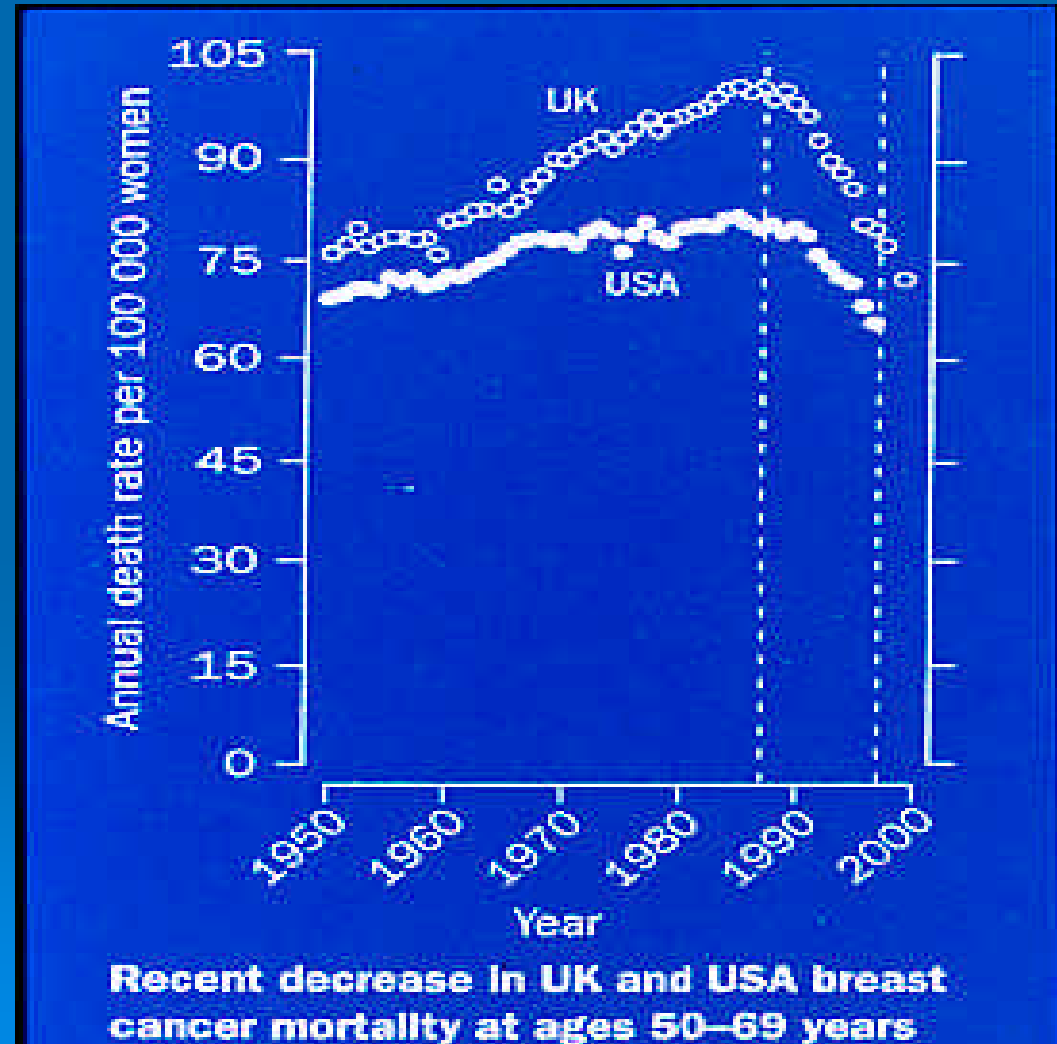


Breast Cancer in New Zealand



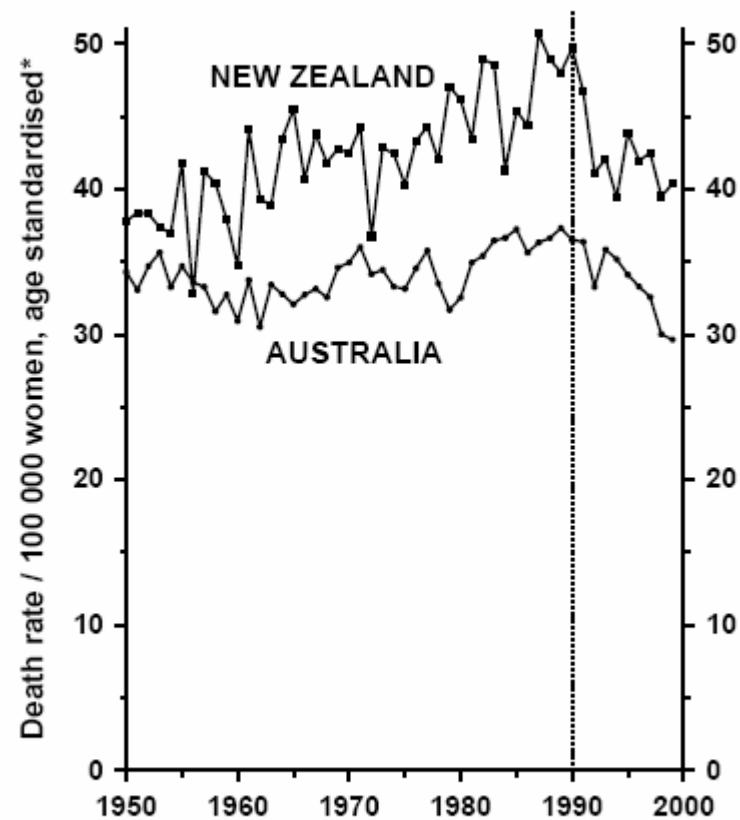
V. Harvey - November 2005

Decrease in Breast Cancer Mortality UK/US 1990 - 2000



Decrease in Breast Cancer Mortality NZ/AUS 1990 - 2000

NZ/Australia, 1950-1999: recent decrease
in breast cancer mortality at ages 20-69



*Mean of annual rates
in component 5-year age groups

Source: WHO mortality &
UN population estimates

10-470-000-10-17-00

Breast Cancer in New Zealand

The Good Things

- Cancer is a National Health Priority
- Establishment of Cancer Control Strategy
 - To ensure national equity
 - To ensure effective screening/early detection
 - To provide optimal treatment for cancer
 - To ensure access to multidisciplinary management
 - To develop defined standards
 - To define and monitor quality
