

“ANDERE” ADJUVANTE BEHANDELINGEN

Adjuvant therapy



Goal

HOW OFTEN DOES SURGERY CURE BREAST CANCER?

Pathological Prognostic Factors in Stage I (T₁N₀M₀) and Stage II (T₁N₁M₀) Breast Carcinoma: A Study of 644 Patients With Median Follow-Up of 18 Years

By Paul Peter Rosen, Susan Groshen, Patricia E. Saigo, David W. Kinne, and Samuel Hellman

J Clin Oncol 7:1239-1251. © 1989 by American Society of Clinical Oncology.

644 pts, all treated with mastectomy and axillary lymph node dissection

**T1N0
19% died of BC**

**T1N(1-3)
28% died of BC**

**T1N(+4)
51% died of BC**

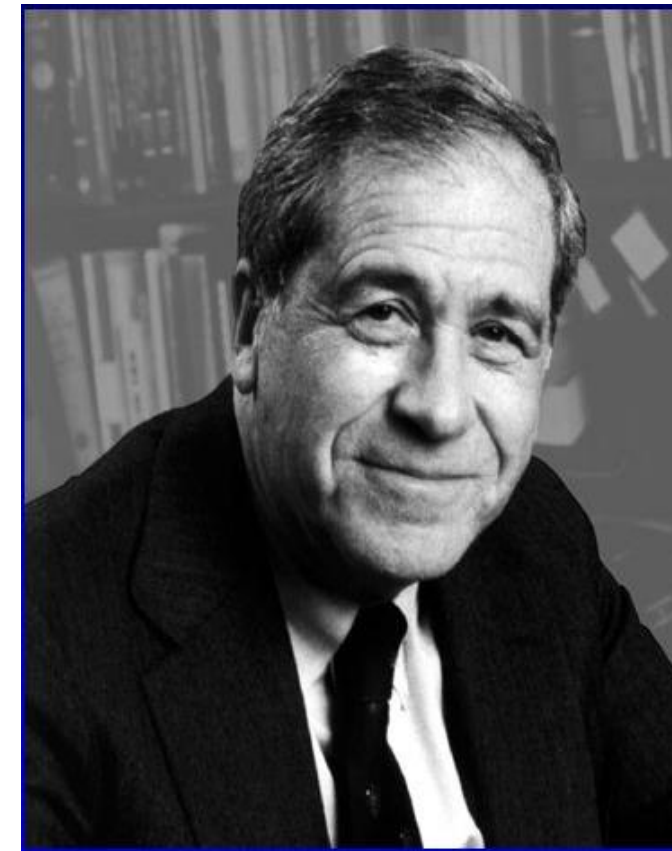
EVOLUTION OF THOUGHT IN BC MANAGEMENT

Halsted (Surgeon)

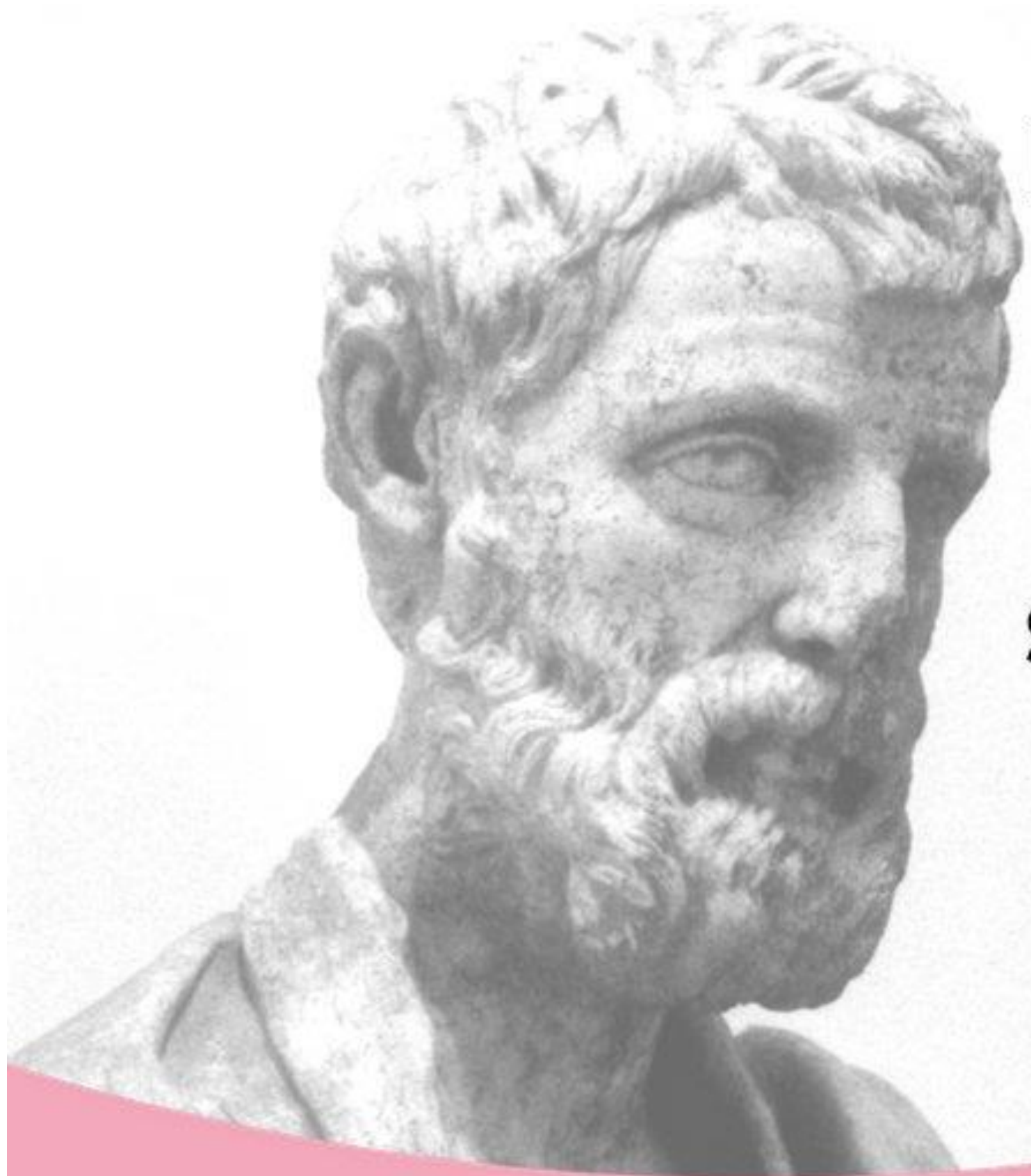


Local control= cure!
Radical (mutilating) mastectomy

Bernard Fisher (Surgeon)



Breast Cancer is a systemic disease,
variations in locoregional treatment
are unlikely to affect survival
substantially



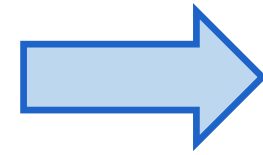
**Did you know, in 160 A.D.
Claudius Galen theorizes
that breast cancer is a
systemic disease affecting
the whole body.**



EVOLUTION OF THOUGHT IN BC MANAGEMENT

Local treatment

Surgery
Radiotherapie



Local treatment

+

Systemic treatment

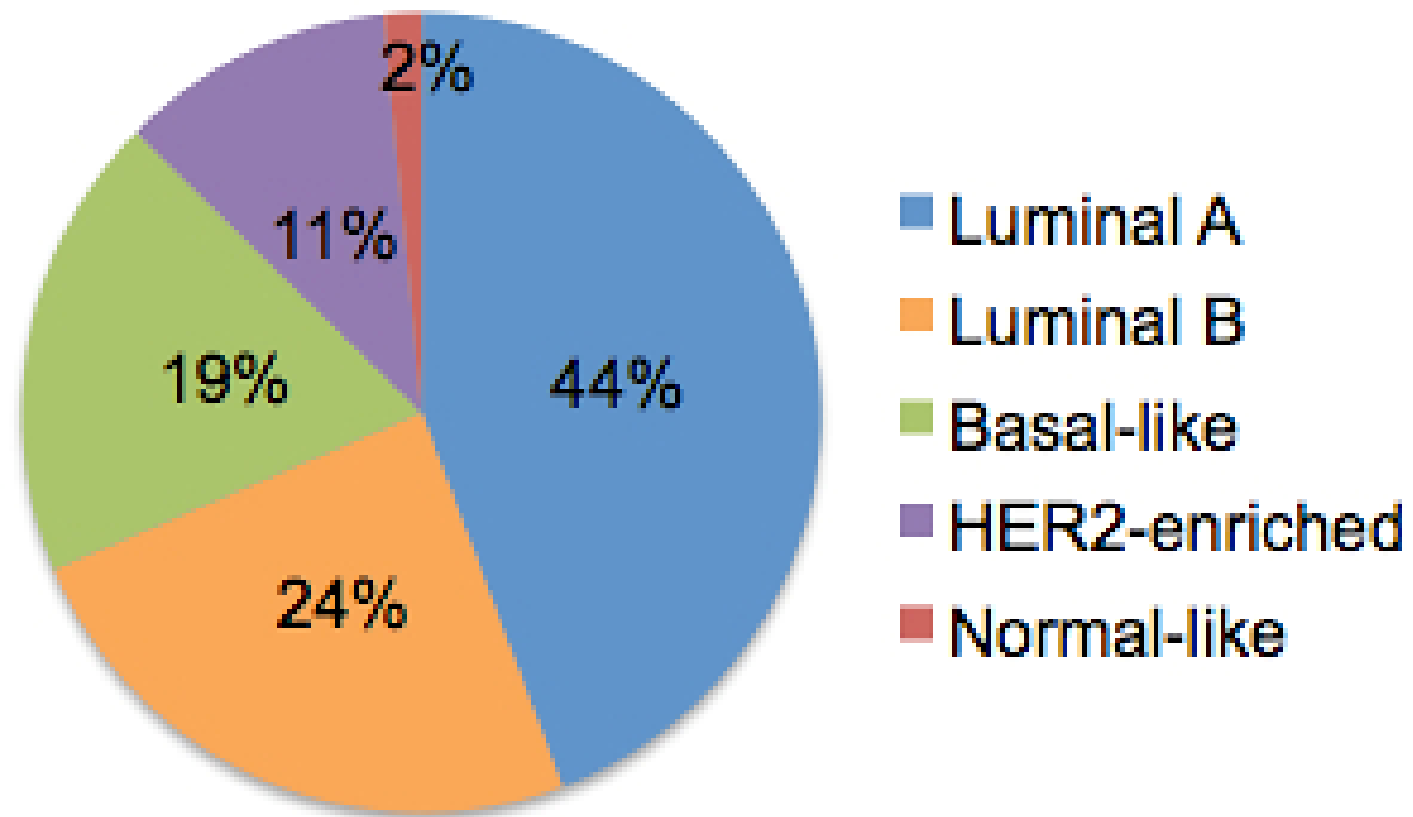
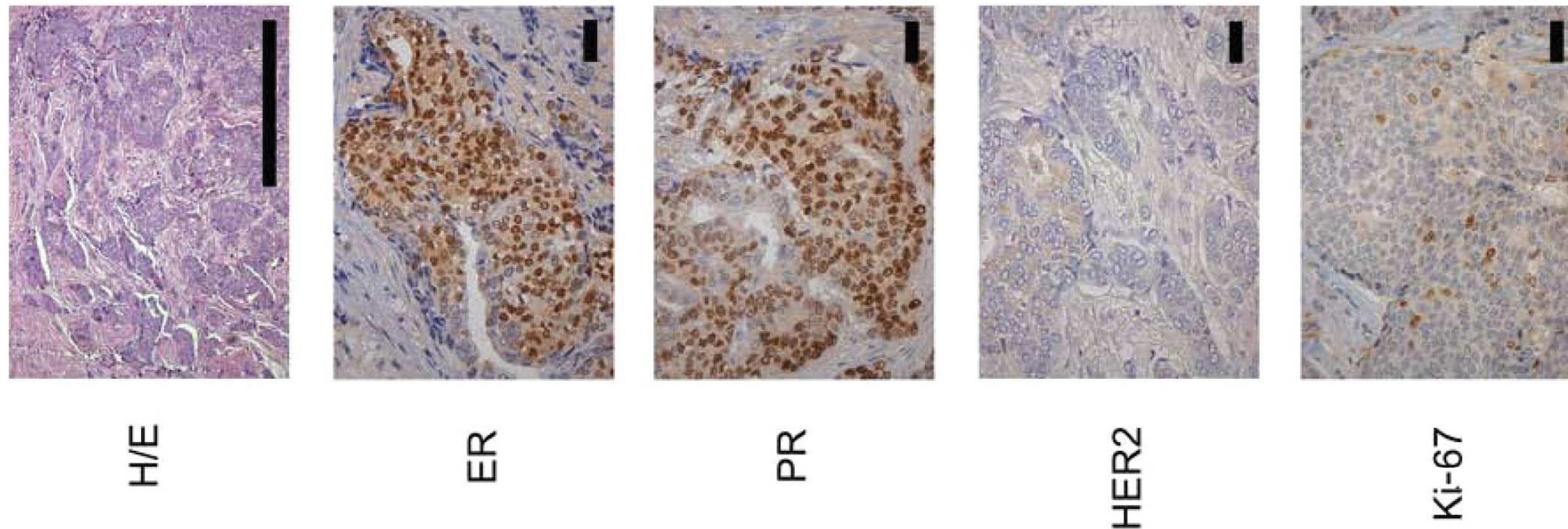
Endocrine treatment
Chemotherapy
Targeted therapy

