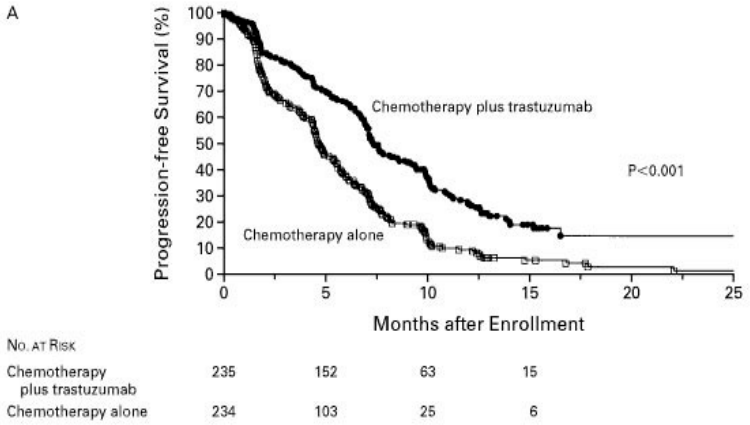
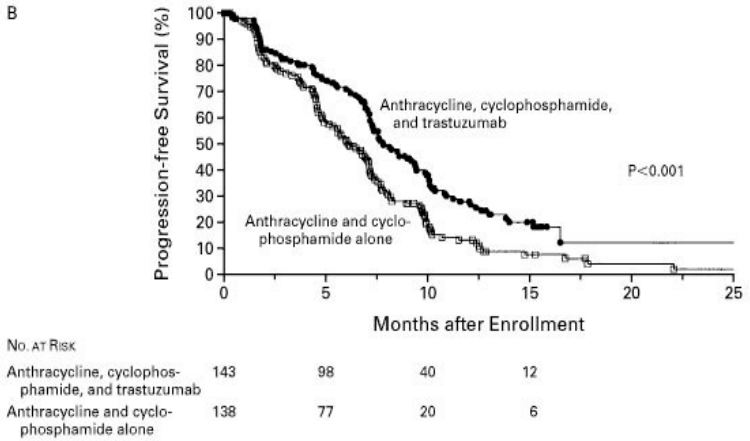
0ne year of herceptin as the gold standard of adjuvant systemic therapy for breast cancer

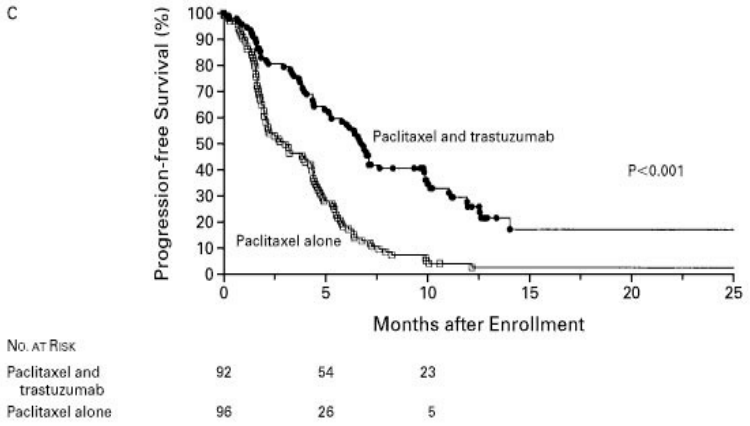
Mike McCrystal

Her-2 overexpression

- Occurs in 15-20% breast cancer cases associated with worse prognosis
- Targeted by humanised murine antibody trastuzumab –signal blockade and immune recognition
- Synergism with cytotoxic therapy







Metastatic disease – Slamon et al, 2001
N=234 chemo (anthracycline +cyclo or paclitaxel) vs same chemo with trastuzumab n=235.

DFS = 7.4 vs 4.6 months p<0.001
ORR = 50 vs 32% p<0.001
DOR 9.1 vs 6.1 months p<0.001
Median OS 25.1 vs 20.3 months

Trastuzumab discontinued in 18/235 cases due to cardiac toxicity, independent cardiac review = 63 pts with cardiac dysfunction 39+12 vs 11+1

Four large adjuvant studies one year as trastuzumab duration

Adjuvant trials

- HERA
- NSABP-B31
- NCCTG 9831
- BCIRG 06

DESIGN OF THE HERA TRIAL

Women with HER2 POSITIVE invasive breast cancer IHC3+ or FISH+ centrally confirmed