 - To increase participation in clinical trials
 - To ensure appropriate introduction of new therapies
 - To define public entitlement

Breast Cancer in New Zealand

Some Good Things

- National screening programme 45-69yrs
- Establishment of Multidisciplinary Clinics/Meetings
- National process for evaluation of new medicines
- Regional Oncology Services

Breast Cancer in New Zealand

Some of the Problems

- A limited workforce
- A limited budget
- High patient expectation
- Highly informed patient population
- Acceptance of therapy for smaller gains
- A technology revolution in medicine

Breast Cancer in New Zealand

The New Drugs

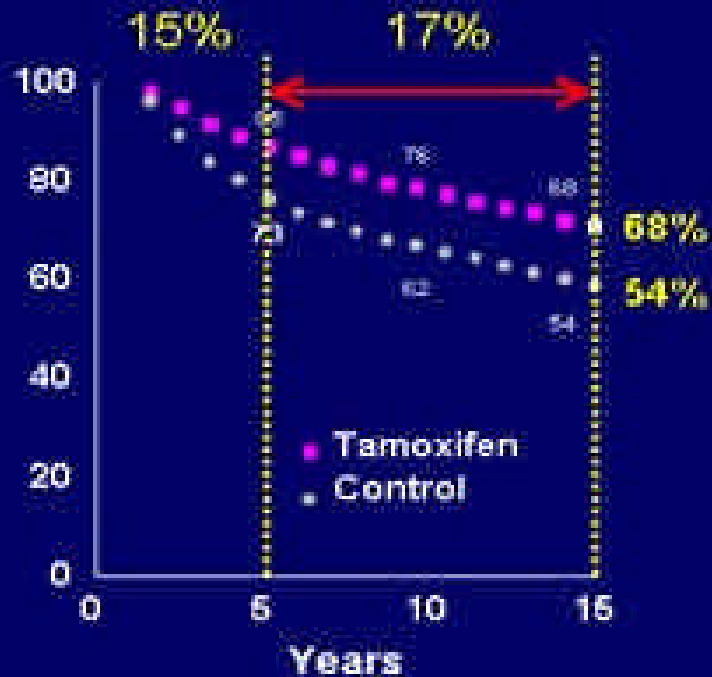
- **Aromatase Inhibitors**
 - Anastrozole (Arimidex)
 - Letrozole (Femara)
- **Taxanes**
 - Paclitaxel (Taxol)
 - Docetaxel (Taxotere)
- **Trastuzumab**
 - Herceptin