Personalised treatment

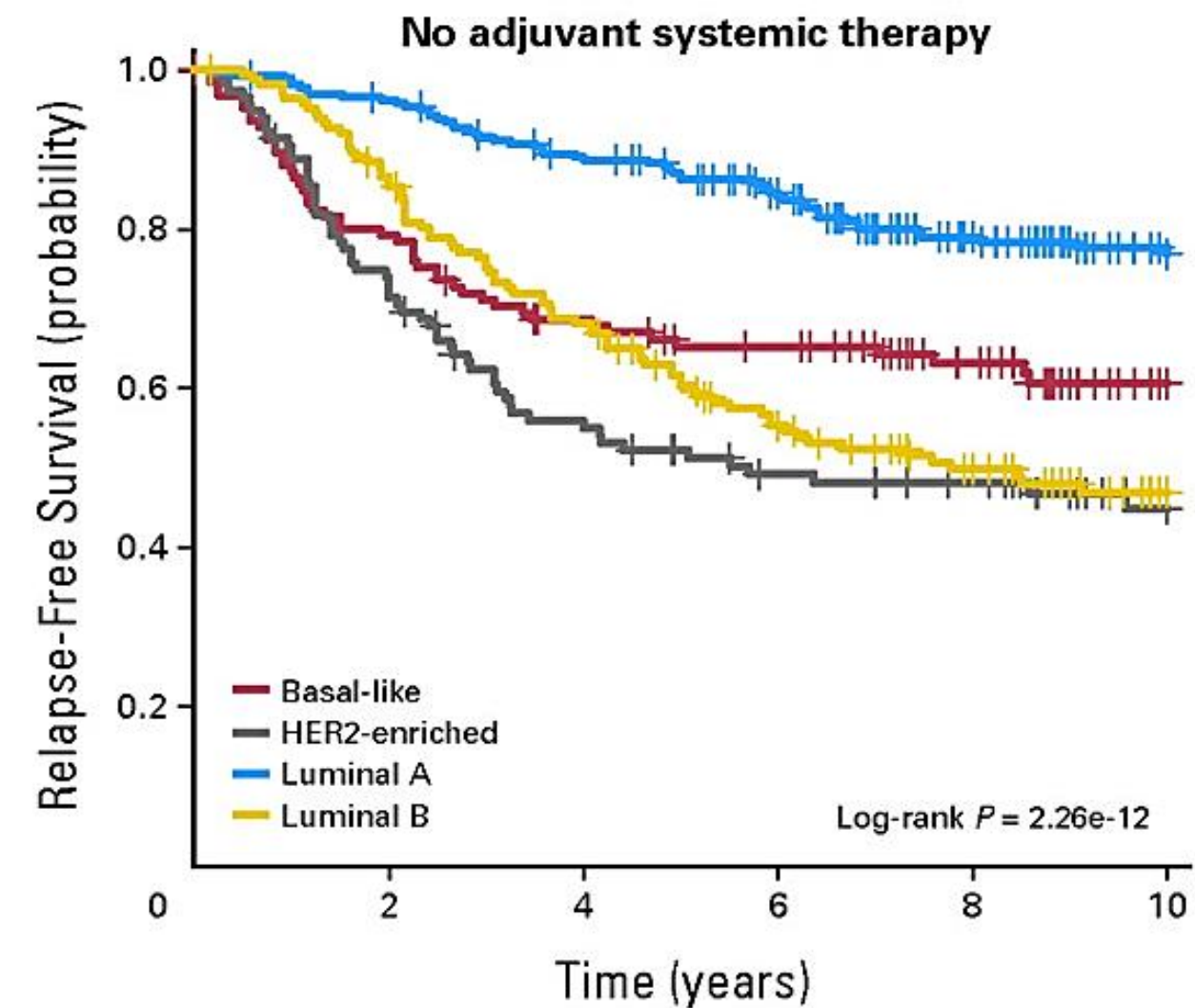


Who needs chemo
(De)Escalation in individualized cases

BC IS NOT ONE DISEASE



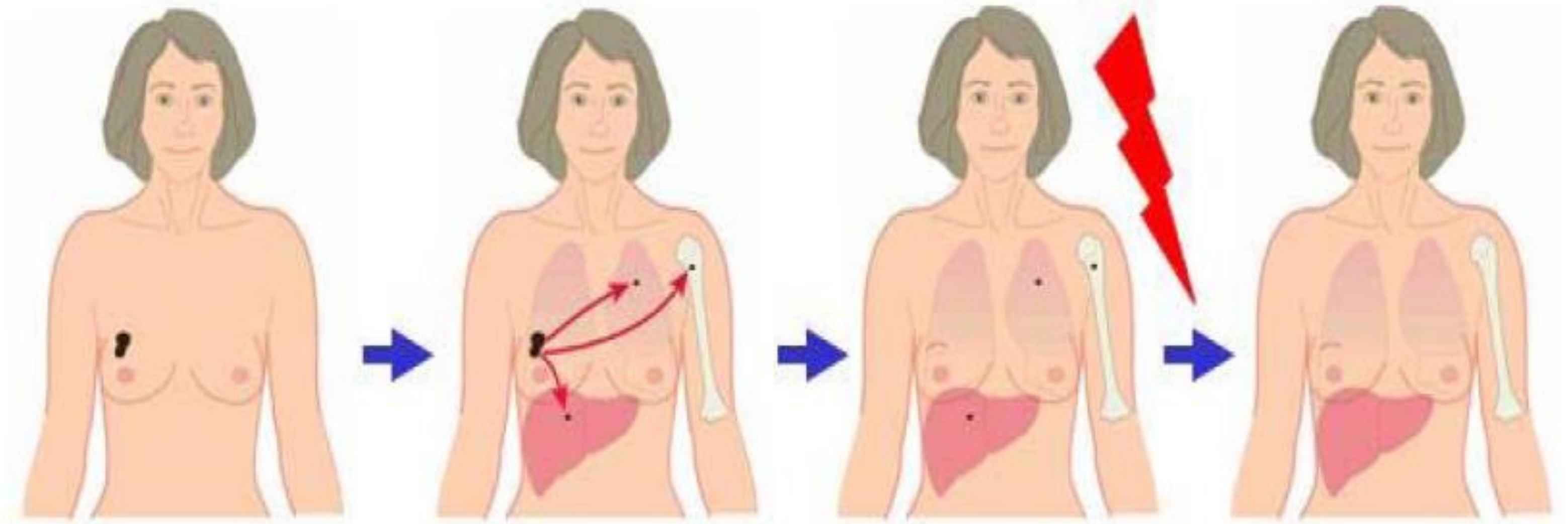
PAM50 intrinsic subtype prognosis for relapse-free survival (RFS)



