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乳癌診療原則

2019年05月31日 第二版

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. 2019）

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

會議討論

上次會議：2019/02/22

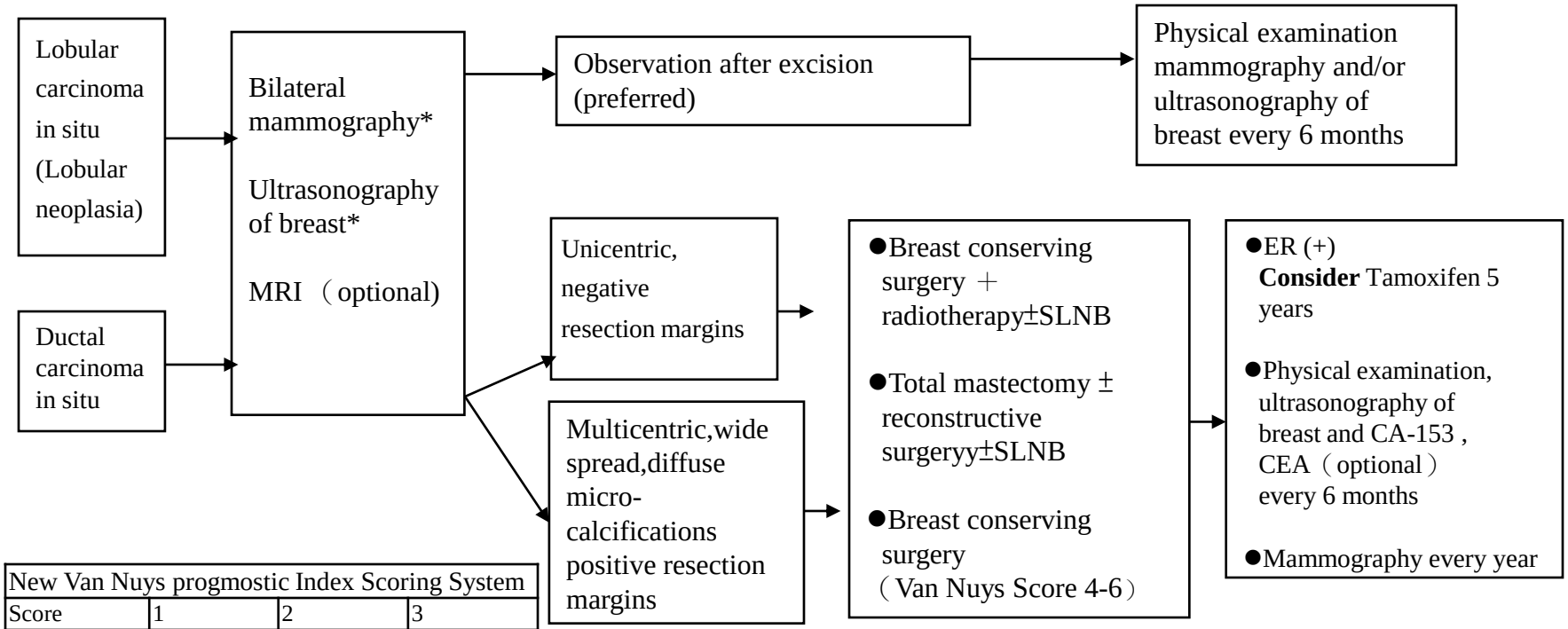
本共識與上一版的差異

上一版	新版
無。	1.新增乳癌標靶治療處方 －Herceptin SC+Perjeta（Loading） －Herceptin SC+Perjeta（Meitenance） －2019/04/17 上線 2. INDICATIONS FOR POST-MASTECTOMY RADIOTHERAPY註記*乳癌放射線治療指引之內容 3.依外評委員建議將Adjuvant、Neoadjuvant 之癌症用藥處方分類。

Breast Cancer

Kaohsiung Veterans General Hospital
Clinical Practice Guideline 2019.01 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

Breast Cancer

Kaohsiung Veterans General Hospital
Clinical Practice Guideline 2019.01 Version

DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	ADJUVANT TREATMENT	FOLLOW-UP

Clinical Stage I

T1N0M0

Clinical Stage II

T0N1M0
T1N1M0
T2N0M0
T2N1M0
T3N0M0

Bilateral mammography*

Ultrasonography of breast*

Ultrasonography of liver or CT*（in 4 months）

Pathology review
（如腫瘤已切除）

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
  T1a or Favorable histology：**hormone therapy**
  Tumor＜2㎝：**hormone therapy ±chemotherapy**
  Tumor＞2㎝：**chemotherapy** + **hormone therapy**
  （If Her2/neu(-) or Ki-67:＜15% or age ＞35歲 **only use hormone therapy**）
- ◆ 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)