The Effect of Tamoxifen

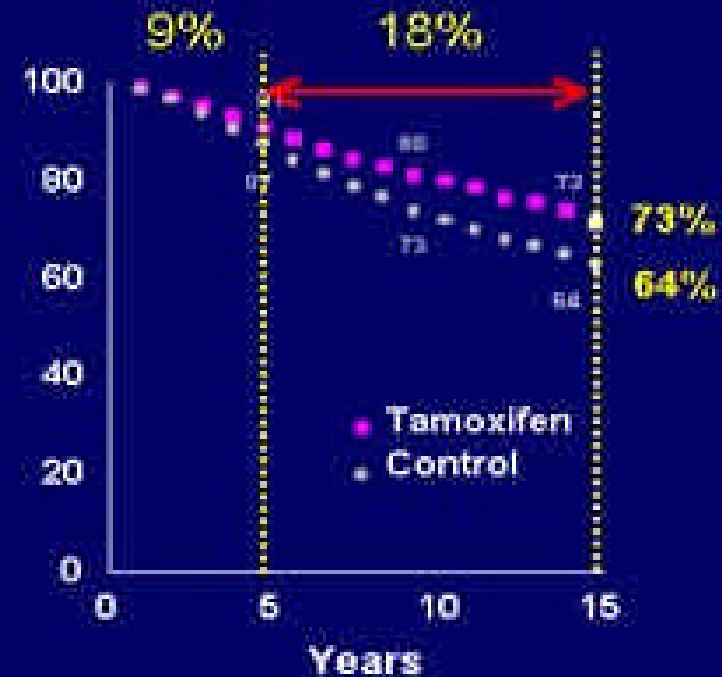
Timing of Breast Cancer Events

Oxford Overview 2000 – adapted with permission

Breast Cancer Recurrences



Breast Cancer Deaths



The Aromatase Inhibitors

Anastrozole/Letrozole

Tamoxifen Challenged

- **Advanced Breast Cancer**
 - greater disease shrinkage than tamoxifen
 - longer disease control than tamoxifen
- **Early Breast Cancer**
 - fewer recurrences than tamoxifen

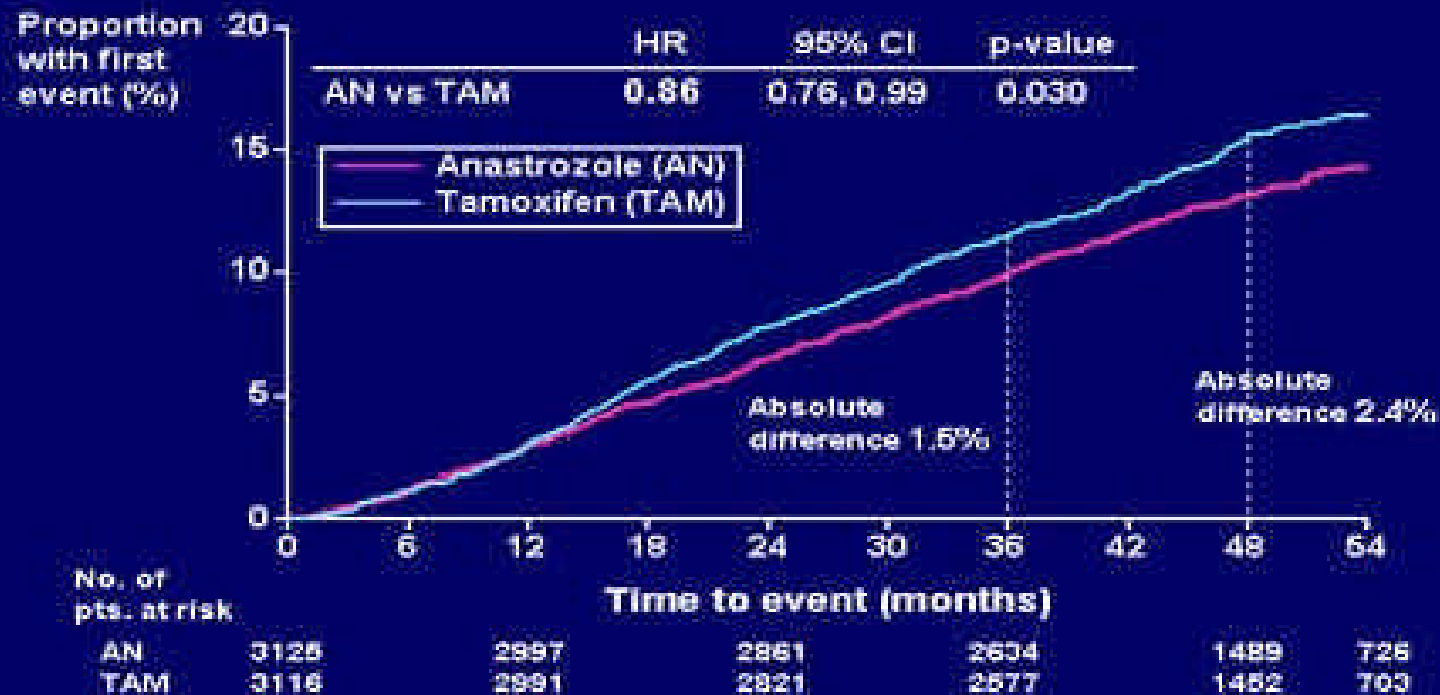
Strategies of using Aromatase Inhibitors



ATAC Trial

Anastrozole vs Tamoxifen

Probability of a first event in overall population



Aromatase Inhibitors

➤ Compared to tamoxifen

- **Similar**
 - Hot flushes
- **Less**
 - Gynaecological problems
 - Venous thromboembolism (DVT)
 - Uterine cancer
- **More**
 - Joint aches (arthralgia/arthritis)
 - Fractures
 - Osteoporosis

Aromatase Inhibitors

➤ Who

- Postmenopausal women

➤ Why

- 2 – 6% lower recurrence rate

➤ When

- Initially – in place of tamoxifen (HER2+: ?ER+ PR-)
- After 2-3 years of tamoxifen (most)
- After 5 years of tamoxifen (if nearing end of 5 years Tamoxifen)

