# Adjuvant chemotherapy in HIGH-RISK EBC 台北榮總趙大中醫師講課

## & which pt (早期乳癌之輔助化學治療)

## which regime (高危險族群選擇處方)

Bonadonna BMJ 2005

(1)乳癌腋下淋巴轉移不作治療，七成復發或轉移

N(+) ↓ 不作 Tx 7 成有事

N(-) 不作 TX 5 成全有事

什麼 pt 作 chemotherpy

LN(+)，premenopause→C/T

(2)乳癌没腋下淋巴結轉移不作治療，五成會復發轉移

(3)什麼情形乳癌一定要作化學治療

a.乳房腋下淋巴結轉移

b.停經期前

c.三陰性乳癌(除非 Tia≤1.0 公分以下，都要考慮

d.her2/neu 有表現的

Tri (-) 除了 T1a

Her2(+)

PT1b1c node(-) → Her2(+) APT trial

ER(+)，LN(+)，ER(-) LN(+) → 用 anthracycline

榮總 FEC → T ⟹ 改成刪~~F~~ EC→ T

⟹ TC x 6 考慮 75/600

(4)her2/neu (+)選擇的化學治療處方

腫瘤≤ 1.0 公分、≤2 公分没有淋巴結轉移，考慮使用依照 NEJM 2015 年 APT Triad (Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer, Tolaney SM,)

(5)

a.如陽性 ER(+)，淋巴結轉移，且為荷爾蒙接受器

b.如腋下淋巴結没轉移，但荷爾蒙接受器陰性 ER(-)

考慮含 anthracycline 蒽環類藥物處方，但處方可考慮由 FEC →T 改為 EC→T，刪去 5-FU 減少肺部副作用

(6)不含 anthracycline 化學治療處方 TC *6 之考慮

常傳訓記錄

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(未經講者修改)

BMJ. 2005 Jan 29;330(7485):217

# 30 years' follow up of randomised studies of adjuvant CMF in operable breast cancer: cohort study

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**Table 1** CMF studies carried out at the Istituto Nazionale Tumori in Milan

| Enrolment period | Study design | Eligible patients | Intervention | No of patients |
|---|---|---|---|---|
| June 1973 to September 1975 | Randomised controlled trial | Node positive, premenopausal, and postmenopausal | Surgery *v* CMF for 12 cycles | 179 *v* 207 |
| September 1975 to May 1978 | Randomised controlled trial | Node positive, premenopausal | CMF for 12 cycles *v* CMF for 6 cycles | 160 *v* 164 |
| May 1978 to October 1980 | Observational study | Node positive, premenopausal | CMF for 12 cycles | 220 |
| December 1980 to October 1985 | Randomised controlled trial | Node negative and oestrogen receptor negative, premenopausal, and postmenopausal | Surgery *v* intravenous CMF for 12 cycles | 45 *v* 45 |

**Table 2** Relapse free and overall survival in the first CMF randomised study (enrolment June 1973 to September 1975). Median observation period 28.5 years

| | No of patients | | % relapse free* | | % surviving* | |
|---|---|---|---|---|---|---|
| Characteristics | Surgery alone | CMF | Surgery alone | CMF | Surgery alone | CMF |
| Total | 179 | 207 | 22 | 29 | 16 | 25 |
| Premenopausal | 86 | 103 | 22 | 33 | 20 | 35 |
| Postmenopausal | 93 | 104 | 23 | 26 | 11 | 14 |
| Age: | | | | | | |
| <50 years | 75 | 95 | 21 | 30 | 21 | 35 |
| ≥50 years | 104 | 112 | 23 | 29 | 12 | 16 |
| Tumour size: | | | | | | |
| <2.0 cm | 96 | 103 | 26 | 31 | 16 | 27 |
| ≥2.0 cm | 83 | 104 | 19 | 27 | 15 | 22 |
| No of affected lymph nodes: | | | | | | |
| 1-3 | 126 | 140 | 26 | 34 | 16 | 29 |
| > 3 | 53 | 67 | 14 | 20 | 15 | 16 |
| Oestrogen receptor status:† | | | | | | |
| Negative | 51 | 54 | 25 | 31 | 19 | 26 |
| Positive | 100 | 132 | 20 | 30 | 13 | 25 |

*Available for 337 of 386 patients (87%).
†Percentage estimates are derived from the Kaplan-Meier product limit method.

