

乳癌診療指引

一、參與討論同仁

| | | |
|--------|---------------|---------------|
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二、討論日期：112年11月27日

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113 年版與上一版差異：

| 112 年版 | 113 年修訂版 |
|---|--|
| <p>《 乳癌診療指引共識 -1 》 術後追蹤 術後五年以上： * 理學檢查、乳房超音波、乳房攝影每年一次</p> | <p>《 乳癌診療指引共識 -1 》 術後追蹤 術後五年以上： * 理學檢查、乳房超音波、乳房攝影或乳房核磁共振，原則上每年一次 (optional)</p> |
| <p>《 乳癌診療指引共識 -1 》 附註：</p> | <p>《 乳癌診療指引共識 -1 》 附註新增： 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。</p> |
| <p>《 乳癌診療指引共識 -2 》 追蹤 術後 5 年以上：各項目每年一次</p> | <p>《 乳癌診療指引共識 -2 》 追蹤 術後 5 年以上：各項目原則上每年一次 (optional)</p> |
| <p>《 乳癌診療指引共識 -2 》 附註： 5. 考慮接受化學治療或 Carrier 血液檢查 (需包含化療前 HBsAg 及 Anti-HCV test) 8. 血液檢查 (包含化療前 HBsAg 及 Anti-HCV test optional)</p> | <p>《 乳癌診療指引共識 -2 》 附註： 刪除第 8 點，合併於第 5 點加上 optiona 考慮接受化學治療或 Carrier 血液檢查 (需包含化療前 HBsAg 及 Anti-HCV test optional)</p> |

112 年版

《乳癌診療指引共識 -2》

附註：

《乳癌診療指引共識 -3》

輔助性治療

2. Her-2 (+) → Consider Trastuzumab* (±Perjeta)or TDM-1(non- PCR)

《乳癌診療指引共識 -3》

追蹤

術後 5 年以上：各項目每年一次

《乳癌診療指引共識 -3》

附註：

4.Anti-Her2 treatment 依健保使用規定或自費使用

《乳癌診療指引共識 -3》

附註：

7. 血液檢查 (包含化療前 HBsAg 及 Anti-HCV test optional)

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《乳癌診療指引共識 -2》

附註新增：

- 11.Pure tubular、Pure mucinous、Pure cribriform、Encapsulated or solid papillary carcinoma(ER+ and/or PR+,HER2-): pT1-3 and pN0: 可考慮 Adjuvant endocrine therapy only(詳見乳癌診療指引共識 -5)
12. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

《乳癌診療指引共識 -3》

輔助性治療

2. Her-2 (+) → Consider Trastuzumab* (±Pertuzumab or TDM-1(non-PCR) 註 4

《乳癌診療指引共識 -3》

追蹤

術後 5 年以上：各項目原則上每年一次 (optional)

《乳癌診療指引共識 -3》

附註：

4.Anti-Her2 treatment 依健保使用規定或自費使用，N+ patients: Consider adjuvant chemotherapy + Trastuzumab + Pertuzumab (category 1)

《乳癌診療指引共識 -3》

附註：

刪除第 7 點

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《乳癌診療指引共識 -3》

附註：

10.ER(-), PR(-) and Her2(+) Node(+) patients: Consider adjuvant chemotherapy+ Trastuzumab ± Pertuzumab

《乳癌診療指引共識 -3》

附註：

《乳癌診療指引共識 -4》

臨床檢查

《乳癌診療指引共識 -4》

輔助治療

3.TNBC with germline BRCA1/2 mutations adjuvant olaparib for 1 y (optional)

《乳癌診療指引共識 -4》

輔助治療

4. HR+, HER2- consider Abemaciclib for 2y (optional)
(≥ 4 LN or 1-3LN and least one of the following:
- Gr.3
 - Ki67 $\geq 20\%$
 - Tumor ≥ 5 cm)

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《乳癌診療指引共識 -3》

附註：

10.Pure tubular、Pure mucinous、Pure cribriform、Encapsulated or solid papillary carcinoma(ER+ and/or PR+,HER2-, pT1-3 and pN0): 可考慮 Adjuvant endocrine therapy only(詳見乳癌診療指引共識 -5)

《乳癌診療指引共識 -3》

附註：新增

11. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

《乳癌診療指引共識 -4》

臨床檢查 新增

腦部磁振造影 (optional)

乳房磁振造影 (optional)

《乳癌診療指引共識 -4》

輔助治療

3.Germline BRCA 1/2 mutations adjuvant olaparib for 1 year (optional)

《乳癌診療指引共識 -4》

輔助治療

4. HR+, HER2- consider Abemaciclib for 2y (optional)
(≥ 4 LN or 1-3LN and least one of the following:
- Gr.3
 - Tumor ≥ 5 cm)

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《乳癌診療指引共識 -4》

附註：

《乳癌診療指引共識 -5》

《乳癌診療指引共識 -6》

《乳癌診療指引共識 -7》

《乳癌診療指引共識 -7》

1. Ajuvant Ado-trastuzumab emtansine alone for 14 cycles. If ado-trastuzumab emtansine discontinued for toxicity, then trastuzumab ± pertuzumab to complete one year of therapy ;

《乳癌診療指引共識 -7》

附註：

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《乳癌診療指引共識 -4》

附註：新增

9. Anti-Her2 treatment 依健保使用規定或自費使用，N+ patients: Consider adjuvant chemotherapy + Trastuzumab + Pertuzumab (category 1)

10. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

新增一頁《乳癌診療指引共識 -5》

原《乳癌診療指引共識 -5》改標題為《乳癌診療指引共識 -6》

原《乳癌診療指引共識 -6》改標題為《乳癌診療指引共識 -7》

原《乳癌診療指引共識 -7》改標題為《乳癌診療指引共識 -8》

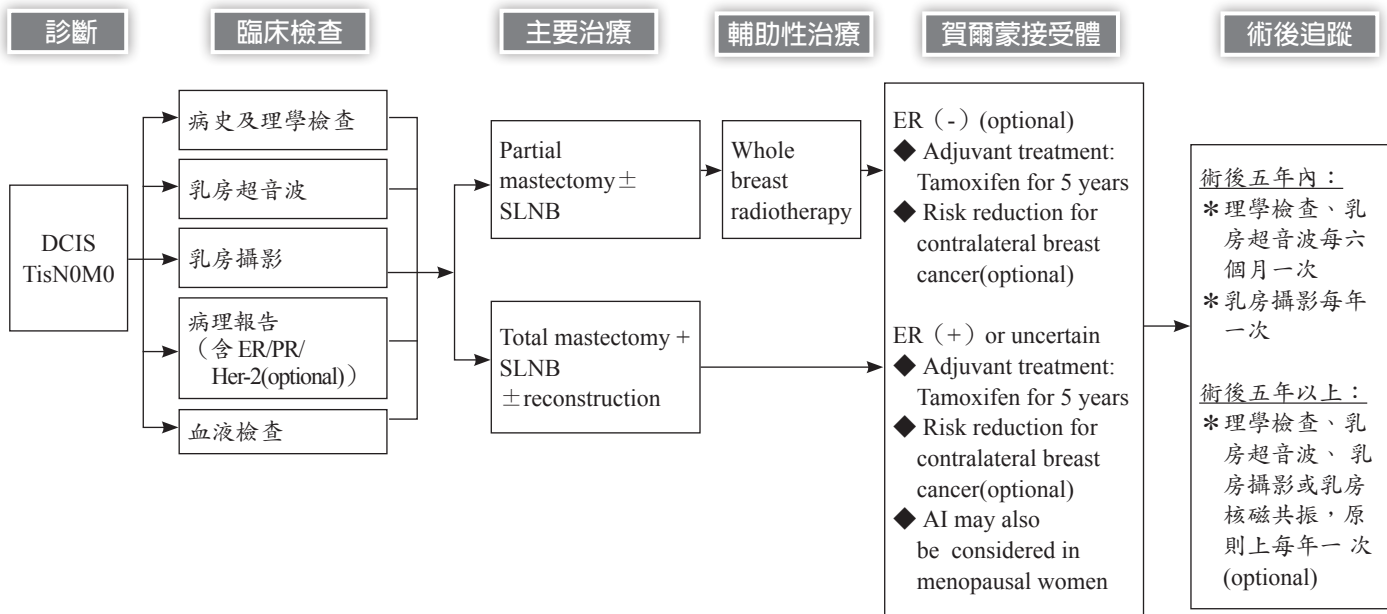
《乳癌診療指引共識 -8》

1. Ajuvant Ado-trastuzumab emtansine alone for 14 cycles. If ado-trastuzumab emtansine discontinued for toxicity, then trastuzumab ± pertuzumab to complete one year of therapy ; If node positive at initial staging, trastuzumab + pertuzumab (category 1)

