

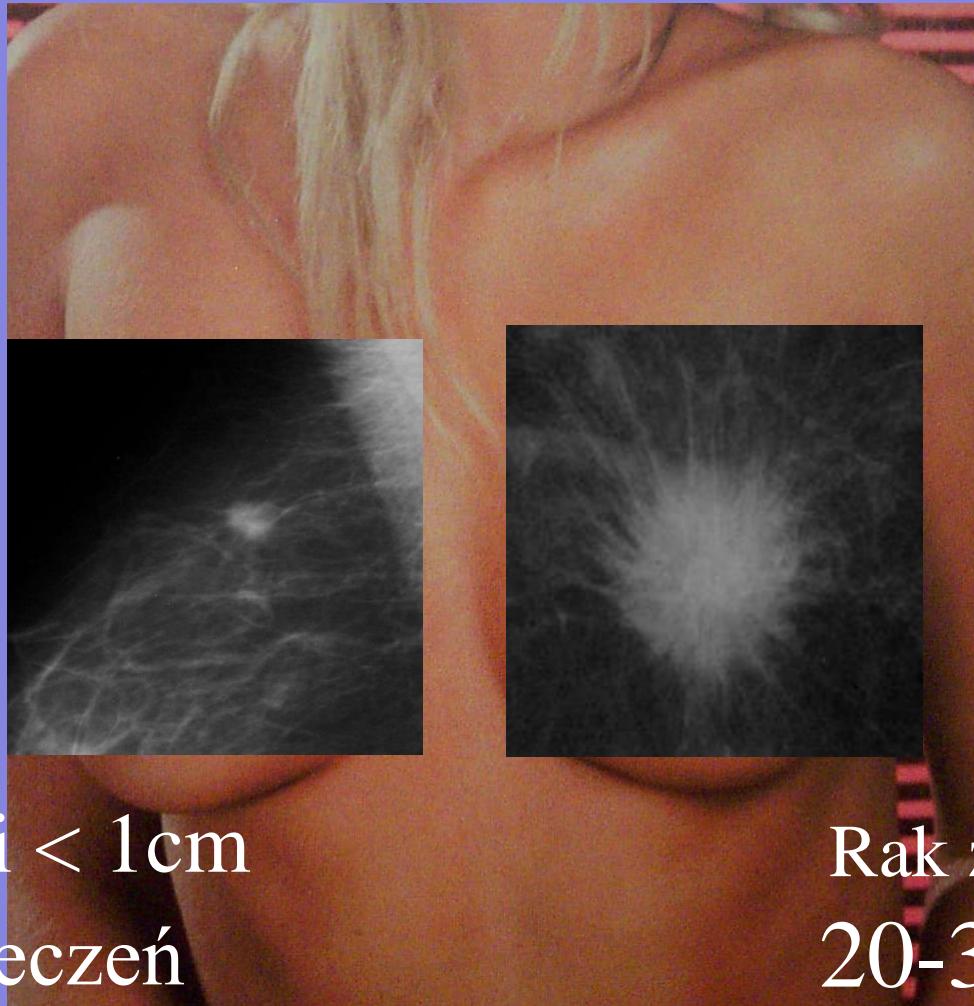
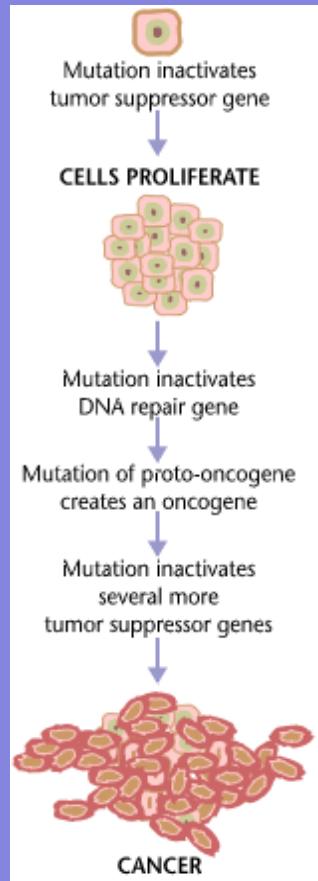
W PERSPEKTYWIE SENOLOGII

Przełomowe terapie uogólnionego raka piersi

2016

PROF. DR HAB. TADEUSZ PIEŃKOWSKI
POLSKIE TOWARZYSTWO DO BADAŃ NAD RAKIEM
PIERSI
CMKP

SZANSA NA WYLECZENIE



Rak piersi < 1cm
95% wyleczeń

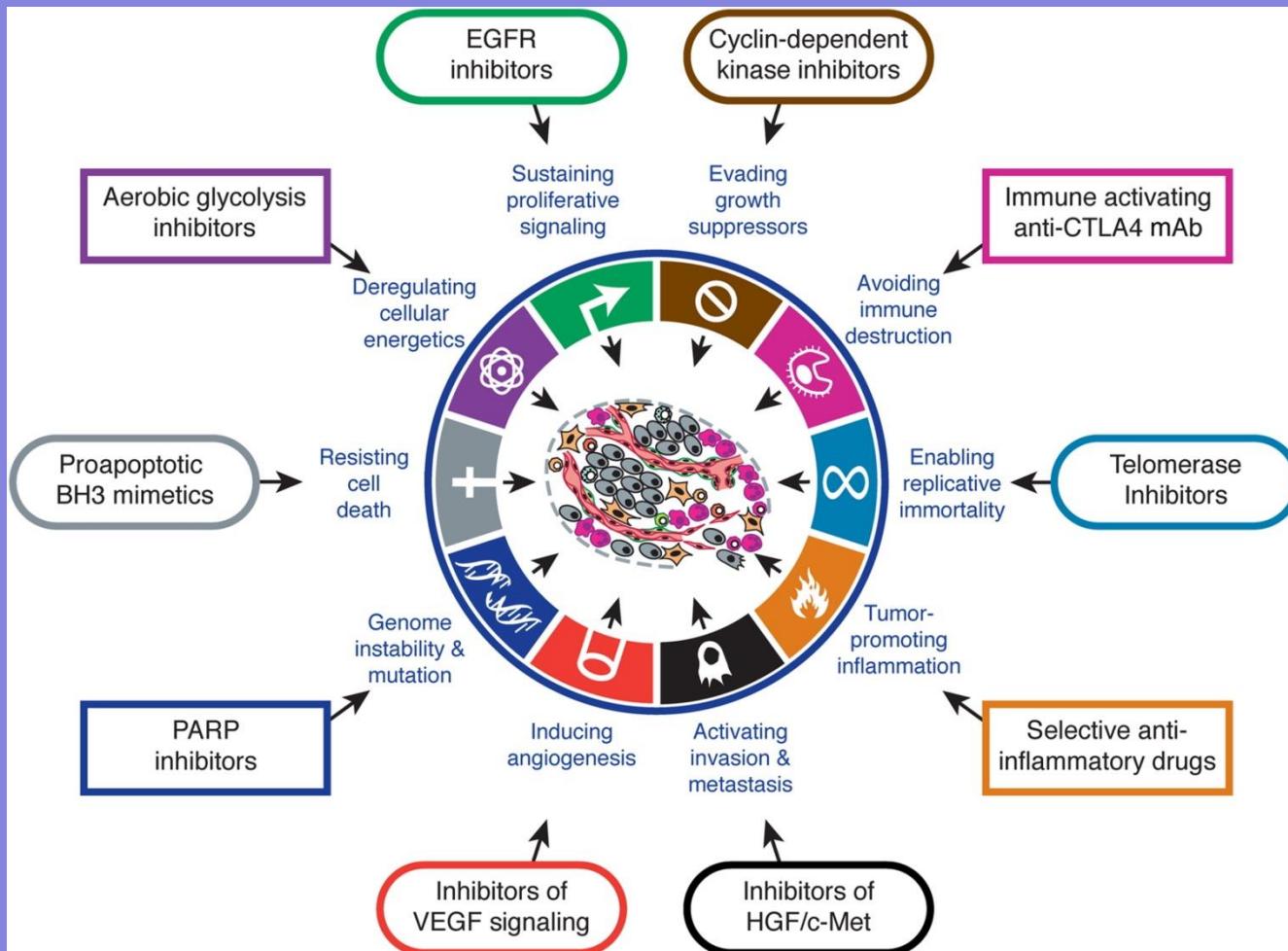
Rak zaawansowany
20-30% wyleczeń

Opóźnienie w postawieniu diagnozy i rozpoczęciu leczenia wpływa na pogorszenie przeżycia kobiet chorych na raka piersi:

