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乳癌診療原則

2022年03月18日 第一版

乳癌醫療團隊擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
  - NCCN Clinical Practical Guidelines in Oncology ™ Breast Cancer（Version 4. 2021）

《停藥機制》
•Progression: image ,tumor marker
•SAE:: severe side effect

會議討論

上次會議：2021/03/26

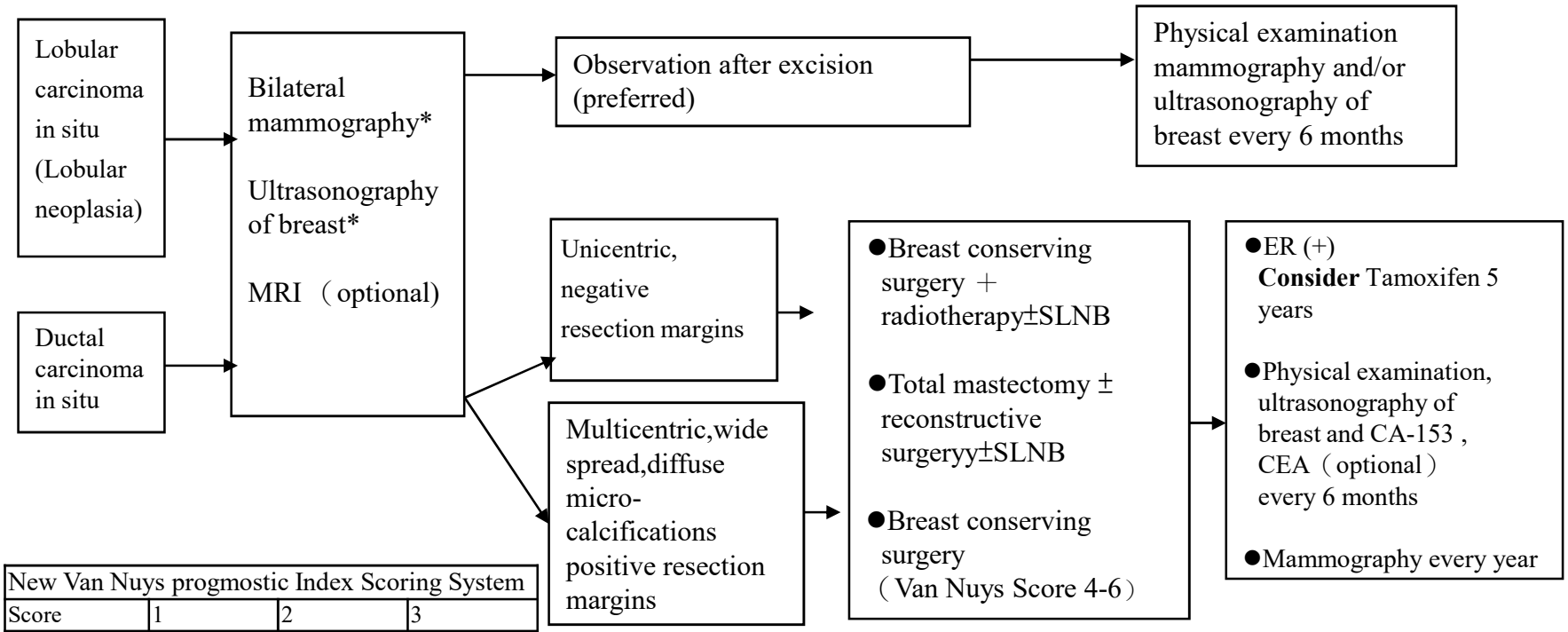
本共識與上一版的差異

上一版	新版
無。	1.新增乳癌治療處方 –Verzenio（Abemaciclib）〈2022/2/15上線〉 –Atezolizumab+Abraxane〈2021/12/2上線〉 –TS-1〈2021/12/2上線〉 –Cisplatin+Etoposide〈2021/12/2上線〉 –Pembrolizumab〈2021/11/24上線〉 2.異動乳癌治療處方 –Palbociclib+Letrozole→Palbociclib –Ribociclib+Letrozole →Ribociclib 3.修改Clinical stage I、II，術後LN(-)、ER(+) ±C/T之條件： （1）unfavorable histology （2）tumor >2cm （3）ki-67>14% （4）age<40 y/o