ADJUVANT SYSTEMIC THERAPY

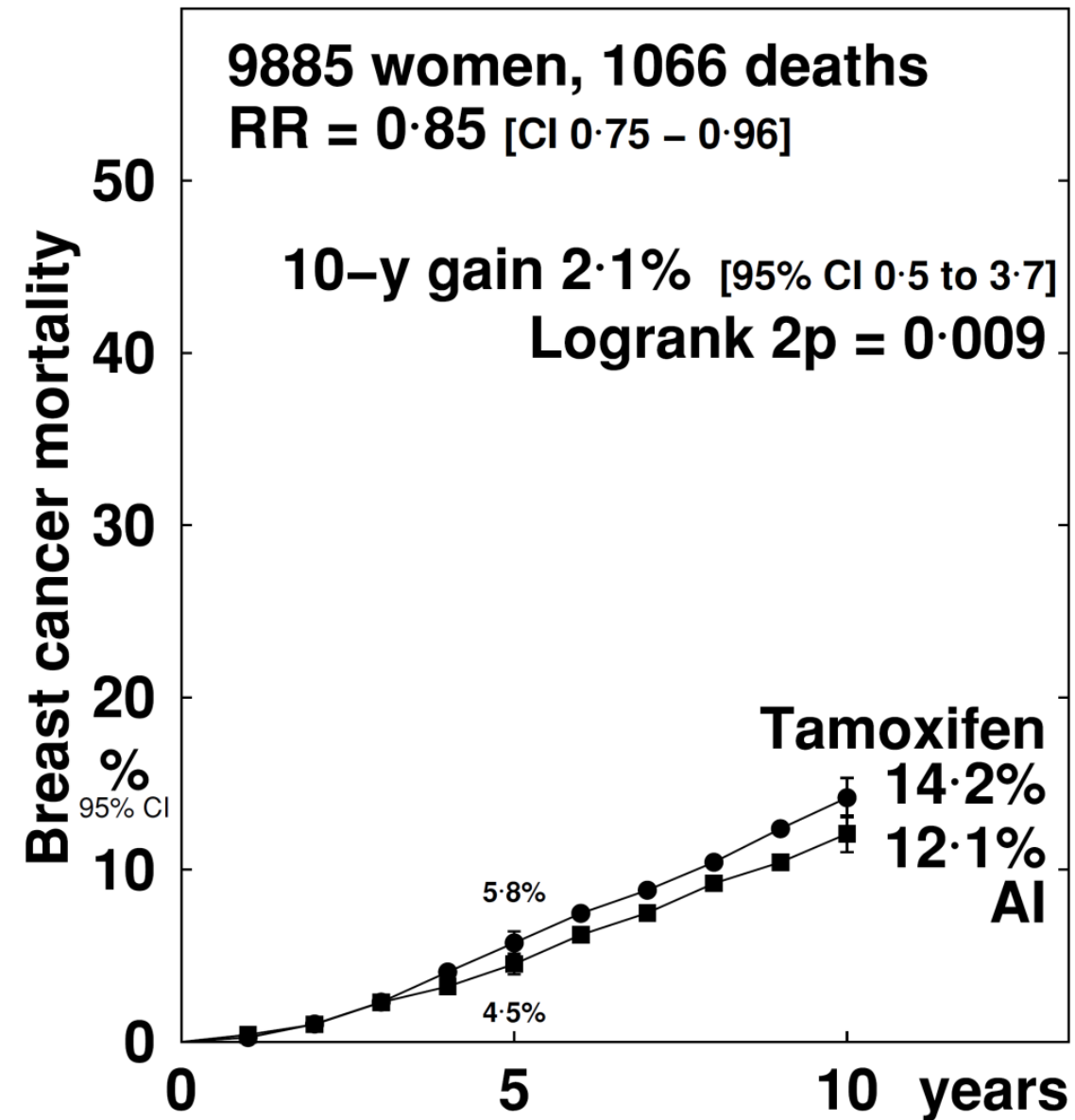
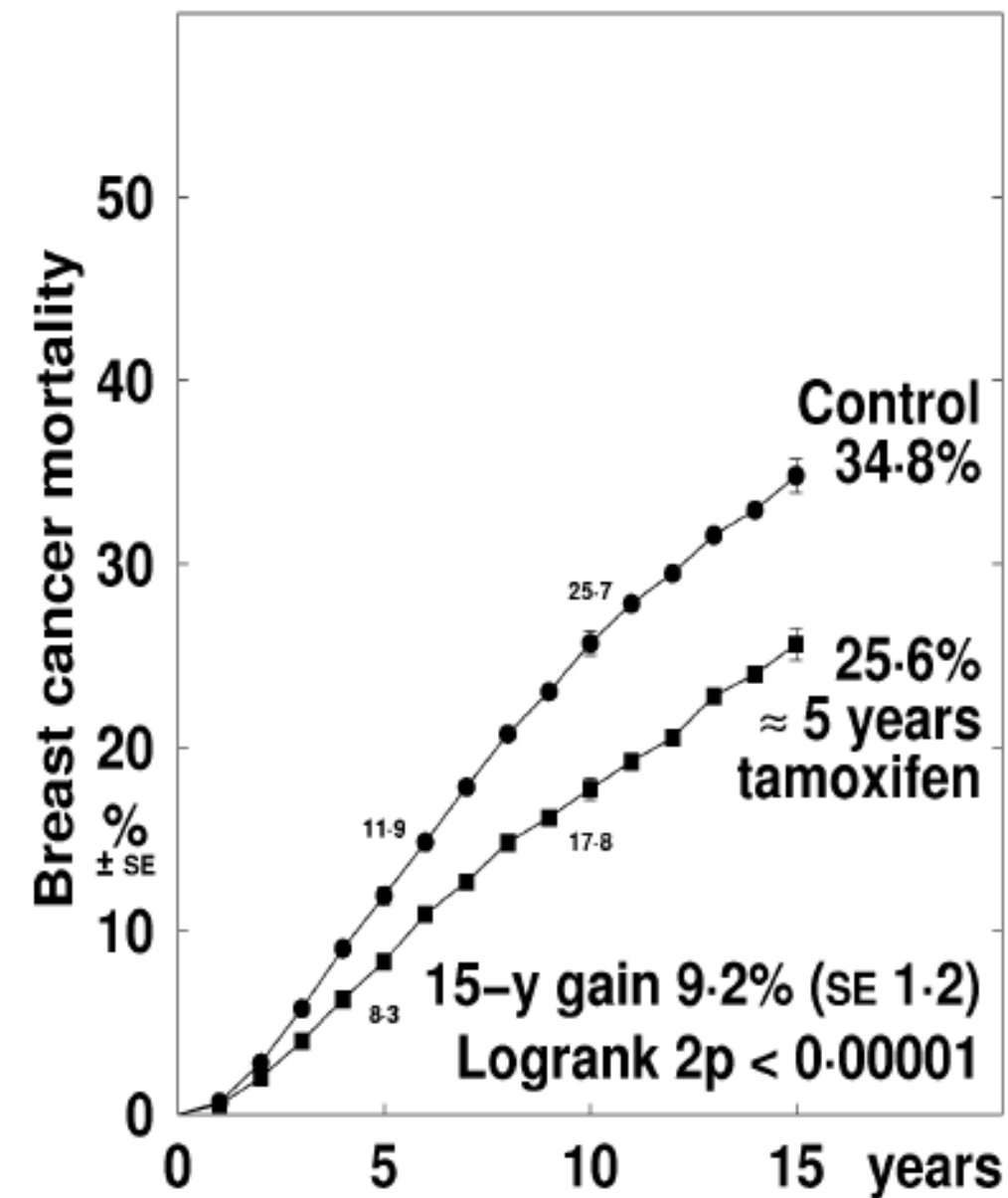
ADJUVANT SYSTEMIC THERAPY

Goal: eradication of micrometastasis and cure of patients



ER+/HER2- BREAST CANCER

ENDOCRINE THERAPY

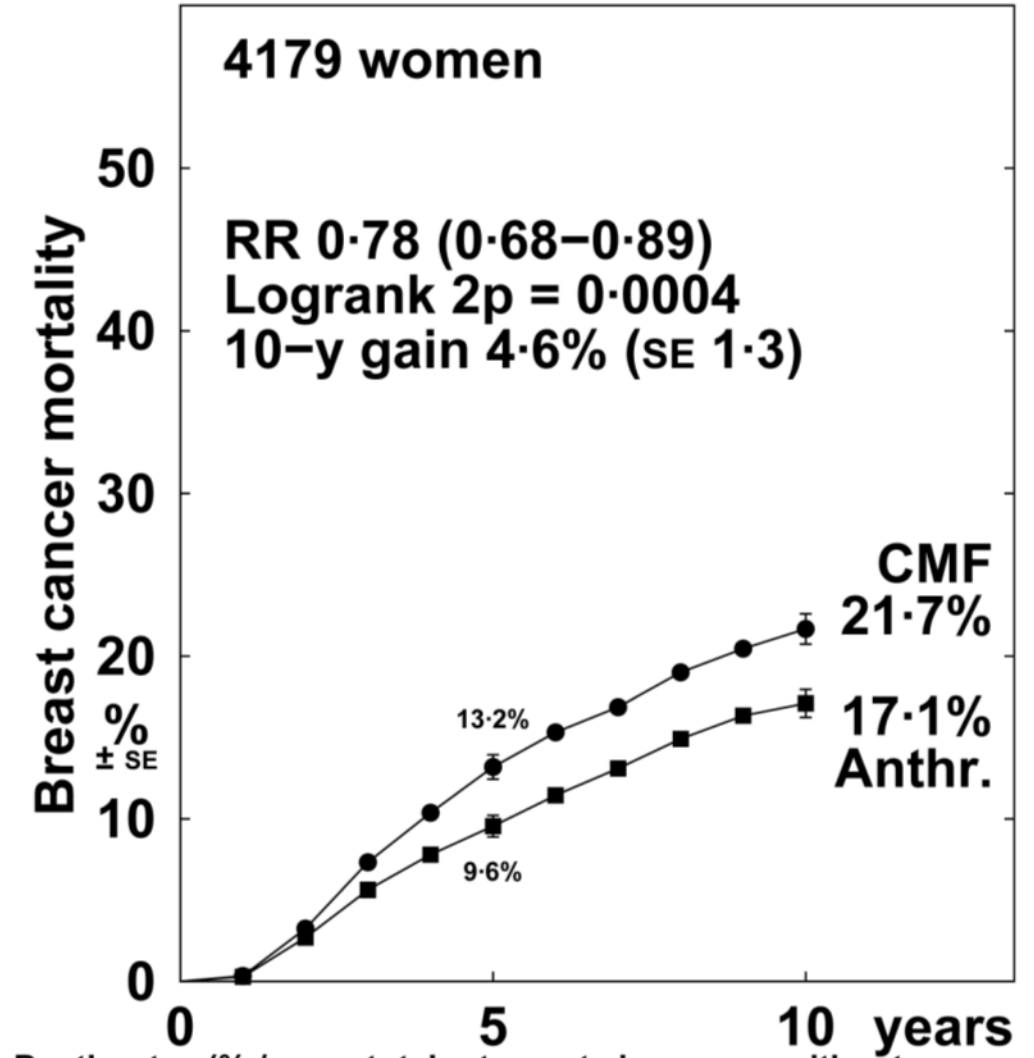


Death rates (% / year: total rate – rate in women without recurrence) & logrank statistics

Allocation	Years 0 – 1	Years 2 – 4	Years 5 – 9	Year 10+
AI	0.52 [CI 0.39 – 0.66]	1.23 [CI 1.05 – 1.41]	1.66 [CI 1.46 – 1.86]	1.93 [CI 0.88 – 2.99]
Tamoxifen	0.51 [CI 0.39 – 0.67]	1.60 [CI 1.38 – 1.83]	1.81 [CI 1.60 – 2.02]	1.88 [CI 0.77 – 2.99]
Rate ratio, from (O-E) / V	0.98 [CI 0.66 – 1.46] -0.4 / 24.3	0.74 [CI 0.60 – 0.91] -27.2 / 90.7	0.90 [CI 0.76 – 1.07] -13.6 / 129.4	1.01 [CI 0.45 – 2.33] 0.1 / 5.6