7%-12% w zakresie 5-letnich przeżyć
w zależności od analizy

Specjalistyczne ośrodki diagnostyki i leczenia raka piersi

- Leczenie skojarzone
 - Więcej chorych otrzymuje najlepszy standard leczenia
- Krótszy czas konsultacji
 - Zmniejszenie lęku u chorych
- Lepsze zastosowanie metod
 - Wcześniejsze wykrycie, lepsze leczenie, wydłużenie życia
- Audyt i badania
 - Poprawa opieki nad chorymi



BIOLOGIA NOWOTWORÓW



DIAGNOSTYKA

MOLEKULARNA

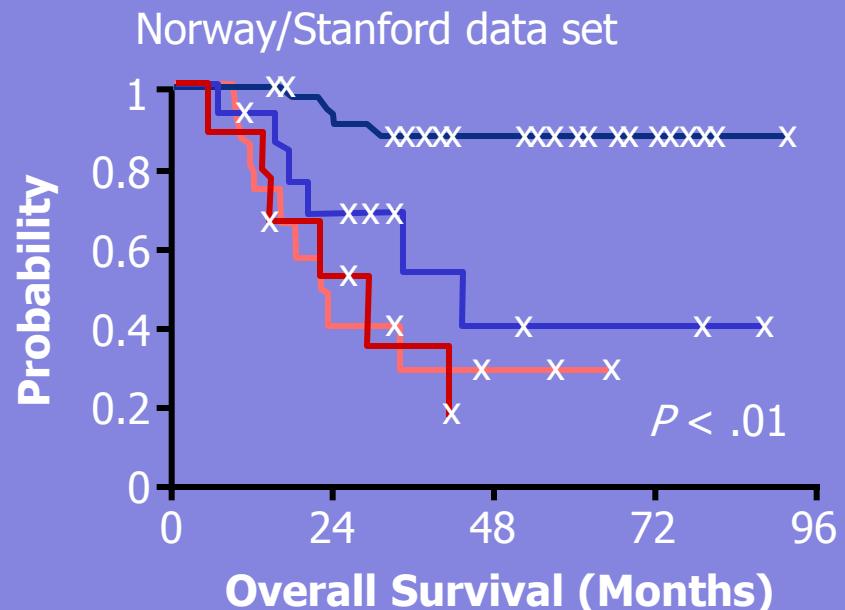
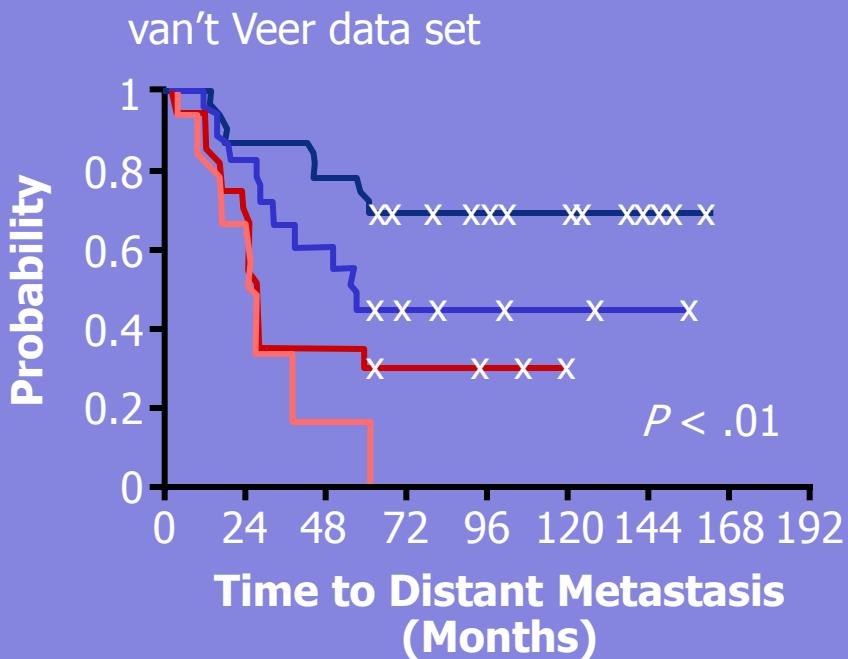