Surgery + (neo)adjuvant chemotherapy (CT) ± radiotherapy

Stratification

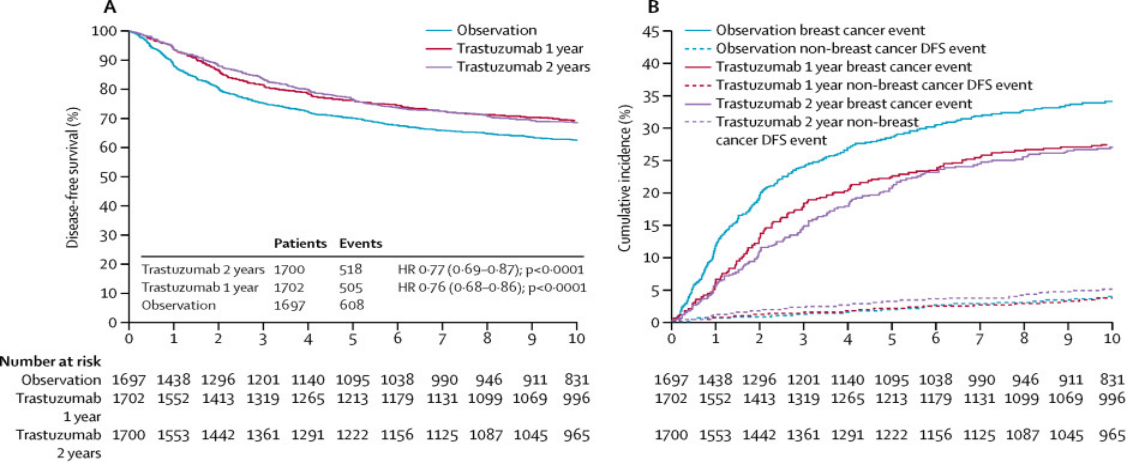
Nodal status, adjuvant CT regimen, hormone receptor status and endocrine therapy, age, region

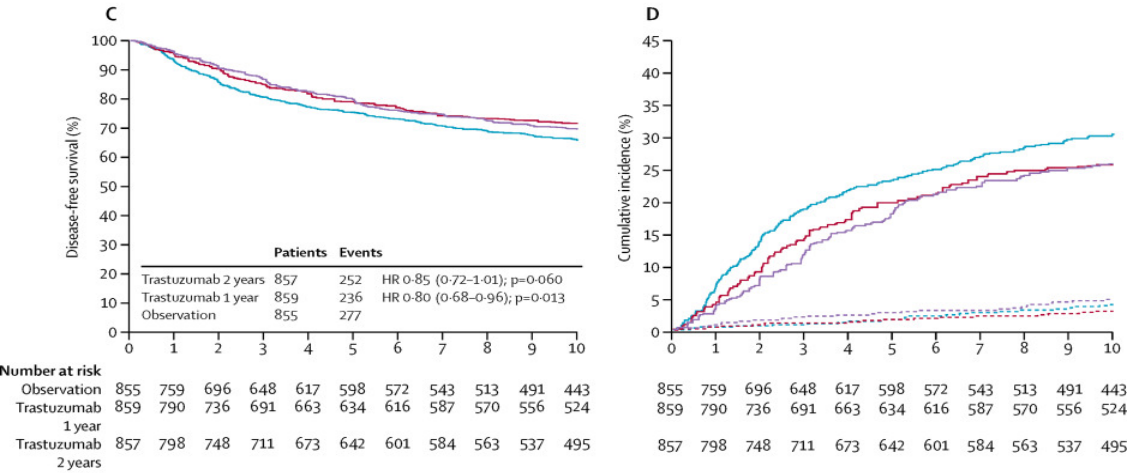
Randomization

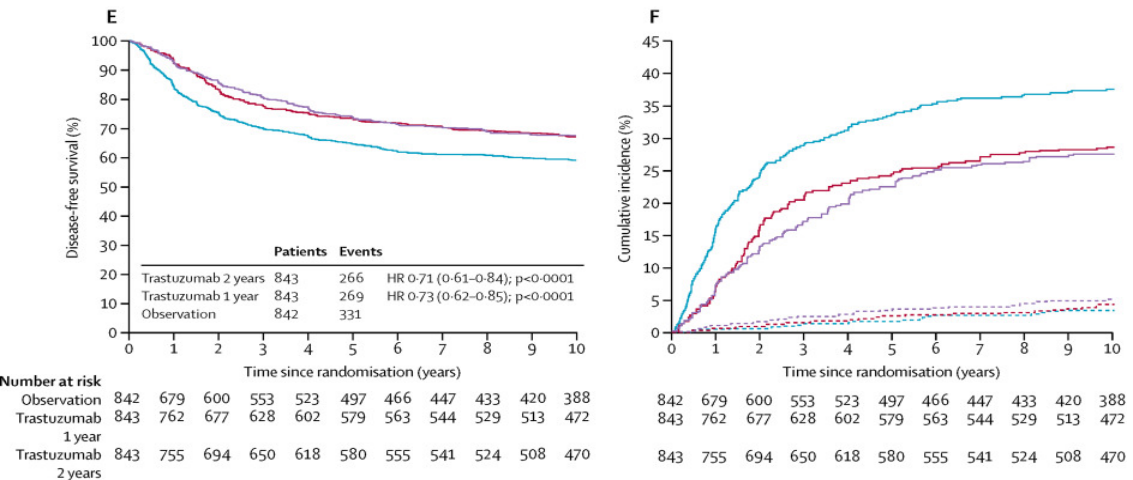
Trastuzumab 8 mg/kg → 6 mg/kg 3 weekly x 2 years	Trastuzumab 8 mg/kg → 6 mg/kg 3 weekly x 1 year	Observation