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

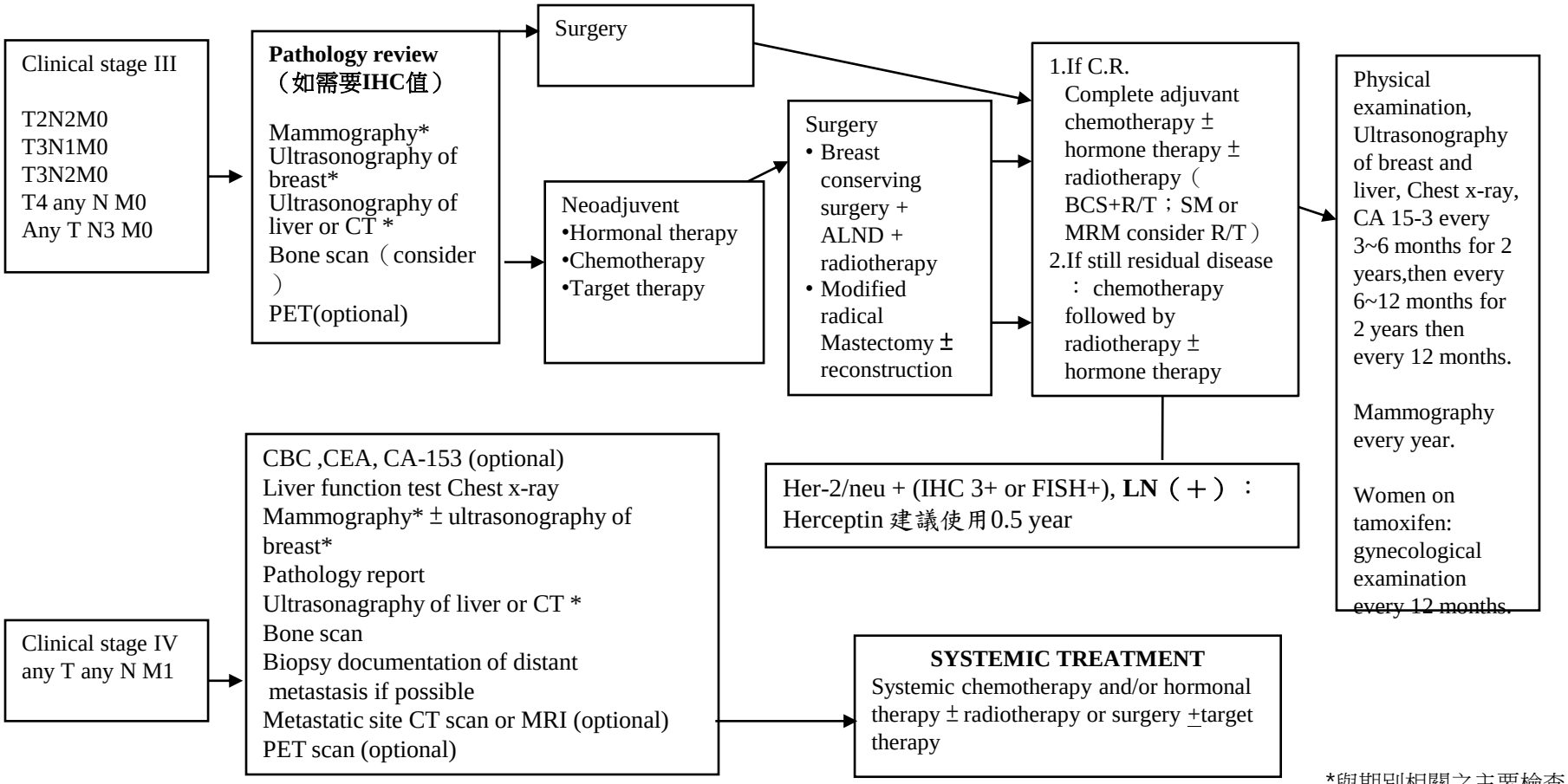
年齡＞70歲或 ECOG功能狀態評分≧2分，可考慮不做化學、放射治療

*與期別相關之主要檢查

Breast Cancer

Kaohsiung Veterans General Hospital
Clinical Practice Guideline 2019.01 Version