➤ Which

- No obvious clinical difference

Aromatase Inhibitors

➤ Who pays

- PHARMAC
 - Advanced disease
 - Early breast cancer
 - Intolerant of tamoxifen
 - Contraindication for tamoxifen
- Patient
 - Early disease
 - Except as above (\$30/month)

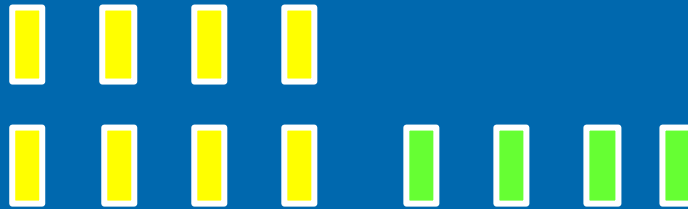
The Taxanes

- Paclitaxel (Taxol)
- Docetaxel (Taxotere)

Strategies to incorporate Taxanes

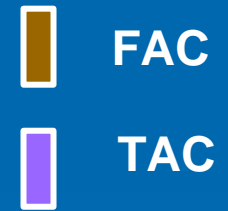
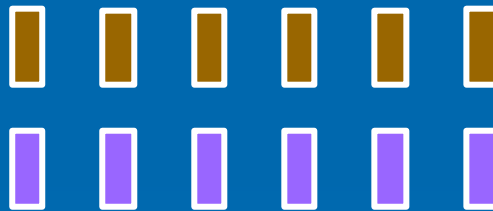
Additional regimen

NSABP B28
CALGB 9344



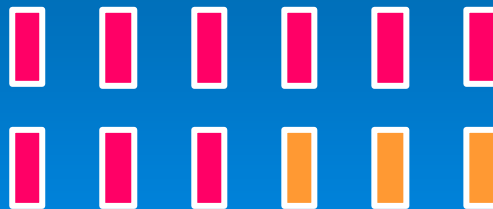
Drug Replacement

BCIRG 001

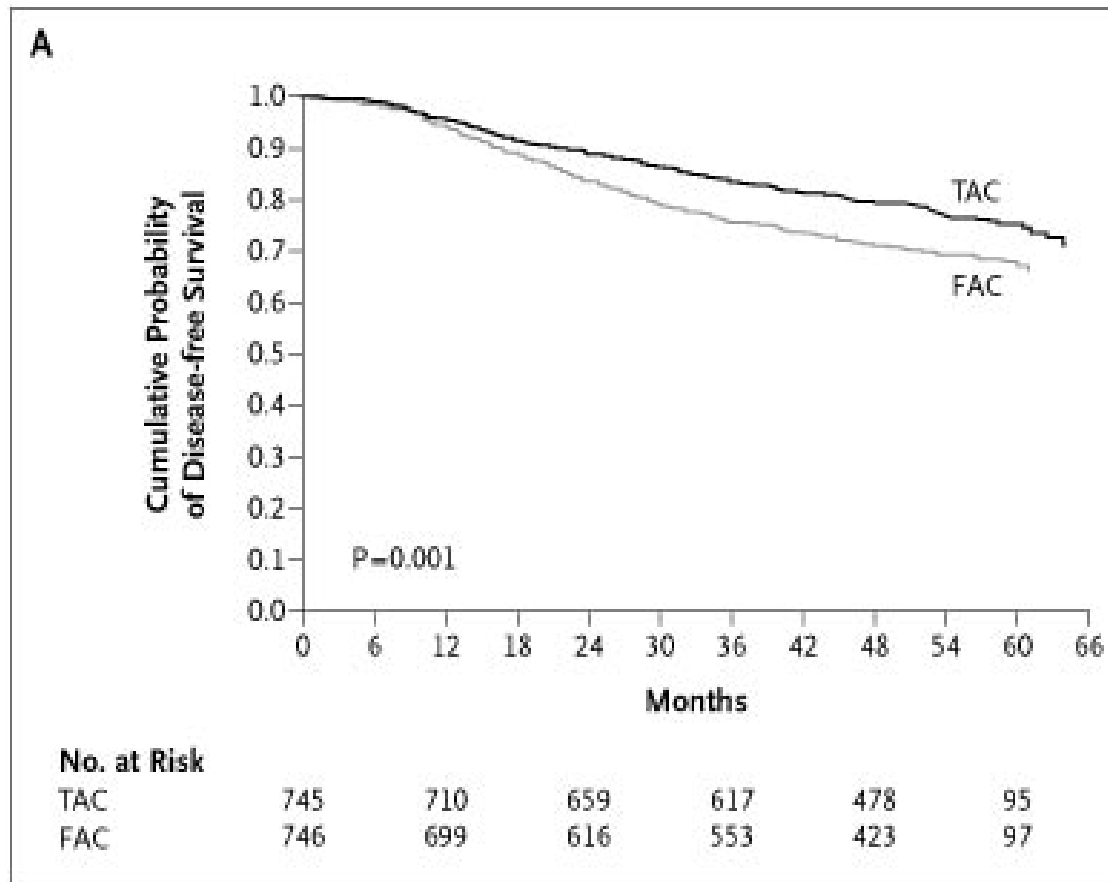


Regimen Replacement

PACS 01



Disease free Survival BCIRG 01 – TAC x6 vs FAC x6



Results of adding Taxanes

5 Year Disease Free Survival

	Control	Taxane Group	Benefit ↑ DFS	Risk of Recurrence	Benefit Overall Survival
CALGB 9344	65%	70%	+5%	↓ 17%	↑ 18%
NSABP B-28	72%	76%	+4%	↓ 17%	None
BCIRG 001	68%	75%	+7%	↓ 28%	↑ 30%
PACS 01	73.2%	78.2%	+5%	↓ 17%	↑ 23%