LECZENIE CELOWANE

Molekularne typy raka

Znaczenie rokownicze

x Censored — Luminal A — Luminal B — Basal — ERBB2+

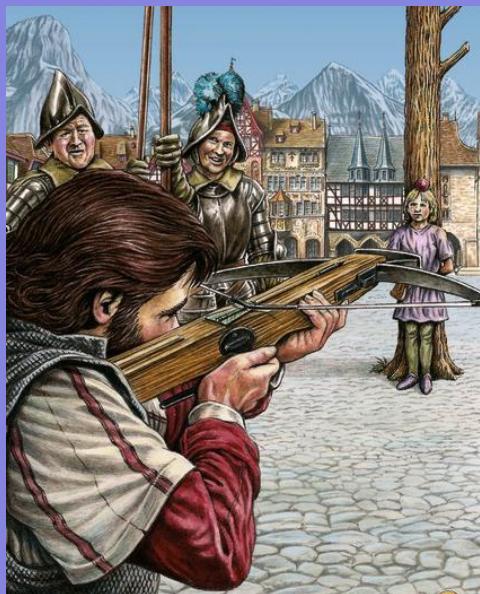


2010

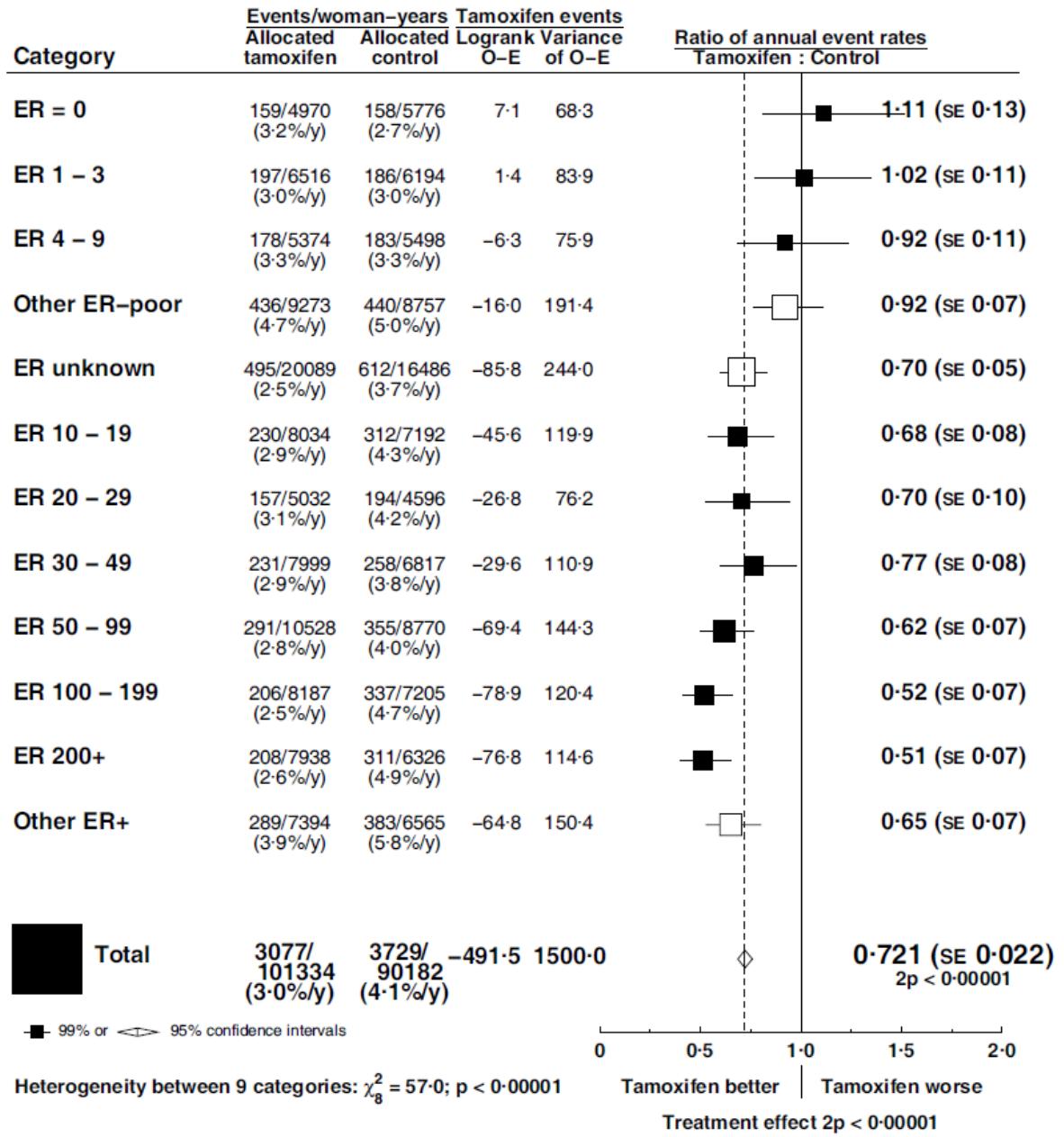
EBCTCG

Zawartość

ER



RECURRENCE in trials of tamoxifen for about 5 years versus the same management, but no tamoxifen



FIRST badanie II fazy. Fulvestrant vs anastrozol w leczeniu pierwszego rzutu chorych na zaawansowanego raka piersi.

Chore na uogólnionego raka piersi po menopauzie uprzednio nie leczone hormonalnie ER dodatni rak

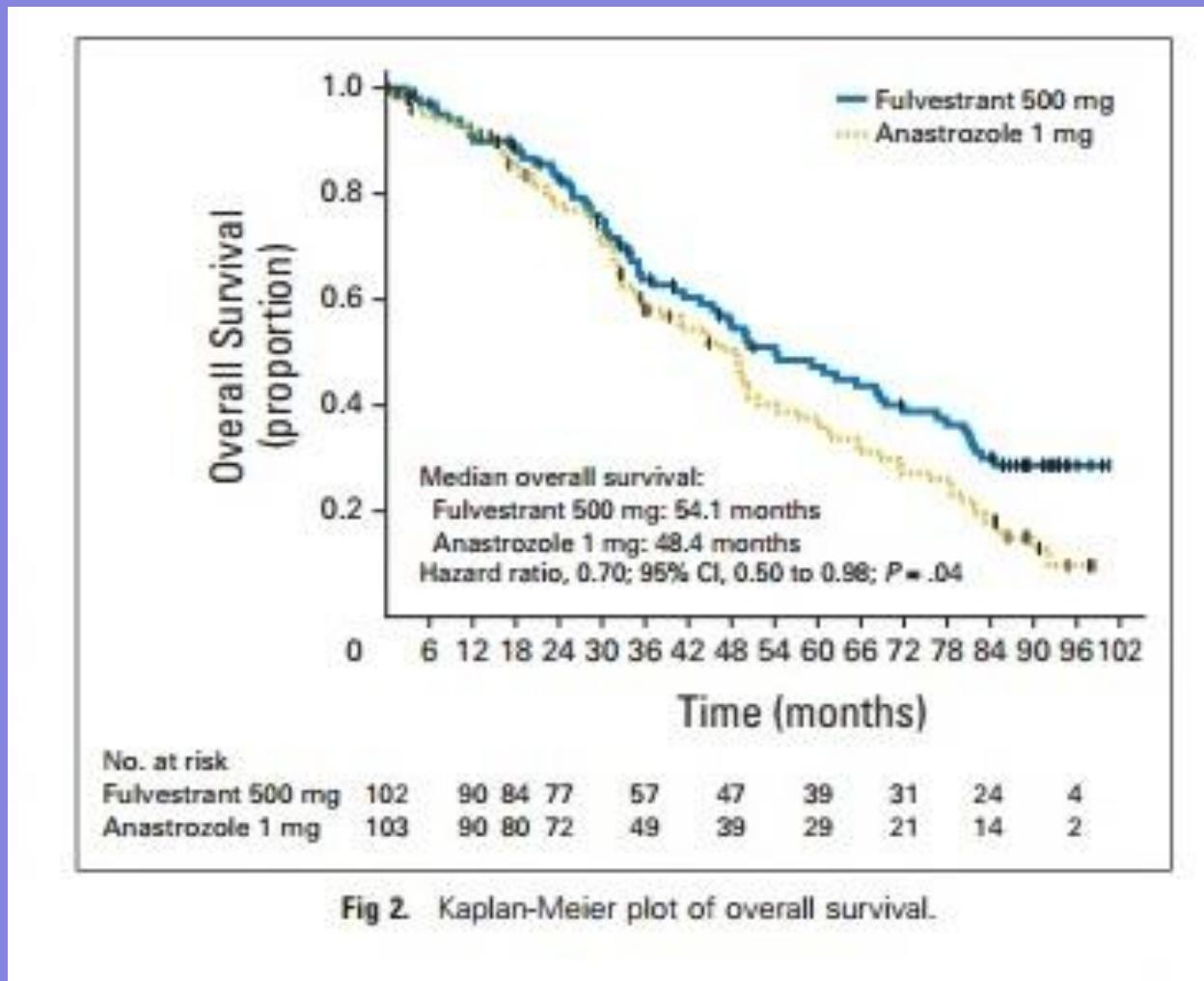
Fulvestrant 500 mg i.m
D 0, 14, 28, i co 28
(n = 102)

Anastrozole 1 mg/day orally
(n = 103)

Leczenie do progresji lub do toksyczności

Główny cel – korzyść kliniczna

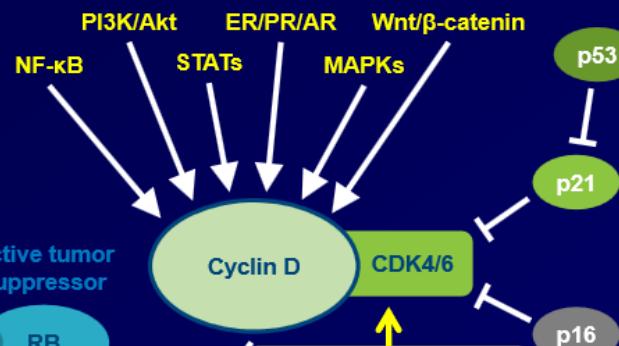
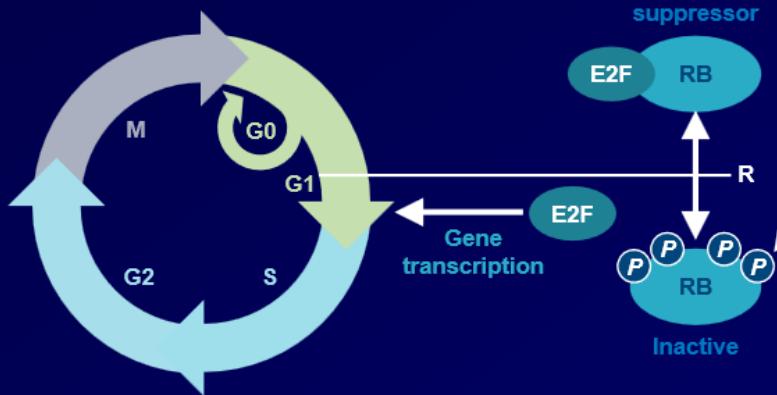
Fulvestrant 500mg vs anastrozol 1 mg w leczeniu pierwszego rzutu uogólnionego hormonozależnego raka piersi



Palbocilib CDK4/6 Inhibitor

Regulation of the G1/S Checkpoint in Breast Cancer

D-type cyclins regulated in response to mitogenic stimuli, including activation of RTKs and steroid hormone receptors¹