《乳癌診療指引共識 -8》

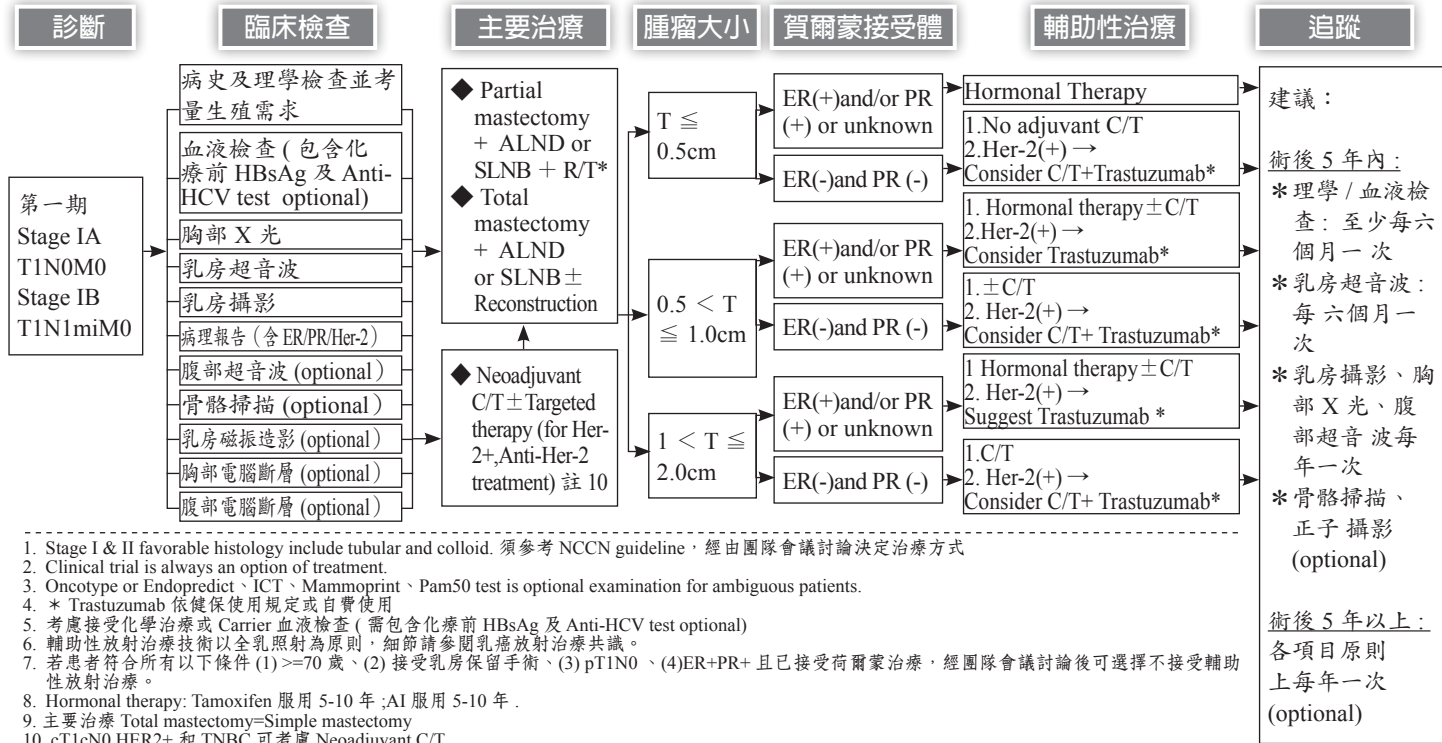
附註：新增

3. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

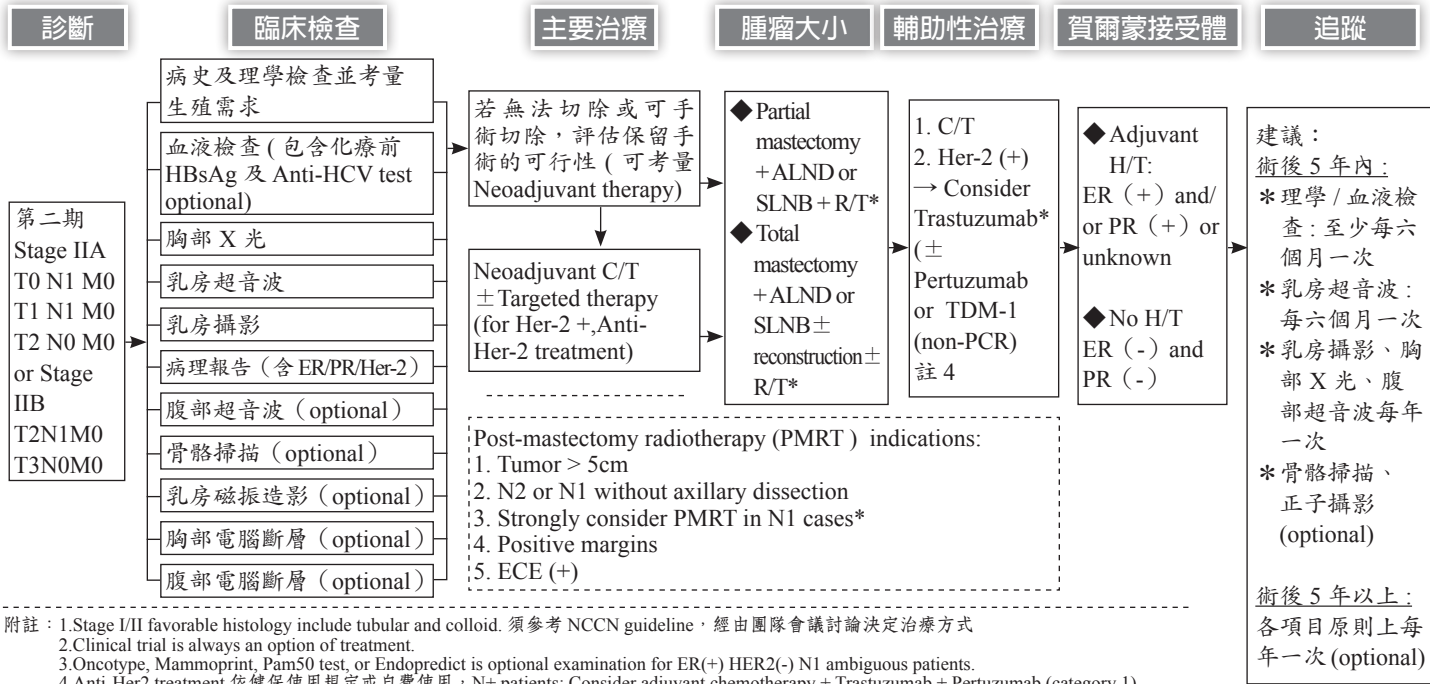


* 乳房保留手術後輔助性全乳放射治療可以顯著減少局部復發達 50%，若患者與乳癌醫療團隊經由醫病共同決策過程 (Shared decision making, SDM) 後同意該個案屬於低復發風險+，有些患者可以選擇只接受局部切除
+ 局部復發的風險因子：可觸及的腫塊、較大的腫瘤、high grade、接近的腫瘤邊緣、年輕患者。
* tamoxifen 的標準劑量為 20 mg/day，持續 5 年。低劑量 * tamoxifen (5 mg/day，連續 3 年) 僅在患者服用 20 毫克劑量時出現症狀或患者不願意或不能服用標準劑量時才可選擇。
* 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

《乳癌診療指引共識 -2》

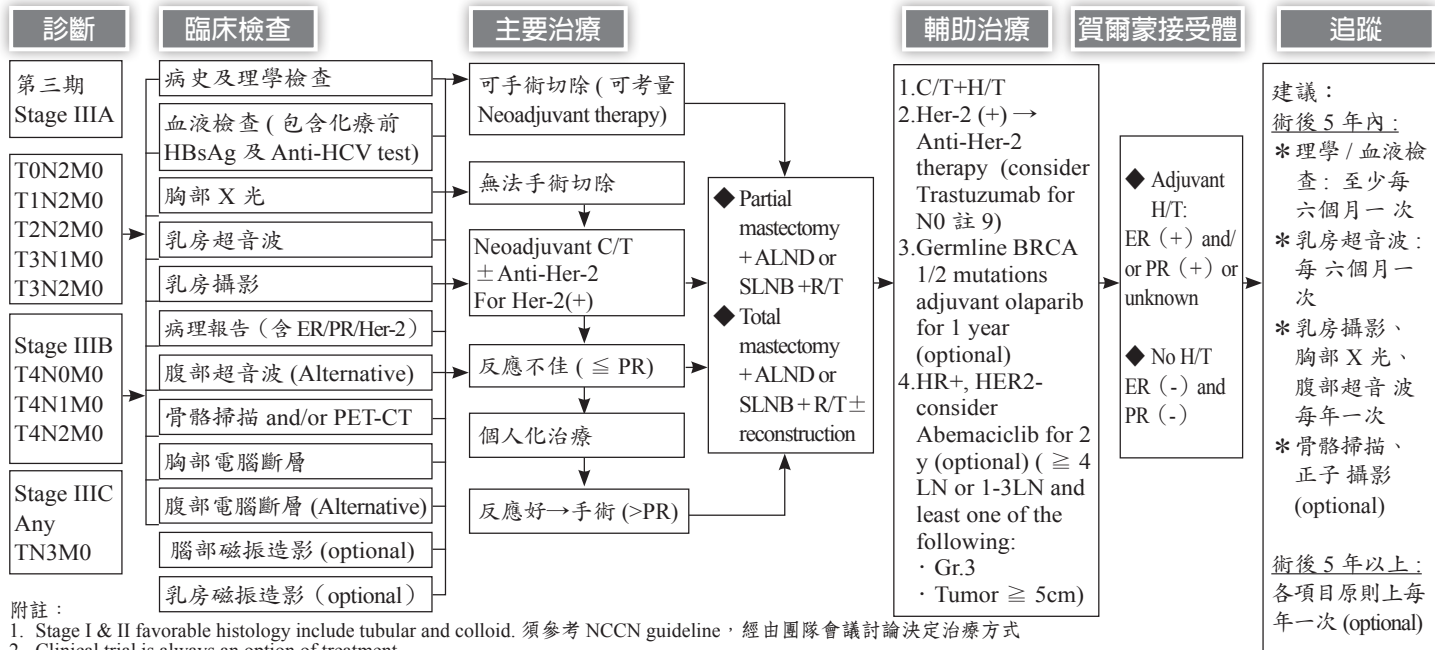


1. Stage I & II favorable histology include tubular and colloid. 須參考 NCCN guideline，經由團隊會議討論決定治療方式
2. Clinical trial is always an option of treatment.
3. Oncotype or Endopredict、ICT、Mammoprint、Pam50 test is optional examination for ambiguous patients.
4. * Trastuzumab 依健保使用規定或自費使用
5. 考慮接受化學治療或 Carrier 血液檢查 (需包含化療前 HBsAg 及 Anti-HCV test optional)
6. 輔助性放射治療技術以全乳照射為原則，細節請參閱乳癌放射治療共識。
7. 若患者符合所有以下條件 (1) ≥70 歲、(2) 接受乳房保留手術、(3) pT1N0、(4) ER+PR+ 且已接受荷爾蒙治療，經團隊會議討論後可選擇不接受輔助性放射治療。
8. Hormonal therapy: Tamoxifen 服用 5-10 年 ;AI 服用 5-10 年。
9. 主要治療 Total mastectomy=Simple mastectomy
10. cT1cN0 HER2+ 和 TNBC 可考慮 Neoadjuvant C/T
11. Pure tubular、Pure mucinous、Pure cribriform、Encapsulated or solid papillary carcinoma(ER+ and/or PR+,HER2-): pT1-3 and pN0: 可考慮 Adjuvant endocrine therapy only(詳見乳癌診療指引共識 -5)
12. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。