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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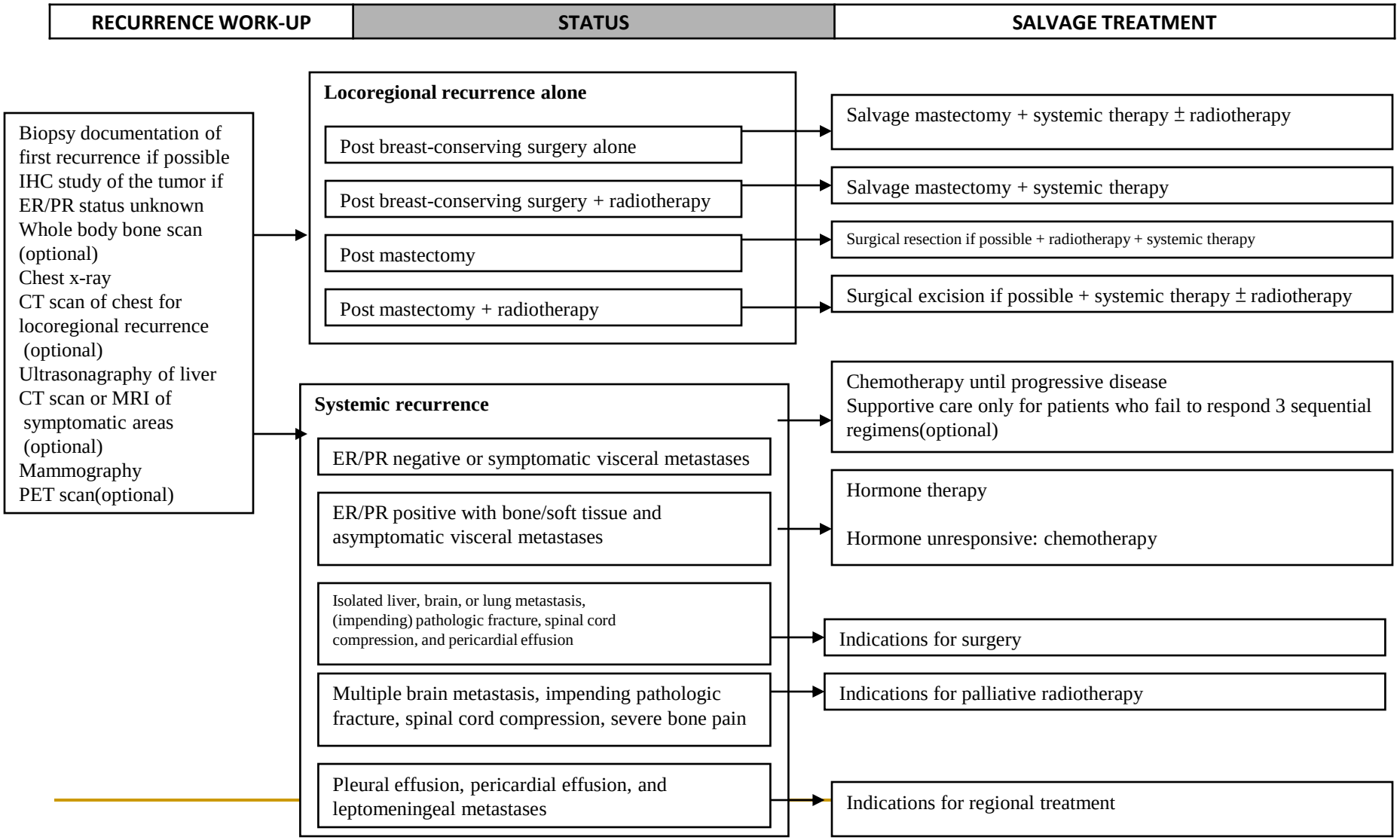

INDICATIONS FOR POST-MASTECTOMY RADIOTHERAPY

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。若為病理險是腫瘤完全消失(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

