 1 followed by 420 mg IV Cycled every 21 days to complete 1 y of therapyq3w**
藥名(學名)	**Pertuzumab**
Ref.	*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, placebocontrolledPhase 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 locallyadvanced, inflammatory, or early HER2-positive breast cancer(NeoSphere): a randomised multicentre, open-label, phase 2 trial.Lancet Oncol 2012;13:25-32*
健保給付	健保規範*:(108/05/01)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。

HER2 過度表現(IHC3+ or FISH+)	
Second-line therapy	
Regimen	**Ado-trastuzumab emtansine(TDM1, Kadcyla) 3.6 mg/kg IV day 1, Cycled every 21 days**
藥名(學名)	**Trastuzumab emtansine**
Ref.	*Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer [supplementary appendix available online]. N Engl J Med2012;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*
健保給付	● 目前健保規範*Trastuzumab emtansine (*如*Kadcyla)*：*(110/2/1*、*113/8/1)*轉移性乳癌*(110/2/1*、*113/8/1)(1)* 限單獨使用於先前未使用過本藥品且*HER2* 過度表現*(IHC3+*或*FISH+)* 之轉移性乳癌患者作為二線治療，並同時符合下列情形： *I.*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。*II.*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。*III.*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。

for HER2 IHC 1+ or 2+/ISH negative)	
Second-line therapy	
Regimen	**Trastuzumab deruxtecan (Enhertu, T-DXd) 5.4 mg/kg iv d1 Q3w**
藥名(學名)	Trastuzumab deruxtecan
Ref.	*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.*

<u>for HER2 IHC 1+ or 2+/ISH negative)、ER(+)</u>	
Adjuvant therapy (EBC)	
Regimen	**Neratinib (Nerlynx) 240 mg PO daily on days 1–28 *12cycle**
藥名(學名)	Neratinib
Ref.	*Chan A, Delaloge S, Holmes FA, et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2016;17:367-377.* *Saura C, Oliveira M, Feng YH, et al. Neratinib plus capecitabine versus lapatinib pluscapecitabine in patients with HER2-positive metastatic breast cancer previously treated with≥2 HER2-directed regimens: Findings from the multinational, randomized, phase 3 NALA trial. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting. May 31-June 4, 2019; Chicago, IL. J Clin Oncol 2019;37(suppl): abstract 1002.*
健保給付	*self-pay*
備註	*suggest* *120 mg PO daily on days 1–7; Followed by:* *160 mg PO daily on days 8–14; Followed by:* *240 mg PO daily on days 15–28*

for TNBC or HR+/HER 2-	
Second-line therapy	
Regimen	**Sacituzumab govitecan-hziy(Trodelvy; SG) 10mg/kg iv d1,8 Q3w**
藥名	Sacituzumab govitecan-hziy
Ref.	*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.*
健保給付	Sacituzumab govitecan(如 Trodelvy）：(113/2/1、114/2/1、114/10/1) 1.用於治療先前已接受兩次以上全身性治療無效(其中一次需為治療晚期疾病)之無法切除的局部晚期或轉移性的三陰性乳癌成人病人。(113/2/1、114/2/1) (1)須符合下列各項條件：I.病人身體狀況良好（ECOG≤1II.須使用過taxane 類藥物至少 1 個療程。 III.先前未接受過trastuzumab deruxtecan 治療。(114/2/1) (2)須經事前審查核准後使用，每次申請之療程以 3 個月為限，初次申請時需檢附ER、PR、HER2 皆為陰性之檢測報告。 (3)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。 (4)Sacituzumab govitecan 和 trastuzumab deruxtecan 僅能擇一給付，不得互換。(114/2/1)。 2.用於治療患有無法切除的局部晚期或轉移性的HR 陽性、HER2 陰性之乳癌成人病人。(114/10/1)(1)須符合下列各項條件： I.須排除活動性腦轉移。 II.曾接受 CDK4/6 抑制劑≦12 個月，並有內臟轉移。III.曾接受至少兩線(每線至少兩個完整療程或於第二個療程中產生疾病惡化)的轉移性乳癌化學治療。 (2)須經事前審查核准後使用，每次申請之療程以 3 個月為限，初次申請時需檢附HR 陽性、HER2 陰性(IHC 0、IHC 1+或 IHC 2+/ISH–)之檢測報告。 (3)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。