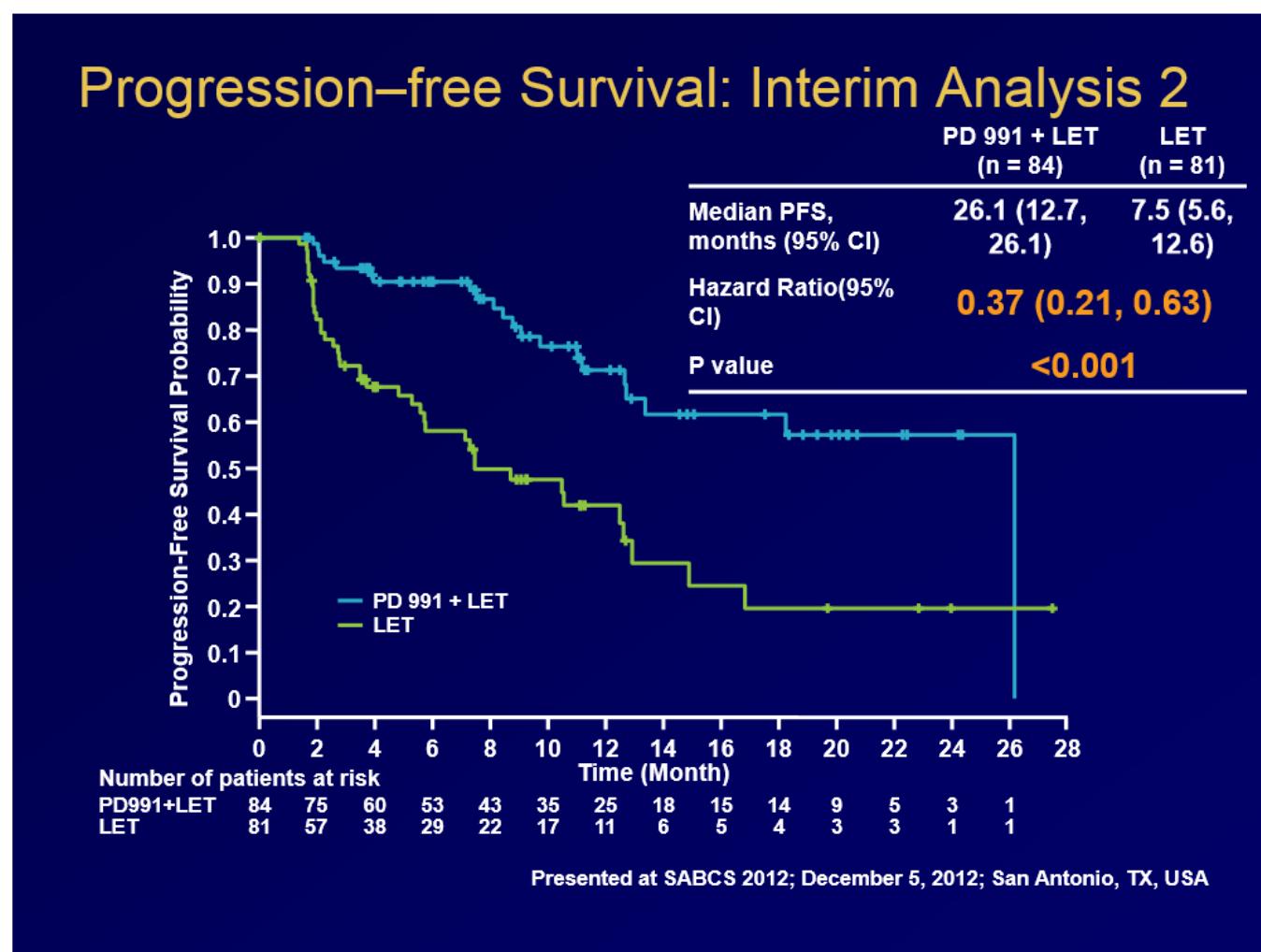
- Cyclin D1 is amplified in 15–20% of breast cancers^{2,3}
- Human ER+ breast cancer cell lines (including those with HER2 amplification) sensitive to G0/G1 arrest⁴

Lange et al. Endocrine-Related Cancer 2011;18:C19–C24; ¹Caldon CE, et al. J Cell Biochem 2006;97:261–274; ²Buckley MF, et al. Oncogene 1993;8:2127–2133; ³Dickson C, et al. Cancer Lett 1995;90:43–50; ⁴Finn RS, et al. Breast Cancer Res 2009;11:R77

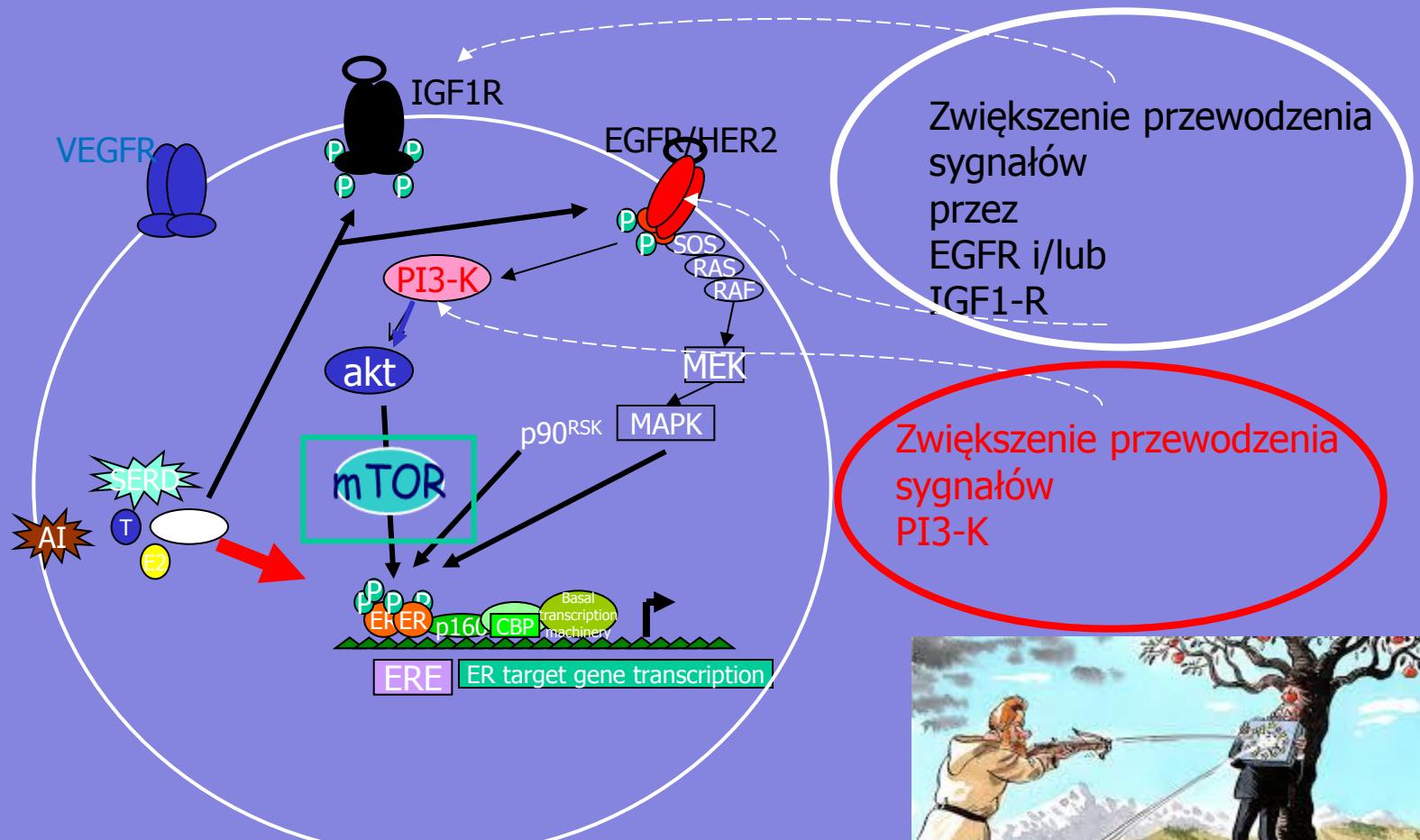
Palbocilib Inhibitor CDK4/6

PALOMA 1

Chore uprzednio nie leczone



Oporość na leczenie hormonalne



Johnston SR. Clin Cancer Res. 2005;11:889s-899s.