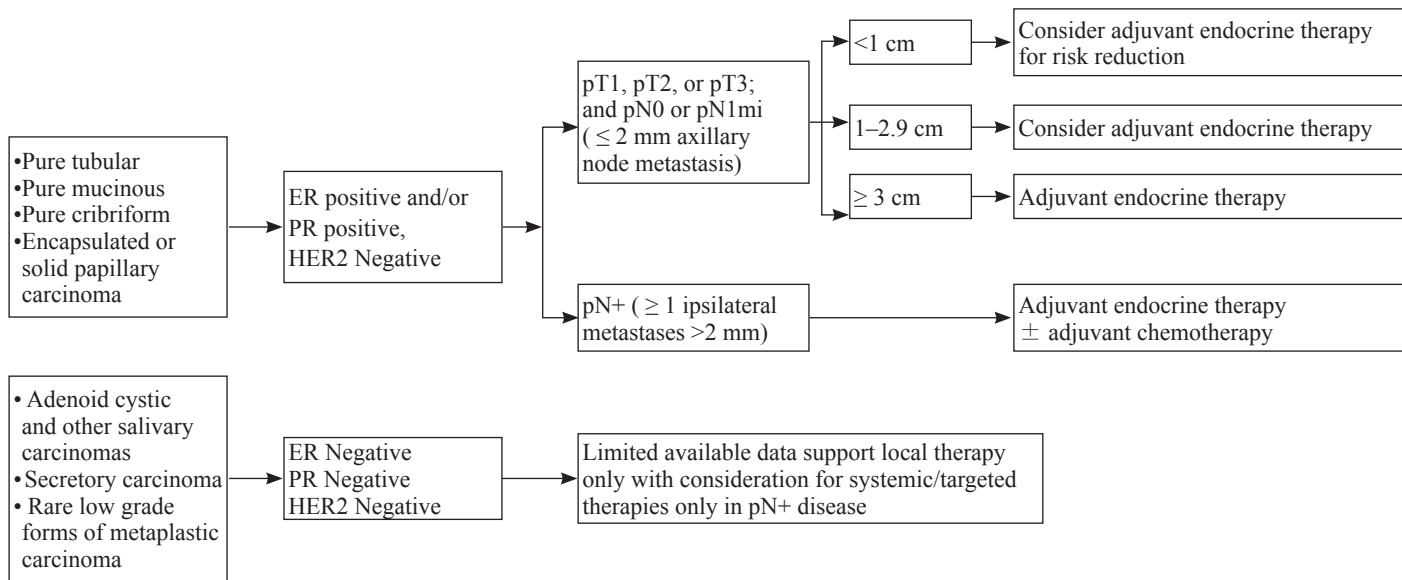
附註: 1. Stage I/II favorable histology include tubular and colloid. 須參考 NCCN guideline, 經由團隊會議討論決定治療方式
 2. Clinical trial is always an option of treatment.
 3. Oncotype, Mammoprint, Pam50 test, or Endopredict is optional examination for ER(+) HER2(-) N1 ambiguous patients.
 4. Anti-Her2 treatment 依健保使用規定或自費使用, N+ patients: Consider adjuvant chemotherapy + Trastuzumab + Pertuzumab (category 1)
 5. 考慮接受化學治療或 Carrier 液檢查 (需包含化療前 HBsAg 及 Anti-HCV test optional)
 6. *N1 低復發風險患者經患者與醫療團隊醫病共同決策過程後, 全乳切除術後可免做輔助放療。低復發風險患者須滿足以下所有條件: 年齡 ≥ 40 歲, T1, 單一淋巴結侵犯, 無淋巴血管侵犯, Her2/Neu (-)
 7. 主要治療 Total mastectomy=Simple mastectomy
 8. TNBC following standard neo/adjuvant therapy: consider Capecitabine maintenance therapy (self-pay)
 9. Stage II/III TNBC neoadjuvant chemotherapy combination with immunotherapy as treatment can be considered
 10. Pure tubular、Pure mucinous、Pure cribriform、Encapsulated or solid papillary carcinoma(ER+ and/or PR+,HER2-, pT1-3 and pN0): 可考慮 Adjuvant endocrine therapy only(詳見乳癌診療指引共識 -5)
 11. 本治療共識謹做為參考, 因每人狀況不同, 而由各醫師選擇最適當之處置方式, 不做為醫療訴訟用。

《乳癌診療指引共識-4》



附註:
 1. Stage I & II favorable histology include tubular and colloid. 須參考 NCCN guideline, 經由團隊會議討論決定治療方式
 2. Clinical trial is always an option of treatment.
 3. RT 參閱乳癌放射治療共識
 4. Abdomen sono or abdomen CT Alternative
 5. 主要治療 Total mastectomy=Simple mastectomy
 6. TNBC with residual invasive cancer following standard neoadjuvant therapy: Consider adjuvant capecitabine (自費使用)
 7. 完全緩解 (Complete Response, CR), 部分緩解 (Partial Response, PR), 無變化 (No Change, NC; 疾病穩定, SD), 疾病進展 (Progressive Disease, PD)
 8. 針對 TNBC high risk 可以考慮 neoadjuvant 及 adjuvant immunotherapy
 9. Anti-Her2 treatment 依健保使用規定或自費使用, N+ patients: Consider adjuvant chemotherapy + Trastuzumab + Pertuzumab (category 1)
 10. 本治療共識謹做為參考, 因每人狀況不同, 而由各醫師選擇最適當之處置方式, 不做為醫療訴訟用。

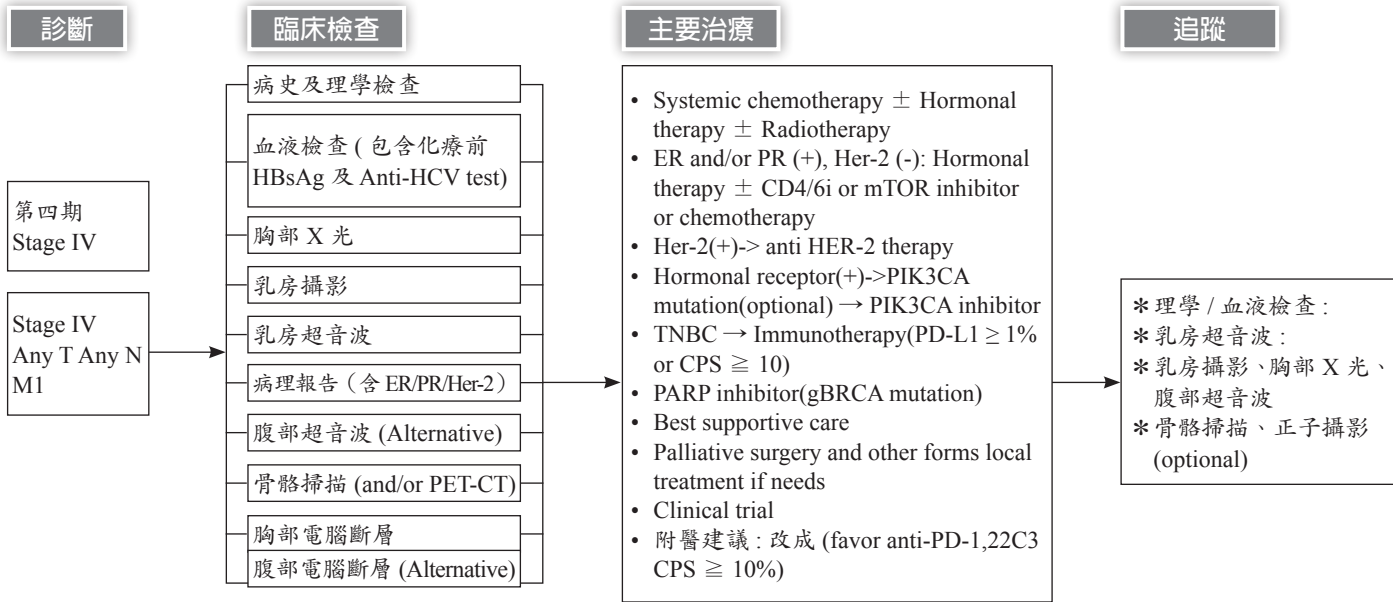
預後良好的病理型態：輔助性藥物指引



附註：

1. There are rare subtypes of metaplastic carcinoma (eg, low-grade adenosquamous and low-grade fibromatosis-like carcinoma) that are considered to have a favorable prognosis without adjuvant systemic therapies.
2. To be associated with favorable prognosis, the favorable histologic type should not be high grade, should be pure (>90% as classified on the surgical excision, not core biopsy alone), and should be HER2 negative. If atypical pathologic or clinical features are present, consider treating as ductal/NST.
3. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

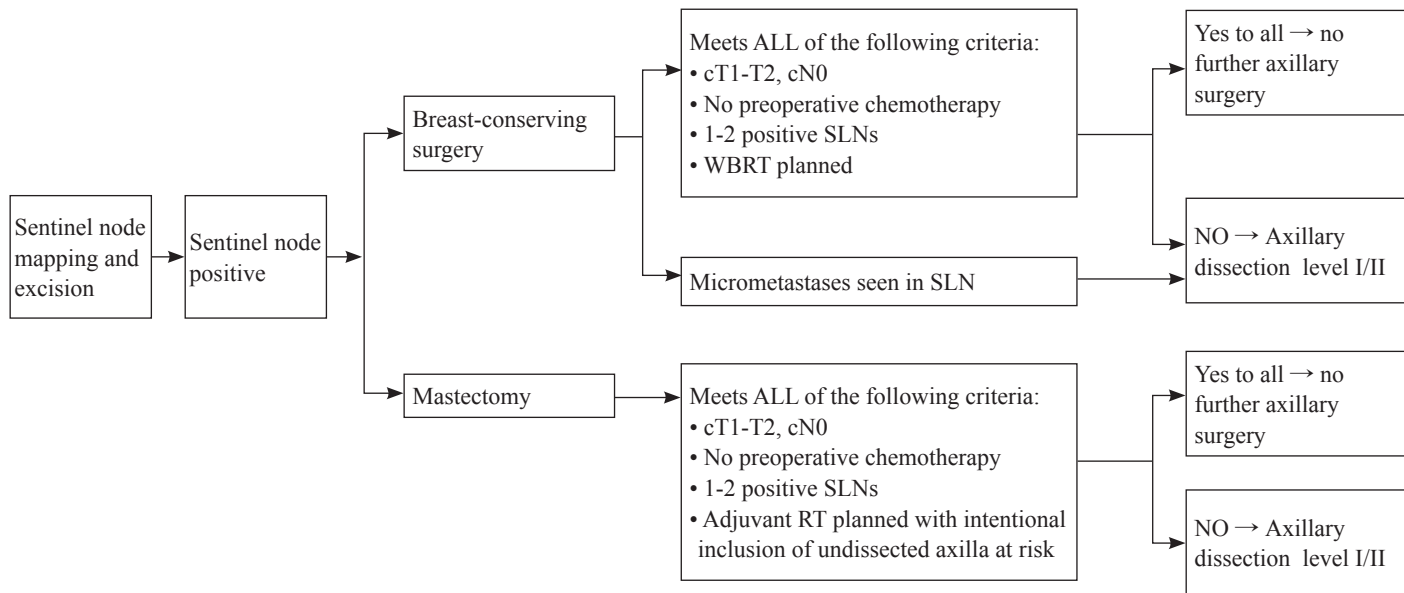
《 乳癌診療指引共識 -6 》



附註：

1. Stage I & II favorable histology include tubular and colloid. 須參考 NCCN guideline，經由團隊會議討論決定治療方式
2. Clinical trial is always an option of treatment.
3. Abdomen sono or abdomen CT Alternative
4. Anti -HER-2 therapy 依健保規範或自費使用
5. CPS: combined positive score
6. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