(PARP) inhibitor indicated:	
BRCA1/2 mutation/ HER2(-) (mBC)	
Regimen	**Olaparib (Lynparza)150mg*2/ Bid, 600mg/day, PO**
藥名	Olaparib
Ref.	*1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025. 2. Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med. 2017;377(6):523-533. 3. Robson ME, Tung N, Conte P, et al. OlympiAD final overall survival and tolerability results: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Ann Oncol. 2019;30(4):558-566. 4. Robson M, Im SA, Senkus E, et al. OlympiAD extended follow-up for overall survival and safety: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Poster presented at: The San Antonio Breast Cancer Symposium; December 10-14, 2019; San Antonio, TX. 5. Data on File, US-47776. AstraZeneca Pharmaceuticals LP. 6. Robson ME, Tung N, Conte P, et al. OlympiAD final overall survival and tolerability results: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Supplementary Appendix. Ann Oncol. 2019;30(4):558-566. 7. Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. Supplementary Appendix. N Engl J Med. 2017;377(6):523-533. 8. Tung NM, Im SA, Senkus-Konefka E, et al. Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer (OlympiAD): efficacy in patients with visceral metastases. Poster presented at: 2018 ASCO Annual Meeting; June 1-5, 2018; Chicago, IL.*
健保給付	三陰性乳癌(olaparib、talazoparib)：(109/11/1、111/6/1、111/8/1、112/1/1、113/6/1) .高復發風險之早期乳癌(olaparib)：(114/6/1) (1)Olaparib 適用於曾接受前導性化療或術後輔助性化療，且具遺傳性 BRCA1/2 (germline BRCA1/2)突變併 HER2 陰性而有高復發風險之早期乳癌成年病人術後輔助治療，依藥品仿單記載以 1 年為上限。 (2)病人須完成至少 6個週期的前導性化療或術後輔助性化療，且化療處方須含有anthracyclines 類藥物、taxane 類藥物，或兩者的複方；亦允許含鉑化療。 (3)病人須在最後一次治療(包括手術、化療或放療)完成後的 12 週內使用olaparib。 (4)須符合下列之高復發風險條件： I.三陰性乳癌： i.針對曾接受前導性化療的病人，須符合於乳房和/或手術切除的淋巴結中發現有殘餘的侵襲性癌症(non-pCR)。 ii.針對曾接受手術且接續術後輔助性化療的病人，須具有腋窩淋巴結陽性(≧pN1)，或腋窩淋巴結陰性(pN0)且原發性病理腫瘤大小≧2 公分(≧pT2)。 II.HR 陽性且 HER2 陰性乳癌： i.針對曾接受前導性化療的病人，須為non-pCR。 ii.針對曾接受手術且接續術後輔助性化療的病人，須具有 4 個以上經病理學證實的陽性淋巴結。 (5)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 HER2 為陰性之檢測報告、ER 和 PR 之檢測報告，以及germline BRCA 1/2 突變之檢測報告，且需符合全民健康保險藥品給付規定之通則十二。 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。 IV. 用於術後輔助治療，olaparib 與 pembrolizumab 僅能擇一給付。 5.Olaparib 每日最多使用 4 粒(112/1/1)

PIK3CA activating mutation	
HR-positive, HER2-negative	
Regimen	**Inavolisib(ltovebi) 9mg PO QD + palbociclib(Ibrance) 125mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W**
藥名	Inavolisib 9mg PO QD + palbociclib 125mg PO QD+ Fulvestrant INJ 250MG/5ML Q1.Q15 Q4W
Ref.	*Turner NC, Im SA, Saura C, et al. Inavolisib-based therapy in PIK3CA-mutated advanced breast cancer. N Engl J Med 2024;391:1584-1596.*
健保給付	*self-pay*

PIK3CA activating mutation	
HR-positive, HER2-negative	
Regimen	**Alpelisib (Piqray)300mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W**
藥名	Alpelisib 300mg PO QD+ Fulvestrant INJ 500 mg IM Q1.Q15 Q4W
Ref.	*Andre F, Ciruelos E, Rubovszky G, et al. Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. N Engl J Med 2019;380:1929-1940.*
健保給付	預計 *2026* 年 *01* 月 *01* 日開始給付， *1.*與*fulvestrant* 併用於曾接受*CDK4/6* 抑制劑治療但疾病惡化的停經後轉移性乳癌病人，且須完全符合下列條件： *(1)* 荷爾蒙受體為：*ER* 或*PR*＞*30%*。 *(2)HER-2* 檢測為陰性。 *(3)* 具有*PIK3CA* 基因突變。 *2.*需經事前審查核准後使用： *(1)* 初次申請需檢附*PIK3CA* 基因突變檢測報告，且需符合全民健康保險藥品給付規定之通則十二。 *(2)* 核准後每 *12* 週需檢附療效評估資料再次申請，若疾病惡化及必須停止使用。 *3.*每日最多處方 *2* 粒。