BOLERO-2: Badanie III fazy ekzemestan +/- ewerolimus u chorych na zaawansowanego raka piersi po uprzednim niepowodzeniu leczenia N IA

N = 724

PMW with HR+, HER2– ABC
refractory to LET or ANA,
defined as

- Recurrence during or within 12 months after end of adjuvant treatment, or
- Progression during or within 1 month after end of treatment for advanced disease

**Everolimus 10
mg/day +
Exemestane 25 mg/day
(n = 485)**

**Placebo +
Exemestane 25 mg/day
(n = 239)**

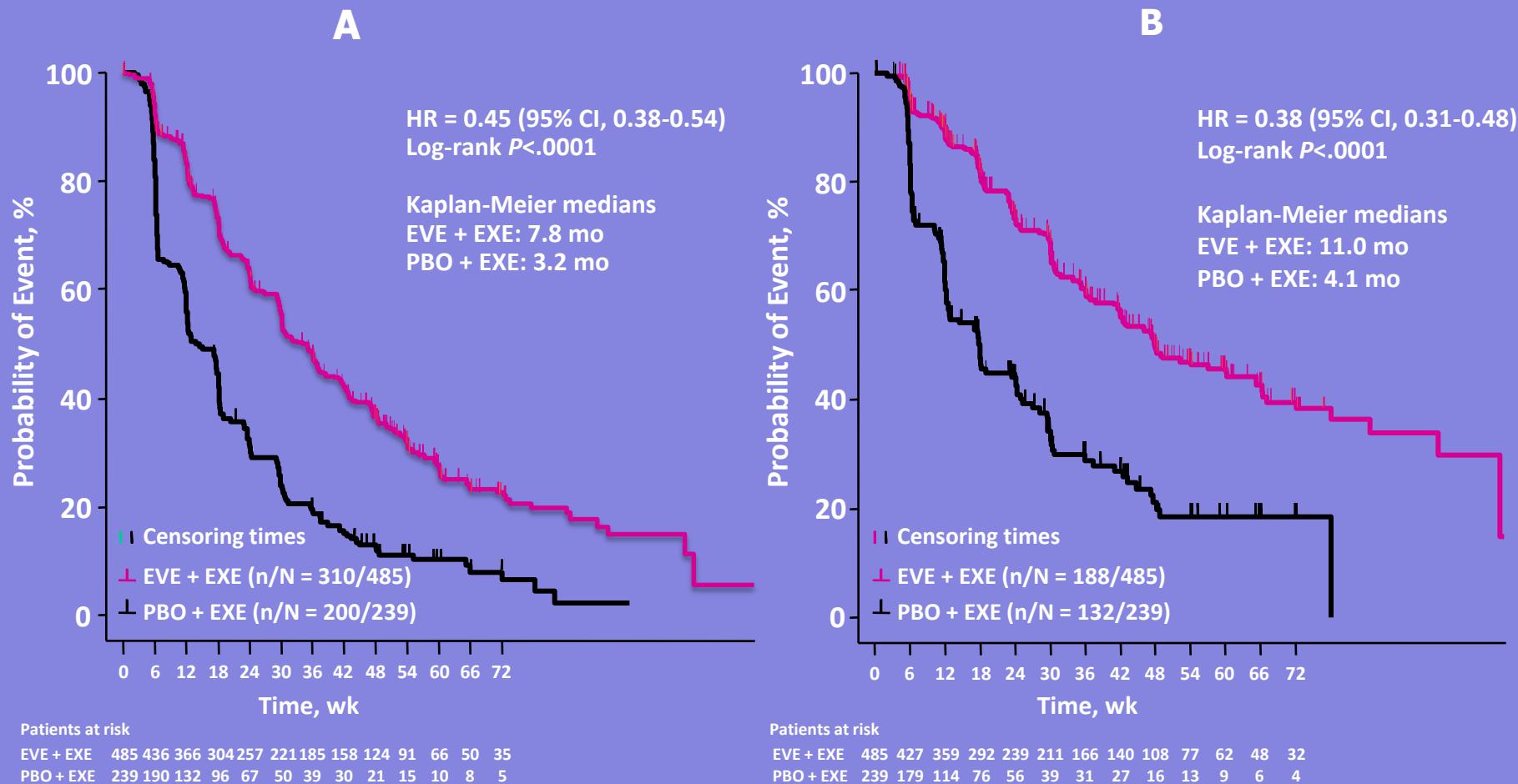
- Stratification
 1. Sensitivity to prior endocrine therapy
 2. Presence of visceral disease
- No crossover

Primary endpoint
PFS

Secondary endpoints
OS, ORR, CBR, safety,
QOL, bone markers

ABC, advanced breast cancer; NSAI, nonsteroidal aromatase inhibitor; PMW, postmenopausal women; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; LET, letrozole; ANA, anastrozole; PFS, progression-free survival; OS, overall survival; ORR; overall response rate; CBR, clinical benefit rate; QOL, quality of life.
Baselga J, et al. *N Engl J Med.* 2012;366(6):520-529.

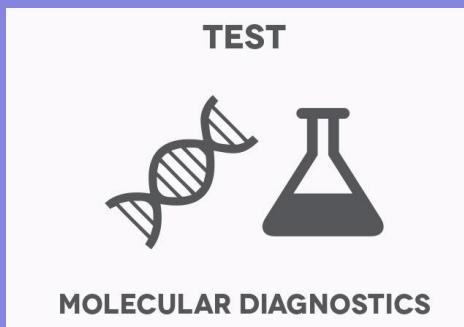
BOLERO-2: Czas do progresji (A) ocena lokalna, (B) ocena centralna.



HR, hazard ratio; CI, confidence interval; EVE, everolimus; EXE, exemestane; PBO, placebo; mo, months.

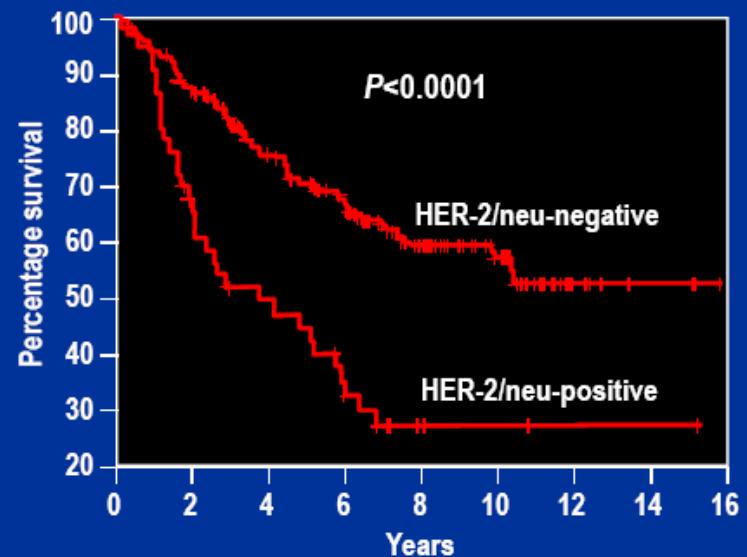
Yardley D et al. *Adv Ther*. 2013; 30(10):870-884.