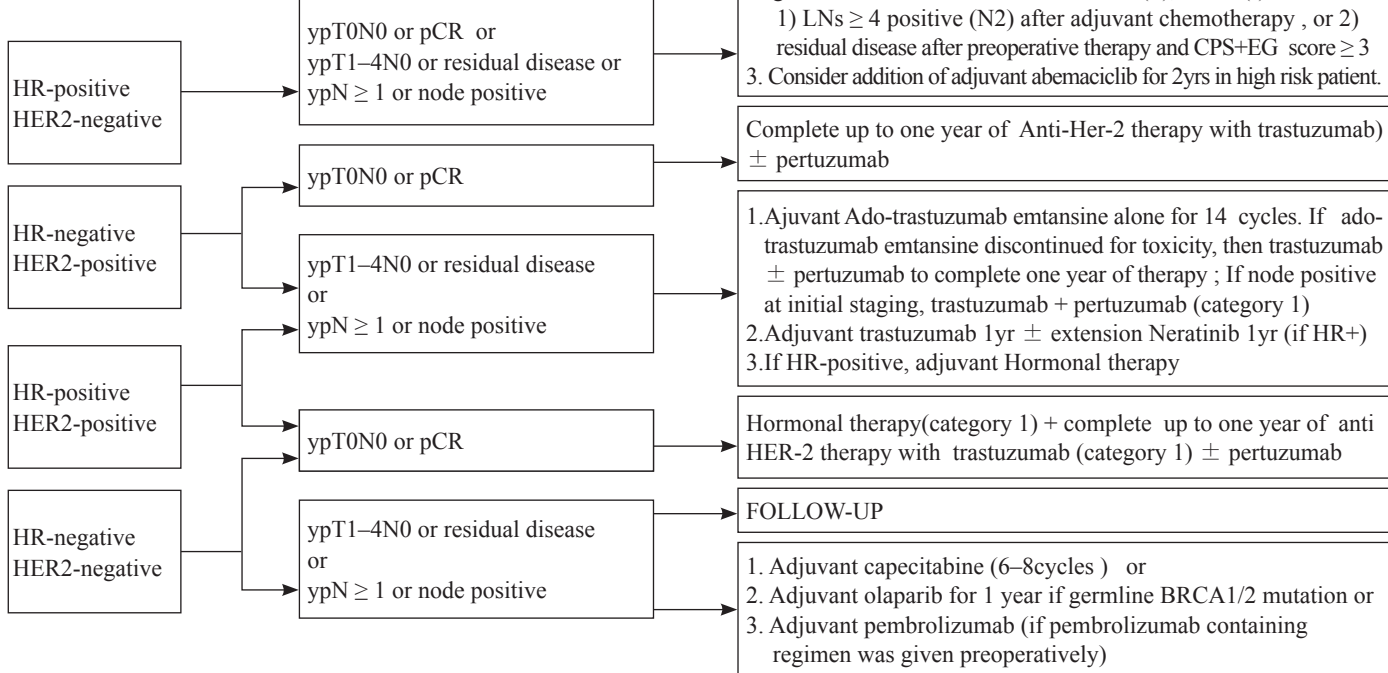
《 乳癌診療指引共識 -7 》



附註：本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

《 乳癌診療指引共識 -8 》

After complete course of neoadjuvant chemotherapy



1. CPS+EG score: a score based on pre-treatment clinical stage (CS) post-treatment pathologic stage (PS), ER status (E) and grade (G) after neoadjuvant therapy
2. pCR 定義為 neoadjuvant chemotherapy 之後，無殘存侵犯性乳癌。(亦若僅殘留原位癌，仍為 pCR)
3. 本治療共識謹做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不做為醫療訴訟用。

《參考文獻》

1. NCCN Clinical Practice in Oncology: Breast Cancer V.5.2023
2. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA CancerJ Clin* 2010;60:277-300.
3. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;365:1687-1717.
4. Edge SB, Byrd DR, Compton CC, et al., eds. *AJCC Cancer Staging Manual*, 7th Edition. New York: Springer; 2010
5. Allred DC, Carlson RW, Berry DA, et al. NCCN Task Force Report:Estrogen Receptor and Progesterone Receptor Testing in Breast Cancer by Immunohistochemistry. *J Natl Compr Canc Netw* 2009;7 Suppl 6:1-1.
6. Dybdal N, Leiberman G, Anderson S, et al. Determination of HER2 gene amplification by fluorescence in situ hybridization and concordance with the clinical trials immunohistochemical assay in women with metastatic breast cancer evaluated for treatment with trastuzumab. *Breast Cancer Res Treat* 2005;93:3-11.
7. Chuba PJ, Hamre MR, Yap J, et al. Bilateral risk for subsequent breast cancer after lobular carcinoma-in-situ: analysis of surveillance, epidemiology, and end results data. *J Clin Oncol* 2005;23:5534-5541.
8. Anderson BO, Calhoun KE, Rosen EL. Evolving concepts in the management of lobular neoplasia. *J Natl Compr Canc Netw* 2006;4:511-522.
9. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 2005;97:1652-1662.
10. International Commission on Radiation Units and Measurements. ICRU Report No 62: Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50). Bethesda, MD: ICRU Publications 1999.
11. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline, *Practical Radiation Oncology*, 2018; 8:145-152
12. Vargas C, Kestin L, Go N, et al. Factors associated with local recurrence and cause-specific survival in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy or mastectomy. *Int J Radiat Oncol Biol Phys* 2005;63:1514-1521.
13. McCormick B. Randomized Trial Evaluating Radiation following Surgical Excision for “Good Risk” DCIS: 12-Year Report from NRG/RTOG 9804. *Int J Radiat Oncol Biol Phys* 2018;102: P1603
14. NCCN Clinical Practice in Oncology: Breast Cancer V.4.2023

《乳癌抗癌藥物治療指引》

Chemotherapy as Primary or Adjuvant Therapy (HER2-POSTIVE)

Preferred Regimens

★ Trastuzumab may be used in fixed dose 600 mg SC

AC followed by Paclitaxel with Trastuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|----------|---------|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 1 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Trastuzumab * | 4 → 2 mg/kg | 1 | QW | 12 | |
| Paclitaxel | 80 | 1 | QW | 12 | |
| Followed by | | | | | |
| Trastuzumab * | 2 (6) mg/kg | 1 | QW (Q3W) | 40 (13) | |

AC followed by Paclitaxel with Trastuzumab ± Pertuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------------------|----------------------|----------|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 6 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Trastuzumab * | 8 → 6 mg/kg | 1 | Q3W | 17 | |
| Pertuzumab (optional) | 840 → 420 mg | 1 | Q3W | 17 | |
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 4 | |

Dose-dense AC followed by Paclitaxel with Trastuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 | |
|--------------------------|----------------------|------|----------|---------|---------|--|
| Doxorubicin | 60 | 1 | Q2W | 4 | 2 | |
| Cyclophosphamide | 600 | 1 | Q2W | 4 | | |
| Followed by | | | | | | |
| Trastuzumab [*] | 4 → 2 mg/kg | 1, 8 | Q2W | 4 | 44 (14) | |
| Paclitaxel | 175 | 1 | Q2W | 4 | | |
| Followed by | | | | | | |
| Trastuzumab [*] | 2 (6) mg/kg | 1 | QW (Q3W) | 44 (14) | | |

TCH

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 | |
|--------------------------|----------------------|----------|-----|----|------|--|
| Trastuzumab [*] | 4 → 2 mg/kg | 1, 8, 15 | Q3W | 6 | 3 | |
| Docetaxel | 75 | 1 | Q3W | 6 | | |
| Carboplatin | 6 AUC | 1 | Q3W | 6 | 11 | |
| Followed by | | | | | | |
| Trastuzumab [*] | 6 mg/kg | 1 | Q3W | 11 | | |

TCH ± Pertuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------------|----------------------|-----|-----|----|------|
| Trastuzumab [*] | 8 → 6 mg/kg | 1 | Q3W | 17 | 4 |
| Pertuzumab (optional) | 840 → 420 mg | 1 | Q3W | 17 | |
| Docetaxel | 75 | 1 | Q3W | 6 | 6 |
| Carboplatin | AUC 6 | 1 | Q3W | 6 | |

Trastuzumab + Pertuzumab + Neratinib

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------------------------------|----------------------|-----|-----|--------|------|
| Trastuzumab * | 8 → 6 mg/kg | 1 | Q3W | 17 | 7 |
| Pertuzumab (optional) | 840 → 420 mg | 1 | Q3W | 17 | |
| Followed by Neratinib (optional) | 240 mg PO QD | | | 1 year | 8 |

T-DM1

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------|----------------------|-----|-----|----|------|
| T-DM1 | 3.6 mg/kg | 1 | Q3W | 14 | 7 |

Other Regimens**AC followed by Docetaxel with Trastuzumab**

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------------------|----------------------|----------|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 3 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by Trastuzumab * | 4 → 2 mg/kg | 1, 8, 15 | Q3W | 4 | |
| Docetaxel | 80-100 | 1 | Q3W | 4 | |
| Followed by Trastuzumab * | 6 mg/kg | 1 | Q3W | 13 | |

AC followed by Docetaxel with Trastuzumab + Pertuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 3 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Trastuzumab [*] | 8 → 6 mg/kg | 1 | Q3W | 17 | |
| Pertuzumab (optional) | 840 → 420 mg | 1 | Q3W | 17 | |
| Docetaxel | 80-100 | 1 | Q3W | 4 | |

Paclitaxel + Trastuzumab (APT trial)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------------|----------------------|-----|----------|---------|------|
| Trastuzumab [*] | 4 → 2 mg/kg | 1 | QW | 12 | 5 |
| Paclitaxel | 80 | 1 | QW | 12 | |
| Followed by | | | | | |
| Trastuzumab [*] | 2 (6) mg/kg | 1 | QW (Q3W) | 40 (13) | |

TC + Trastuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------------|----------------------|--------------|-----|----|------|
| Trastuzumab [*] | 4 → 2 (8 → 6) mg/kg | 1, 8, 15 (1) | Q3W | 4 | 6 |
| Docetaxel | 75 | 1 | Q3W | 4 | |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Trastuzumab [*] | 6 mg/kg | 1 | Q3W | 13 | |

Paclitaxel + Trastuzumab + Pertuzumab

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------------------|----------------------|----------|-----|----|------|
| Trastuzumab * | 8 → 6 mg/kg | 1 | Q3W | 4 | 11 |
| Pertuzumab (optional) | 840 → 420 mg | 1 | Q3W | 4 | |
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 4 | |

Neratinib (adjuvant setting only)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|-----------------------|-------|-----|-----|------|
| Neratinib | 120 mg PO | 1-7 | Q4W | 1 | 9 |
| | 160 mg PO | 8-14 | | | |
| | Followed by 240 mg PO | 15-28 | | | |
| Neratinib | 240 mg PO | 1-28 | Q4W | 12? | |

T-DM1 (adjuvant setting only)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------|----------------------|-----|-----|----|------|
| T-DM1 | 3.6 mg/kg | 1 | Q3W | 17 | 10 |

參考文獻

1. 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.
2. Dang C, Fomier M, Sugarman S, et al. The safety of dose-dense doxorubicin and cyclophosphamide followed by paclitaxel with trastuzumab in HER2/neu over expressed/amplified breast cancer. J Clin Oncol. 2008;26(8):1216-1222.

3. Slamon D, Eiermann W, Robert N, et al. Adjuvant trastuzumab in HER2-positive breast cancer. *N Engl J Med* 2011;365:1273-1283.
4. 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.
5. 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.
6. Jones SE, Collea R, Paul D, et al. Adjuvant docetaxel and cyclophosphamide plus trastuzumab in patients with HER2-amplified early stage breast cancer: a singlegroup, open-label, phase 2 study. *Lancet Oncol* 2013;14:1121-8.
7. Minckwitz G, Huang C, Mano M, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. *N Engl J Med* 2019;380:617-628.
8. Miguel Martin, Frankie A Holmes, Bent Ejlersen, et al. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2017;18: 1688–700.
9. Chan A, Delalogue 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.
10. Tolaney SM, Tayob N, Dang C, et al. Adjuvant trastuzumab emtansine versus paclitaxel in 8combination with trastuzumab for stage I HER2-positive breast cancer (ATEMPT): A randomized clinical trial. *J Clin Oncol* 2021;39:2375-2385.
11. Nitz UA, Gluz O, Christgen M, et al. De-escalation strategies in HER2-positive early breast cancer (EBC): final analysis of the WSG-ADAPT HER2+/HR- phase II trial: efficacy, safety, and predictive markers for 12 weeks of neoadjuvant dual blockade with trastuzumab and pertuzumab ± weekly paclitaxel. *Ann Oncol* 2017;28:2768-27723.