Breast Cancer

Kaohsiung Veterans General Hospital
Clinical Practice Guideline 2022.01 Version

DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	FOLLOW-UP



New Van Nuys progmostic Index Scoring System			
Score	1	2	3
Size	≦m	16	≧
Margin width	≧m	1	＜m
Pathologic classification	Non-high-Grade w/o necrosis	Non-high-Grade with necrosis	High-grade With or w/o necrosis
Age	>60	40-60	<40

*與期別相關之主要檢查

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DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	ADJUVANT TREATMENT	FOLLOW-UP

Clinical Stage I

T1N0M0

Clinical Stage II

T0N1M0
T1N1M0
T2N0M0
T2N1M0
T3N0M0

Chest X-ray*

Bilateral mammography*

Breast sono*

Liver sono or CT * （in 4 months）

Whole body bone scan（optional）

Pathology review
（如腫瘤已切除）

Criteria of sentinel node biopsy：
early breast cancer and clinically lymph node negative

Systemic treatment

Clinical LN（－）
- Breast conserving surgery + SLNB + R/T
- Simple mastectomy + SLNB ± reconstruction
- Modified radical Mastectomy ± reconstruction

Clinical LN（＋）
- Breast conserving surgery + ALND + R/T
- Modified radica Mastectomy ± reconstruction **(+/-R/T)**

If SLNB(+)
- axillary lymph node dissection
- BCS:If tumor ＜3cm, consider SLNB only then R/T

LN（－）
- ER positive
  hormone therapy ±chemotherapy
  1) unfavorable histology
  2) tumor ＞ 2cm
  3) ki-67 ＞14%
  4) age ＜40y/o
- ER negative : **chemotherapy**
  （Exclude T1a）

LN（＋）
- ER positive:
  Chemotherapy+hormone therapy
- ER negative :
  Chemotherapy

※更年期後婦女，LN(+)≦3顆，ER(+)可以使用Hormal therapy即可

pN1
- TNBC
- non TNBC if age ≦50 or LVI(+)

Strongly consider PMRT

Favorable histology: medullary, mucinous, papillary, tubular carcinoma

Physical examination, Ultrasonography of breast and liver, Chest x-ray, CA 15-3 every 3~6 months for 2 years, then every 6~12 months for 2 years then every 12 months. Mammography every year Women on tamoxifen: pelvic examination every 12 months

Post-mastectomy radiotherapy: see page 7

Her-2/neu + (IHC 3+ or FISH+)
Herceptin x for 1 year (optional)