Disadvantages of Adding Taxanes

➤ Increased side-effects

- Muscular aches and pains
- Febrile neutropenia (TAC vs FAC)

➤ Increased duration of treatment

- AC vs AC → Taxol - 3 vs 6 months

➤ Increased cost

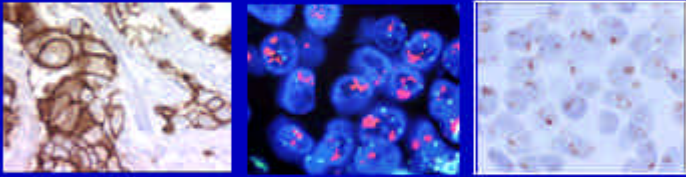
- \$20 – 25,000 (Not yet funded by PHARMAC)

Herceptin (Trastuzumab)

- HER2 receptor found on 20-30% of breast cancers
- Associated with
 - More aggressive disease
 - Destroyed by Herceptin

HER2 status evaluation

Visualisation of invasive cells harbouring the signal

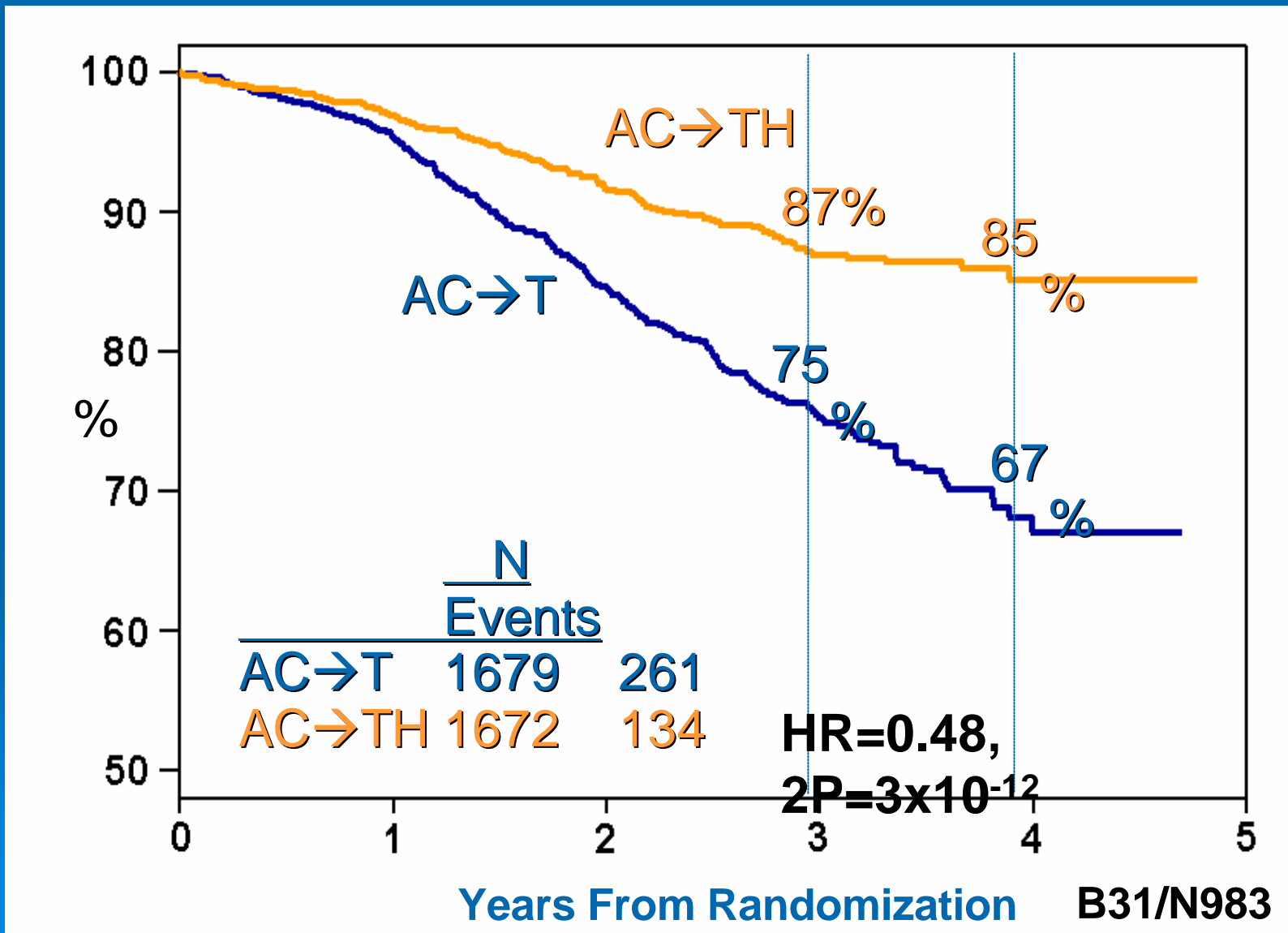


IHC Protein FISH DNA CISH

IHC = Immunohistochemistry
FISH = Fluorescence In-Situ Hybridization
CISH = Chromogenic In-Situ Hybridization