Chemotherapy as Primary or Adjuvant Therapy (HER2-NEGATIVE)

Preferred Regimens

Dose-dense AC followed by Paclitaxel

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q2W | 4 | 1 |
| Cyclophosphamide | 600 | 1 | Q2W | 4 | |
| Followed by | | | | | |
| Paclitaxel | 175 | 1 | Q2W | 4 | |

Dose-dense AC followed by weekly Paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q2W | 4 | 1 |
| Cyclophosphamide | 600 | 1 | Q2W | 4 | |
| Followed by | | | | | |
| Paclitaxel | 80 | 1 | QW | 12 | |

TC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Docetaxel | 75 | 1 | Q3W | 4 | 2 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|-----|------|
| Capecitabine | 1000-1250 PO BID | 1-14 | Q3W | 6-8 | 18 |

(If triple-negative breast cancer and residual disease after preoperative therapy with taxane, alkylator, and anthracycline based chemotherapy)

For germline BRCA1/2 mutations

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------|----------------------|-----|-----|------------|------|
| Olaparib | 300 mg PO BID | | Q4W | For 1 year | 23 |

For High-risk triple-negative breast cancer (TNBC)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|----------|-----|----|------|
| Pembrolizumab | 200 mg | 1 | Q3W | 4 | 22 |
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 4 | |
| Carboplatin | AUC 5 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Pembrolizumab | 200 mg | 1 | Q3W | 4 | |
| Doxorubicin* | 60* | 1 | Q3W | 4 | |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Pembrolizumab | 200 mg | 1 | Q3W | 9 | |

*may be transferred to Epirubicin 90 mg/m²

Useful in certain circumstances

Dose-dense AC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q2W | 4 | 1 |
| Cyclophosphamide | 600 | 1 | Q2W | 4 | |

AC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 3 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |

TAC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Docetaxel | 75 | 1 | Q3W | 6 | 4 |
| Doxorubicin | 60 | 1 | Q3W | 6 | |
| Cyclophosphamide | 500 | 1 | Q3W | 6 | |

TEC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Docetaxel | 75 | 1 | Q3W | 6 | 14 |
| Epirubicin | 75 | 1 | Q3W | 6 | |
| Cyclophosphamide | 500 | 1 | Q3W | 6 | |

FAC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|--------------|-----|----|------|
| 5-FU | 500 | 1, 8 or 1, 4 | Q3W | 6 | 5, 6 |
| Doxorubicin | 50 | 1 | Q3W | 6 | |
| Cyclophosphamide | 500 | 1 | Q3W | 6 | |

CEF

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|----|------|
| Cyclophosphamide | 500 | 1, 8 | Q3W | 6 | 7 |
| Epirubicin | 80 | 1, 8 | Q3W | 6 | |
| 5-FU | 500 | 1, 8 | Q3W | 6 | |

CMF

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|----|------|
| Cyclophosphamide | 100 PO | 1-14 | Q4W | 6 | 8 |
| Methotrexate | 40 | 1, 8 | Q4W | 6 | |
| 5-FU | 600 | 1, 8 | Q4W | 6 | |

AC followed by Docetaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 9 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| Docetaxel | 80-100 | 1 | Q3W | 4 | |

AC followed by Paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 10 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by Paclitaxel | 175 | 1 | Q3W | 4 | |

AC followed by weekly Paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 4 | 10 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by Paclitaxel | 80 | 1 | QW | 4 | |

EC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Epirubicin | 90-100 | 1 | Q3W | 4 | 11 |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |

FEC followed by Docetaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| 5-FU | 500 | 1 | Q3W | 3 | 12 |
| Epirubicin | 100 | 1 | Q3W | 3 | |
| Cyclophosphamide | 500 | 1 | Q3W | 3 | |
| Followed by | | | | | |
| Docetaxel | 100 | 1 | Q3W | 3 | |

FEC followed by weekly Paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------------|----------------------|-----|-----|----|------|
| 5-FU | 600 | 1 | Q3W | 4 | 13 |
| Epirubicin | 90 | 1 | Q3W | 4 | |
| Cyclophosphamide | 600 | 1 | Q3W | 4 | |
| Followed by | | | | | |
| 3 Weeks no treatment | | | | | |
| Followed by | | | | | |
| Paclitaxel | 100 | 1 | QW | 8 | |

FLC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| 5-FU | 500 | 1 | Q3W | 6 | 17 |
| Lipo-Doxorubicin | 35-40 | 1 | Q3W | 6 | |
| Cyclophosphamide | 500 | 1 | Q3W | 6 | |

Cisplatin + Docetaxel (Triple negative)

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|----|----|--------|
| Cisplatin | 60 | 1 | | | 15, 16 |
| Docetaxel | 60 | 1 | | | |

Carboplatin + Docetaxel (Triple negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|-----|----|--------|
| Cisplatin | AUC 6 | 1 | Q3W | | 19, 20 |
| Docetaxel | 75 | 1 | Q3W | | |

Weekly Paclitaxel + Carboplatin

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|------|
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 4 | 21 |
| Carboplatin | AUC 6 | 1 | Q3W | 4 | |

Weekly Paclitaxel + weekly Carboplatin (Triple negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|--------|
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 6 | 24, 25 |
| Carboplatin | AUC 1.5-2 | 1, 8, 15 | Q3W | 6 | |

Weekly Paclitaxel + weekly Carboplatin (Triple negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|--------|
| Paclitaxel | 80 | 1, 8, 15 | Q3W | 6 | 24, 25 |
| Carboplatin | AUC 1.5-2 | 1, 8, 15 | Q3W | 6 | |

Capecitabine (maintenance therapy for TNBC after adjuvant chemotherapy)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|--------|------|
| Capecitabine | 650 PO BID | 1-28 | Q4W | 1 year | 26 |

★三院有個別版本

參考文獻

1. Citron ML, Berry DA, 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. 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.
3. 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.
4. Martin, Pienkowsky T, Mackey L, et al. Adjuvant docetaxel for node-positive breast cancer. N Engl J Med 2005;352:22.

5. 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.
6. Assikis V, Buzdar A, Yang Y, et al. A Phase III Trial of Sequential Adjuvant Chemotherapy for Operable Breast Carcinoma. Final Analysis with 10-Year Follow-Up. *Cancer* 2003;97:2716-23.
7. Levine MN, Bramwell VH, Pritchard KI, 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.
8. Bonadonna G, Brusamolino E, Valagussa P, et al. Combination chemotherapy as an adjuvant treatment in operable breast cancer. *N Engl J Med.* 1976;294(8):405-410.
9. von Minckwitz G1, Raab G, Caputo A, et al. Doxorubicin with cyclophosphamide followed by docetaxel every 21 days compared with doxorubicin and docetaxel every 14 days as preoperative treatment in operable breast cancer: the GEPARDUO study of the German Breast Group. *J Clin Oncol* 2005;23(12):2676-85.
10. Sparano JA, Wang M, Martino S, et al. Weekly Paclitaxel in the Adjuvant Treatment of Breast Cancer. *N Engl J Med* 2008;258:1663-1671.
11. 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.
12. Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: the FNCLCC PACS 01 Trial. *J Clin Oncol* 2006; 24:5664-5671.
13. 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.
14. Bayo J, Prieto B, Rivera F. Comparison of Doctors' and Breast Cancer Patients' Perceptions of Docetaxel, Epirubicin, and Cyclophosphamide (TEC) Toxicity. *Breast J* 2016; 22: 293–302.
15. Y. Fan, B. H. Xu*, P. Yuan, F. Ma, et al. Docetaxel–cisplatin might be superior to docetaxel–capecitabine in the first-line treatment of metastatic triple-negative breast cancer. *Annals of Oncology* 24: 1219–1225, 2013.
16. Park SH, et al. Docetaxel plus cisplatin is effective for patients with metastatic breast cancer resistant to previous anthracycline

- treatment: a phase II clinical trial. *BMC Cancer*. 2005; 5: 21.
17. Rau KM, Lin YC, Chen YY, et al. Pegylated liposomal doxorubicin (Lipo-Dox®) combined with cyclophosphamide and 5-fluorouracil is effective and safe as salvage chemotherapy in taxane-treated metastatic breast cancer: an open-label, multi-center, non-comparative phase II study. *BMC Cancer*. 2015; 15: 423.
 18. Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 2017;376:2147-2159.
 19. Sharma P, López-Tarruella S, García-Saenz JA, et al. Pathological Response and Survival in Triple-Negative Breast Cancer Following Neoadjuvant Carboplatin plus Docetaxel. *Clin Cancer Res* December 1 2018 (24) (23) 5820-5829.
 20. Perez EA, Suman VJ, Fitch TR, et al. A Phase II Trial of Docetaxel and Carboplatin as First-Line Chemotherapy for Metastatic Breast Cancer: NCCTG Study N9932. *Oncology* 2005;69:117–121.
 21. Loibl S, O'Shaughnessy J, 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: 497–509.
 22. Schmid P, Cortes J, Puztai L, et al. Pembrolizumab for early triple-negative breast cancer. *N Engl J Med*, 2020;382(9):810-821.
 23. Tutt ANJ, Garber JE, Kaufman B, et al. Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. *N Engl J Med*. 2021 Jun 3.
 24. 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.
 25. 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.
 26. Wang X, Wang SS, Huang H, et al. Effect of Capecitabine Maintenance Therapy Using Lower Dosage and Higher Frequency vs Observation on Disease-Free Survival Among Patients With Early-Stage Triple-Negative Breast Cancer Who Had Received Standard Treatment: The SYSUCC-001 Randomized Clinical Trial. *JAMA*. 2021;325(1):50-58.