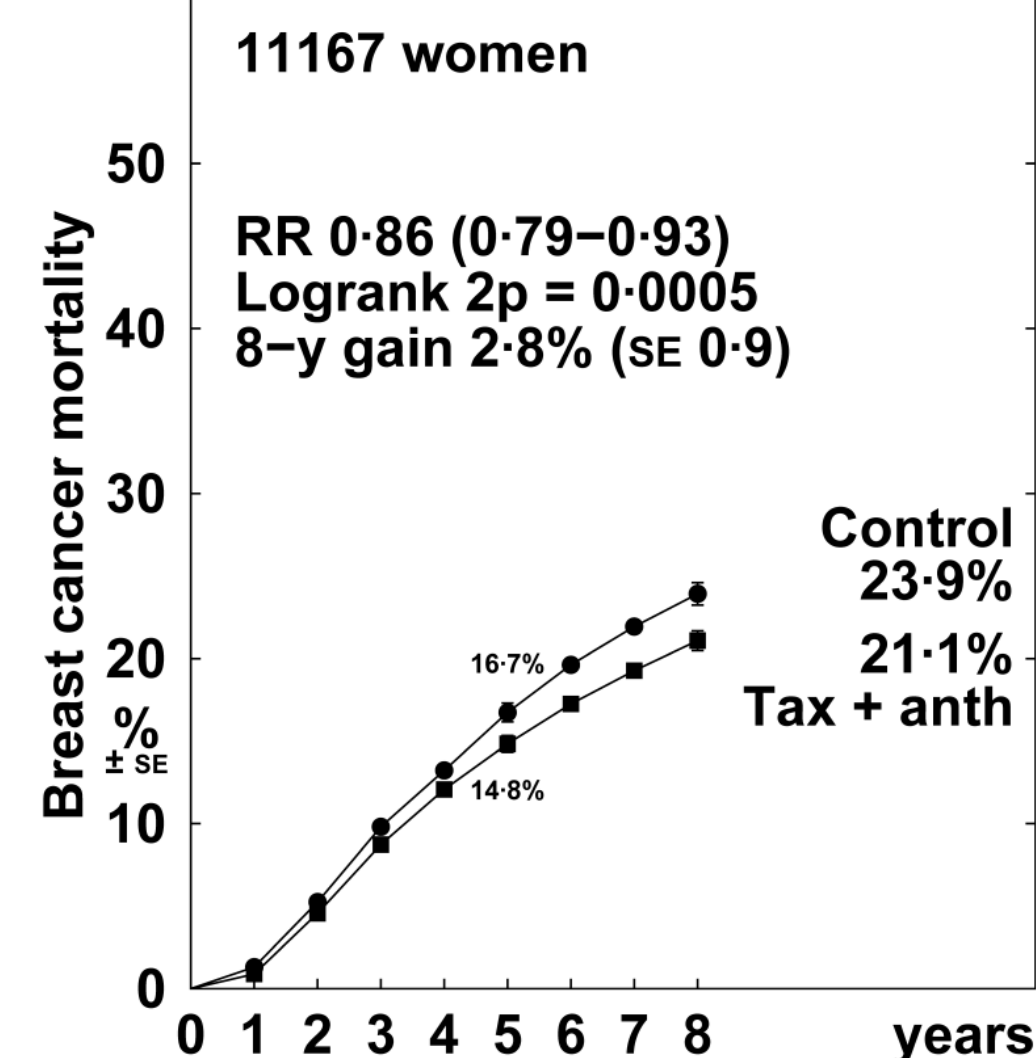
CHEMOTHERAPY EVOLUTION

CMF \implies Antracyclines \implies Antra/taxanes \implies Dose dense



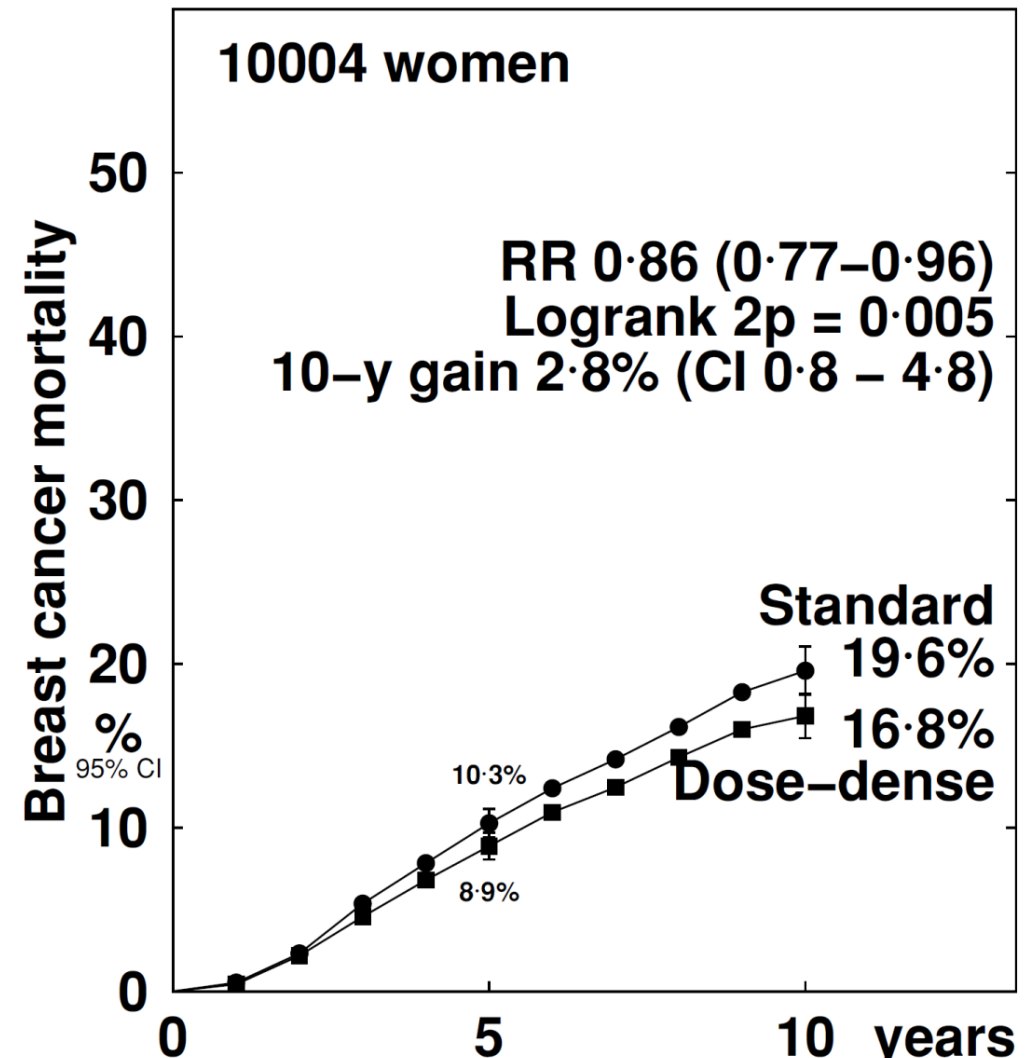
Death rates (% / year: total rate – rate in women without recurrence)

Allocation	Years 0 – 4	Years 5 – 9	Year 10+
Anthr.	2.03 SE 0.14	1.75 SE 0.15	0.88 SE 0.15
CMF	2.76 SE 0.17	2.11 SE 0.16	0.93 SE 0.15
Rate ratio	0.71 SE 0.08	0.85 SE 0.11	0.94 SE 0.24
(O-E) / V	-37.0 / 109.0	-11.8 / 72.2	-1.1 / 16.7



Death rates (% / year: total rate – rate in women without recurrence)

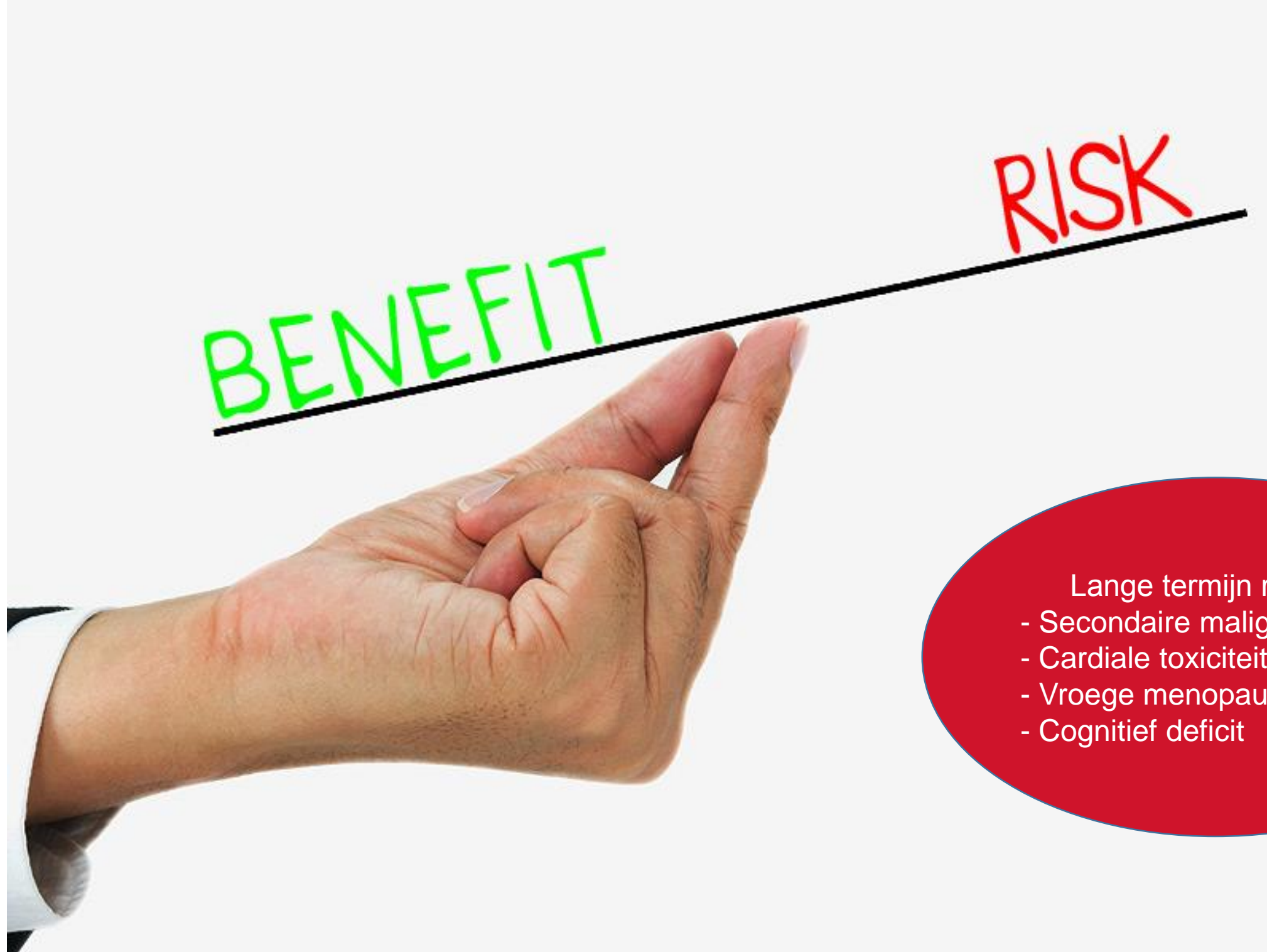
Allocation	Years 0 – 4	Year 5+
Tax + anth	3.21 SE 0.11	2.48 SE 0.13
Control	3.58 SE 0.13	3.06 SE 0.16
Rate ratio	0.88 SE 0.05	0.82 SE 0.07
(O-E) / V	-46.4 / 348.5	-33.3 / 172.3



CHEMOTHERAPY COMES AT A COST



CHEMO OR NO CHEMO



- Lange termijn risico's:
- Secondaire maligniteit
 - Cardiale toxiciteit
 - Vroege menopauze
 - Cognitief deficit

GENOMIC TESTS MOSTLY USED IN ER + BREAST CANCER

GENOMIC TESTS

oncotype[®] DX[®]
Breast Cancer Assa



mammaprint[®]

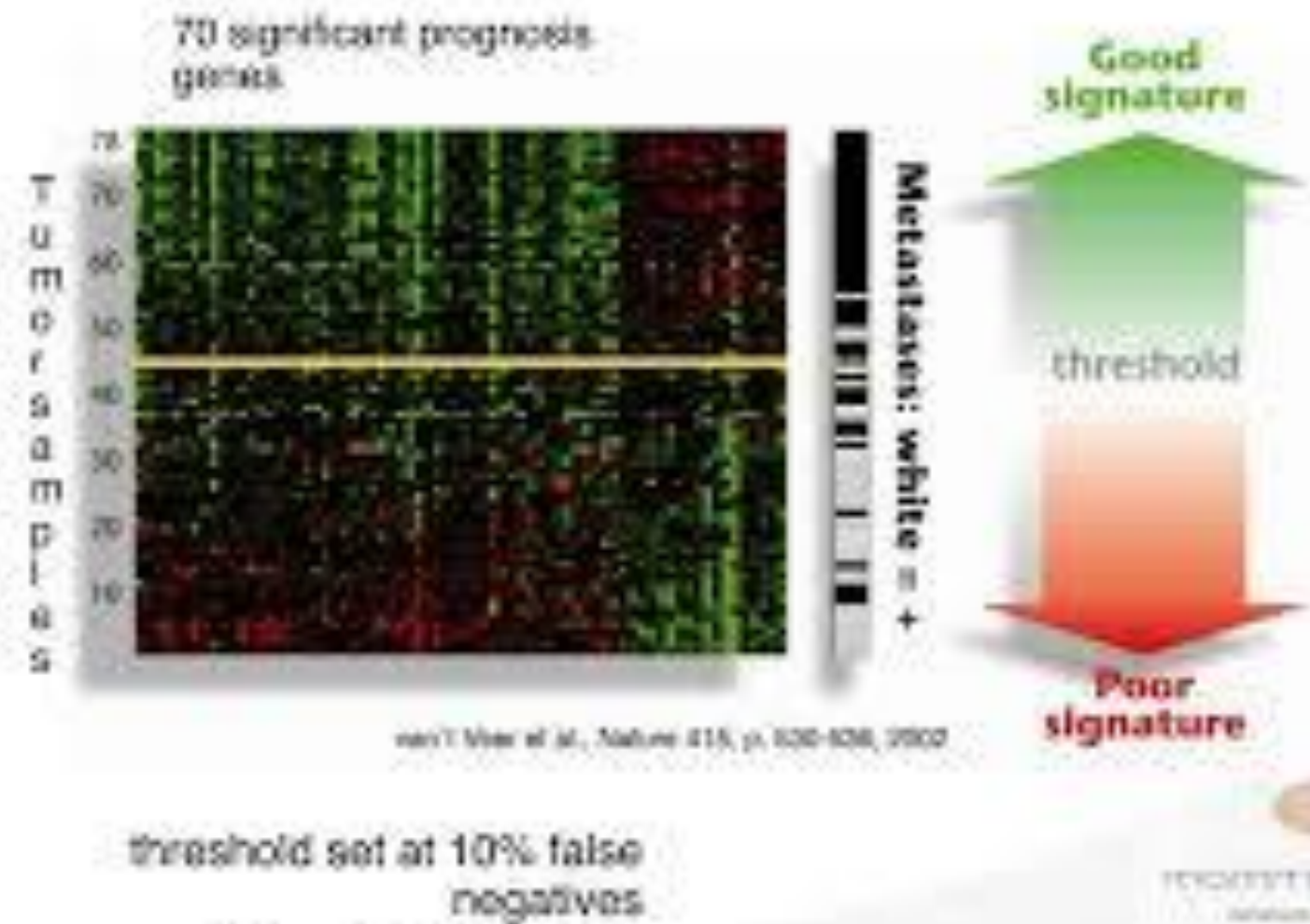


prosigna[™]