癌別：乳癌2018年

Neoadjuvant	最近改版	**2019/02/22**		
	處方內容	**Chemotherapy formula**	**schedule**	**Reference (No) /strength of evidence**
		EC or LC (Epirubicin g/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	4-6 cycles	No 16 / Level I
		Taxol 80 mg/m	QWKLY	No 27,28,29/Level I
		Docetaxel 75mg/m^2	Q3WKLY	No 31 / Level I
		Herceptin 2~8 mg/kg	QWKLY or Q3WKLY	No 53 / Level I
		Herceptin（Trastuzumab）600mg SC	Q3WKLY	No 22 / Level I
		Herceptin + Perjeta（meitanance）	Q3WKLY	No 21 / Level I
		Herceptin + Perjeta（loading）	Q3WKLY	No 21 / Level I
		Bevacizumab	(D1 & D15)	No 19,56 / Level I
		Herceptin SC + Perjeta（meitanance）	Q3WKLY	No 67/ Level I
		Herceptin SC + Perjeta（loading）	Q3WKLY	No 67/Level I
Adjuvant	處方內容	Carboplatin AUC x5mg+ Docetaxel 75mg/m^2	Q3WKLY	No 23 / Level I
		Carboplatin AUC 4~6+ 5-FU 1000mg/m^2	Q3WKLY（新增2015/9/11	No 54,59 / Level I
		Cisplatin 50mg/m^2	Q3WKLY	No 24 / Level I
		Cisplatin 50mg/m^2 + 5-FU 500mg/m^2	Q3WKLY	No 57 / Level I
		Gemcitabine 1250mg/m^2	Q3WKLY	No 25 / Level I
		Lipo-Dox 50mg/m^2	Q3WKLY	No 16,60 / Level I
		~~Mitoxantrone 12mg/m^2~~	~~Q3WKLY~~（刪2019/2/22）	No 17 / Level I
		Taxol 80 mg/m + Gemcitabine 800mg/m^2	QWKLY ~~Q3WKLY~~（刪2017/10/6）	No 26 / Level I
		Taxol 80 mg/m + Cisplatin 50mg/m^2	Q3WKLY	No 57 / Level I
		Taxol 80 mg/m	QWKLY	No 27,28,29/ Level I
		Taxol g/m	Q3WKLY	No 29 / Level I
		Docetaxel 60mg/m^2 + Cisplatin 50mg/m^2	Q3WKLY	No 30 / Level I
		~~Docetaxel 75mg/m^2 + Gemcitabine 1000mg/m^2~~	~~Q3WKLY~~（刪2017/10/6）	No 17 / Level I
		Docetaxel 75mg/m^2	Q3WKLY	No 31 / Level I
		TC（Docetaxel 75mg/m^2+Cyclophosphamide 500mg/m^2）	Q3WKLY	No 32 / Level I
		Vinorelbine 25~30mg/m	D1 or D8	No 33 / Level I

		Docetaxel 75mg/m^2 x1 + Xeloda 2.5tab x14 day	Q3WKLY+14 day	No 34 / Level I
		Afinitor 5mg	2tab QD × 14 day	No 35,36 / Level I
		Xeloda 500mg	2tab Bid × 14 day	No 37 / Level I
		Cyclophosphamide	2tab QD × 14 day	No 38 / Level I
		Methotrexate	2tab（BIW）x14 day	No 62 / Level I
		Ufur	3cap（Bid）x14 day	No 61 / Level I
		Vinorelbine 30mg + Vinorelbine 20mg	2 cap1 + 1cap（QW）x 14 day	No 39 / Level I
		Bleomycin 50mg	once	No 65 / Level I
		FEC(5-FU500mg/m^2,Epirubicin75mg/m，cyclophosphamide g/m^2)	2-6 cycles	No 2 / Level I
		FLC (5-FU g/m^2，Lipo-Dox g/m^2，cyclophosphamide g/m^2)	2-6 cycles	No 16 / Level I
		FEC or FLC + Taxol(taxol g/m^2)（Q3W） (taxol 80 mg/m)（QW）	2-4 cycles（Q3W）or 2-12 cycles（QW）	No 7 / Level I
		FEC or FLC + Taxotere (taxotere g/m^2)	2-4 cycles（Q3W）	No 9 / Level I
		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 g/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 16 / Level I
		TEC (Docetaxel 75mg/m^2 + Epirubicin 75mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 3 / Level I
		Mitoxantrone 10mg/m^2 + Leucovorine 170mg/m^2 + 5-FU 600mg/m^2 + Cisplantin 60 mg/m^2	Q3WKLY	No 66 / Level I
		IAIC for Epicin 60mg	once	No 64 / Level I
		Eribulin:1.4mg/ m^2	on days 1 and 8, 21-day cycle	No 40 / Level I
		~~Bevacizumab + Paclitaxel~~	~~(D1 & D8& D15)~~（刪 2019/2/22）	No 19 / Level I
Hormone therapy	最新改版	**2019/02/22**		
	處方內容	Faslodex 250mg	Q28D	No 41 / Level I
		Goserelin 3.6mg	Q28D	No 42,43 / Level I
		Leuprorelin 3.75mg	Q28D	No 44 / Level I
		Anastrozole 1mg	1tab（QD）x14 day	No 45 / Level I
		Exemestane 25mg	1tab（QD）x14 day	No 46 / Level I
		Letrozole 2.5 mg	1tab（QD）x14 day	No 47 / Level I
		Palbociclib and Letrozole	1tab（QD）x21 day	No 20,48 / Level I
		Tamoxifen 10mg	1tab（BID）x28 day	No 49 / Level I
		Toremifene	1tab（QD）x28 day	No 63 / Level I