年齡＞70歲或 ECOG功能狀態評分≧2分，可考慮不做化學、放射治療

*與期別相關之主要檢查

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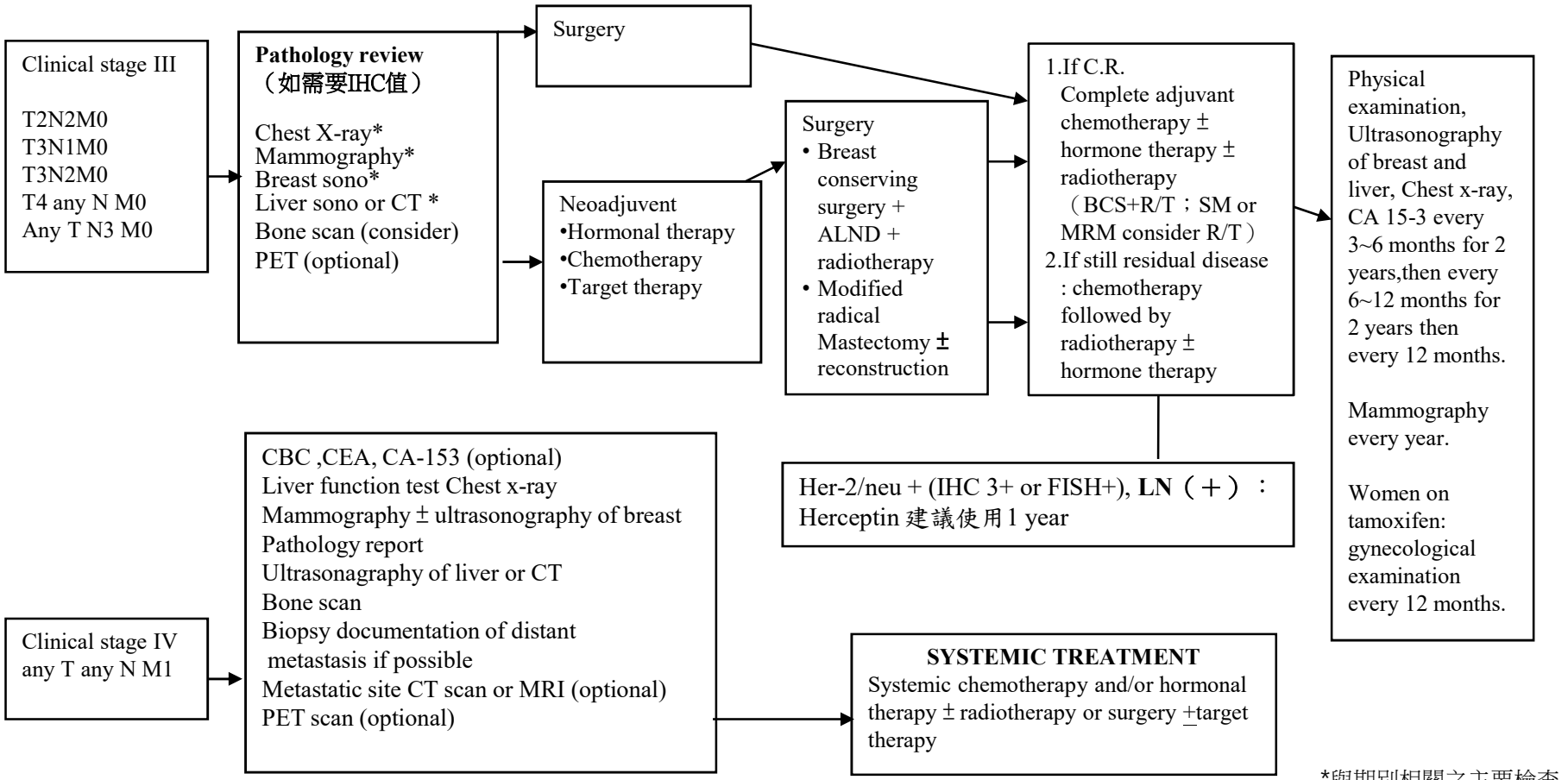
DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	ADJUVANT TREATMENT	FOLLOW-UP