USE OF GENOMIC TUMOR CHARACTERISTICS TO DECIDE WHO NEEDS CHEMO AND WHO DOESN'T

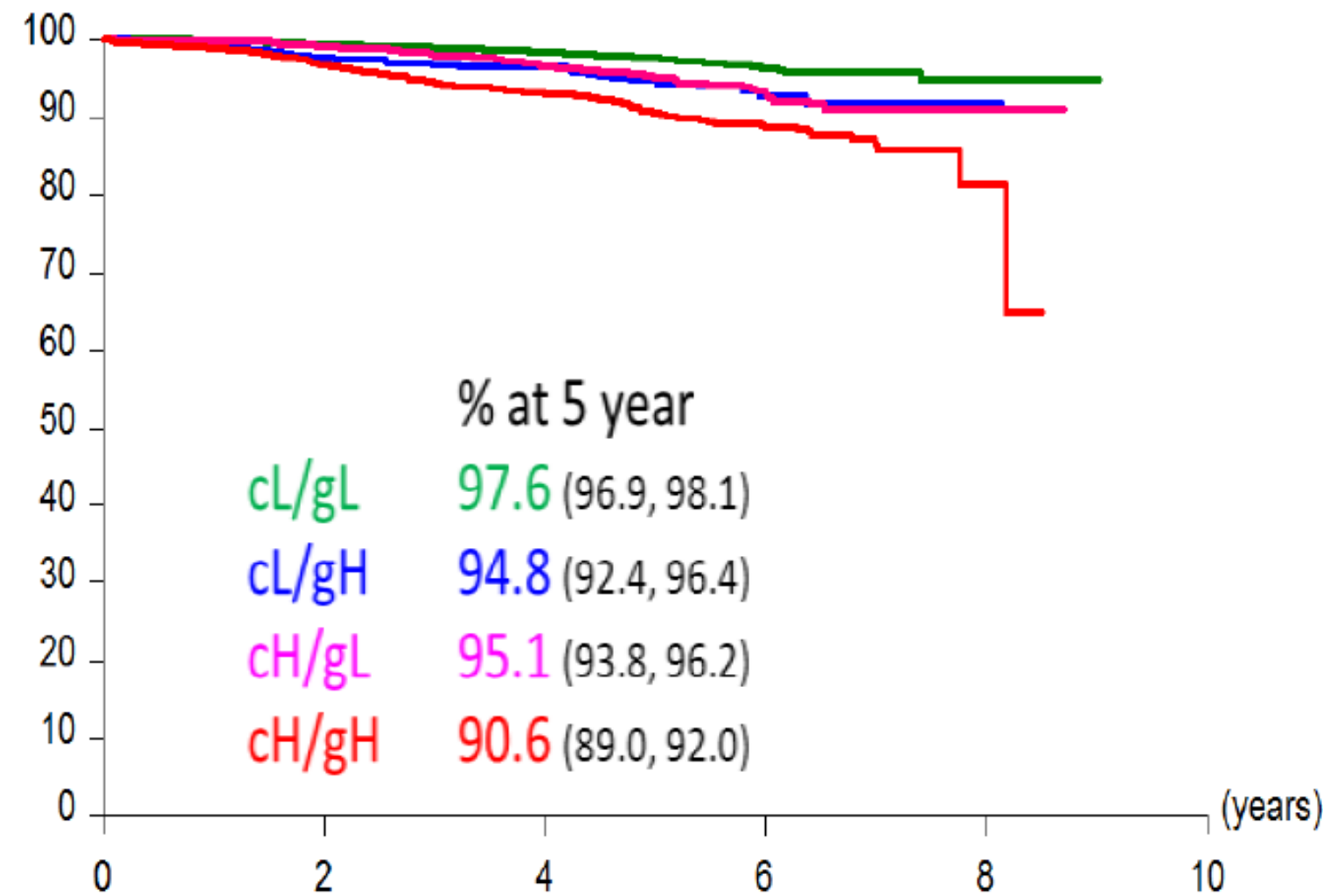


MammaPrint prognosis Profile
"the 70 gene profile"



CLINICAL OUTCOME IN MINDACT TRIAL

Distant Metastasis Free Survival



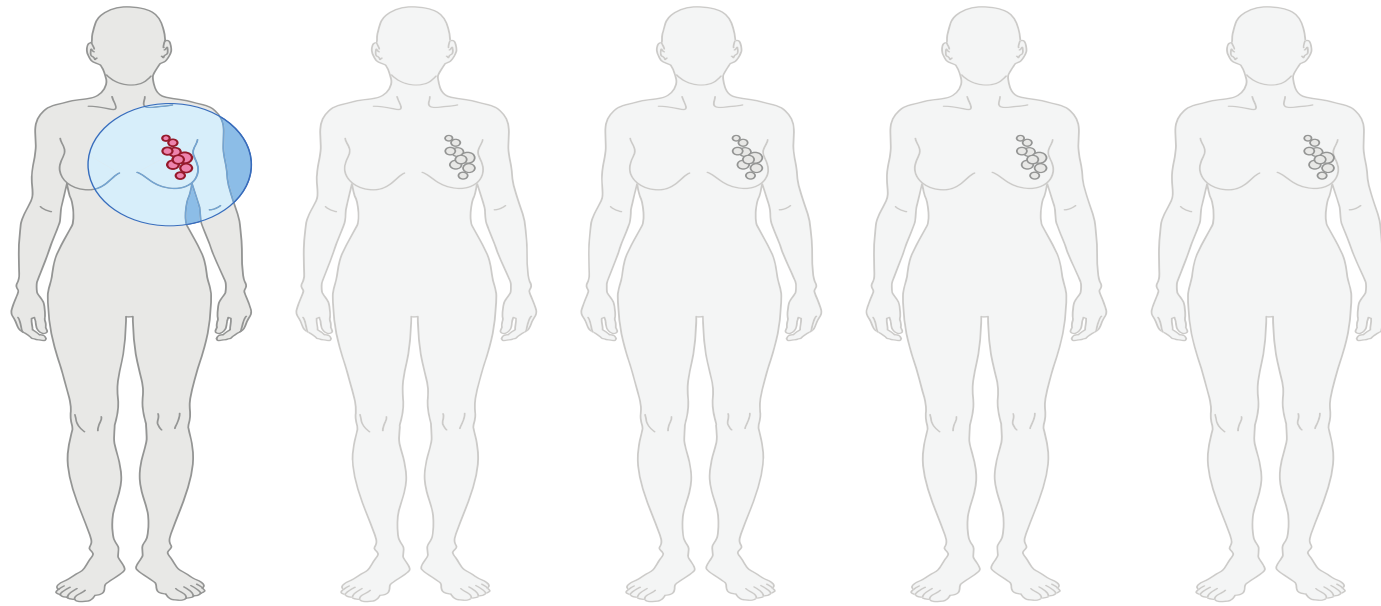
O	N	Number of patients at risk :				corrected risk
77	2745	2628	2331	735	33	cL/gL
32	592	550	484	136	2	cL/gH
82	1550	1457	1317	311	9	cH/gL
171	1806	1689	1462	395	11	cH/gH

MAMMAPRINT

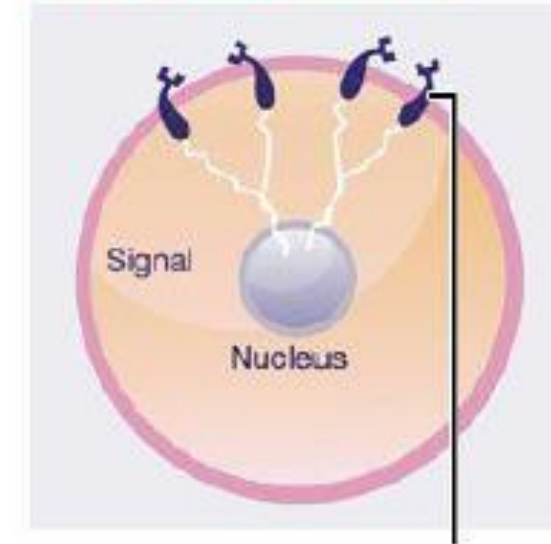
- Not for all BC patients
- Not for low risk patients
- Not for HER2 or high risk TN BC
- Not for patients who want chemo even for little benefit
- Goal: identification of **clinical high, genomic low** patients who will have limited benefit from chemotherapy (Moc decision)