Target therapy	最近改版	**2019/02/22**		
	處方內容	~~Docetaxel 75mg/m^2 + Herceptin 6~8 mg/kg~~	~~Q3WKLY~~（刪）	No 17 / Level I
		~~Perjeta 420~840mg + Herceptin 6~8 mg/kg + Docetaxel 75mg/m^2~~	~~Q3WKLY~~（刪2018/9/7）	No 17 / Level I
		Kadcyla 3.6 mg/kg	Q3WKLY	No 50 / Level I
		Tykerb 250mg + Xeloda 500mg	5 tab（QD）+2tab（Bid x14 day	No 51 / Level I
		Tykerb 250mg	5 tab（QD）x14 day	No 52 / Level I
		Herceptin 2~8 mg/kg	QWKLY or Q3WKLY	No 53 / Level I
		Herceptin（Trastuzumab）600mg SC	Q3WKLY	No 22 / Level I
		Herceptin + Perjeta（meitanance）	Q3WKLY	No 21 / Level I
		Herceptin + Perjeta（loading）	Q3WKLY	No 21 / Level I
		Herceptin SC + Perjeta（meitanance）	Q3WKLY	No 67/
		Herceptin SC + Perjeta（loading）	Q3WKLY	No 67/
Metastasis First line prescription	最近改版	**2019/02/22**		
	處方內容	Taxol 80 mg/m	QWKLY	No 29 / Level I
		Docetaxel 75mg/m^2	Q3WKLY	No 55 / Level I
		EC or LC (Epirubicin g/m^2 or Lipo-Dox 35mg/m^2 + cyclophosphamide 500mg/m^2)	6 cycles	No 16 / Level I
		~~Bevacizumab + Paclitaxel~~	~~(D1 & D8& D15)~~（刪 2019/2/22）	No 19 / Level I
		Faslodex 250mg	Q28D	No 41 / Level I
		Goserelin 3.6mg	Q28D	No 42,43 / Level I
		Leuprorelin 3.75mg	Q28D	No 44 / Level I
		Letrozole 2.5 mg	1tab（QD） x14 day	No 47 / Level I
		Tamoxifen 10mg	1tab（BID） x28 day	No 49 / Level I
		Bevacizumab	(D1 & D15)	No 19,56 / Level I
		~~Perjeta 420~840mg + Herceptin 6~8 mg/kg + Docetaxel 75mg/m^2~~	~~Q3WKLY~~（刪2018/9/7）	No 17 / Level I
		Kadcyla 3.6 mg/kg	Q3WKLY	No 50 / Level I
		Herceptin 2~8 mg/kg	QWKLY or Q3WKLY	No 53 / Level I