Adjuvant Endocrine Therapy

Anti-estrogen

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|----|----|------|
| Tamoxifen | 20-40 mg PO QD | | | | 1 |

Aromatase inhibitor

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|----|----|------|
| Exemestane | 25 mg PO QD | | | | 2 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Anastrozole | 1 mg PO QD | | | | 3 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|----|----|------|
| Letrozole | 2.5 mg PO QD | | | | 4 |

Ovarian suppression or ablation

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------------|----------------------|-----|-----|----|------|
| Goserelin Acetate | 3.6 mg SC | 1 | Q4W | | 5 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------|----------------------|-----|-----|----|------|
| Leuprolide Acetate | 3.75 mg SC | 1 | Q4W | | 6 |

參考文獻

1. Product Information: tamoxifen citrate oral tablets, tamoxifen citrate oral tablets. Watson Laboratories (per manufacturer), Corona, CA, 2011.
2. Product Information: AROMASIN(R) oral tablets, exemestane oral tablets. Pharmacia & Upjohn Company (per FDA), New York, NY, 2013.
3. Product Information: ARIMIDEX(R) oral tablet, anastrozole oral tablet. AstraZeneca Pharmaceuticals LP, Wilmington, DE, 2009.
4. Product Information: Femara oral tablets, letrozole oral tablets. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 2010.
5. Product Information: ZOLADEX(R) implant 3.6mg, goserelin acetate implant implant 3.6mg. AstraZeneca, Wilmington, DE, 2009.
6. Boccardo F, Rubagotti A, Amoroso D, et al: Endocrinological and clinical evaluation of two depot formulations of leuprolide acetate in pre- and perimenopausal breast cancer patients. Cancer Chemother Pharmacol 1999; 43:461-466

Chemotherapy for Recurrent or Metastatic Breast Cancer

HER2-NEGATIVE

Preferred Single Agents

Anthacyclins

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60-75 | 1 | Q3W | 7 | 1 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Doxorubicin | 20 | 1 | QW | | 2 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Lipo-Doxorubicin | 50 | 1 | Q4W | | 3 |

Taxanes

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|-----|----|------|
| Paclitaxel | 175 | 1 | Q3W | | 4 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|----|----|------|
| Paclitaxel | 80 | 1 | QW | | 5 |

Antimetabolites

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|----|------|
| Capecitabine | 1000-1250 PO BID | 1-14 | Q3W | 6 | 6 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|------|
| Gemcitabine | 800-1200 | 1, 8, 15 | Q4W | | 7 |

Other microtubule inhibitors

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Vinorelbine | 25 | 1 | QW | | 8 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------|----------------------|------|-----|----|------|
| Eribulin | 1.4 | 1, 8 | Q3W | | 9 |

PARP inhibitors

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------|----------------------|-----|----|----|------|
| Olaparib | 300 mg PO BID | | | | 46 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|-----|----|------|
| Talazoparib | 1 mg PO QD | | Q4W | | 47 |

Atezolizumab + albumin-bound paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------|----------------------|----------|-----|----|------|
| Atezolizumab | 840 mg | 1, 15 | Q4W | | 48 |
| Nab-Paclitaxel | 100 | 1, 8, 15 | Q4W | | |

(An option for patients with PD-L1-positive TNBC)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|-----|----|------|
| Pembrolizumab | 200 mg | 1 | Q3W | | 55 |

TNBC, CPS ≥ 10

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|---------|----|------|
| Carboplatin | AUC 6 | 1 | Q3W-Q4W | | 11 |

(An option for patients with triple-negative tumors and germline BRCA1/2 mutation)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|-----|----|------|
| Cisplatin | 75 | 1 | Q3W | 4 | 17 |

(An option for patients with triple-negative tumors and germline BRCA1/2 mutation)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------------------------------|----------------------|-----|-----|----|------|
| Fam-trastuzumab deruxtecan-nxk | 5.4 mg/kg | 1 | Q3W | | 61 |

(For HER2 IHC 1+ or 2+/ISH negative)

Other Single Agents

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|----|------|
| Cyclophosphamide | 50 PO QD | 1-21 | Q4W | | 10 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|-----|----|--------|
| Docetaxel | 60-100 | 1 | Q3W | 6 | 12, 13 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|----------------------|-----|----|------|
| Docetaxel | 35 | 1, 8, 15, 22, 29, 36 | Q8W | | 14 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------|----------------------|----------|-----|----|--------|
| Nab-Paclitaxel | 100 or 150 | 1, 8, 15 | Q4W | | 15, 16 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------|----------------------|-----|-----|----|------|
| Nab-Paclitaxel | 260 | 1 | Q3W | | 15 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|-----|----|------|
| Epirubicin | 75 | 1 | Q3W | | 18 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------------------|----------------------|------|-----|----|------|
| Sacituzumab govitecan-hziy | 10 | 1, 8 | Q3W | | 61 |

 For TNBC (HER2 negative 2nd line)

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|----|----|------|
| Larotrectinib | 100 mg BID PO | | | | 56 |

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|-------------|
| Entrectinib | 600 mg QD PO | | | | 57 |
| | | | | | NTRK fusion |

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|-----|----|-------------------------------------|
| Pembrolizumab | 200 mg | 1 | Q3W | | 58, 59 |
| | | | | | MSI-H/dMMR and TMB-H (≥ 10 muts/mb) |

Combinations

Carboplatin + Docetaxel (triple negative)

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|-----|----|--------|
| Carboplatin | AUC 6 | 1 | Q3W | 6 | 49, 50 |
| Docetaxel | 75 | 1 | Q3W | 6 | |

Paclitaxel+Carboplatin (Triple negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|-----|----|------|
| Paclitaxel | 175-200 | 1 | Q3W | | 51 |
| Carboplatin | AUC 6 | 1 | Q3W | | |

Paclitaxel+Carboplatin (weekly)(Triple negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|------|
| Paclitaxel | 100 | 1, 8, 15 | Q3W | | 52 |
| Carboplatin | AUC 2 | 1, 8, 15 | Q3W | | |

Albumin-bound Paclitaxel + Carboplatin (weekly) (Triple negative, preoperative setting)

| 藥品名 * | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|----------------|----------------------|------|-----|----|------|
| Nab-Paclitaxel | 125 | 1, 8 | Q3W | | 53 |
| Carboplatin | AUC 2 | 1, 8 | Q3W | | |

CAF

| 藥品名 * | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|----|------|
| Cyclophosphamide | 100 PO | 1-14 | Q4W | | 19 |
| Doxorubicin | 30 | 1, 8 | Q4W | | |
| 5-FU | 500 | 1, 8 | Q4W | | |

FAC

| 藥品名 * | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|--------------|-----|----|------|
| 5-FU | 500 | 1, 8 or 1, 4 | Q3W | | 20 |
| Doxorubicin | 50 | 1 | Q3W | | |
| Cyclophosphamide | 500 | 1 | Q3W | | |

FEC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|-----|------|
| Cyclophosphamide | 400 | 1, 8 | Q4W | 6-9 | 21 |
| Epirubicin | 50 | 1, 8 | Q4W | | |
| 5-FU | 500 | 1, 8 | Q4W | | |

AC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Doxorubicin | 60 | 1 | Q3W | 8 | 22 |
| Cyclophosphamide | 600 | 1 | Q3W | 8 | |

EC

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|-----|-----|----|------|
| Epirubicin | 75 | 1 | Q3W | 6 | 23 |
| Cyclophosphamide | 600 | 1 | Q3W | 6 | |

CMF

| 藥品名 * | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------------|----------------------|------|-----|----|--------|
| Cyclophosphamide | 100 PO QD | 1-14 | Q4W | | 24, 45 |
| Methotrexate | 40 | 1, 8 | Q4W | | |
| 5-FU | 600 | 1, 8 | Q4W | | |

Docetaxel + Capecitabine

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|----|------|
| Docetaxel | 75 | 1 | Q3W | 6 | 25 |
| Capecitabine | 950 PO BID | 1-14 | Q3W | 6 | |

GT

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Paclitaxel | 175 | 1 | Q3W | | 26 |
| Gemcitabine | 1250 | 1, 8 | Q3W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|------|
| Paclitaxel | 80 | 1, 8, 15 | Q4W | | 44 |
| Gemcitabine | 800 | 1, 8, 15 | Q4W | | |

Gemcitabine + Carboplatin

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Gemcitabine | 1250 | 1, 8 | Q3W | | 27 |
| Carboplatin | AUC 2 | 1, 8 | Q3W | | |

Bevacizumab + Paclitaxel

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|----------|-----|----|------|
| Bevacizumab | 10 mg/kg | 1, 8 | Q4W | | 28 |
| Paclitaxel | 90 | 1, 8, 15 | Q4W | | |

HER2-POSITIVE

Preferred Agents

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|-----|----|------|
| Pertuzumab | 840 → 420 mg | 1 | Q3W | | 29 |
| Trastuzumab * | 8 → 6 mg/kg | 1 | Q3W | | |
| Docetaxel | 75-100 | 1 | Q3W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|----------|----|--------|
| Pertuzumab | 840 → 420 mg | 1 | Q3W | | 30, 31 |
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | |
| Paclitaxel | 175 (80) | 1 | Q3W (QW) | | |

Other Agents

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|----------|----|--------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 32 |
| Paclitaxel | 175 | 1 | Q3W | | |
| Carboplatin | AUC 6 | 1 | Q3W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|----------|----|------------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 33, 34 |
| Paclitaxel | 175 (80-90) | 1 | Q3W (QW) | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|--------------|----------|----|------------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 35, 36 |
| Docetaxel | 80-100 (35) | 1, 8, 15 (1) | Q3W (QW) | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|----------|----------|----|--------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 37 |
| Vinorelbine | 30-35 (25) | 1, 8 (1) | Q3W (QW) | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|------|----------|----|----------------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 33, 38, 39 |
| Capecitabine | 1000-1250 | 1-14 | Q3W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------|----------------------|-----|-----|----|------|
| T-DM1 | 3.6 mg/kg | 1 | Q3W | | 40 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|----|------|
| Lapatinib | 1250 mg PO QD | 1-21 | Q3W | | 41 |
| Capecitabine | 1000 PO BID | 1-14 | Q3W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|---------------|----------------------|-----|----------|----|--------|
| Trastuzumab * | 8 → 6 (4 → 2) mg/kg | 1 | Q3W (QW) | | 31, 43 |
| Lapatinib | 1000 mg PO QD | | Q3W | | |

| 藥品名* | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------|----------------------|------|-----|----|------|
| Neratinib | 240 mg PO QD | 1-21 | Q3W | | 54 |
| Capecitabine | 750 PO BID | 1-14 | Q3W | | |

*三院有個別版本

參考文獻

1. Chan S, Friendrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. *J Clin Oncol*. 1999 Aug;17(8):2341-54.
2. Gasparini G, Dai 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 Feb;14(1):38-44.
3. O'Brien ME, Wigler N, Inbar M, et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCl (CAELYX/Doxil) versus conventional doxorubicin for first-line treatment of metastatic breast cancer. *Ann Oncol*. 2004 Mar;15(3):440-9.
4. 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 Oncol* 1995;13:2575-2581.
5. Perez EA, Vogel CL, Irwin DH, et al. Multicenter Phase II Trial of Weekly Paclitaxel in Women With Metastatic Breast Cancer. *J Clin Oncol* 2001;19:4216-4223.
6. Safety and Efficacy of Two Different Doses of Capecitabine in the Treatment of Advanced Breast Cancer in Older Women. *J Clin Oncol* 2005;23:2155-2161.
7. Seidman AD, Gemcitabine as Single-Agent Therapy in the Management of Advanced Breast Cancer. *Oncology (Williston Park)*2001;15:11-14.
8. 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 Nov 1;92(9):2267-72.
9. Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. *Lancet* 2011;377:914-923.
10. Licchetta A, Correale P, Migali C, et al. Oral Metronomic Chemo-Hormonal-Therapy of Metastatic Breast Cancer with