HERA

- 3 arms, n= 1694 in each, chemotherapy (at least 4 cycles) followed by observation, 1 year or 2 years of herceptin.
- Herceptin started after chemo (sequential)
- LVEF >55% after chemo
- Cross-over from observation arm 2005, 885 pts (52%) median time from original randomisation = 22.8 months







No difference 1 year vs 2 years. With median follow up 11 years, DFS 1 yr over observation
HR 0.76 (0.68-0.86)
OS 0.74 (0.64—0.86)

Incidence cardiac events 7.3% 2 year arm, 7.4% 1 year and 0.9% in observation arm

NSABP B-31

Control: AC→T

Arm 1

Arm 2

NCCTG N9831

Arm A

Investigational: AC→T+H

Arm B

Arm C

= doxorubicin/cyclophosphamide (AC) 60/600 mg/m2 q 3 wk x 4

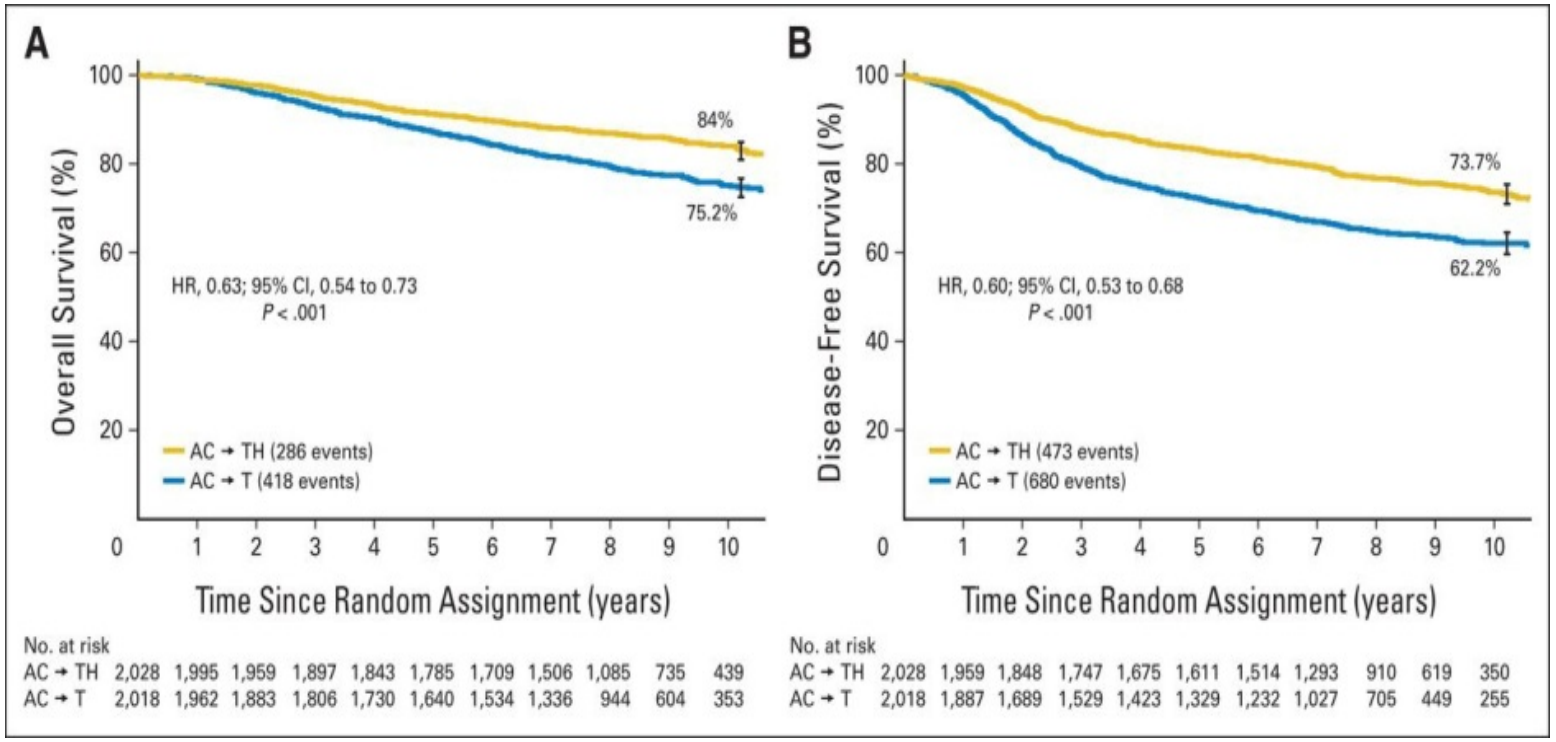
= paclitaxel (T) 175 mg/m2 q 3 wk x 4