Reference for Neoadjuvant / Adjuvant Chemotherapy Regimens

1. Citron ML, Berry DA, Cirrincione, et al: Randomized Trial of Dose-Dense Versus Conventionally Scheduled and Sequential Versus Concurrent Combination Chemotherapy as Postoperative Adjuvant Treatment of Node-Positive Primary Breast cancer: First Report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741.J Clin Oncol 2003;21:1431-1439.
2. Fisher B, Brown AM, Dimitrov NV, et al: Two months of doxorubicin-cyclophosphamide with and without interval reinduction therapy compared with 6 months of cyclophosphamide, methotrexate, and fluorouracil in positive-node breast cancer patients with tamoxifen-nonresponsive tumors: results from the National Surgical Adjuvant Breast and Bowel Project B-15. J Clin Oncol 1990;8:1483-1496.
3. Martin, Pienkowski T, Mackey J, et al: Adjuvant Docetaxel for Node-Positive Breast Cancer. N Engl J Med 2005; 352:22.
4. Buzdar AU, Kau SW, Smith TL, Hortobagyi GN. Ten-year results of FAC adjuvant chemotherapy trial in breast cancer. Am J Clin Oncol 1989;12;123-128.
5. Levine MN,Bramwell VH, Pritchard Kl, et al:Randomized trial of intensive cyclophosphamide, epirubicin, and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer. National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1998;16:2651-8.
6. Goldhirsch A,Colleoni M, Coates AS, et al: Adding adjuvant CMF chemotherapy to either radiotherapy or tamoxifen: Are all CMFs alike? The International Breast Cancer Study Group (IBCSG).Ann Oncol 1998;9:489-93.
7. Sparano JA, Wang M, Martino S, et al: Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008;258:1663-1671.
8. Piccart MJ, Di Leo A, Beauduin M, 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;19:3103-3110.
9. Roche H, Fumoleau P, Spielmann M, et al: Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCC PACS 001 trial. J Clin Oncol 2006;24:5664-5671.
10. Martin M, Rodriguez-Lescure A, Ruiz A, et al: Randomized phase 3 trial of fluorouracil, epirubicin, and cyclophosphamide alone or followed by Paclitaxel for early breast cancer. J Natl Cancer Inst 2008;100:805-814.
11. Romond EH, Perez EZ, Bryant J, et al: Trastuzumab plus adjuvant Chemotherapy for operable HER2-positive breast cancer.N Engl J Med 2005;353:1673-1684.
12. Dang C, Fornier M, Sugarman S, et al: The Safety of Dose-Dense Doxorubicin and Cyclophosphamide Followed by Paclitaxel With Trastuzumab in HER-2/*neu* Overexpressed/Amplified Breast Cancer. J Clin Oncol.2008;26(8):1216-22.
13.Joensuu H, Kellokumpu-Lehtinen P-L, Bono P, et al: Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. N Engl J Med 2006;354:809-20.

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

15.Slamon D, Eiermann W, Robert N, et al: Adjuvant Trastuzumab in HER2-Positive Breast Cancer. N Engl J Med 2011;365:1273-1283.

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

17. NCCN clinical practice Guidelines in oncology (NCCN Guidelines) version 4. 2018

18. Cortes J, O'Shaughnessy J, Loesch D, et al. EMBRACE (Eisai Metastatic Breast Cancer Study Assessing Physician's Choice Versus E7389) investigators:Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011 Mar 12;377(9769):914-23. doi: 10.1016/S0140-6736(11)60070-6. Epub 2011 Mar 2.

19. Kathy Miller, M.D., Molin Wang, Ph.D., Julie Gralow, M.D., Maura Dickler, M.D., Melody Cobleigh, M.D., Edith A. Perez, M.D., Tamara Shenkier, M.D., David Cella, Ph.D., and Nancy E. Davidson, M.D.; Paclitaxel plus Bevacizumab versus Paclitaxel Alone for Metastatic Breast Cancer N Engl J Med 2007; 357:2666-2676December 27, 2007DOI: 10.1056/NEJMoa072113

20. Richard S. Finn, M.D., Miguel Martin, M.D., Hope S. Rugo, M.D., Stephen Jones, M.D., Seock Ah Im, M.D., Ph.D.,Karen Gelmon, M.D., Nadia Harbeck, M.D., Ph.D., Oleg N. Lipatov, M.D., Janice M. Walshe, M.D.,Stacy Moulder, M.D., Eric Gauthier, Pharm.D., Ph.D., Dongrui R. Lu, M.Sc., Sophia Randolph, M.D., Ph.D.,Veronique Dieras, M.D., and Dennis J. Slamon, M.D., Ph.D. Palbociclib and Letrozole in Advanced Breast CancerN Engl J Med. 2016 Nov 17;375(20):1925-1936.

21. Gunter von Minckwitz, MD, et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med 2017;377:122-131

22. Christian Jackisch, et. al. HannaH phase III randomized study: Association of otal pathological complete response with event-free survival in HER2-positive early breast Cancer treated with neoadjuvant-adjuvant trastuzumab after 2 years of treastment-free follow up. European Journal of Cancer. 2016:62-75

23. Robert N, Leyland-Jones B, Asmar L, et al. Randomized phase III study of trastuzumab, paclitaxel, and carboplatin compared with trastuzumab and paclitaxel inwomen with HER-2-overexpressing metastatic breast cancer. J Clin Oncol 2006;24:2786-2792.

24. Silver DP, Richardson AL, Eklund AC, et al. Efficacy of neoadjuvant cisplatinin triple-negative breast cancer. J Clin Oncol 2010;28(7):1145-53.

25. Seidman AD. Gemcitabine as single-agent therapy in the management of advanced breast cancer. Oncology (Williston Park) 2001;15:11-14.