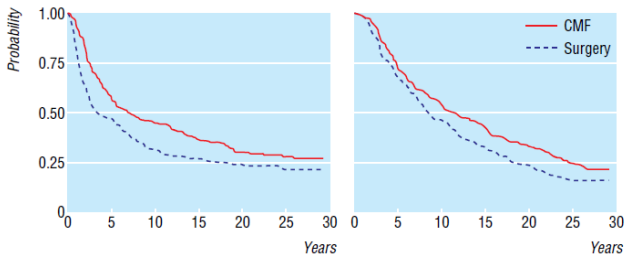


**Fig 1** Treatment outcome in the first randomised CMF study after a median observation of 28.5 years. Left: Relapse free survival after surgery alone (179 patients) *v* CMF (207 patients). Univariate analysis: hazard ratio 0.71 (95% confidence interval 0.56 to 0.91; P=0.005). Right: Overall survival after surgery alone (179 patients) *v* CMF (207 patients). Univariate analysis: hazard ratio 0.79 (0.63 to 0.98; P=0.04)

**Table 3** Multivariate analysis of the first CMF study in 337 patients with known oestrogen receptor status. Final model

| | Hazard ratio* | 95% CI | P value (Wald test) |
|---|---|---|---|
| Relapse-free survival: | | | |
| CMF *v* surgery alone | 0.66 | 0.51 to 0.85 | 0.002 |
| >3 affected lymph nodes *v* 1-3 affected lymph nodes | 1.67 | 1.28 to 2.18 | 0.0001 |
| Overall survival: | | | |
| CMF *v* surgery alone | 0.78 | 0.61 to 0.98 | 0.04 |
| >3 affected lymph nodes *v* 1-3 affected lymph nodes | 1.40 | 1.09 to 1.80 | 0.009 |
| Age ≥50 *v* <50 years | 1.43 | 1.12 to 1.82 | 0.004 |

*A ratio of <1.0 favours CMF.

**Table 4** Cumulative incidence of first recurrence of cancer in the first CMF randomised study. Values are percentage estimates derived by applying the method of Marubini and Valsecchi

| | At 5 years | | At 10 years | | In current analysis | |
|---|---|---|---|---|---|---|
| Recurrence | Surgery alone | CMF | Surgery alone | CMF | Surgery alone | CMF |
| Total first recurrence: | 53 | 44 | 68 | 54 | 78 | 71 |
| Locoregional only* | 12 | 10 | 14 | 12 | 15 | 14 |
| Contralateral breast | 2 | 2 | 3 | 4 | 5 | 10 |
| Distant | 39 | 32 | 51 | 38 | 58 | 47 |

*Includes ipsilateral supraclavicular nodes.

**Table 5** Incidence of iatrogenic amenorrhea in premenopausal women who had monthly periods at study entry (first three studies in table 1)

| | CMF for 12 cycles | | CMF for 6 cycles | |
|---|---|---|---|---|
| | No | No with amenorrhoea (%) | No | No with amenorrhoea (%) |
| Total | 397 | 299 (75) | 145 | 90 (62) |
| Age in years: | | | | |
| <35 | 48 | 6 (12.5) | 8 | 0 0 |
| 35-39 | 87 | 52 (60) | 38 | 11 (29) |
| 40-44 | 110 | 94 (85) | 50 | 32 (64) |
| >44 | 152 | 147 (97) | 49 | 47 (96) |

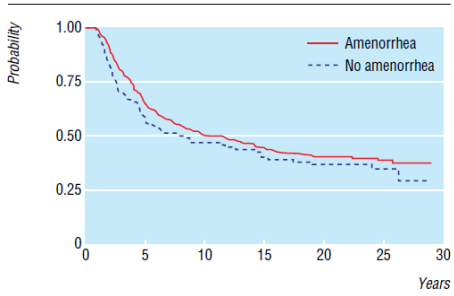


**Fig 2** Relapse free survival in premenopausal women who had monthly periods at entry to the study and given 12 cycles of CMF. Influence of iatrogenic amenorrhoea

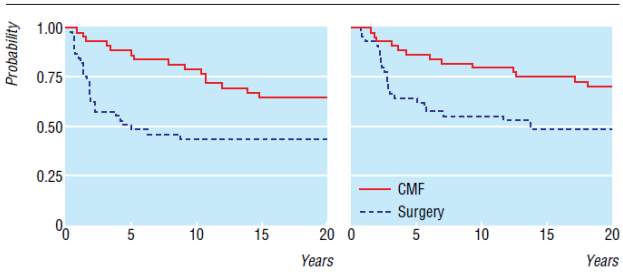


**Fig 3** Treatment outcome in node negative and oestrogen receptor negative tumours: 20 year results. Left: Relapse free survival after surgery alone (45 patients) compared with intravenous CMF (45 patients). Univariate analysis: hazard ratio 0.65 (95% confidence interval 0.47 to 0.90; P=0.009). Right: Overall survival after surgery alone (45 patients) compared with intravenous CMF (45 patients). Univariate analysis: hazard ratio 0.65 (0.47 to 0.92; P=0.01)