PIK3CA or AKT1 activating mutations or PTEN alterations	
HR-positive, HER2-negative	
Regimen	**Capivasertib (Truqap) 400mg(200mg/tab) BID PO + Fulvestrant 500 mg IM Q1.Q15 Q4W**
藥名	Capivasertib 400mg(200mg/tab) BID PO + Fulvestrant 500 mg IM Q1.Q15 Q4W
Ref.	Turner NC, Oliveira M, Howell SJ, et al. Capivasertib in hormone receptor–positive advanced breast cancer. N Engl J Med 2023;388:2058-2070.
健保給付	*self-pay*

CDK4/6 inhibitor	
HR-positive, HER2-negative	
Regimen	**Ribociclib(kisqali) 400mg PO QD Q3W (in combination with an aromatase inhibitor)**
藥名	Ribociclib
Ref.	*Slamon D, Lipatov O, Nowecki Z, et al. Ribociclib plus endocrine therapy in early breast cancer. N Engl J Med 2024;390:1080-1091* *Hortobagyi GN, Stemmer SM, Burris HA, et al. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2- negative advanced breast cancer. Ann Oncol 2018;29:1541-1547*
健保給付	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、113/1/1、113/3/1、114/7/1) 1.用於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、113/1/1) (1) 荷爾蒙接受體為：ER 或 PR>30%。（109/10/1、113/1/1) (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 (visceralcrisis)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.用於停經前/正在停經乳癌婦女及男性乳癌發生遠端轉移後之全身性藥物治療，須與芳香環轉化酶抑制劑及 GnRH analogue 併用。（113/1/1、114/7/1）

	(1) 荷爾蒙接受體為：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。 (4)骨轉移不可為唯一轉移部位。 3. 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） 4. 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。 5. 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，使用至總療程(即終生 24 個月)或總療程期間疾病惡化為止，且後續不得再申請使用本類藥品。（110/10/1、113/1/1） 6. 若先前使用 everolimus 無效後，不得再申請本類藥品。(109/4/1) 7. 若先前於早期乳癌使用 abemaciclib 無效後，不得再申請本類藥品。(113/3/1)

CDK4/6 inhibitor	
HR-positive, HER2-negative	
Regimen	**Abemaciclib(Verzenio) 150mg/200mg PO QD Q3W (in combination with an aromatase inhibitor)**
藥名	Abemaciclib
Ref.	*Jhaveri KL, Neven P, Casalnuovo ML, et al. Imlunestrant with or without abemaciclib in advanced breast cancer. N Engl J Med 2025;392:1189-1202.*
健保給付	1. 早期乳癌： 併用內分泌療法 (tamoxifen 或芳香環酶抑制劑)，可做為荷爾蒙受體(HR)陽性、第二型人類表皮生長因子受體(HER2)陰性、淋巴結陽性，高復發風險之早期乳癌成年病人的輔助治療。 2. 晚期乳癌： (1) 併用芳香環酶抑制劑(aromatase inhibitor)，可做為治療荷爾蒙受體(HR)陽性、第二型人類表皮生長因子受體(HER2)陰性之晚期或轉移性乳癌之停經後婦女及男性的第一線內分泌療法(endocrine-based therapy)。 (2) 併用 fulvestrant，可治療荷爾蒙受體(HR)陽性、第二型人類表皮生長因子受體(HER2)陰性，且接受內分泌療法後疾病惡化之晚期或轉移性乳癌的成人病人。

	(3) 單獨用於治療荷爾蒙受體(HR)陽性、第二型人類表皮生長因子受體(HER2)陰性，曾經接受過內分泌治療及於轉移後接受化學治療後又發生疾病惡化之晚期或轉移性乳癌的成人病人。

Endocrine Therapy

藥名(學名)	Tamoxifen 10mg BID

藥名(學名)	Letrozole 2.5mg QD for 3-5years
健保給付	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)。