26. Albain KS, Nag S, Calderillo-Ruiz G, et al. Global phase III study of gemcitabine plus paclitaxel (GT) vs. paclitaxel (T) as frontline therapy for metastatic breast cancer (MBC): First report of overall survival [Abstract]. J Clin Oncol 2004;22:Abstract 510 Available at:http://meeting.ascopubs.org/cgi/content/abstract/22/14_suppl/510.

27.Sparano JA, Wang M, Martino S, et al. Weekly paclitaxel in adjuvant treatment of breast cancer. N Engl J Med 2008;258:1663-1671.

28. 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.

29. Seidman AD, Tiersten A, Hudis C, et al. Phase II trial of paclitaxel by 3-hour infusion as initial and salvage chemotherapy for metastatic breast cancer. J Clin Oncol1995;13:2575-2581.

30. Hurley J, Doliny P, Reis I, et al. Docetaxel, cisplatin, and trastuzumab as primary systemic therapy for human epidermal growth factor receptor 2-positive locally advanced breast cancer. J Clin Oncol 2006;24:1831-1838. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16549824.

31. 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.

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

33. Zelek L, Barthier S, Riofrio M, et al. Weekly vinorelbine is an effective palliative regimen after failure with anthracyclines and taxanes in metastatic breast carcinoma. Cancer 2001;92:2267-2272.

34. Mavroudis D, Papakotoulas P, Ardavanis A, et al. Randomized phase III trial comparing docetaxel plus epirubicin versus docetaxel plus capecitabine as first-line treatment in women with advanced breast cancer. Ann Oncol 21:48(2010).

35. Yardley DA, Noguchi S, Pritchard KI, et al. Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis. Adv Ther 2013;30:870-884. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24158787.

36. 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. Available at:http://www.ncbi.nlm.nih.gov/pubmed/22149876.

37. Capecitabine 1,000-1,250 mg/m2 PO twice daily on Days 1-14. Cycled every 21 days for 6-8 cycles. Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. N Engl J Med 2017;376:2147- 2159.

38. Licchetta A, Correale P, Migali C, et al. Oral metronomic chemo-hormonal-therapy of metastatic breast cancer with cyclophosphamide and megestrol acetate. Chemother 2010;22(3):201-4.

39. Zelek L, Barthier S, Riofrio M, et al. Weekly vinorelbine is an effective palliative regimen after failure with anthracyclines and taxanes in metastatic breast carcinoma.Cancer 2001;92:2267-2272.

40. Gasparini G, Dal Fior S, Panizzoni GA, et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinical trial. Am J Clin Oncol 1991;14:38-44.

41. Robertson JF, Llombart-Cussac A, Rolski J, et al. Activity of fulvestrant 500 mg versus anastrozole 1 mg as first-line treatment for advanced breast cancer: results from the FIRST study. J Clin Oncol 2009;27:4530-4535. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19704066.

42. Moore HC, Unger JM, Phillips KA, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. N Engl J Med 2015;372:923-932. Available at:http://www.ncbi.nlm.nih.gov/pubmed/25738668.

43. Francis PA, Regan MM, Fleming GF, et al. Adjuvant ovarian suppression in premenopausal breast cancer. N Engl J Med 2015;372:436-446. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25495490.

44. Schmid P, Untch M, Wallwiener D, et al. Cyclophosphamide, methotrexate and fluorouracil (CMF) versus hormonal ablation with leuprorelin acetate as adjuvant treatment of node-positive, premenopausal breast cancer patients: preliminary results of the TABLE-study (Takeda Adjuvant Breast cancer study with Leuprorelin Acetate). Anticancer Res 2002;22:2325-2332. Available at:http://www.ncbi.nlm.nih.gov/pubmed/12174922.

45. Vergote I, Bonneterre J, Thurlimann B, et al. Randomised study of anastrozole versus tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women. Eur J Cancer 2000;36 Suppl 4:S84-85. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11056332.

46. Johnston SR, Kilburn LS, Ellis P, et al. Fulvestrant plus anastrozole or placebo versus exemestane alone after progression on non-steroidal aromatase inhibitors in postmenopausal patients with hormone-receptor-positive locally advanced or metastatic breast cancer (SoFEA): a composite, multicentre, phase 3 randomised trial. Lancet Oncol 2013;14:989-998. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23902874.

47. Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med 2003;349:1793- 1802. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14551341.

48. Johnston S, Pippen J, Pivot X, et al. Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. J Clin Oncol 2009;27:5538-5546. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19786658.

49. Fyles AW, McCready DR, Manchul LA, et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med 2004;351:963-970. Available at:http://www.ncbi.nlm.nih.gov/pubmed/15342804.

50. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer [supplementary appendix available online]. N Engl J Med 2012;367:1783-1791.