## What is already known on this topic

At a median follow up of about 15 years, adjuvant systemic therapy with cyclophosphamide, methotrexate, and fluorouracil (CMF) can benefit patients with operable breast cancer

## What this study adds

Adjuvant systemic therapy has long lasting effects even after 30 years, and these are achieved at the cost of minimal long term sequelae

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The poor prognosis associated with unfavourable indicators in patients treated locoregionally alone was improved by administration of adjuvant CMF

# Adjuvant Paclitaxel and Trastuzumab for Node-Negative, HER2-Positive Breast Cancer

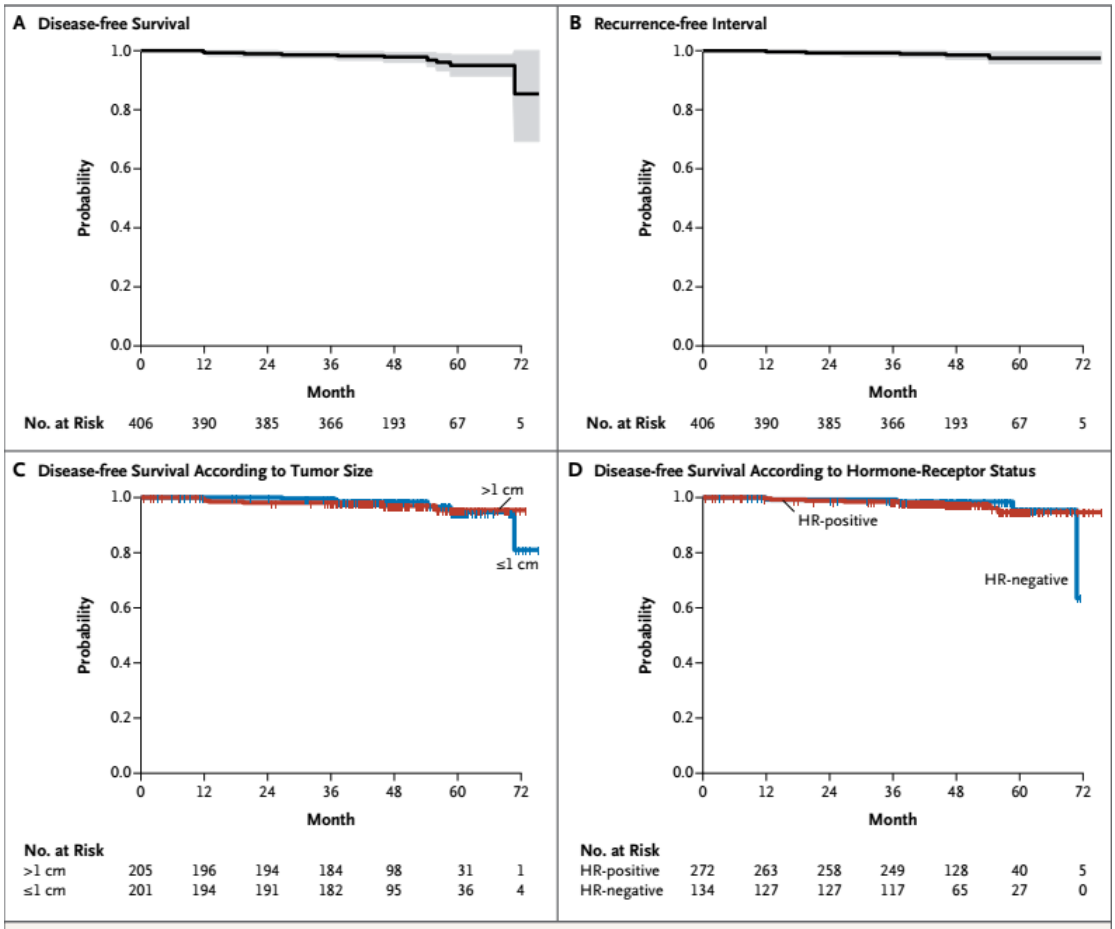


**Figure 2. Probabilities of Disease-free Survival and Recurrence-free Interval.**

Panel A shows the probability of disease-free survival in the intention-to-treat population, and Panel B the recurrence-free interval in the intention-to-treat population (unlike recurrence-free survival, the recurrence-free interval did not include death from cancer other than breast cancer). The shading in Panels A and B denotes the 95% confidence intervals. Panel C shows the probability of disease-free survival according to tumor size, and Panel D the probability of disease-free survival according to hormone-receptor (HR; estrogen receptor or progesterone receptor) status. Tick marks represent the time of censoring for patients who were recurrence-free.