= paclitaxel (T) 80 mg/m2/wk x 12

= trastuzumab (H) 4mg/kg LD + 2 mg/kg/wk x 51

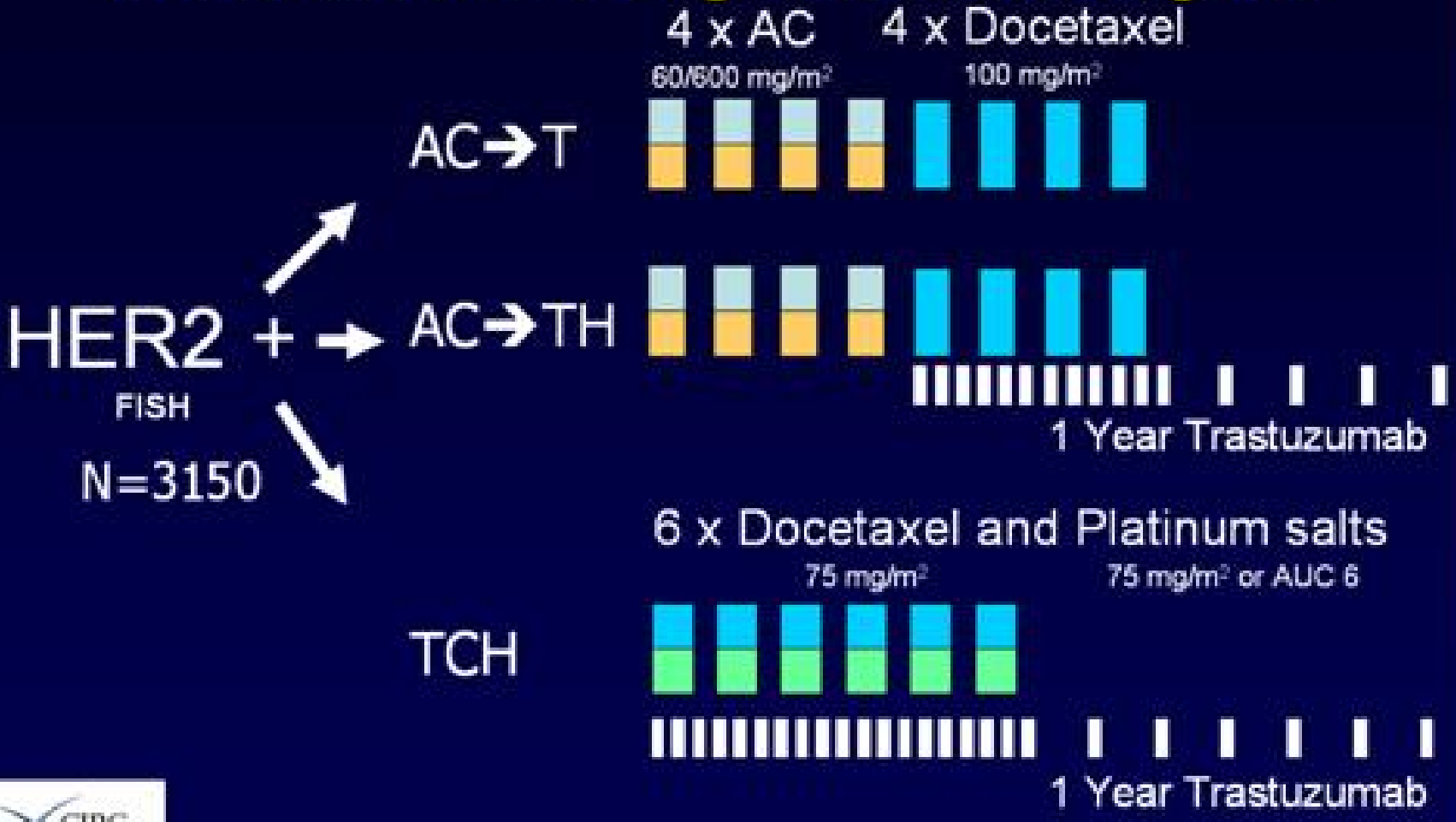
Combination NSABP B-31 and NCCTG9831

- 2102 patients from B31 in total and 1944 patients from N9831



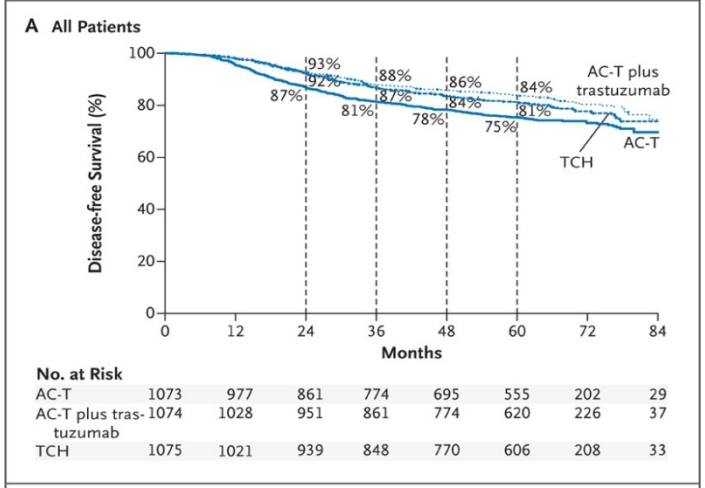
BCIRG 006

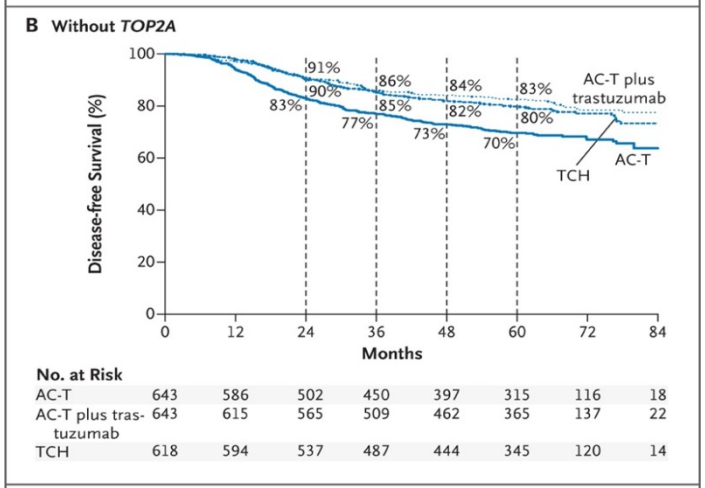
Adjuvant Treatment of Breast Cancer
Node Positive and High Risk Node Negative