HER2 + BREAST CANCER

1 IN 5 BREAST CANCERS IS HER2-POSITIVE

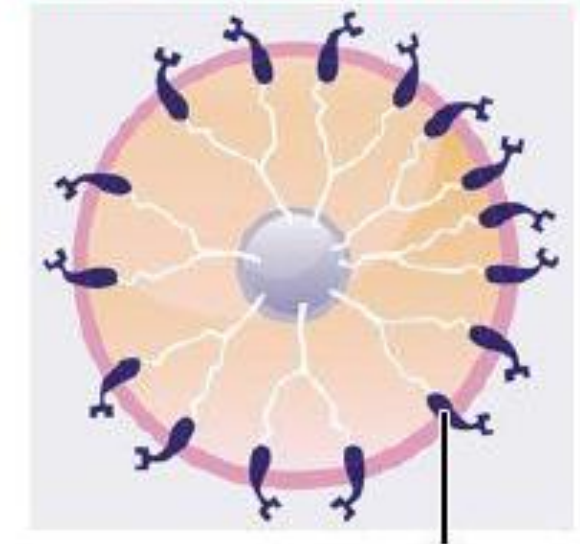


Normal breast cancer cell



Normal amount of HER2 receptors send signals telling cells to grow and divide.¹

Abnormal HER2+ breast cancer cell

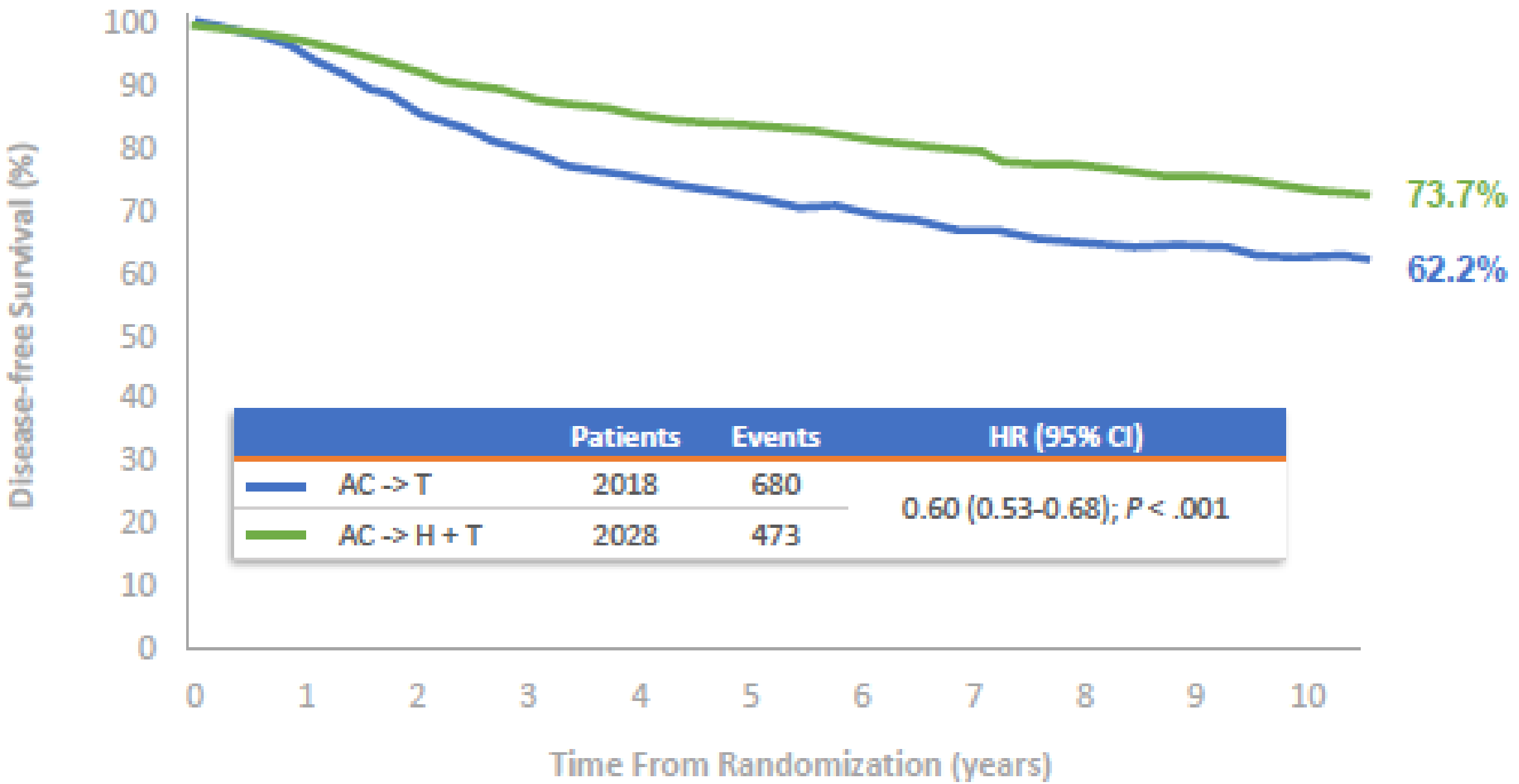


Too many HER2 receptors send more signals, causing cells to grow too quickly.¹

HER2-positive breast cancer is an **aggressive** form of the disease.
If left untreated, it is linked to poor chances of survival.

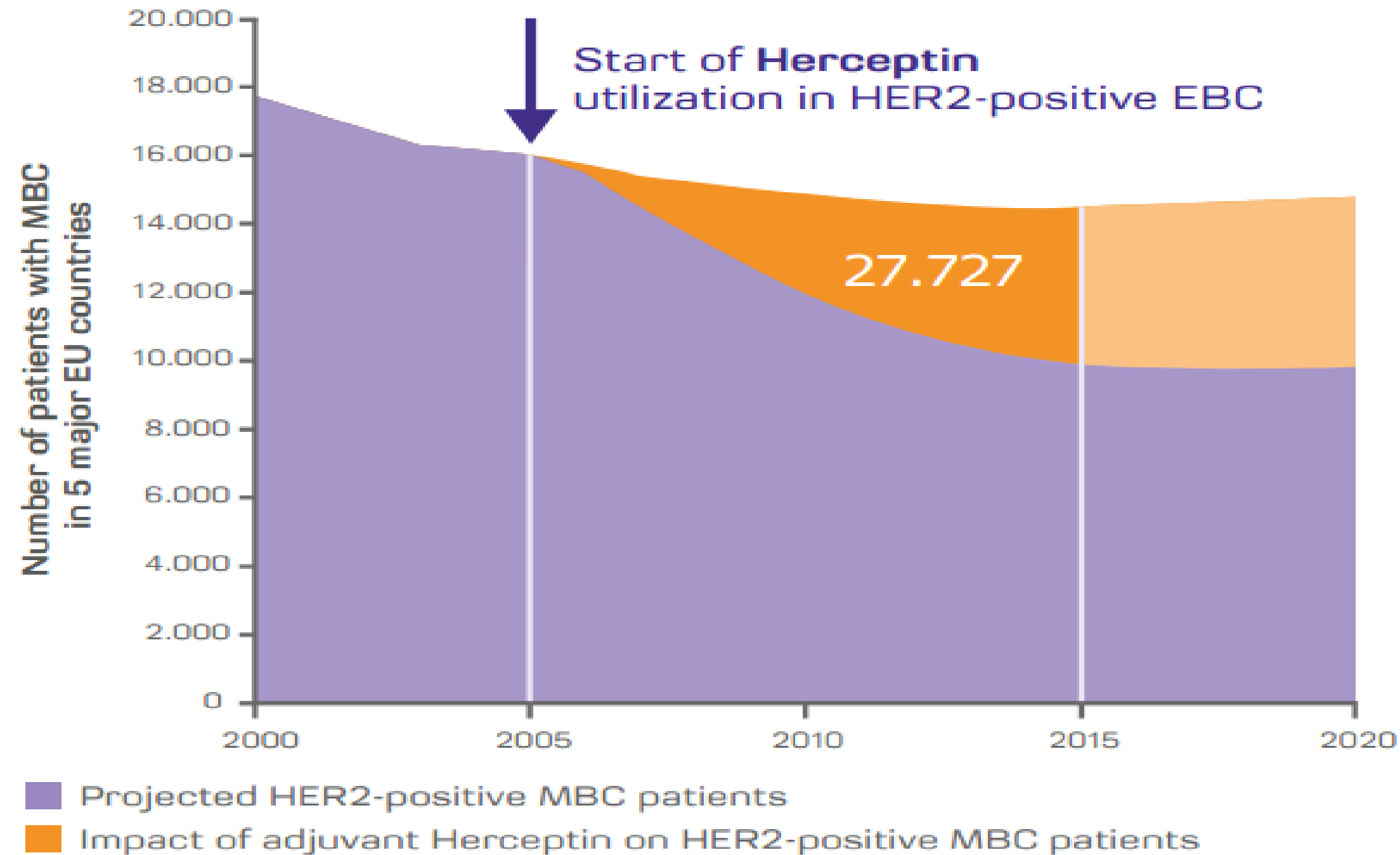
ADJUVANT HERCEPTIN SIGNIFICANTLY IMPROVES RISK OF RECURRENCE IN HER2+ EBC

NCCTG N9831 and NSABP B-31 Joint Analysis²



Impact of Herceptin on numbers of patients with HER2+ mBC

Impact of Herceptin on numbers of patients with HER2-positive MBC



TRIPLE NEGATIVE BREAST CANCER

TRIPLE NEGATIVE BC

- ER-
- PR-
- HER2-



CHEMOTHERAPY

NEO-ADJUVANT THERAPY: HOLD THAT SCAPEL

ADJUVANTE CHEMO



NEOADJUVANT CHEMOTHERAPY

- Her2 or TNBC

- downstaging

- pCR, prognostic

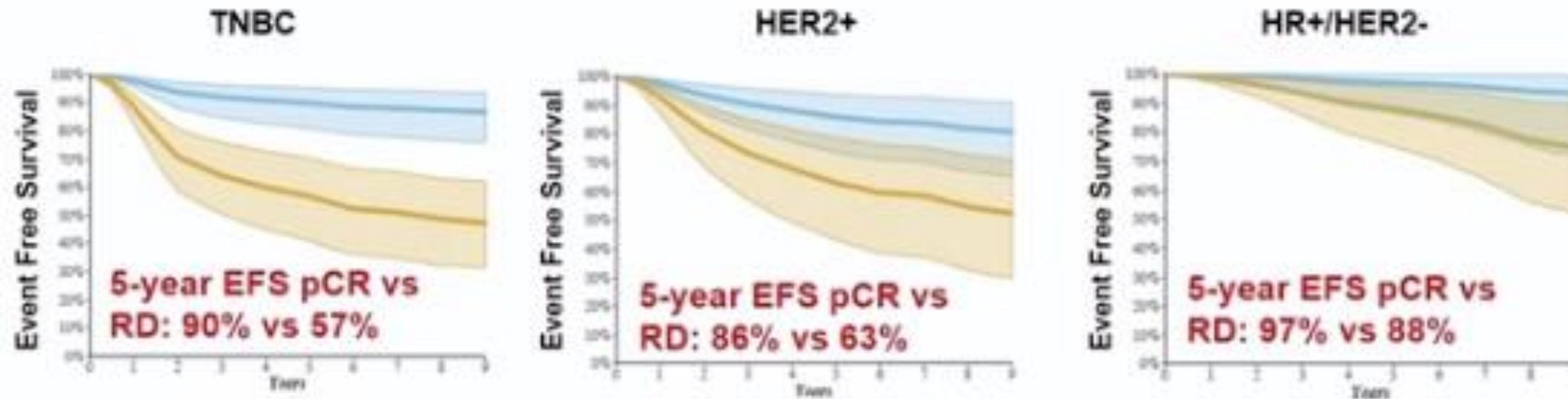
- **Adjustement post therapy**

- ER+/HER2- BC

- pCR less frequent, prognostic less important

PCR AFTER NEOADJUVANT CHEMOTHERAPY AND IMPACT ON BREAST CANCER RECURRENCE AND SURVIVAL : META-ANALYSIS OF OVER 27.000 PATIENTS