- Cyclophosphamide and Megestrol Acetate. *J Chemother* 2010;22(3):201-4.
11. Isakoff, SJ, Goss PE, et al. (2011). TBCRC009: A multicenter phase II study of cisplatin or carboplatin for metastatic triple-negative breast cancer and evaluation of p63/p73 as a biomarker of response[abstract]. *J Clin Oncol* 29(15_suppl):Abstract 1025.
 12. Burris HA, 3rd. Single-agent docetaxel(Taxotere) in randomized phase III trials, *Semin Oncol* 1999;26:1-6.
 13. Harvey V, Mouridsen H, Semiglazov V, et al. Phase III Trial Comparing Three Doses of Docetaxel for Second-Line Treatment of Advanced Breast Cancer. *J Clin Oncol* 2006;24(31):4963-70.
 14. Rivera E, Mejjia JA, Arun BJ, et al. Phase 3 study comparing the use of docetaxel on an every-3-week versus weekly schedule in the treatment of metastatic breast cancer. *Cancer* 2008 Apr 1;112(7):1455-61.
 15. Gradishar WJ, Tjulandin S, Davidson N, et al. Phase III Trial of Nanoparticle Albumin-Bound Paclitaxel Compared With Polyethylated Castor Oil-Based Paclitaxel in Women With Breast Cancer. *J Clin Oncol* 2005;23:7794-7803.
 16. Gradishar W, Dimitry K, Sergey C, et al. Significantly Longer Progression-Free Survival With nab-Paclitaxel Compared With Docetaxel As First-Line Therapy for Metastatic Breast Cancer. *J Clin Oncol* 2009;27(22):3611-9.
 17. Silver DP, Richardson AL, Eklund AC, et al. Efficacy of Neoadjuvant Cisplatin in Triple-Negative Breast Cancer. *J Clin Oncol* 2010;28(7):1145-53.
 18. Bastholt L, Dalmark M, Gjedde SB, 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;14:1146-1155.
 19. Bull JM, Tormey DC, Li SH, et al. A randomized comparative trial of adriamycin versus methotrexate in combination drug therapy. *Cancer* 1978;41:1649-1657.
 20. Hortobagyi GN, Gutterman JU, Blumenschein GR, et al. Combination chemoimmunotherapy of metastatic breast cancer with 5-FU, fluorouracil, adriamycin, cyclophosphamide, and BCG. *Cancer* 1979;43:1225-33.
 21. Ackland SP, Anton A, Breitbach GP, et al. Dose-Intensive Epirubicin-Based Chemotherapy Is Superior to an Intensive Intravenous Cyclophosphamide, Methotrexate, and Fluorouracil Regimen in Metastatic Breast Cancer: A Randomized Multinational Study. *J Clin Oncol* 2001;19:943-953.

22. Nabholz JM, Falkson C, Campos D, et al. Docetaxel and Doxorubicin Compared With Doxorubicin and Cyclophosphamide as First-Line Chemotherapy for Metastatic Breast Cancer: Results of a Randomized, Multicenter, Phase III Trial. *J Clin Oncol* 2003;21(6):968-75.
23. Langley RE, Camichel J, Jones AL, et al. Phase III Trial of Epirubicin Plus Paclitaxel Compared With Epirubicin Plus Cyclophosphamide As First-Line Chemotherapy for Metastatic Breast Cancer: United Kingdom National Cancer Research Institute. *J Clin Oncol* 2005;23:8322-8330.
24. Bonadonna G, Brusamolino E, Valagussa P, et al. Combination Chemotherapy as an Adjuvant Treatment in Operable Breast Cancer. *N Engl Med* 1976;294:405-410.
25. 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).
26. Albani KS, Nag S, Calderillo-Ruiz G, et al. Gemcitabine Plus Paclitaxel Versus Paclitaxel Monotherapy in Patients With Metastatic Breast Cancer and Prior Anthracycline Treatment. *J Clin Oncol* 2008;26(24):3950-7.
27. O'Shaughnessy J, Schwartzberg LS, Danso MA, et al. A randomized phase III study of iniparib (BSI-201) in combination with gemcitabine/carboplatin (G/C) in metastatic triple-negative breast cancer (TNBC). [abstract]. *J Clin Oncol* 2011;29(Suppl_15):Abstract 1007.
28. Miller K, Wang M, Gralow J, et al. Paclitaxel plus Bevacizumab versus Paclitaxel Alone for Metastatic Breast Cancer. *N Engl J Med* 2007;357:2666-2676.
29. 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.
30. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with HER2-overexpressing metastatic breast cancer [abstract]. *Cancer Research* 2012;72:Abstract P5-18-20.
31. Leyland-Jones B, Gelmon K, Ayoub JP, et al. Pharmacokinetics, Safety, and Efficacy of Trastuzumab Administered Every Three Weeks in Combination With Paclitaxel. *J Clin Oncol* 2003;21:3965-3971.
32. Perez EA, Suman VJ, Rowland KM, et al. Two Concurrent Phase II Trials of Paclitaxel/Carboplatin/Trastuzumab (Weekly or Every-3-Week Schedule) as First-Line Therapy in Women with HER2-Overexpressing Metastatic Breast Cancer: NCCTG Study 983252. *Clin Breast Cancer* 2005;6:425-432.

33. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of Chemotherapy plus a Monoclonal Antibody against HER2 for Metastatic Breast Cancer That Overexpresses HER2. *N Engl J Med* 2001;344:783-792.
34. Seidman A, Berry DA, Cirincione C, 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;26:1642-1649.
35. Marty M, Cognetti F, Maraninchi D, et al. Randomized Phase II Trial of the Efficacy and Safety of Trastuzumab Combined With Docetaxel in Patients With Human Epidermal Growth Factor Receptor 2–Positive Metastatic Breast Cancer Administered As First-Line Treatment: The M77001 Study Group. *J Clin Oncol* 2005;23:4265-4274.
36. Esteva FJ, Valero V, Booser D, et al. Phase II Study of Weekly Docetaxel and Trastuzumab for Patients With HER-2–Overexpressing Metastatic Breast Cancer. *J Clin Oncol* 2002;20:1800-1808.
37. Burstein HJ, Keshaviah A, Baron AD, et al. Trastuzumab plus vinorelbine or taxane chemotherapy for HER2-overexpressing metastatic breast cancer: The trastuzumab and vinorelbine or taxane study. *Cancer* 2007;110:965-972.
38. von Minckwitz G, du Bois A, Schmidt M, et al. Trastuzumab Beyond Progression in Human Epidermal Growth Factor Receptor 2–Positive Advanced Breast Cancer: A German Breast Group 26/Breast International Group 03-05 Study. *J Clin Oncol* 2009;27:1999-2006.
39. Cobleigh MA, Vogel CL, Tripathy D, 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;17:2639-2648.
40. 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.
41. 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.
42. Bartsch R, Wenzel C, Altorjai G, et al. Capecitabine and Trastuzumab in Heavily Pretreated Metastatic Breast Cancer. *J Clin Oncol* 2007;25:3853-3858.

43. Blackwell KL, Burstein H, et al. Randomized Study of Lapatinib Alone or in Combination With Trastuzumab in Women With ErbB2-Positive, Trastuzumab-Refractory Metastatic Breast Cancer. *J Clin Oncol* 2010;28(7):1124-30.
44. Kun-Ming Rau, Shan-Hsuan Li, 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.
45. Jin Hyun Park, Seock-Ah Im, et al. Cyclophosphamide, Methotrexate, and 5-Fluorouracil as Palliative Treatment for Heavily Pretreated Patients with Metastatic Breast Cancer: A Multicenter Retrospective Analysis. *J Breast Cancer*. 2017 Dec; 20(4): 347-355.
46. Mark Robson, Seock-Ah Im, Elzbieta Senkus, et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. *N Engl J Med* 2017; 377:523-533.
47. Litton J, Rugo H, Ettl J, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med* 2018;379:753-63.
48. Schmid P, Adams S, Rugo HS, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. [supplementary appendix appears online]. *N Engl J Med*. 2018 Nov 29;379:2108-2121.
49. Pathological Response and Survival in Triple-Negative Breast Cancer Following Neoadjuvant Carboplatin plus Docetaxel. *Clin Cancer Res* December 1 2018 (24) (23) 5820-5829.
50. A Phase II Trial of Docetaxel and Carboplatin as First-Line Chemotherapy for Metastatic Breast Cancer: NCCTG Study N9932. *Oncology* 2005;69:117-121.
51. Perez EA, Hillman DW, Stella PJ, et al. A phase II study of paclitaxel plus carboplatin as first-line chemotherapy for women with metastatic breast carcinoma. *Cancer* 2000;88(1):124-131.
52. Loesch D, Robert N, Asmar L, et al. Phase II multicenter trial of a weekly paclitaxel and carboplatin regimen in patients with advanced breast cancer. *J Clin Oncol* 2002;20(18):3857-3864.
53. Yardley DA, Coleman R, Conte P, et al. nab-Paclitaxel plus carboplatin or gemcitabine versus gemcitabine plus carboplatin as first-line treatment of patients with triple-negative metastatic breast cancer: results from the tnAcity trial. *Ann Oncol* 2018;29(8):1763-1770.
54. Saura C, Oliveira M, Feng YH, et al. Neratinib plus capecitabine versus lapatinib plus capecitabine 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; abstr 1002).
55. Cortes J, Cescon DW, Rugo HS, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial. *Lancet*. 2020 Dec 5;396(10265):1817-1828.
 56. Drilon A, Laetsch TW, Kummar W, et al. Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. *N Engl J Med* 2018;378(8):731-739.
 57. Drilon A, Siena S, Ou SI, et al. Safety and antitumor activity of the multitargeted pan-TRK, ROS1, and ALK inhibitor entrectinib: Combined results from two phase I trials (ALKA-372-001 and STARTRK-1). *Cancer Discov* 2017;7(4):400-409.
 58. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 2017;357(6349):409-413.
 59. Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab:prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. *Lancet Oncol*. 2020;21(10):1353-1365.
 60. 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.
 61. Bardia A, Mayer IA, Vahdat LT, et al. Sacituzumab govitecan-hziy in refractory metastatic triple negative breast cancer. *N Engl J Med*. 2019;380:741-751.