*與期別相關之主要檢查

年齡＞70歲或 ECOG功能狀態評分≧2分，可考慮不做化學、放射治療

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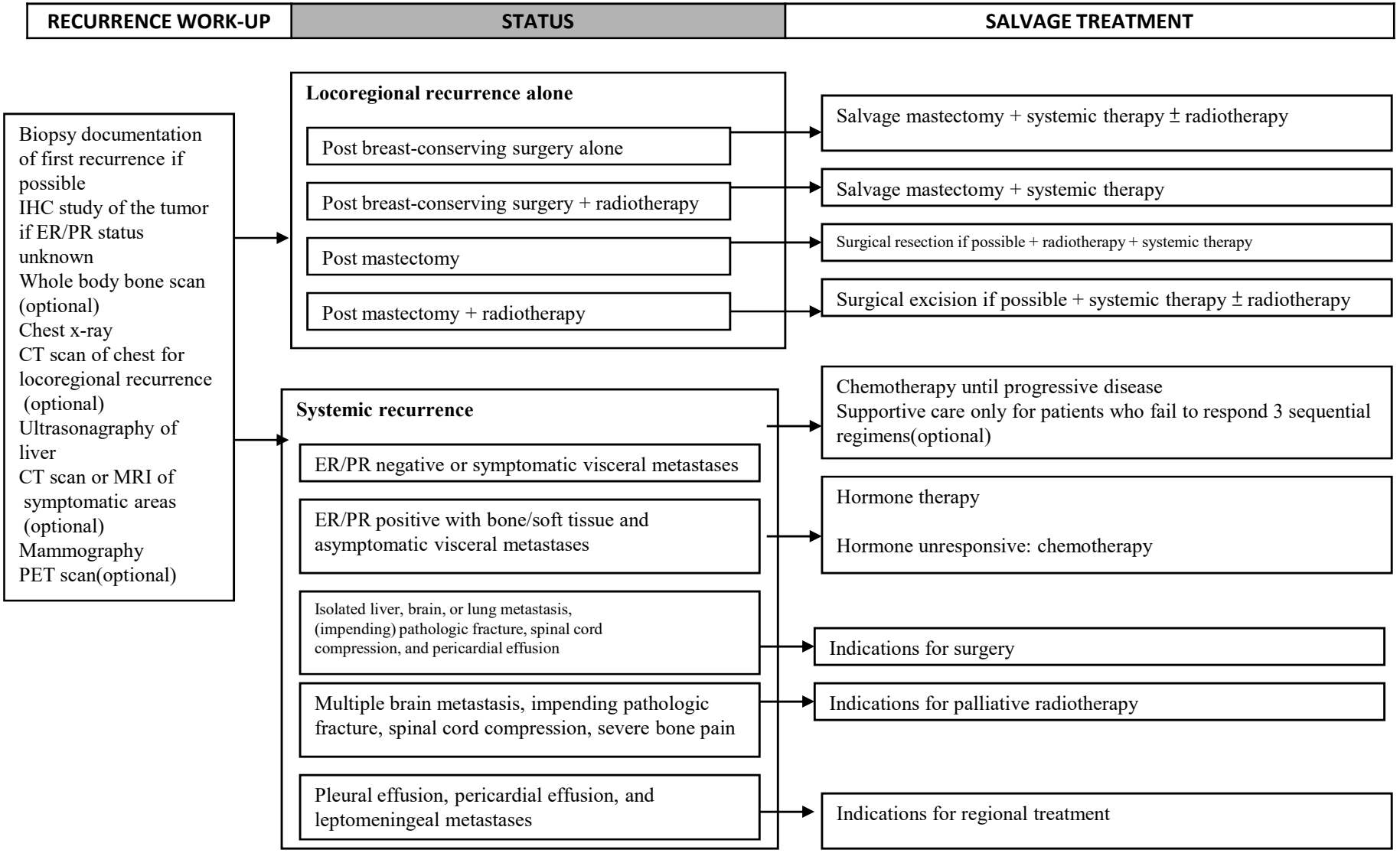

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INDICATIONS FOR POST-MASTECTOMY RADIOTHERAPY

1.skin involvement(skin nodule, ulceration, dorms lymphatic involvement)
2.Chest wall involvement
3.positive axillary lymph nodes ≥4, lymph nodes positive 1-3（Strongly consider*）
4.positive or close surgical margin
5.tumor ≥5㎝, lymph nodes negative（optional）, lymph nodes positive recommendation
6.gross multicentric disease(tumor in more than one quadrant and serpent at least 4cm by clinical or pathology)
7. for breast conservative treatment（if DCIS Van Nuys Score ≥7）

*乳房切除術(modified radical mastectomy)後之放射治療：
1. T3N+，T4或腋下淋巴結被癌細胞侵犯超過四顆(含)以上者
2. 手術範圍邊緣仍被癌細胞侵犯者
3. 腋下淋巴結被癌細胞侵犯一至三顆者，應與醫師討論是否需輔助性放射治療。年齡小於50歲、血管淋巴侵犯或三陰性患者，強烈建議接受輔助性放射治療
4. 若手術前接受過化學治療者應以化學治療前的疾病狀態及術後病理來考慮是否需輔助性放射治療。若為病理顯示腫瘤完全消失(pCR)，可考慮不需術後放射治療。
5. T3N0,手術界邊陽性或小於1mm，建議照射胸廓，是否加上局部淋巴區則依臨床判斷。
6. 如果病情需要施以術後放射治療與化學治療，通常以化學治療為先。

BASIC REQUIREMENTS OF RADIOTHERAPY

- Radiation fields should include ipsilateral chest wall, internal mammary chain and supraclavicular fossa
- Excluding heart from radiation fields
- Central lung distance of the tangential fields < 3 cm
- No axillary irradiation if axillary clearance is adequate

Excision biopsy with no prior suspicion for malignancy

- Exact tumor size and type of tumor
- Tumor histological and/or nuclear grade
- Margin status (exact distance in mm)
- Status of lymphovascular permeation
- ER and PR study