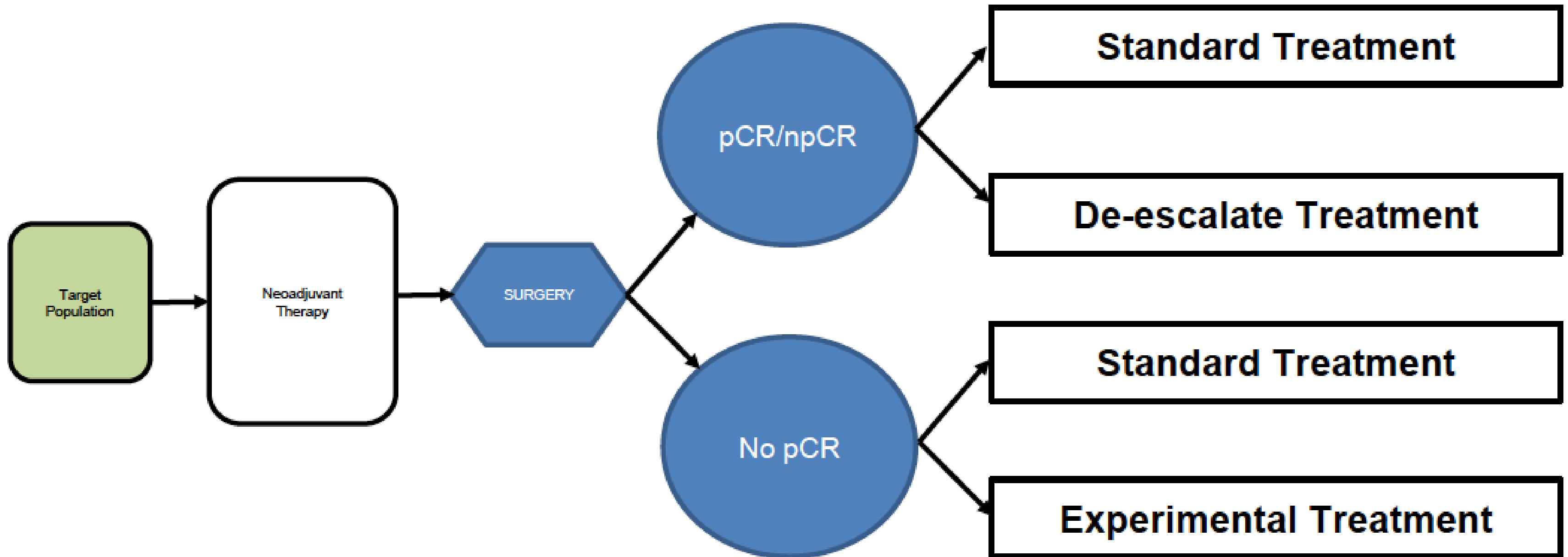
Results: EFS and OS by Subtype



Blue: pCR group

Orange: Residual disease (RD) group

DESIGNS BASED ON RESPONSE TO THERAPY



HER2+ EBC

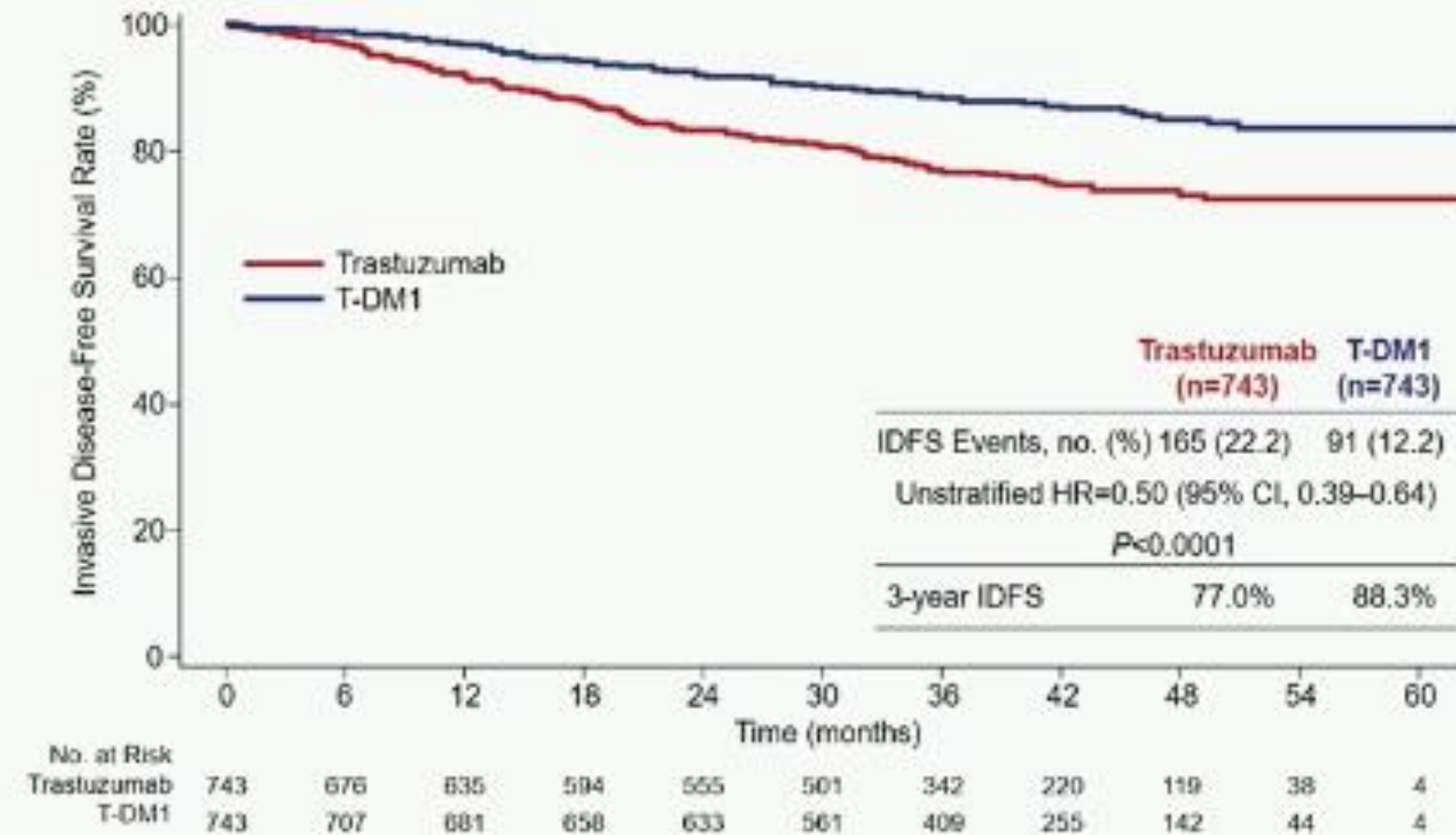
KATHERINE Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
 - Minimum of 6 cycles of chemotherapy
 - Minimum of 9 weeks of taxane
 - Anthracyclines and alkylating agents allowed
 - All chemotherapy prior to surgery
 - Minimum of 9 weeks of trastuzumab
 - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



Stratification factors:

- Clinical presentation: Inoperable (stage cT4 or cN2-3) vs operable (stages cT1-3)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs negative/not done



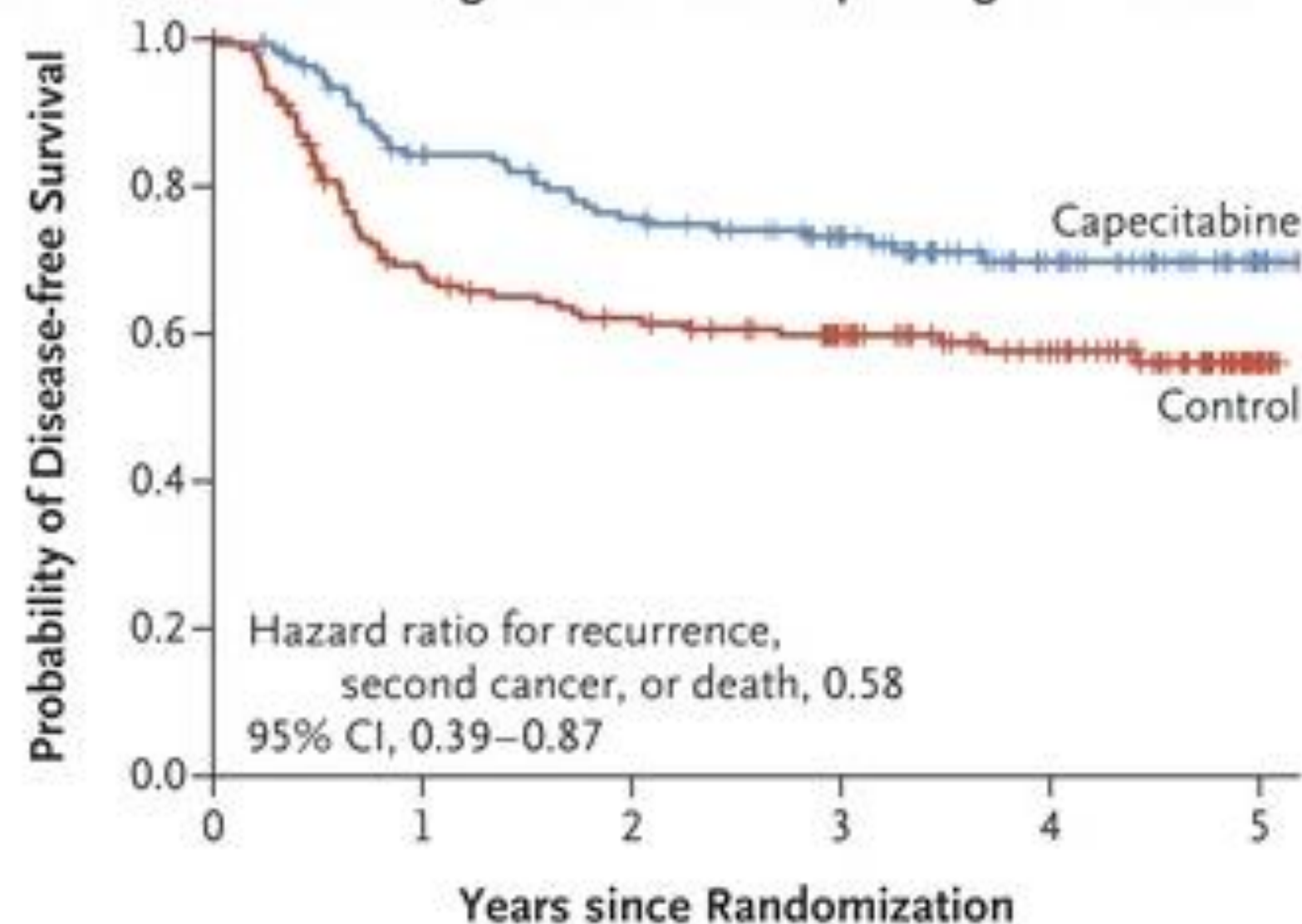
TNBC



Stratification factors:
ER, Age, NAC, ypN,
5FU and institution

Standard therapy:
HR+: Hormone therapy
HR-: No further systemic treatment

Disease-free Survival among Patients with Triple-Negative Disease

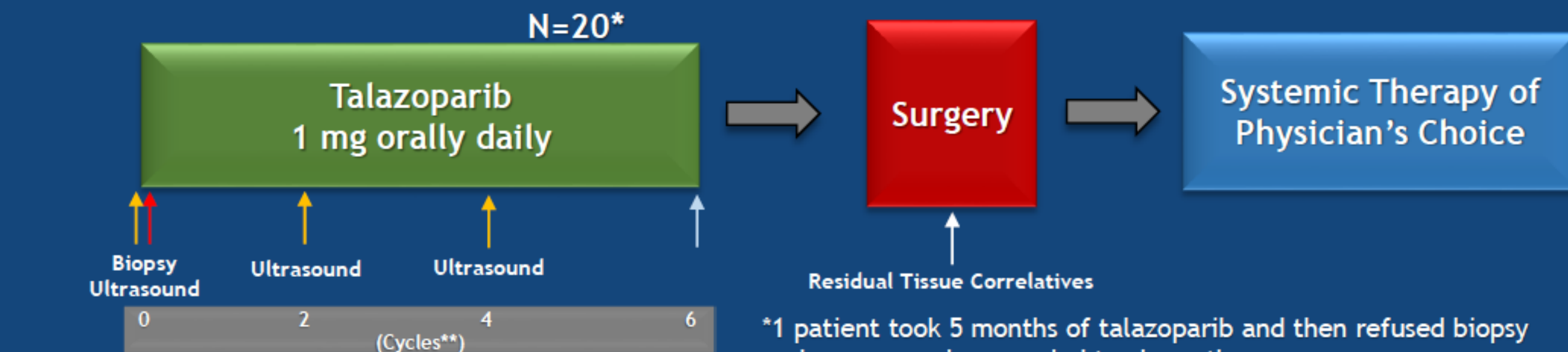


No. at Risk

Capecitabine	139	109	96	76	42	11
Control	147	95	84	69	47	6

BRCA+ BREAST CANCER

Study Design



*1 patient took 5 months of talazoparib and then refused biopsy and surgery and proceeded to chemotherapy

** 1 cycle=28 days

Eligibility

- Tumors > 1 cm
- Clinical Stage I-III
- Germline BRCA mutation
- No previous therapy