51. Geyer C, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 2006;355:2733-2743.

52. Johnston S, Pippen J, Pivot X, et al. Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. J Clin Oncol 2009;27:5538-5546. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19786658.

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

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

54. M.P. Decatris, D. Sundar, K.J. O'Byrne. Platinum-based chemotherapy in metastatic breast cancer: current status. CANCER TREATMENT 2004;4:53-81

55. Chan S, Friedrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999;17:2341-2354.

56. E.Smith, J-Y Pierga, L. Biganzoil, et al. First-line bevacizumab plus taxane-based chemotherapy for locally recurrent or metastatic breast cancer:safety and efficacy in an open-label study in 2251 patients.Annals of Oncology 2011;22:595-602

57. Lekakis L, Tryfonopoulos D, Pistamatzian N, et al. Salvage chemotherapy with cisplatin and 5-fluorouracil in metastatic breast cancer. Particular activity against liver metastases. Anticancer Res. 2012 May;32(5):1833-7.

58. Liheng Zhou,1 Shuguang Xu,1 Wenjin Yin, et al. Weekly paclitaxel and cisplatin as neoadjuvant chemotherapy with locally advanced breast cancer: a prospective, single arm, phase II study. Oncotarget. 2017 Oct 3;8(45): 79305–79314.

59. M. V. Fiorentino & A. Brandes. Carboplatin plus 5-fluorouracil and leucovorin in previously treated patients with metastatic breast cancer. Annals of Oncology 3 (Suppl.3): S29-S32, 1992.

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

61. SATORU TANAKA, MITSUHIKO IWAMOTO, KOSEI KIMURA,et al. A Phase II Study of Adjuvant Chemotherapy of Tegafur–Uracil for Patients with Breast Cancer with HER2-negative Pathologic Residual Invasive Disease After Neoadjuvant Chemotherapy. 2016;36:6505-6510.

62. VITTORIO GEBBIA, HAMOUDA BOUSSEN and MARIA ROSARIA VALERIO. Oral Metronomic Cyclophosphamide with and without Methotrexate as Palliative Treatment for Patients with Metastatic Breast Carcinoma. ANTICANCER RESEARCH 2012;32:529-536.

63. T. Qin, MD, Z.Y. Yuan, MD, R.J. Peng, MD, et al. Efficacy and tolerability of toremifene and tamoxifen therapy in premenopausal patients with operable breast cancer: a retrospective analysis. Curr Oncol. 2013;20(4):196–204.

64. Hsiao JH, Chang HT, Tseng YD,et al. Hepatic Arterial Infusion Chemotherapy Is a Feasible Treatment Option for Breast Cancer with Liver-predominant Metastatic Disease. 2018 Nov-Dec;32(6):1635-1641.

65. Carol Tan, Artyom Sedrakyan , John Browne , et al. The evidence on the effectiveness of management for malignant pleural effusion: a systematic review. European Journal of Cardio-thoracic Surgery. 2006;29:829－838

66. Lazzaro Repetto, Loredana Miglietta, Giovanni Gardin, et al. Phase II study of weekly mitoxantrone, 5-fluorouracil, and leucovorin in metastatic breast cancer. Breast Cancer Research and Treatment. 1994;30(2):133-7.

67. Joseph Gligorov a, Giuseppe Curigliano b, Volkmar Müller c, et al. Switching between intravenous and subcutaneous trastuzumab:Safety results from the PrefHer trial. The Breast 2017(34): 89-95

Reference：

美國癌症聯合委委員會(第八版AJCC)乳腺癌TNM分期
American Joint Committee on Cancer (AJCC)第8 版
NCCN Chemotherapy Order Templates (NCCN Templates™)
The National Comprehensive Cancer Network (NCCN)
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NCCN Drugs & Biologics Compendium (NCCN Compendium™)
NCCN Oncology Research Program (ORP)
NCCN Annual Conference: Clinical Practice Guidelines & Quality Cancer Care™
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.
衛生福利部國民健康署「癌症篩檢與診療測量指標」公告版102年12月修訂
PLOS ONE, December 2013, Volume 8 (12), e81765
Ann Surg Oncol (2013) 20:3169–3174
Cancer. 2013 Jul 1;119(13):2366-74. doi: 10.1002/cncr.28085. Epub 2013 Apr 10.
Annals of Oncology 25 (Supplement 1): i3, 2014
J Clin Oncol. 2011 Jul 20;29(21):2852-8. doi: 10.1200/JCO.2010.33.4714. Epub 2011 Jun 13.