Ductal carcinoma in situ with wide excision only

- Nuclear grade
- Status of tumor necrosis
- Tumor size
- Margin status (exact distance in mm)
- ER/PR study

Invasive carcinoma with wide excision and axillary lymph node dissection or modified radical mastectomy

- Exact tumor size and type of tumor
- Tumor histological grade
- Margin status (exact distance in mm)
- Status of multifocality and multicentricity
- Presence of DCIS and status of extensive intraductal component
- Status of peritumoral LVI
- Number of involved and total axillary lymph nodes with extranodal extension, total number of axillary nodes examined should not be less than 10.
- If any involvement of skin
- ER and PR study Her-2/neu
- Ki-67

住院放置人工血管術前一天 *篩選具心臟毒性用藥／評估CRS分數*	會診心臟內科醫師	後續追蹤

➢**Cardiotoxicity Risk Score(CRS)**

Medication-relted risk	**Example**
High (risk score 4)	Anthracyclines; trastuzumab; cyclophosphamide; 5-fluorouracil
Intermediate (risk score 2)	Pertuzumab; vinblastine; capecitabine; ponatinib
Low (risk score 1)	Bevacizumab; imatinib
Rare (risk score 0)	Carboplatin; fludarabine; paclitaxel; rituximab

心臟功能評估項目：

- Echo
- NT-proBNP
- High sensitivity Troponin-I

- Trastuzumab治療中，每3個月追蹤滿一年。
- Epirubicin療程結束後，每6個月追蹤，滿2年。

➢使用以下藥物，必須於首次治療前評估心臟功能：

- **Trastuzumab**
- **Pertuzumab**
- **TDM-1**
- **Lapatinib**

➢使用以下藥物，評估以下危險因子，大於**5**分者必須於首次治療前評估心臟功能：

- **Epirubicin**

Patient risk factors (1 point per item)

- Cardiomyopathy or heart failure
- Coronary artery disease or equivalent (including peripheral artery disease)
- Hypertension
- Diabetes mellitus
- Prior or concurrent anthracyclines
- Prior or concurrent chest radiation
- Age <15 years or >65years
- Female gender