Exclusion

- HER2 positive

Primary Objectives

- pCR (ypT0/is ypN0)
- RCB-0 + RCB-I

Secondary Objective

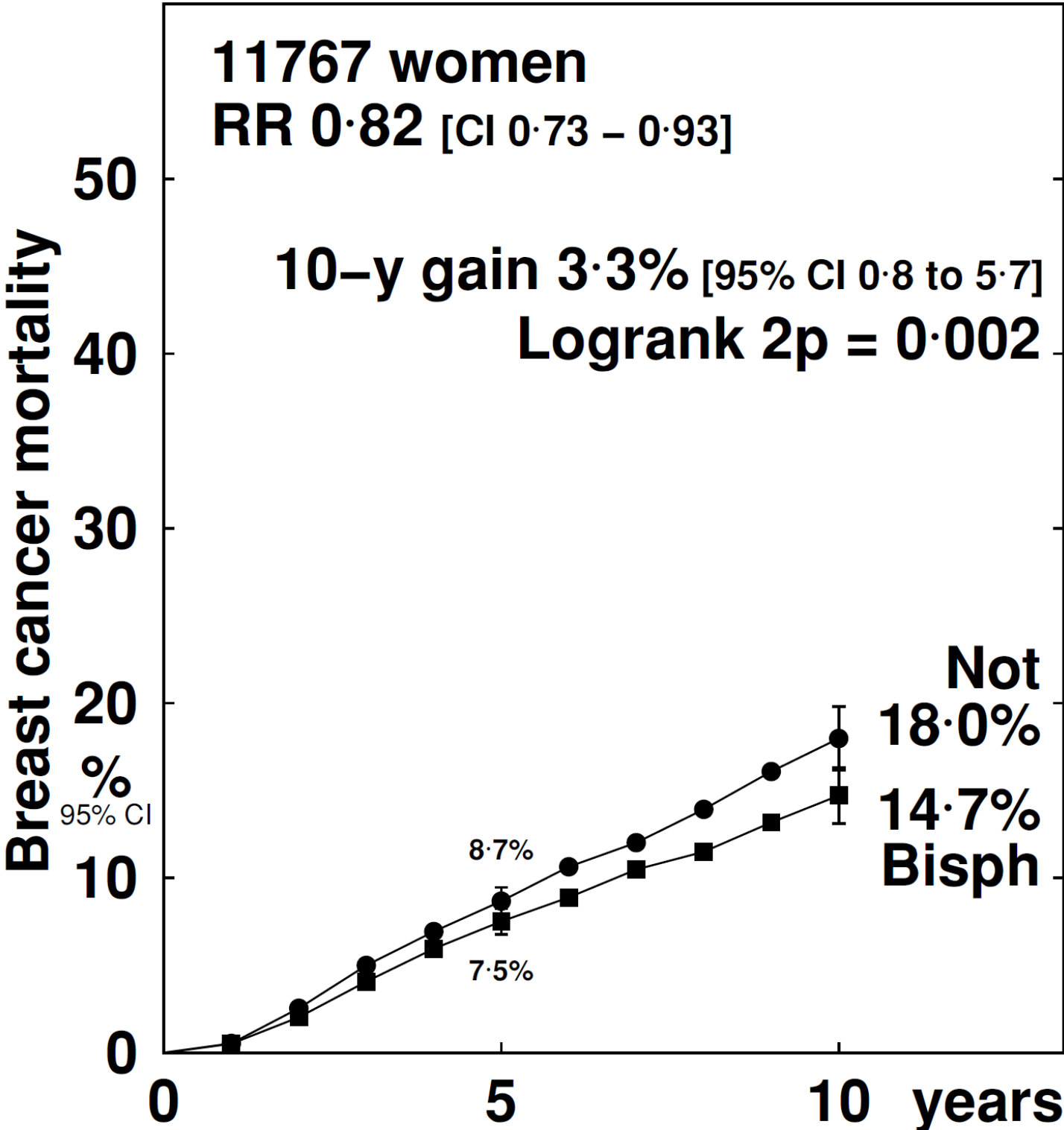
- Evaluate toxicity

pCR 63%

BISPHOSPHONATES

BISFOSFONATEN

Every 6months, in total 6x



Death rates (% / year: total rate – rate in women without recurrence) & logrank statistics

Allocation	Years 0 – 4	Years 5 – 9	Year 10+
Bisph	1.56 [CI 1.41 – 1.72]	1.57 [CI 1.30 – 1.84]	1.30 [CI 0.34 – 2.26]
Not	1.74 [CI 1.58 – 1.91]	2.04 [CI 1.74 – 2.35]	2.73 [CI 1.30 – 4.16]
Rate ratio, from (O–E) / V	0.86 [CI 0.72 – 0.99] –27.1 / 174.9	0.76 [CI 0.55 – 0.97] –18.0 / 65.0	0.52 [CI 0.18 – 1.44] –2.4 / 3.6

CONCLUSION:

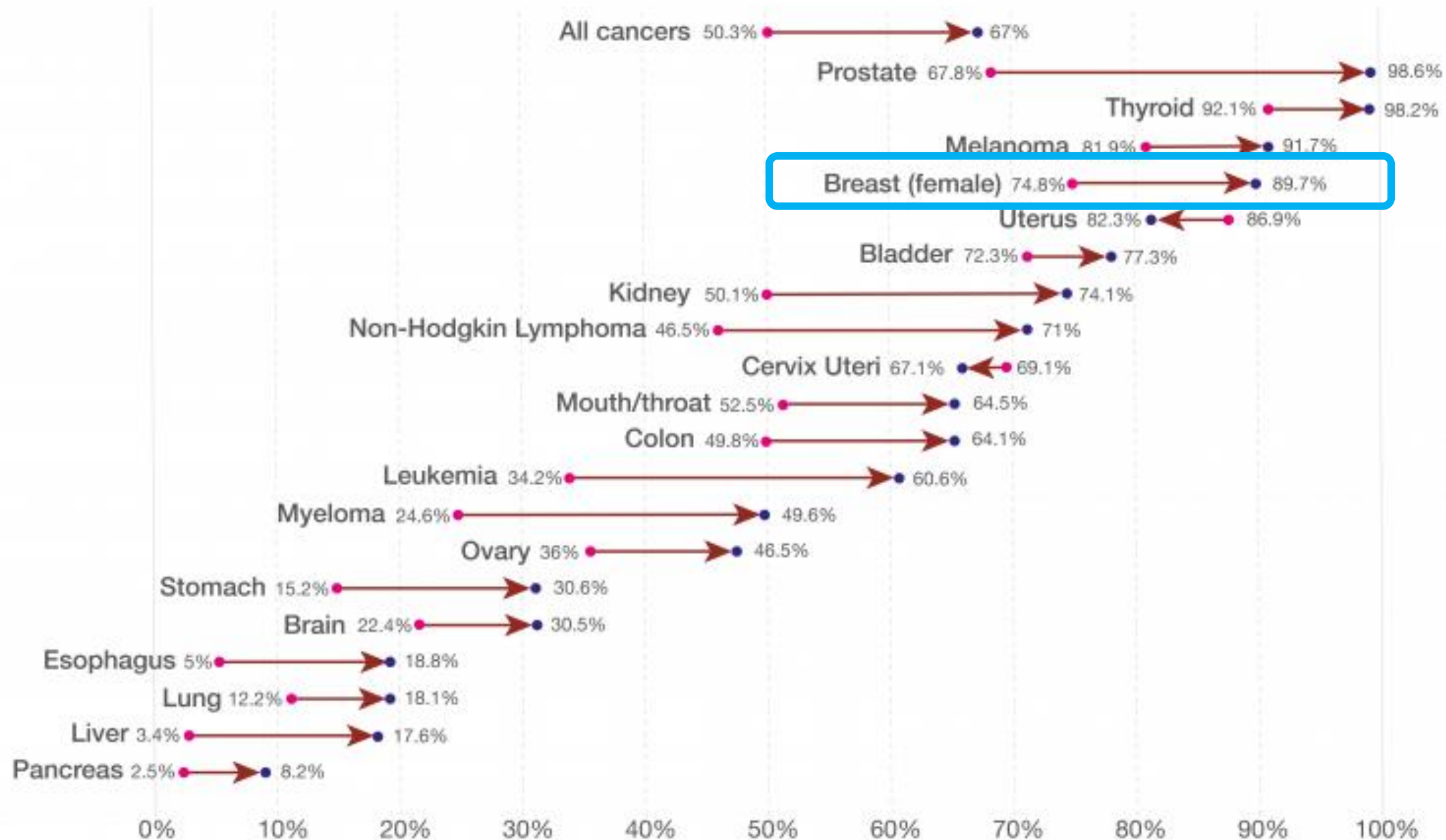
PILING UP SMALL IMPROVEMENTS LEADS TO BETTER PROGNOSIS



EVOLUTION BC PROGNOSIS

Five-year cancer survival rates in the USA

Average five-year survival rates from common cancer types in the United States, shown as the rate over the period 1970-77 [●] and over the period 2007-2013 [●]: 1970-77 → 2007-2013
This five-year interval indicates the percentage of people who live longer than five years following diagnosis.

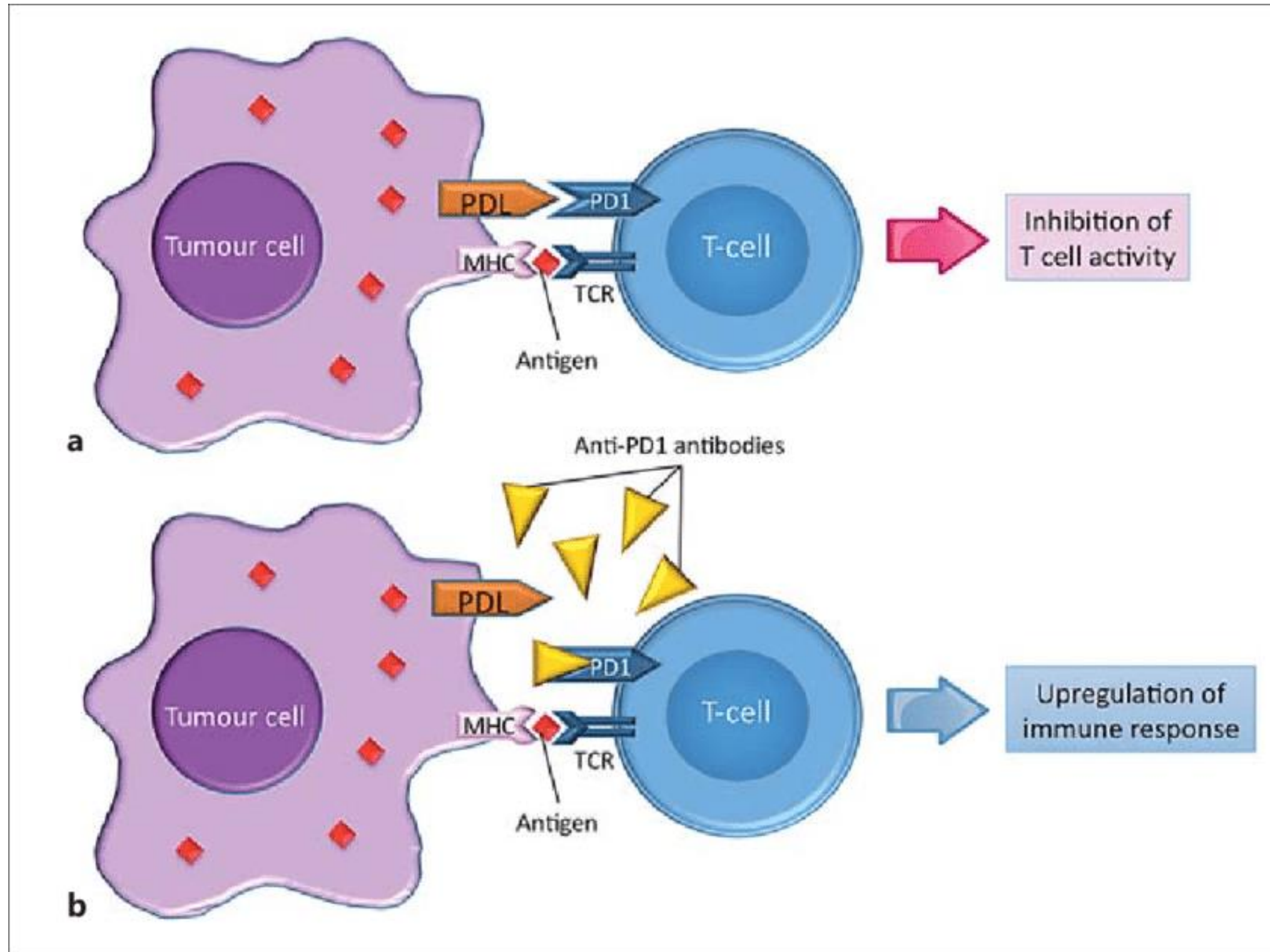


Based on data by Journal of the National Cancer Institute; Surveillance, Epidemiology and End Results Program.
The data visualization is available at [OurWorldinData.org](https://ourworldindata.org). There you find research and more visualizations on this topic.

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EXAMPLES OF NEW ADJUVANT THERAPIES/COMBINATIONS IN CLINICAL TRIALS

IMMUNOTHERAPY



CDK4/6 INHIBITORS