Endocrine Therapy Regimens for Recurrent or Metastatic Breast Cancer

Premenopausal

SERM

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|----|----|------|
| Tamoxifen | 20-40 mg PO QD | | | | 1 |

Ovarian ablation or suppression

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------------|----------------------|-----|-----|----|------|
| Goserelin Acetate | 3.6 mg SC | | Q4W | | 5 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|--------------------|----------------------|-----|-----|----|------|
| Leuprolide Acetate | 3.75 mg SC | | Q4W | | 6 |

Postmenopausal

Aromatase inhibitor

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|----|----|------|
| Exemestane | 25 mg PO QD | | | | 2 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Anastrozole | 1 mg PO QD | | | | 3 |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-----------|----------------------|-----|----|----|------|
| Letrozole | 2.5 mg PO QD | | | | 4 |

SERD

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|-----|----|------|
| Fulvestrant | 500 IM | | Q4W | | 7 |

CDK4/6 inhibitor+AI (for Her2-negative)

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Palbociclib | 125 mg PO QD | 1-21 | Q4W | | 8 |
| Letrozole | 2.5 mg PO QD | 1-21 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Palbociclib | 125 mg PO QD | 1-21 | Q4W | | 8 |
| Anastrozole | 1 mg PO QD | 1-21 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Palbociclib | 125 mg PO QD | 1-21 | Q4W | | 8 |
| Exemestane | 25 mg PO QD | 1-21 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|------|-----|----|------|
| Ribociclib | 600 mg PO QD | 1-21 | Q4W | | 9 |
| Letrozole | 2.5 mg PO QD | 1-21 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|------|-----|----|------|
| Ribociclib | 600 mg PO QD | 1-21 | Q4W | | 9 |
| Anastrozole | 1 mg PO QD | 1-21 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|------|-----|----|------|
| Ribociclib | 600 mg PO QD | 1-21 | Q4W | | 9 |
| Exemestane | 25 mg PO QD | 1-28 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Abemaciclib | 150 mg PO BID | | | | 15 |
| Letrozole | 2.5 mg PO QD | | | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Abemaciclib | 150 mg PO BID | | | | 15 |
| Anastrozole | 1 mg PO QD | | | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Abemaciclib | 150 mg PO BID | | | | 15 |
| Exemestane | 25 mg PO QD | | | | |

CDK4/6 inhibitor + SERD

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----------|-----|----|------|
| Palbociclib | 125 mg PO QD | 1-21 | Q4W | | 10 |
| Fulvestrant | 500 IM | 1, 15 → 1 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----------|-----|----|------|
| Palbociclib | 600 mg PO QD | 1-21 | Q4W | | 11 |
| Fulvestrant | 500 IM | 1, 15 → 1 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----------|-----|----|------|
| Abemaciclib | 150 mg PO BID | | | | 16 |
| Fulvestrant | 500 IM | 1, 15 → 1 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|----|----|------|
| Everolimus | 10 mg PO QD | | | | 12 |
| Exemestane | 25 mg PO QD | | | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----------|-----|----|------|
| Everolimus | 10 mg PO QD | | Q4W | | 13 |
| Fulvestrant | 500 IM | 1, 15 → 1 | Q4W | | |

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|------------|----------------------|-----|----|----|------|
| Everolimus | 10 mg PO QD | | | | 14 |
| Tamoxifen | 20-40 mg PO QD | | | | |

Fulvestrant + Alpelisib for PIK3CA-mutated tumors

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----------|-----|----|------|
| Alpelisib | 300 mg PO QD | | | | 17 |
| Fulvestrant | 500 IM | 1, 15 → 1 | Q4W | | |

Useful in certain circumstances**Abemaciclib**

| 藥品名 | 劑量 mg/m ² | 給藥日 | 頻率 | 週期 | 參考文獻 |
|-------------|----------------------|-----|----|----|------|
| Abemaciclib | 200 mg PO BID | | | | 18 |

參考文獻

1. Product Information: tamoxifen citrate oral tablets, tamoxifen citrate oral tablets. Watson Laboratories (per manufacturer), Corona, CA, 2011.
2. Product Information: AROMASIN(R) oral tablets, exemestane oral tablets. Pharmacia & Upjohn Company (per FDA), New York, NY, 2013.
3. Product Information: ARIMIDEX(R) oral tablet, anastrozole oral tablet. AstraZeneca Pharmaceuticals LP, Wilmington, DE, 2009.
4. Product Information: Femara oral tablets, letrozole oral tablets. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 2010.
5. Product Information: ZOLADEX(R) implant 3.6mg, goserelin acetate implant implant 3.6mg. AstraZeneca, Wilmington, DE, 2009.
6. Boccardo F, Rubagotti A, Amoroso D, et al: Endocrinological and clinical evaluation of two depot formulations of leuprolide acetate in pre- and perimenopausal breast cancer patients. Cancer Chemother Pharmacol 1999; 43:461-466.

7. Rita S. Mehta, M.D., William E. Barlow, Ph.D., et al. Combination Anastrozole and Fulvestrant in Metastatic Breast Cancer.
8. Turner NC, Ro J, Andre F, et al. Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. *N Engl J Med* 2015;373:209-219.
9. Gabor N. Hortobagyi, M.D., Salomon M. Stemmer, M.D., et al. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. *N Engl J Med* 375;18 November 3, 2016
10. Massimo Cristofanilli, Nicholas C Turner, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. *Lancet Oncol* 2016; 17: 425–39.
11. Dennis J. Slamon, Patrick Neven, et al. Phase III Randomized Study of Ribociclib and Fulvestrant in Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Advanced Breast Cancer: MONALEESA-3. *J Clin Oncol* 36:2465-2472.
12. José Baselga, M.D., Ph.D., Mario Campone, M.D., et al. Everolimus in Postmenopausal Hormone Receptor–Positive Advanced Breast Cancer. *N Engl J Med* 366;6 nejm.org february 9, 2012.
13. Noah Kornblum, Fengmin Zhao, et al. Randomized Phase II Trial of Fulvestrant Plus Everolimus or Placebo in Postmenopausal Women With Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer Resistant to Aromatase Inhibitor Therapy: Results of PrE0102. *J Clin Oncol* 36:1556-1563.
14. Thomas Bachelot, Céline Bourcier, et al. Randomized Phase II Trial of Everolimus in Combination With Tamoxifen in Patients With Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer With Prior Exposure to Aromatase Inhibitors: A GINECO Study. *J Clin Oncol* 30:2718-2724.
15. Goetz MP, Toi M, et al. MONARCH 3: Abemaciclib As Initial Therapy for Advanced Breast Cancer. *J Clin Oncol*. 2017;35(32):3638-3646.

16. Sledge GW Jr, Toi M, et al. The Effect of Abemaciclib Plus Fulvestrant on Overall Survival in Hormone Receptor–Positive, ERBB2-Negative Breast Cancer That Progressed on Endocrine Therapy—MONARCH 2. *AMA Oncol.* 2020;6(1):116-124.
17. André F, Ciruelos E, et al. Alpelisib for PIK3CA-Mutated, Hormone Receptor–Positive Advanced Breast Cancer. *N Engl J Med* 2019; 380:1929-1940.
18. Dickler MN, Tolaney SM, et al. MONARCH 1, a phase 2 study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2– metastatic breast cancer. *Clin Cancer Res.* 2017; 23(17): 5218–5224.

一、全乳放射治療

應以電腦斷層影像定義標靶體積與正常危急器官

適應症：侵襲癌或原位癌經乳房保留手術術後

◎照射範圍：患側乳房

◎照射劑量：50-50.4Gy / GyE 次數：25-28 次 或 40-42.5Gy / GyE 次數：15-16 次

◎追加照射範圍：腫瘤切除空腔與其周圍

◎追加照射劑量：10-16Gy / GyE 次數：4-8 次

治療技術：使用斜角對照配合強度調控放射治療技術，包含弧形及螺旋放射規劃，可考慮搭配影像導引治療，與心肺保護技術。可選擇先後給予胸壁照射與追加照射，或是在放療計畫中同步規劃高低劑量區，同步進行兩部位照射。質子治療屬放射治療新興技術，其處方劑量、分次與危急器官之劑量限制須考慮質子射束相對生物效應的格雷當量。

二、胸壁放射治療

應以電腦斷層影像定義標靶體積與正常危急器官

適應症：侵襲癌經乳房全切除手術術後有較大的原發腫瘤 (T stage \geq T3)，臨床或病理認定腫瘤侵犯淋巴結 (N stage \geq N1)，腫瘤細胞存在於外科邊緣或距離邊緣 $< 1\text{mm}$

◎照射範圍：患側胸壁、手術疤痕與其周圍

◎照射劑量：50-50.4Gy / GyE 次數：25-28 次 (或若未進行乳房重建時可考慮 40-42.5 Gy/GyE 次數：15-16 次)

◎追加照射範圍：手術疤痕周圍

◎追加照射劑量：10-16Gy / 次數：4-8 次

治療技術：使用斜角對照配合強度調控放射治療技術，包含弧形及螺旋放射規劃，以及質子治療，可考慮搭配影像導引治療，與心肺保護技術。可選擇先後給予胸壁照射與追加照射，或是在放療計畫中同步規劃高低劑量區，

同步進行兩部位照射。質子治療屬放射治療新興技術，其處方劑量、分次與危急器官之劑量限制須考慮質子射束相對生物效應的格雷當量。

三、淋巴引流區放射治療

應以電腦斷層影像定義標靶體積與正常危急器官

適應症：較大的原發腫瘤 (T stage \geq T3)、臨床或病理認定腫瘤侵犯至少一個淋巴結 (N stage \geq N1)

◎照射範圍：患側高風險淋巴轉移範圍，包括腋下、鎖骨下、鎖骨上淋巴引流區。臨床懷疑內乳淋巴結轉移或正常組織容受許可時，可選擇性考慮照射內乳淋巴引流區。

◎照射劑量：50-50.4Gy / GyE 次數：25-28 次 追加照射劑量 (或若未進行乳房重建時可考慮 40-42.5 Gy/GyE 次數：15-16 次)

◎追加照射範圍：未能手術之侵犯或腫大淋巴腺

◎追加照射劑量：10-16Gy / 次數：4-8 次

治療技術：使用強度調控放射治療技術，選擇性使用斜角對照，包含弧形及螺旋放射規劃，可考慮搭配影像導引治療，與心肺保護技術。

《參考文獻》

1. NCCN Clinical Practice in Oncology: Breast Cancer V.4.2023
2. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010;60:277-300.
3. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687-1717.
4. Edge SB, Byrd DR, Compton CC, et al., eds. AJCC Cancer Staging Manual, 7th Edition. New York: Springer; 2010
5. Allred DC, Carlson RW, Berry DA, et al. NCCN Task Force Report: Estrogen Receptor and Progesterone Receptor Testing in Breast Cancer by Immunohistochemistry. J Natl Compr Canc Netw 2009;7 Suppl 6:1-1.
6. Dybdal N, Leiberman G, Anderson S, et al. Determination of HER2 gene amplification by fluorescence in situ hybridization and concordance with the clinical trials immunohistochemical assay in women with metastatic breast cancer evaluated for treatment with trastuzumab. Breast Cancer Res Treat 2005;93:3-11.

7. Chuba PJ, Hamre MR, Yap J, et al. Bilateral risk for subsequent breast cancer after lobular carcinoma-in-situ: analysis of surveillance, epidemiology, and end results data. *J Clin Oncol* 2005;23:5534-5541.
8. Anderson BO, Calhoun KE, Rosen EL. Evolving concepts in the management of lobular neoplasia. *J Natl Compr Canc Netw* 2006;4:511-522.
9. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 2005;97:1652-1662.
10. International Commission on Radiation Units and Measurements. ICRU Report No 62: Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50). Bethesda, MD: ICRU Publications 1999.
11. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline, *Practical Radiation Oncology*, 2018; 8:145-152
12. Vargas C, Kestin L, Go N, et al. Factors associated with local recurrence and cause-specific survival in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy or mastectomy. *Int J Radiat Oncol Biol Phys* 2005;63:1514-1521.
13. McCormick B. Randomized Trial Evaluating Radiation following Surgical Excision for “Good Risk” DCIS: 12-Year Report from NRG/RTOG 9804. *Int J Radiat Oncol Biol Phys* 2018;102: P1603