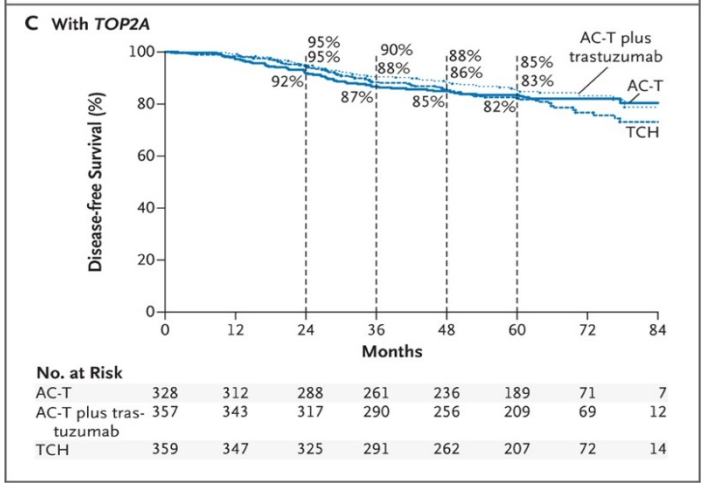


CIRG

Courtesy of M. Buyse



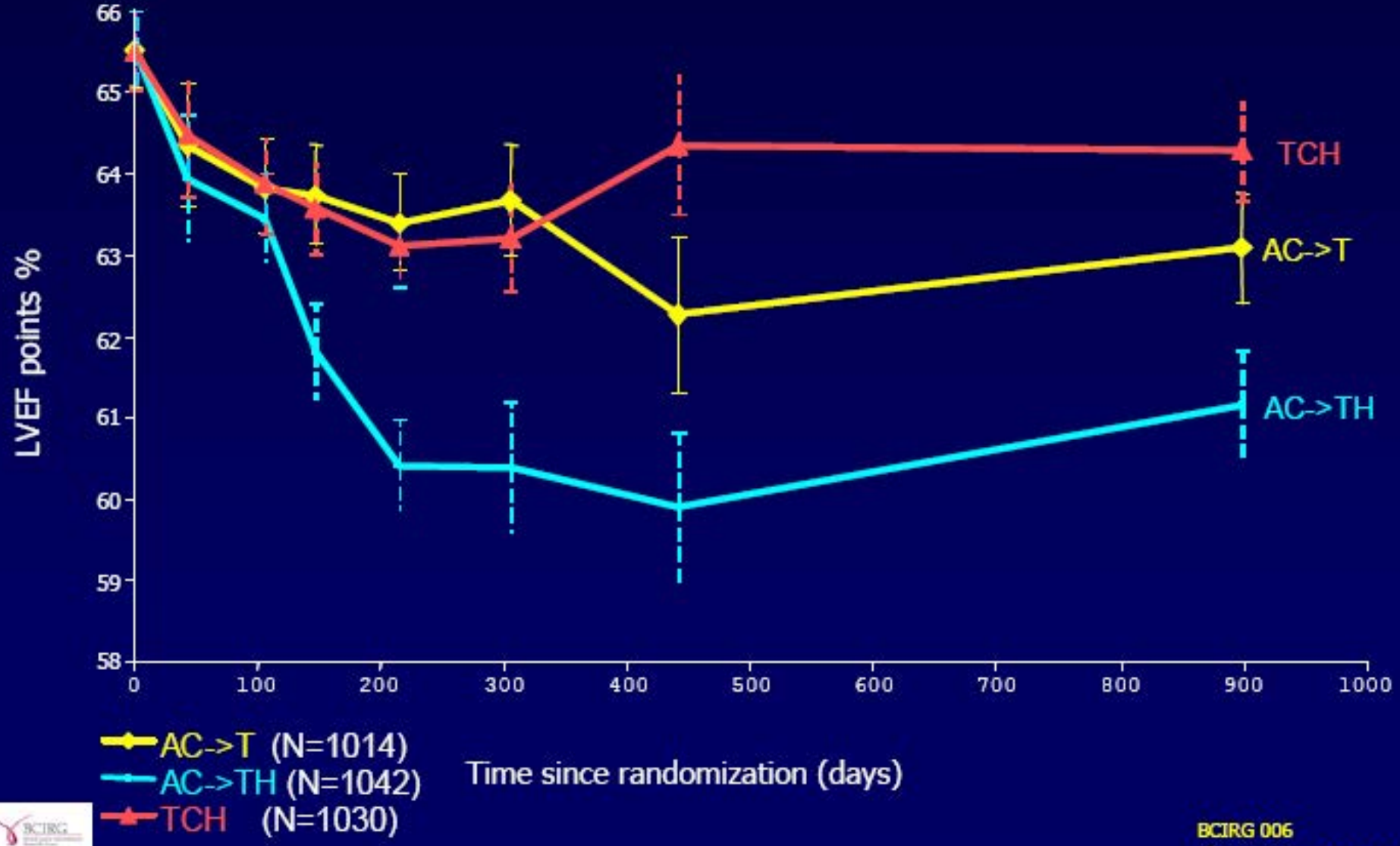




Median follow up 6.5 years,
estimated 5 year DFS 75 % vs 84%
for AC-TH and 81% for TCH
)S is 87% 92% and 91%
respectively, no differenec
between AC-TH and TCH
statistically.
Evidence cardiomyopathy
incidence worse for AC-TH vs TCH