NSABP B-31/NCCTG 9831

Disease-Free Survival



Results of adding Herceptin

Disease Free Survival

	Control	Herceptin Group	Benefit DFS	Benefit HR
NSABP B-31 N9871	75%	87%	+12%	52%
	74%	87%	+13%	55%
	78%	87%	+ 9%	45%
HERA	77%	86%	+9%	46%
BCIRG 006		AC → TH TCH		51% 39%

Disadvantages of Adding Herceptin

➤ Increased side-effects

- Fevers & chills – usually minor
- Cardiac impairment - reversible

➤ Increased duration of therapy

- Currently 1 year (possibly longer)

➤ Increased Cost

- \$90 – 150,000 (Not funded by PHARMAC)

What do the New Chemotherapies Add?

Conclusions

➤ Taxanes

- Reduces risk of recurrence (↓ 17-28%)
- Increases survival (↑ 18-30%)

➤ Herceptin

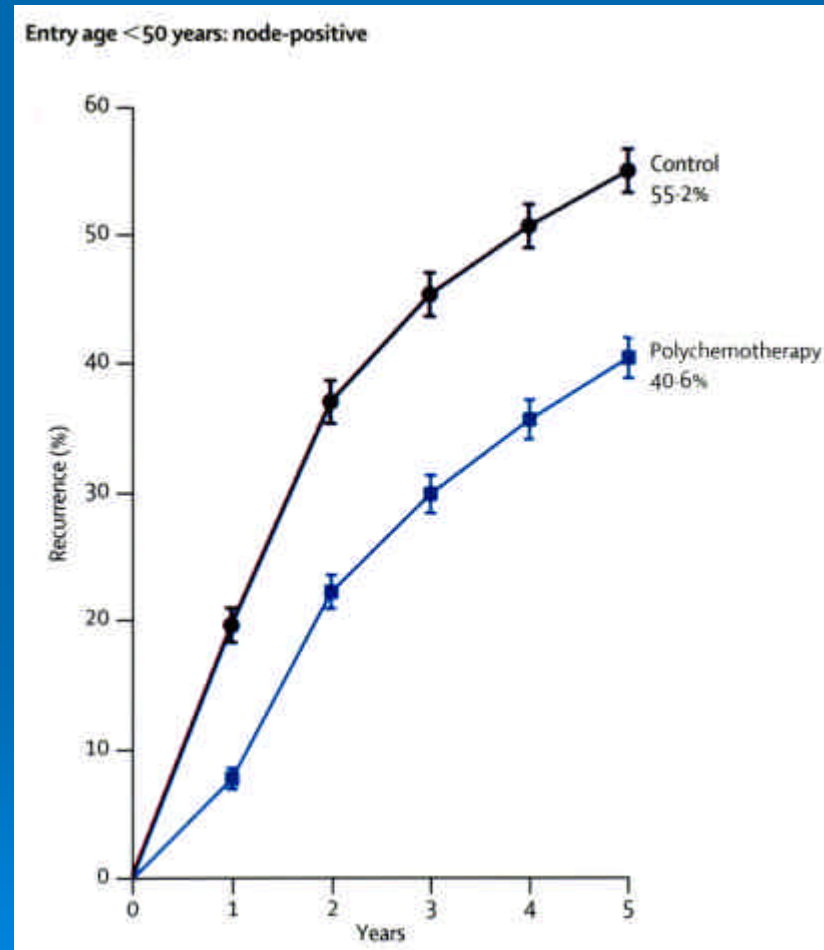
- Reduces risk of recurrence (↓ ~50%)
- Possible increase in survival