藥名(學名)	Exemestane 25mg QD
健保給付	1. 限停經後或卵巢切除後，且女性荷爾蒙受體(estrogen receptor)陽性之晚期乳癌病患，經使用 tamoxifen 無效後，方可使用。 1. 具有雌激素受體陽性之停經婦女，使用 tamoxifen 至少兩年之高危險早期侵犯性乳癌的輔助治療，且不得與 tamoxifen 或其他 aromatase inhibitor 併用。使用時需同時符合下列規定：(105/8/1) (1) 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)。 (2) 本案藥品使用不得超過三年。

藥名(學名)	Anastrozole 1mg QD
健保給付	1. 停經後雌激素接受器為陽性或不清楚之局部晚期或轉移性乳癌第一線治療。 (92/3/1) 2. 停經後婦女晚期乳癌，雌激素接受器為陰性，但曾對 tamoxifen 有陽性反應者。(92/3/1) 3. 停經後婦女罹患早期侵犯性乳癌，經外科手術切除後且雌激素接受器為陽性，且有血栓栓塞症或子宮內膜異常 增生的高危險群，而無法使用 tamoxifen 治療者。 (93/6/1) 備註：療程期間以不超過五年為原則。血栓栓塞症或子宮內膜異常增生的高危險群需符合下列情形之一： (1) 有腦血管梗塞病史者。 (2) 有靜脈血栓栓塞症病史者。 (3) 有子宮異常出血病史，且「經陰道超音波檢查」判定為子宮內膜異常增生的高危險群。

藥名(學名)	Goserelin 3.6mg QM
健保給付	停經前(或更年期前)之早期乳癌，且須完全符合以下六點：(100/2/1、106/2/1、109/2/1) I. 與 tamoxifen 合併使用，作為手術後取代化學治療之輔助療法。 II. 荷爾蒙接受體為強陽性：ER/PR 為 2+或 3+。 III. Her-2 Fish 檢測為陰性或 IHC 為 1+。 IV. 淋巴結轉移數目須≦3 個。 V. 使用期限：leuprorelin、goserelin 或 triptorelin 使用 3 年，tamoxifen 使用 5 年。(106/2/1、109/2/1) VI. 須事前審查，並於申請時說明無法接受化學治療之原因。

藥名(學名)	Triptorelin 11.25mg Q3M
健保給付	停經前(或更年期前)之早期乳癌，且須完全符合以下六點：(100/2/1、106/2/1、109/2/1) I. 與 tamoxifen 合併使用，作為手術後取代化學治療之輔助療法。 II. 荷爾蒙接受體為強陽性：ER/PR 為 2+或 3+。 III. Her-2 Fish 檢測為陰性或 IHC 為 1+。 IV. 淋巴結轉移數目須≦3 個。 V. 使用期限：leuprorelin、goserelin 或 triptorelin 使用 3 年，tamoxifen 使用 5 年。(106/2/1、109/2/1) VI. 須事前審查，並於申請時說明無法接受化學治療之原因。

藥名(學名)	Fulvestrant 250mg loading dose 500mg then 250mg QM

藥名(學名)	Leuprorelin 22.5mg Q3M
健保給付	停經前(或更年期前)之早期乳癌，且須完全符合以下六點：(100/2/1、106/2/1、109/2/1) I. 與 tamoxifen 合併使用，作為手術後取代化學治療之輔助療法。 II. 荷爾蒙接受體為強陽性：ER/PR 為 2+或 3+。 III. Her-2 Fish 檢測為陰性或 IHC 為 1+。 IV. 淋巴結轉移數目須≦3 個。 V. 使用期限：leuprorelin、goserelin 或 triptorelin 使用 3 年，tamoxifen 使用 5 年。(106/2/1、109/2/1) VI. 須事前審查，並於申請時說明無法接受化學治療之原因。

Ref. of Endocrine therapy

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七、放射線治療原則

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。

(1). 全乳房放射治療（Whole Breast Irradiation, WBI）

放射治療目標為整個乳房組織。

- **放射治療劑量：**

a. 中度低分次放射治療（Moderate hypofractionation）：

40 Gy / 15 fractions **或** 42.5 Gy / 16 fractions，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。加強劑量為以 4-8 放射次數接受 10-16 Gy 的劑量。

b. 傳統分次放射治療（Conventional fractionation）：

50-50.4 Gy / 25-28 fractions，可用於不適合低分次之病人，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。加強劑量為以 4-8 放射次數接受 10-16 Gy 的劑量。

c. 超低分次放射治療（Ultra-hypofractionation）：

於**選擇性早期乳癌病人**，可考慮採用 **5 Gy × 5 fractions（總劑量 25 Gy，1 週完成）**。現有大型隨機試驗顯示，其局部控制與毒性結果與中度低分次相近。