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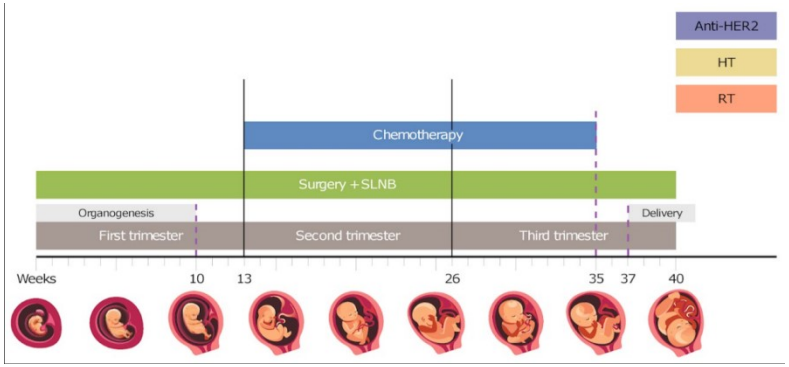
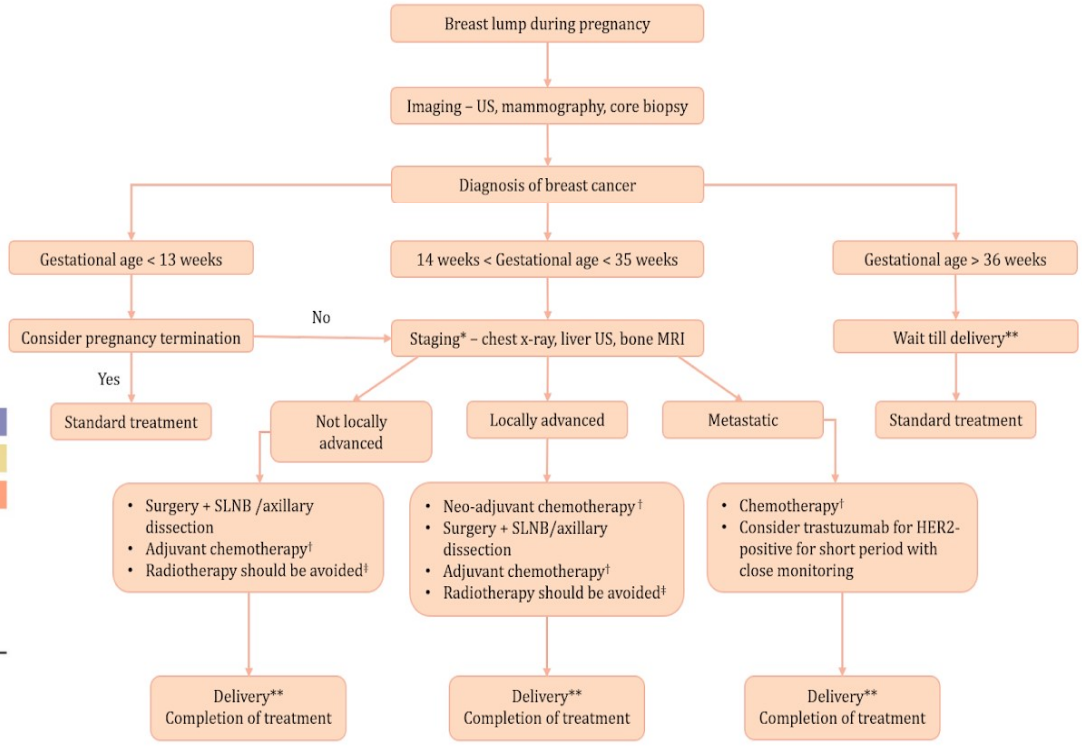
- 針對骨鬆者：依台灣骨鬆照護規範，50歲以上婦女有骨鬆風險者（如接受化學治療或Aromatase Inhibiter荷爾蒙治療），應每一到兩年檢查骨質密度（ DXA： dual energy X-ray absorptiometry ），鈣攝取量每天1000 – 1500 mg（胃酸不足，便祕，腎結石病史者使用檸檬酸鈣），並搭配Vitamin D3 400 – 800 IU，對於DXA檢查T-score -2.5以下，建議每日服用Clodronate(Sinclot)400 – 800 mg，或每週服用Alendronate (Fosamax)70mg，或每半年皮下注射Danosumab 60mg(Prolia)，或每半年靜脈注射Zoledronic acid 5mg，或每半年靜脈注射Pamidronate 90mg

- 針對懷孕者：13週以前不考慮墮胎及超過13週而少於35週

1. 早期乳癌患者：進行手術，之後可視病理狀況執行輔助化學治療
2. 局部晚期乳癌患者：先行術前化學治療，再進行手術，之後執行輔助化學治療
3. 轉移性乳癌患者：進行化學治療，若HER2 陽性，可視狀況施打短期trastuzumab





* Indicated only when might alter clinical management
** Avoiding iatrogenic preterm delivery is recommended
† Allowed only when gestational age is between 14 and 35 weeks
‡ Radiotherapy may be considered in highly selected patients before 20 weeks' gestation