Problem is how to fund





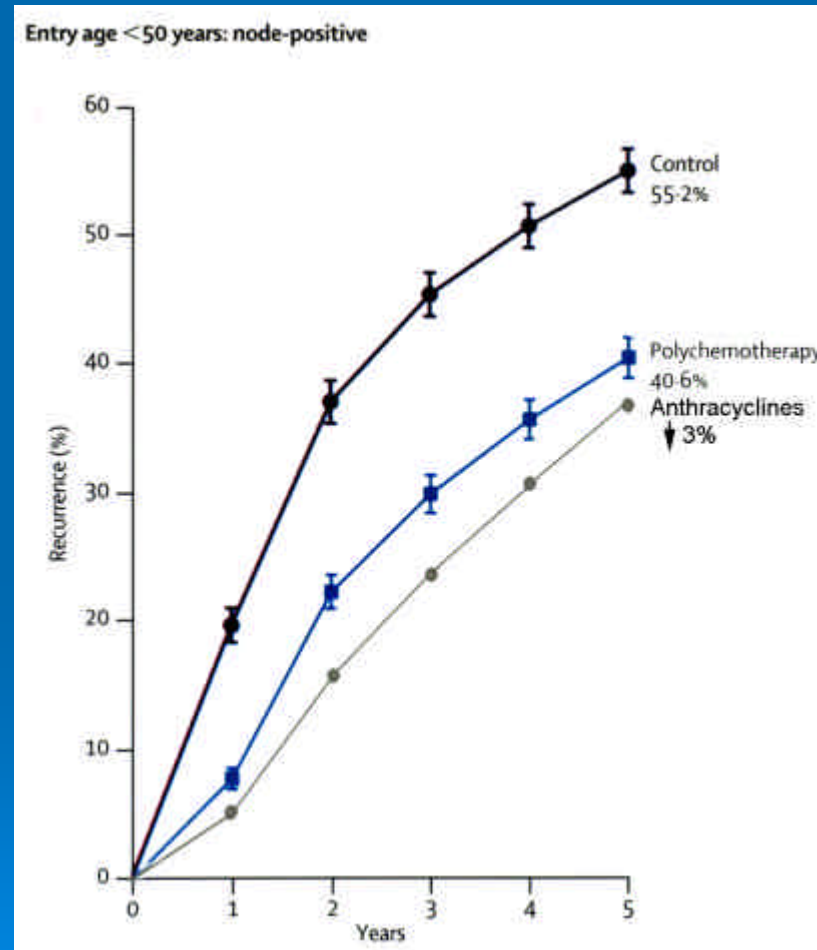
Breast Cancer Recurrence Benefit of Chemotherapy