Zwiększoną ekspresją receptora HER2 występuje u około 20 - 25% chorych na raka piersi



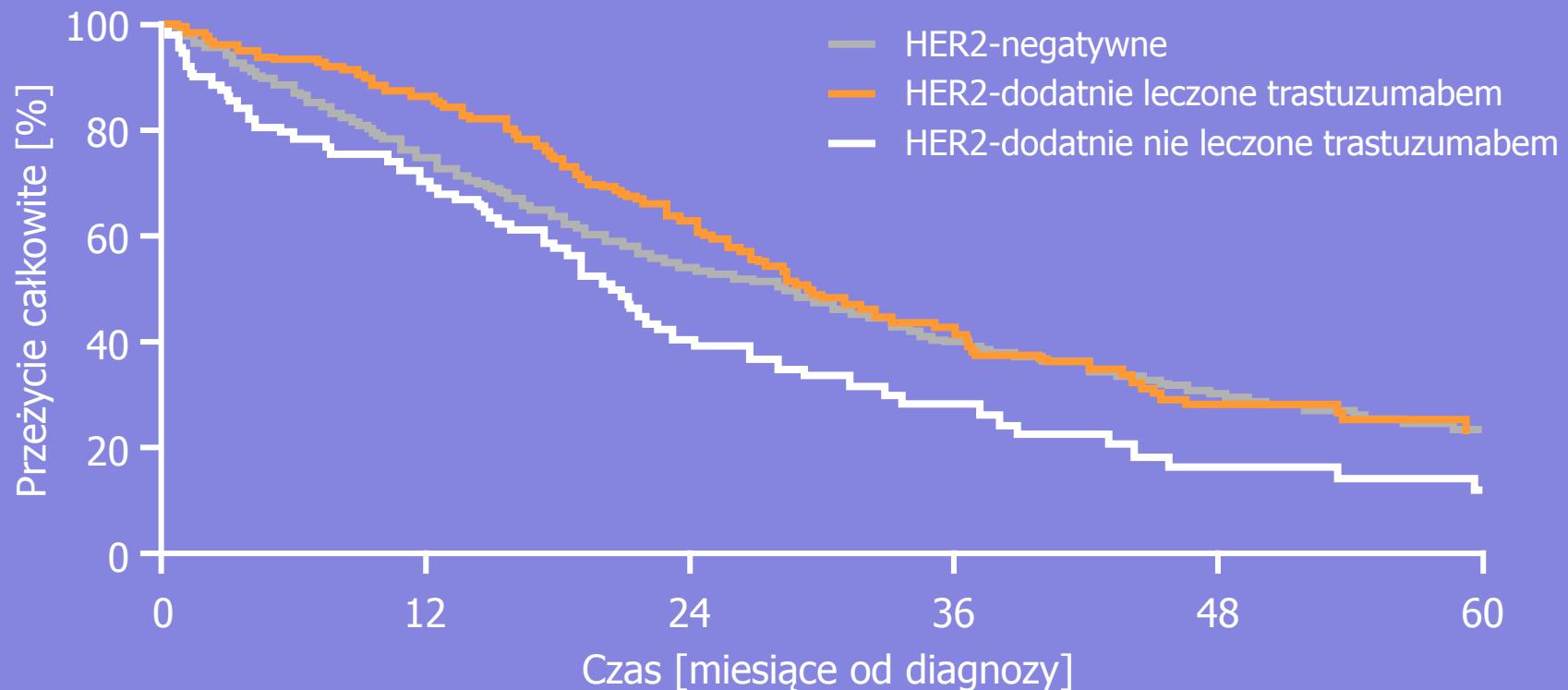
HER-2/neu Positivity Correlates with Decreased Survival in Breast Cancer

In this study, strongly positive IHC scores (3+) were associated with significantly decreased survival



IHC = immunohistochemistry.
Witton CJ et al. J Pathol. 2003;200:290-297.

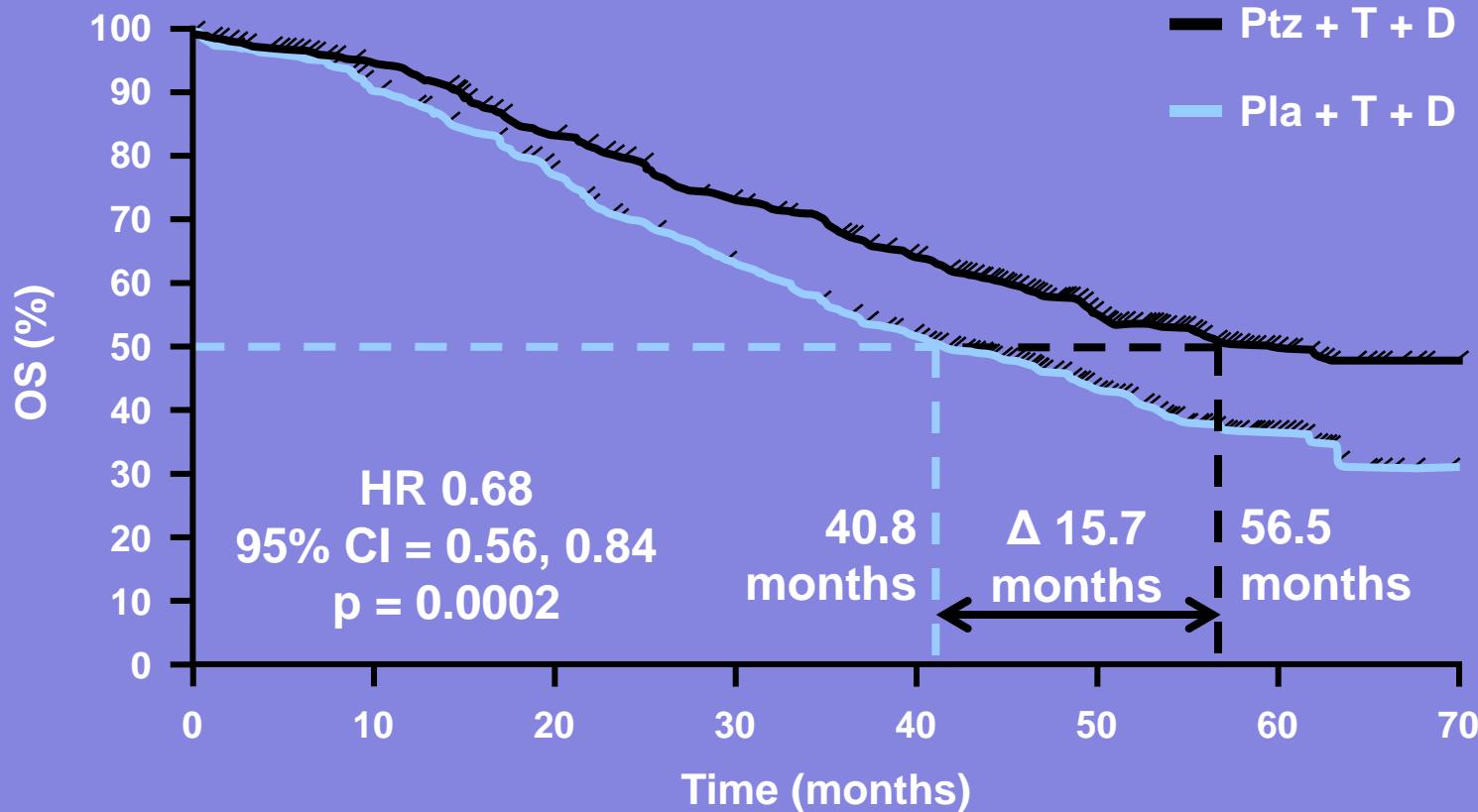
Trastuzumab zmienia naturalny przebieg choroby w zaawansowanym raku piersi



Badanie CLEOPATRA

Przeżycie całkowite

Mediana follow-up 50 miesięcy (0–70)