癌別：乳癌2022年				
Neoadjuvant	最近改版	**2022/03/18**		
	處方內容	**Chemotherapy formula**	**schedule**	**Reference (No) /strength of evidence**
		EC or LC (Epirubicin 90mg/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	4-6 cycles	No 10 / Level I
		Taxol 80 mg/m^2	QWKLY	No 20, 21/Level I
		Docetaxel 75mg/m^2	Q3WKLY	No 5 / Level I
		Trastuzumab 2~8 mg/kg	QWKLY or Q3WKLY	No 8 / Level I
		Trastuzumab SC	Q3WKLY	No 15 / Level I
		Trastuzumab + Pertuzumab（maintenance）	Q3WKLY	No 14 / Level I
		Trastuzumab + Pertuzumab（loading）	Q3WKLY	No 14 / Level I
		Bevacizumab	(D1 & D15)	No 12, 39 / Level I
		Trastuzumab SC + Pertuzumab（maintenance）	Q3WKLY	No 48 / Level I
		Trastuzumab SC + Pertuzumab（loading）	Q3WKLY	No 48 /Level I
		Letrozole 2.5 mg	1tab（QD） x14 day	No 36 / Level I
		Cisplatin+Etoposide	Q3WKLY	No 58 / Level I
Adjuvant	處方內容	Carboplatin AUC x5mg+ Docetaxel 75mg/m^2	Q3WKLY	No 16 / Level I
		Carboplatin AUC 4~6+ 5-FU 1000mg/m^2	Q3WKLY	No 42 / Level I
		Cisplatin 50mg/m^2	Q3WKLY	No 17 / Level I
		Cisplatin 50mg/m^2 + 5-FU 500mg/m^2	Q3WKLY	No 40 / Level I
		Gemcitabine 1250mg/m^2	Q3WKLY	No 18 / Level I
		Lipo-Dox 50mg/m^2	Q3WKLY	No 10, 43 / Level I
		~~Mitoxantrone 12mg/m^2~~	~~Q3WKLY~~	（刪2019/2/22）
		Taxol 80mg/m^2 + Gemcitabine 800mg/m^2	QWKLY ~~Q3WKLY~~	（刪2017/10/6）
		Taxol 80mg/m^2 + Cisplatin 50mg/m^2	Q3WKLY	No 40 / Level I
		Taxol 80mg/m^2	QWKLY	No 20, 21/ Level I
		Taxol 175mg/m^2	Q3WKLY	No 21 / Level I
		Docetaxel 60mg/m^2 + Cisplatin 50mg/m^2	Q3WKLY	No 22 / Level I
		~~Docetaxel 75mg/m^2 + Gemcitabine 1000mg/m^2~~	~~Q3WKLY~~	（刪2017/10/6）
		Docetaxel 75mg/m^2	Q3WKLY	No 1 / Level I
		TC（Docetaxel 75mg/m^2 + Cyclophosphamide 500mg/m^2）	Q3WKLY	No 23 / Level I
		Vinorelbine 25~30mg/m	D1 or D8	No 24 / Level I

Adjuvant	處方內容	Docetaxel 75mg/m^2 x1 + Xeloda 2.5tab x14 day	Q3WKLY+14 day	No 25 / Level I
		Afinitor 5mg	2tab QD × 14 day	No 26, 27 / Level I
		Xeloda 500mg	2tab Bid × 14 day	No 28 / Level I
		Cyclophosphamide	2tab QD × 14 day	No 29 / Level I
		Methotrexate	2tab（BIW） x14 day	No 45 / Level I
		Ufur	3cap（Bid） x14 day	No 44 / Level I
		Vinorelbine 30mg + Vinorelbine 20mg	2 cap1 + 1cap（QW） x 14 day	No 24 / Level I
		Bleomycin 50mg	once	No 55 / Level I
		FEC (5-FU500mg/m^2, Epirubicin75mg/m, cyclophosphamide 500mg/m^2)	2-6 cycles	No 6 / Level I
		FLC (5-FU 500mg/m^2, Lipo-Dox 35g/m^2, cyclophosphamide 500mg/m^2)	2-6 cycles	No 43 / Level I
		~~FEC or FLC + Taxol (Q3W) (QW)~~	~~2-4 cycles（Q3W）or 2-12 cycles（QW）~~	（刪2020/3/20）
		~~FEC or FLC + Taxotere (taxotere 75mg/m^2)~~	~~2-4 cycles（Q3W）~~	（刪2020/3/20）
		CMF (Cyclophosphamide 2tab/m^2 + Methotrexate g/m^2 + Fluorouracil 500~600mg/m^2)	6-12 cycles	No 2 / Level I
		EC or LC (Epirubicin 90mg/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 10 / Level I
		TEC (Docetaxel 75mg/m^2 + Epirubicin 75mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 1 / Level I
		Mitoxantrone 10mg/m^2 + Leucovorine 170mg/m^2 + 5-FU 600mg/m^2 + Cisplantin 60 mg/m^2	Q3WKLY	No 54 / Level I
		IAIC for Epicin 60mg	once	No 47 / Level I
		Eribulin:1.4mg/ m^2	on days 1 and 8, 21-day cycle	No 11 / Level I
		~~Bevacizumab + Paclitaxel~~	~~(D1 & D8& D15)~~	（刪2019/2/22）
		Lynparza (Oraparib) 150mg	2 tabs BID	No 52 / Level I
		Nerlynx (Neratinib) 40mg	6 tabs QD	No 51 / Level I
		Ixempra(Ixabepilone)	Q3WKLY	No 53 / Level I
		TALZENNA (Talazoparib) 0.25mg	4 caps QD	No 56 / Level I
		TS-1	14 day	No 57 / Level I
		Cisplatin+Etoposide	Q3WKLY	No 58 / Level I