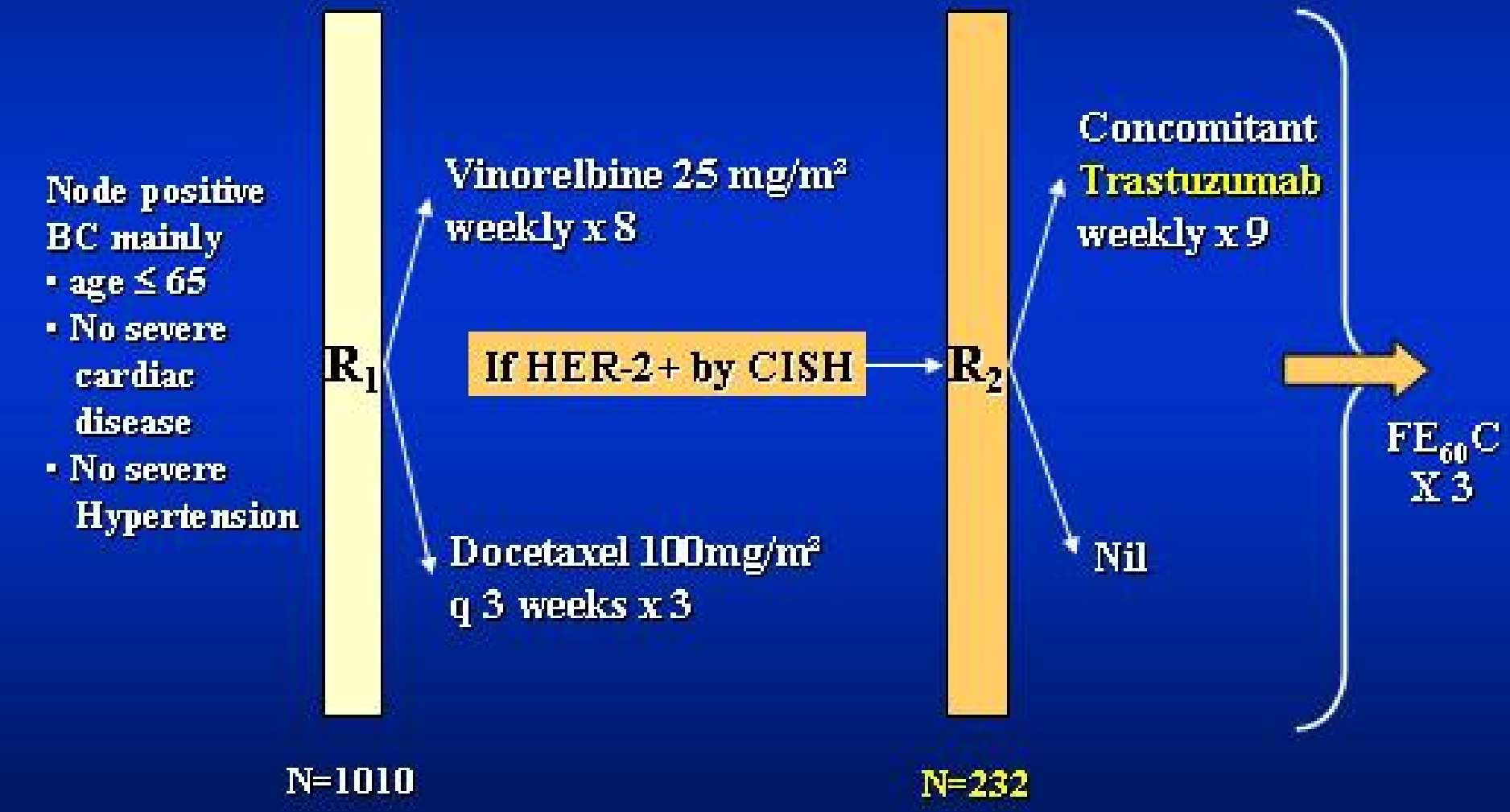
Mean LVEF - All Observations

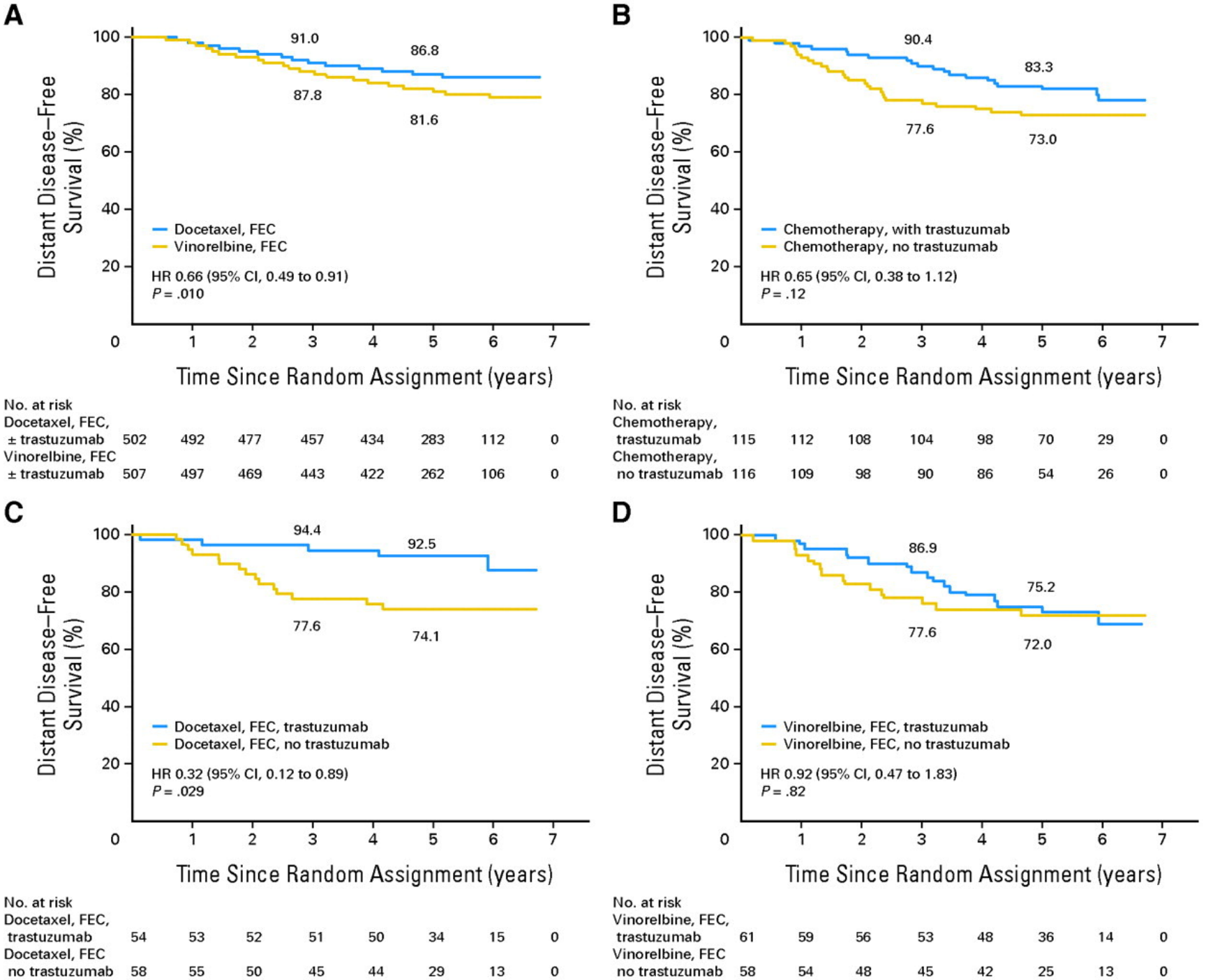
2nd Interim Analysis



BCIRG 006
Slamon D., SABCS 2006

THE "FINHER" TRIAL




A
Distant Disease–Free Survival (%)
100
80
60
40
20
0
91.0
86.8
87.8
81.6
Docetaxel, FEC
Vinorelbine, FEC
HR 0.66 (95% CI, 0.49 to 0.91)
P = .010
1
2
3
4
5
6
7
Time Since Random Assignment (years)
No. at risk
Docetaxel, FEC, ± trastuzumab 502 492 477 457 434 283 112 0
Vinorelbine, FEC ± trastuzumab 507 497 469 443 422 262 106 0
B
Distant Disease–Free Survival (%)
90.4
83.3
77.6
73.0
Chemotherapy, with trastuzumab
Chemotherapy, no trastuzumab
HR 0.65 (95% CI, 0.38 to 1.12)
P = .12
Time Since Random Assignment (years)
No. at risk
Chemotherapy, trastuzumab 115 112 108 104 98 70 29 0
Chemotherapy, no trastuzumab 116 109 98 90 86 54 26 0
C
Distant Disease–Free Survival (%)
94.4
92.5
77.6
74.1
Docetaxel, FEC, trastuzumab
Docetaxel, FEC, no trastuzumab
HR 0.32 (95% CI, 0.12 to 0.89)
P = .029
Time Since Random Assignment (years)
No. at risk
Docetaxel, FEC, trastuzumab 54 53 52 51 50 34 15 0
Docetaxel, FEC no trastuzumab 58 55 50 45 44 29 13 0
D
Distant Disease–Free Survival (%)
86.9
75.2
77.6
72.0
Vinorelbine, FEC, trastuzumab
Vinorelbine, FEC, no trastuzumab
HR 0.92 (95% CI, 0.47 to 1.83)
P = .82
Time Since Random Assignment (years)
No. at risk
Vinorelbine, FEC, trastuzumab 61 59 56 53 48 36 14 0
Vinorelbine, FEC no trastuzumab 58 54 48 45 42 25 13 0

Could a shorter duration than a year yield the same results?

- Reduced cost
- Possibly less cardiac toxicity
- ……..but a difficult space to conduct trials in NZ

  -hard fought gain of 12 months funding

  - drug company interests


OUR
WOMEN