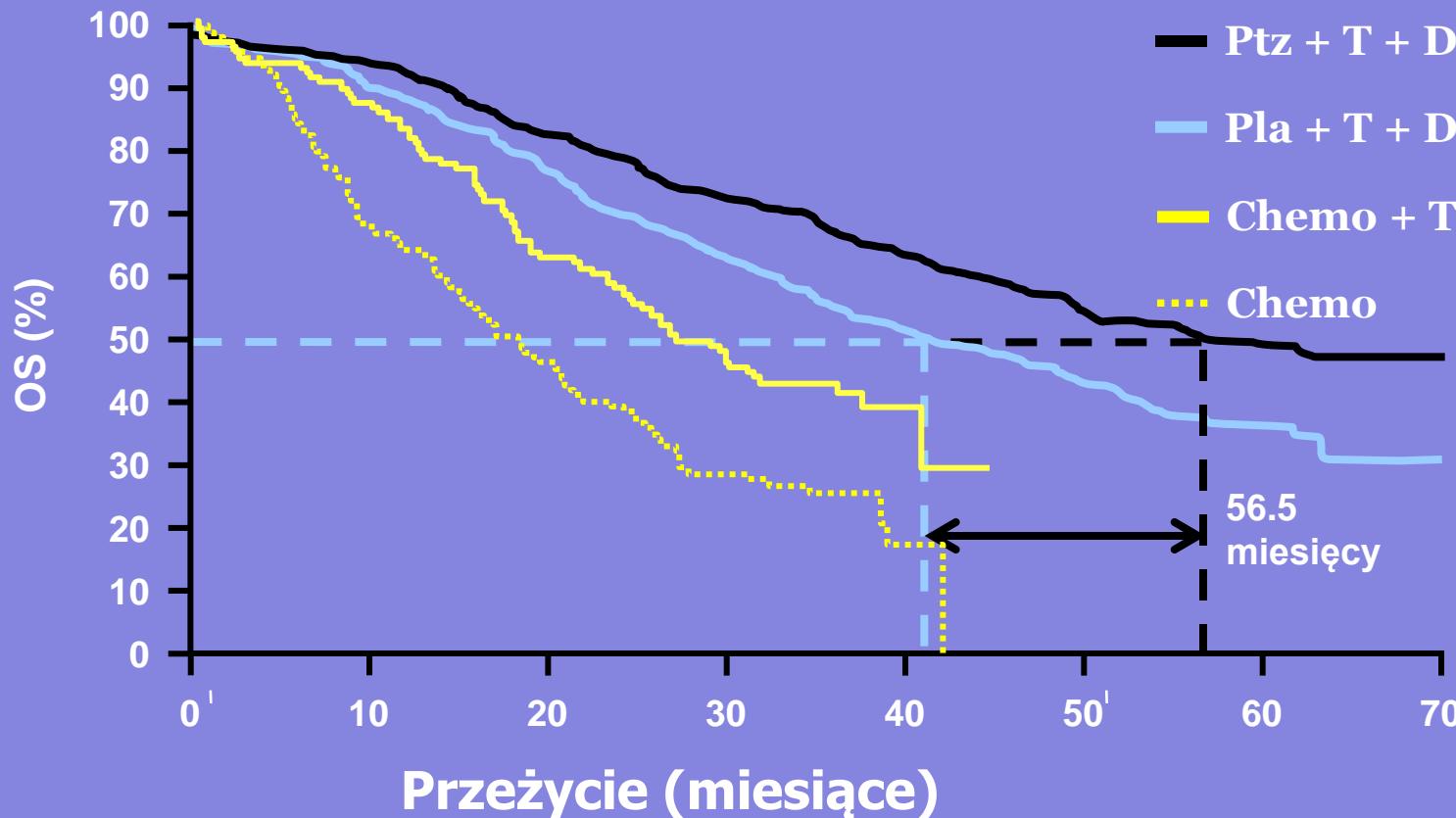
n at risk

—	Ptz + T + D	402	371	318	268	226	104	28	1
—	Pla + T + D	406	350	289	230	179	91	23	0

ITT population. Stratified by geographic region and neo/adjuvant chemotherapy.

CI, confidence interval; Pla, placebo; Ptz, pertuzumab.

Zestawienie wyników leczenia chorych na zaawansowanego raka piersi z nadmierną ekspresją HER2



od chemioterapii do pertuzumabu z trastuzumabem

Badanie EMILIA

**HER2+ (central)
LABC or MBC
(N=980)**

- Prior taxane and trastuzumab
- Progression on metastatic tx or within 6 mos of adjuvant tx

1:1

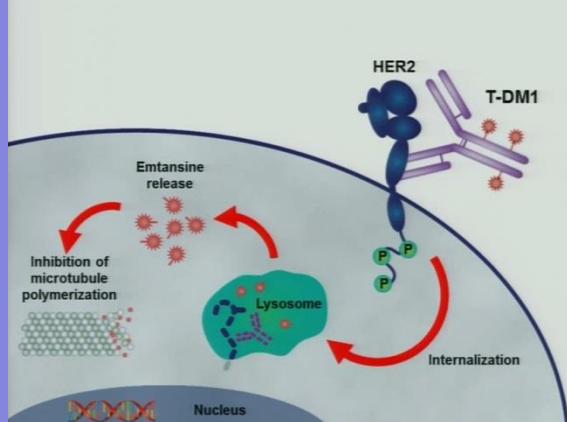
**T-DM1
3.6 mg/kg q3w IV**

PD

**Capecitabine
1000 mg/m² orally bid, days 1–14, q3w
+
Lapatinib
1250 mg/day orally qd**

PD

T-DM1: Mechanism of Action

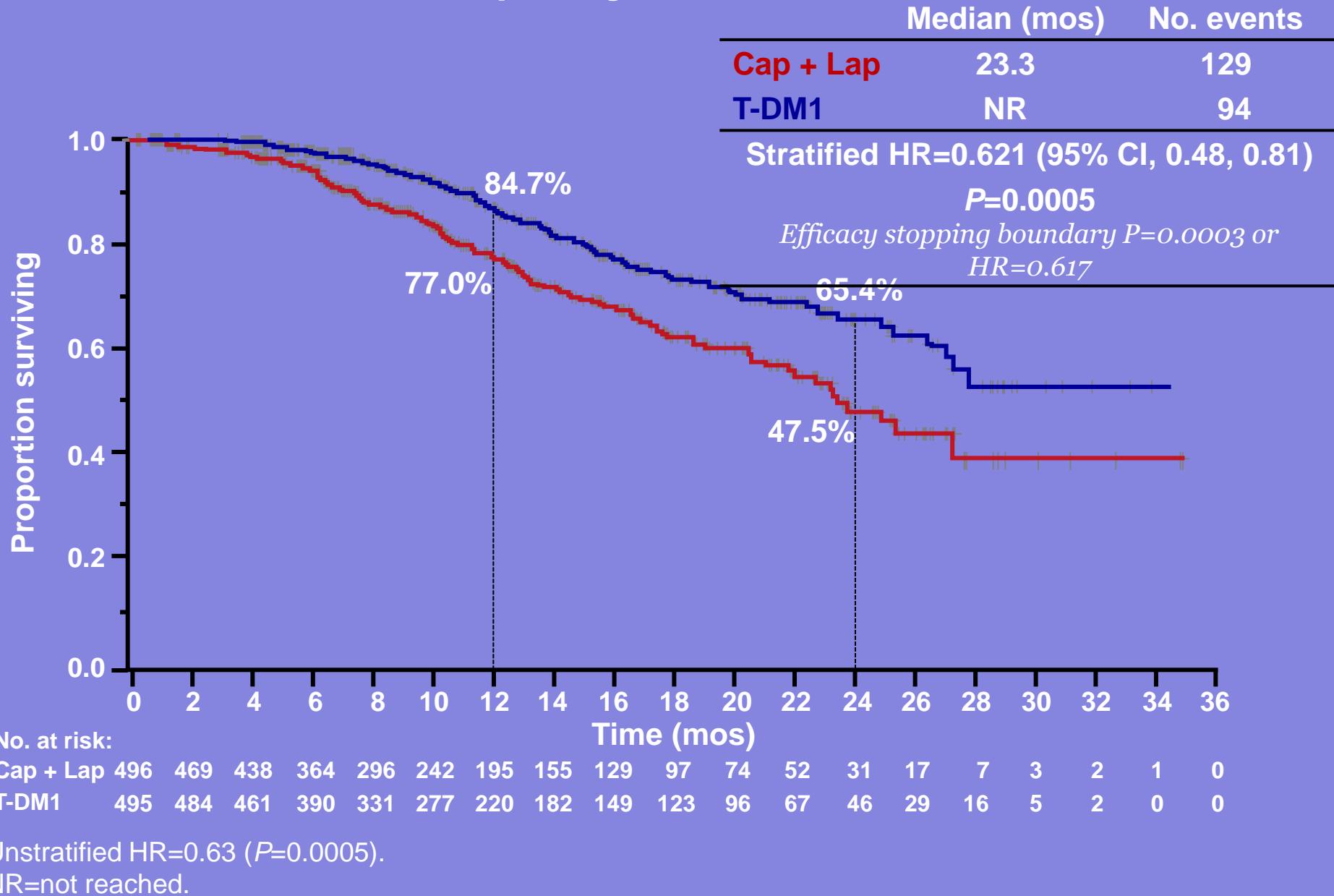


Adapted from LoRusso PM, et al. Clin Cancer Res 2011.

3



Badanie Emilia przeżycie całkowite analiza przejściowa.