Hormone therapy	最近改版	**2022/03/18**		
	處方內容	Faslodex 250mg	Q28D	No 30 / Level I
		Goserelin 3.6mg	Q28D	No 31,32 / Level I
		Leuprorelin 3.75mg	Q28D	No 33 / Level I
		Anastrozole 1mg	1tab（QD） x28 day	No 34 / Level I
		Exemestane 25mg	1tab（QD） x28 day	No 35 / Level I
		Letrozole 2.5 mg	1tab（QD） x28day	No 36 / Level I
		Palbociclib	1tab（QD） x21 day	No 13 / Level I
		Ribociclib	3cap（QD）x21 day	No 50 / Level I
		Abemaciclib	1tab（BID）x28 day	No 59, 60, 61/ Level 1
		Tamoxifen 10mg	1tab（BID） x28 day	No 34, 36 / Level I
		Toremifene	1tab（QD） x28 day	No 46 / Level I
Target therapy	最近改版	**2022/03/18**		
	處方內容	~~Docetaxel 75mg/m^2 + Herceptin 6~8 mg/kg~~	~~Q3WKLY~~（刪2018/9/7）	
		~~Perjeta 420~840mg + Herceptin 6~8 mg/kg + Docetaxel 75mg/m^2~~	~~Q3WKLY~~（刪2018/9/7）	
		Kadcyla 3.6 mg/kg	Q3WKLY	No 37 / Level I
		Tykerb 250mg + Xeloda 500mg	5 tab（QD）+2tab（Bid x14 day	No 38 / Level I
		Tykerb 250mg	5 tab（QD）x14 day	No 38 / Level I
		Trastuzumab 2~8 mg/kg	QWKLY or Q3WKLY	No 8, 9/ Level I
		Trastuzumab SC	Q3WKLY	No 9 / Level I
		Trastuzumab + Pertuzumab（meitanance）	Q3WKLY	No 14 / Level I
		Trastuzumab + Pertuzumab（loading）	Q3WKLY	No 14 / Level I
		Trastuzumab SC + Pertuzumab（maintenance）	Q3WKLY	No 48 / Level I
		Trastuzumab SC + Pertuzumab（loading）	Q3WKLY	No 48 /Level I

Metastasis First line prescription	最新改版	**2022/03/18**		
	處方內容	Taxol 80 mg/m	QWKLY	No 21 / Level I
		Docetaxel 75mg/m^2	Q3WKLY	No 5 / Level I
		EC or LC (Epirubicin 90mg/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 10 / Level I
		~~Bevacizumab + Paclitaxel~~	~~(D1 & D8& D15)~~（刪2019/2/22）	
		Faslodex 250mg	Q28D	No 30 / Level I
		Goserelin 3.6mg	Q28D	No 31, 32 / Level I
		Leuprorelin 3.75mg	Q28D	No 33 / Level I
		Letrozole 2.5 mg	1tab（QD） x28 day	No 36 / Level I
		Tamoxifen 10mg	1tab（BID） x28 day	No 34, 36 / Level I
		Bevacizumab	(D1 & D15)	No 12, 39 / Level I
		~~Perjeta 420~840mg + Herceptin 6~8 mg/kg + Docetaxel 75mg/m^2~~	~~Q3WKLY~~（刪2018/9/7）	
		Kadcyla 3.6 mg/kg	Q3WKLY	No 37 / Level I
		Trastuzumab 2~8 mg/kg	QWKLY or Q3WKLY	No 9 / Level I
		Atezolizumab 840mg	Q2WKLY	No 49 / Level I
		Lynparza (Oraparib) 150mg	2 tabs BID	No 52 / Level I
		Ixempra(Ixabepilone)	Q3WKLY	No 53 / Level I
		TALZENNA (Talazoparib) 0.25mg	4 caps QD	No 56 / Level I
Immuno-oncology therapy	最近改版	**2022/03/18**		
	處方內容	Atezolizumab+Abraxane	Q3WKLY	N0 63 / Level I
		Pembrolizumab 200mg	Q3WKLY	No 62 / Level I

Reference for Neoadjuvant / Adjuvant Chemotherapy Regimens

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