然而，對於需合併區域淋巴結照射、立即或一期乳房重建，或器官風險劑量限制不易達成者，**不建議常規使用**，宜採用中度低分次方案。

(2). 胸壁放射治療(含乳房重建)(Chest Wall Irradiation)

放射治療目標為手術後胸壁及皮下組織。

- **放射治療劑量：**

a. 40 Gy / 15 fractions 或 50 Gy / 25 fractions。

b. 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。加強劑量為以 4-8 放射次數接受 10-16 Gy 的劑量

(3). **區域淋巴結放射治療（Regional Nodal Irradiation, RNI）**

照射範圍可包括鎖骨上、腋窩及內乳淋巴結，依病理分期與風險因子決定

- **放射治療劑量：**

a. 40 Gy / 15 fractions 或 50 Gy / 25 fractions。

b. 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。加強劑量為以 4-8 放射次數接受 10-16 Gy 的劑量

(4). **術前放射治療（Neoadjuvant Radiotherapy, Neo-RT）**

術前放射治療屬於研究中

- **放射治療劑量：**

8 Gy × 3 fractions（總劑量 24 Gy），於短期內完成

備註：其長期局部控制、乳房外觀與最佳治療時序仍需更多成熟證據，應以臨床試驗結果為依據。

主要參考文獻

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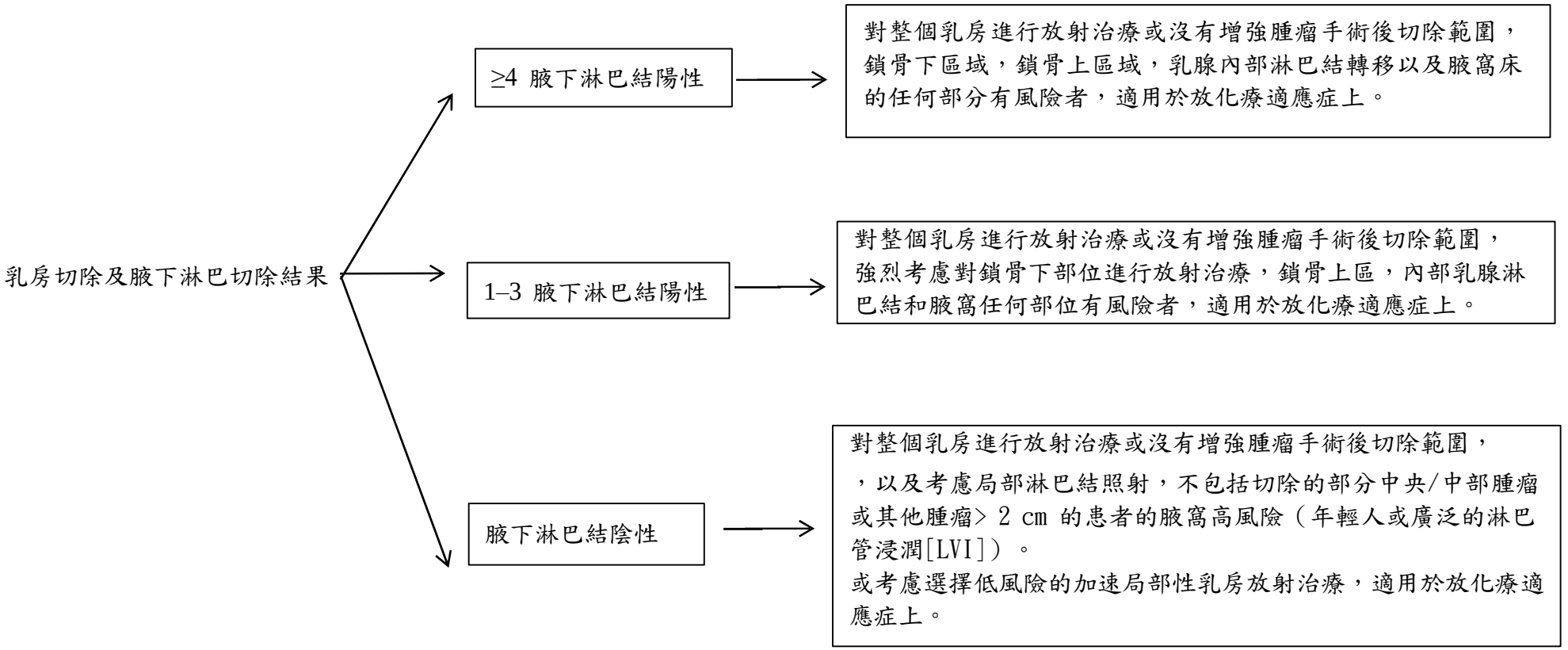
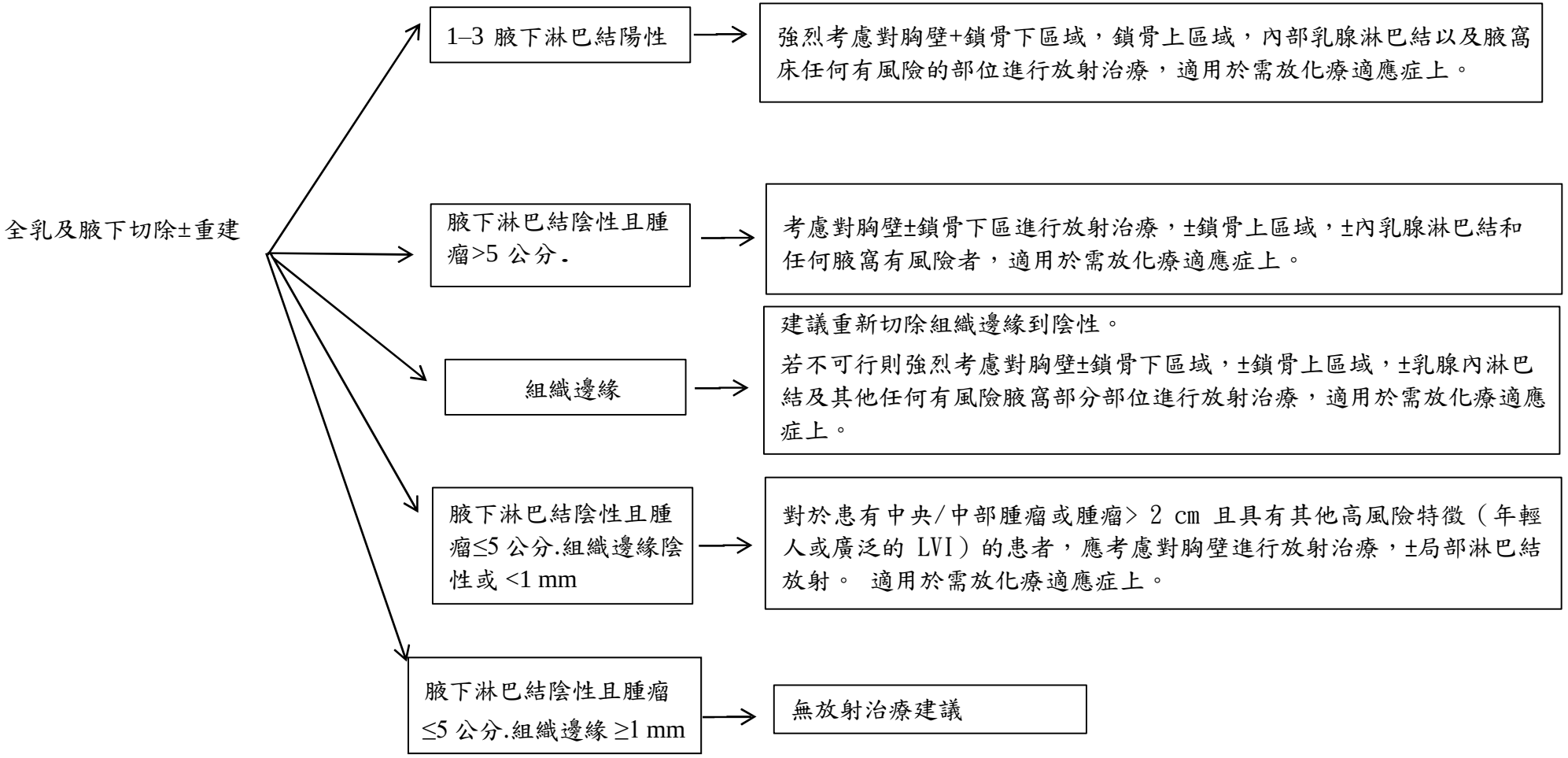
Accelerated Partial Breast Irradiation (APBI)/Partial Breast Irradiation (PBI)

- 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114年檢視