EBCTCG Lancet 2005;365:1687-1717

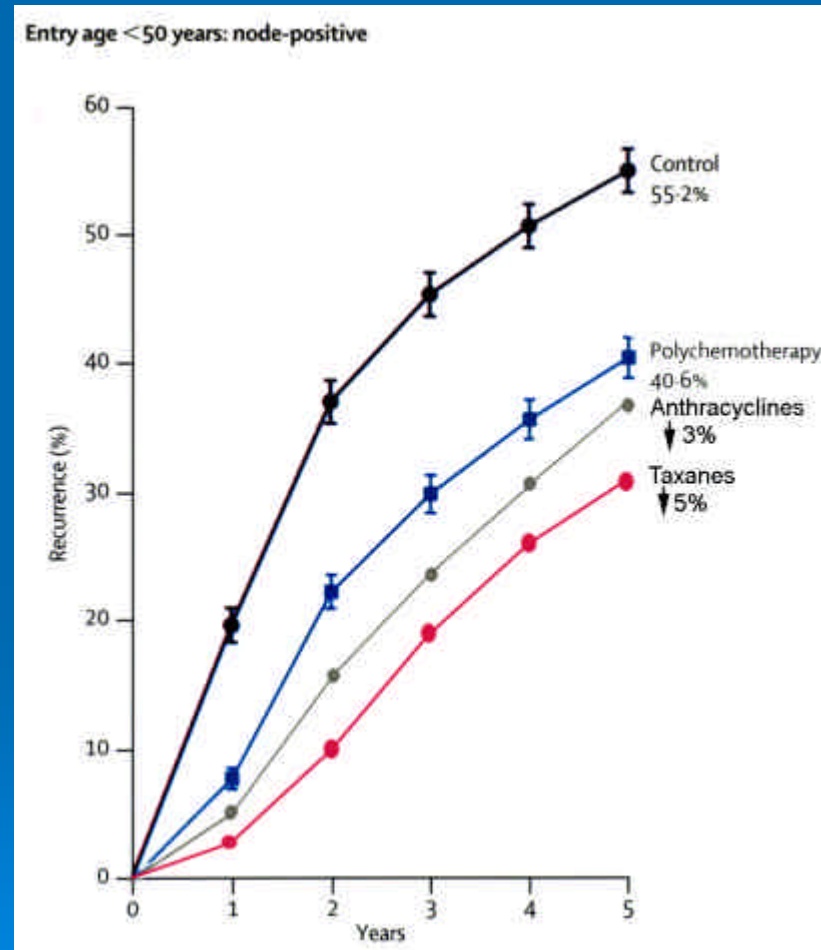
Breast Cancer Recurrence

Additional Benefit of Anthracyclines



Breast Cancer Recurrence

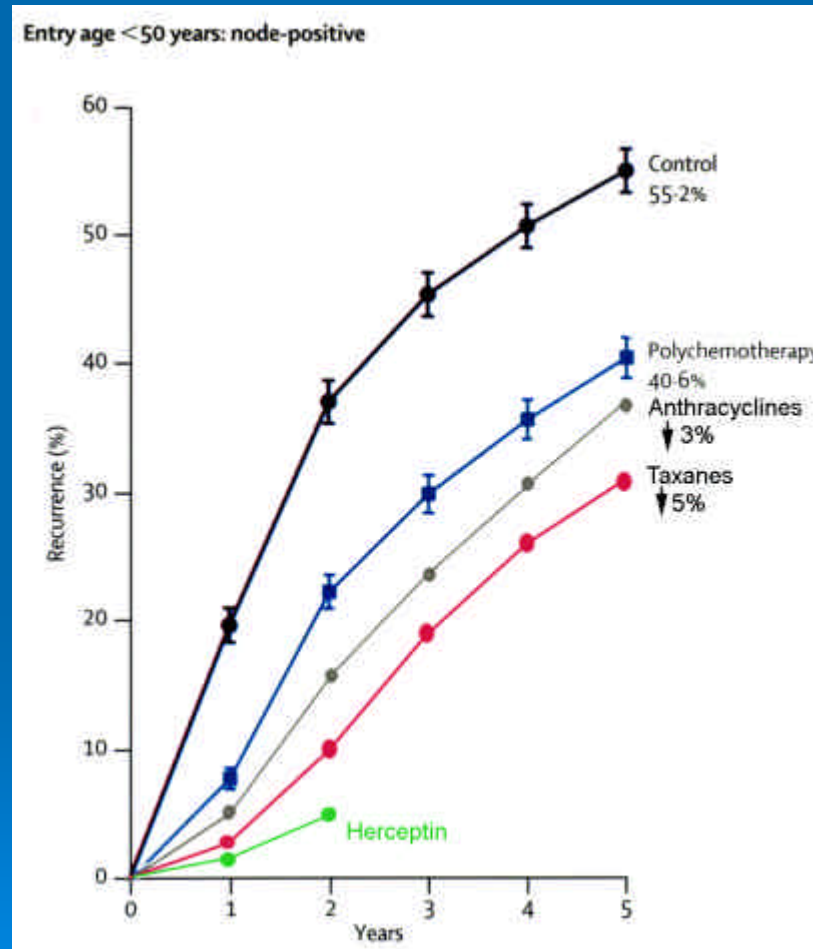
Additional Benefit of Taxanes



Adapted from EBCTCG Lancet 2005;365:1687-1717

Breast Cancer Recurrence

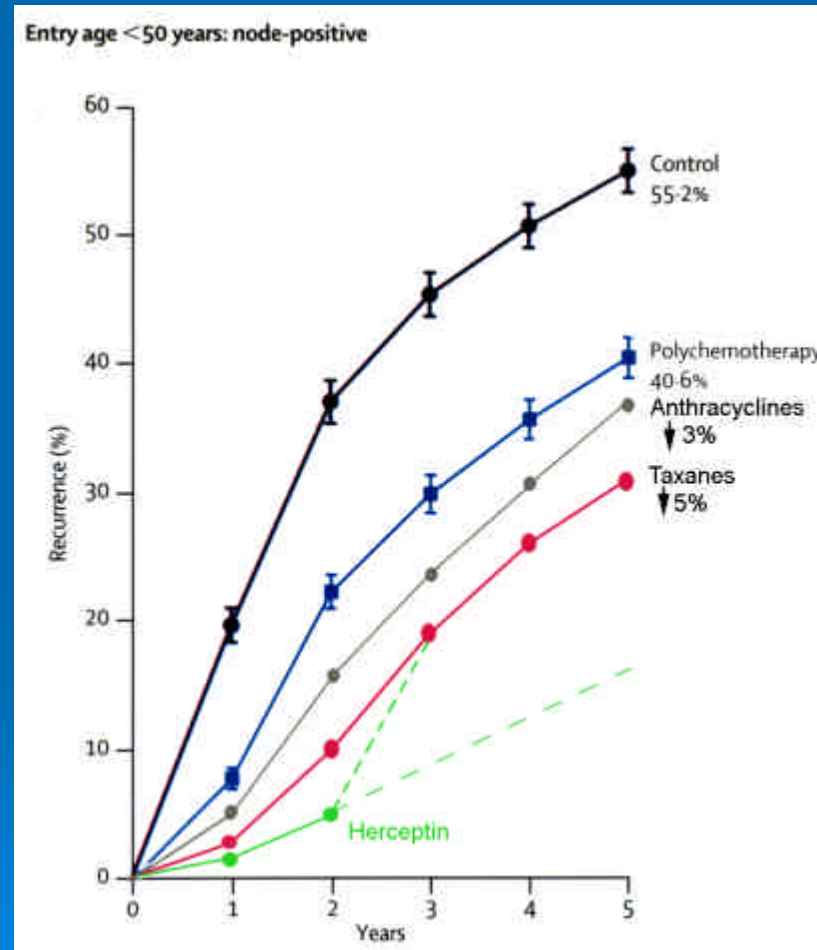
Additional Benefit of Herceptin



Adapted from EBCTCG Lancet 2005;365:1687-1717

Breast Cancer Recurrence

Additional Benefit of Herceptin - Possibilities



Adapted from EBCTCG Lancet 2005;365:1687-1717