Zalecenia NCCN

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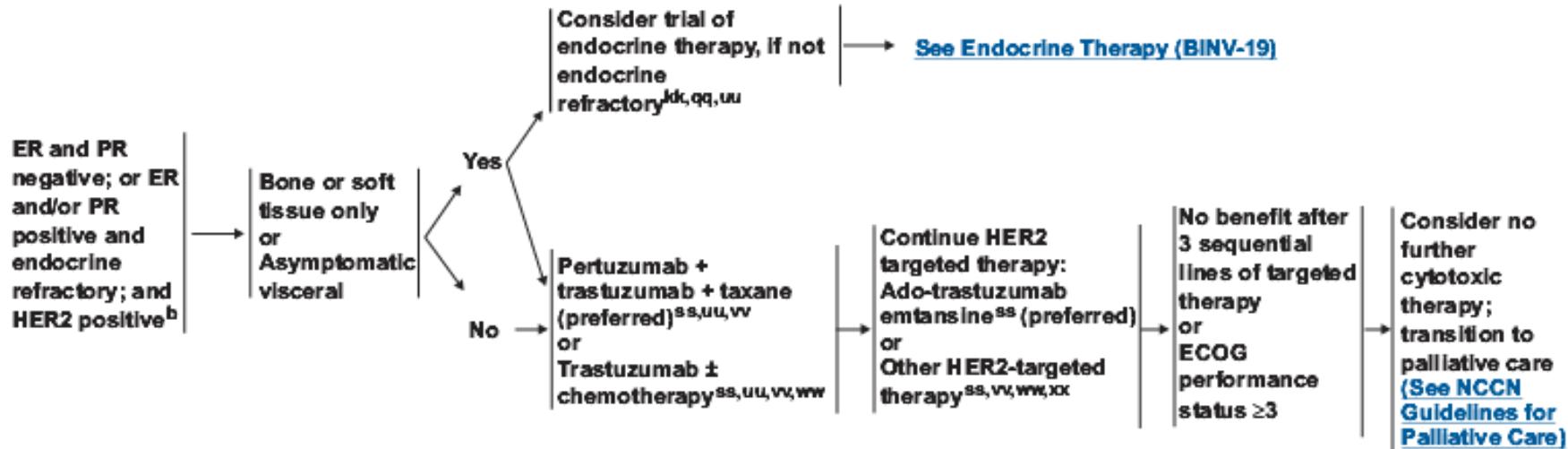


NCCN Guidelines Version 3.2014 Invasive Breast Cancer

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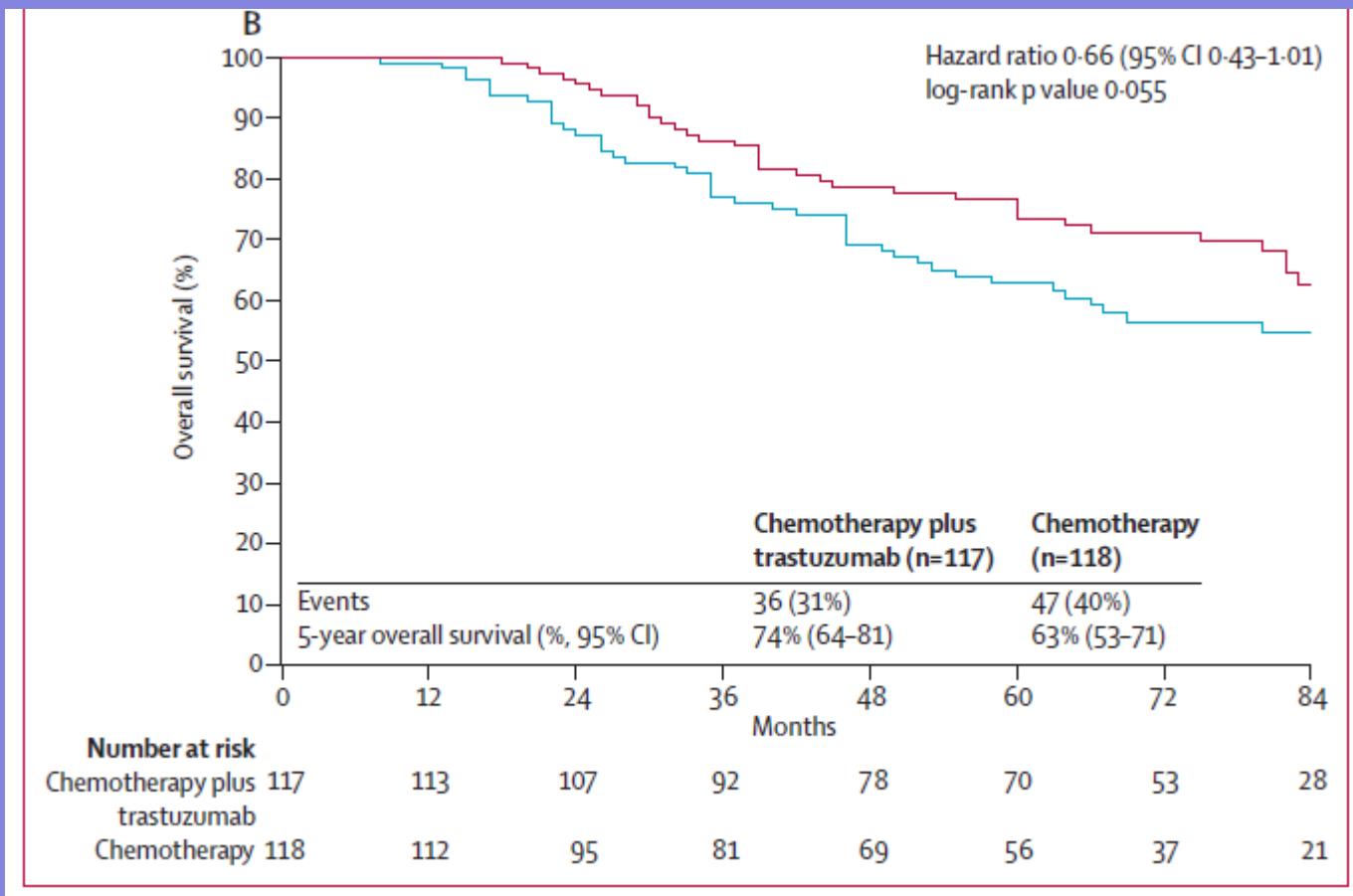
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE

ER and PR NEGATIVE; or ER and/or PR POSITIVE and ENDOCRINE REFRACTORY; and HER2 POSITIVE

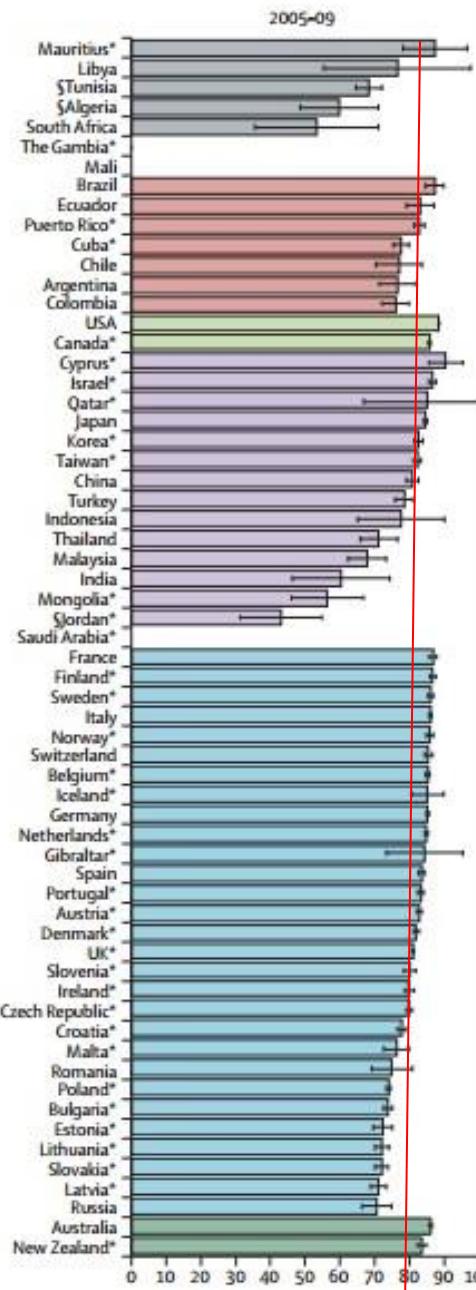
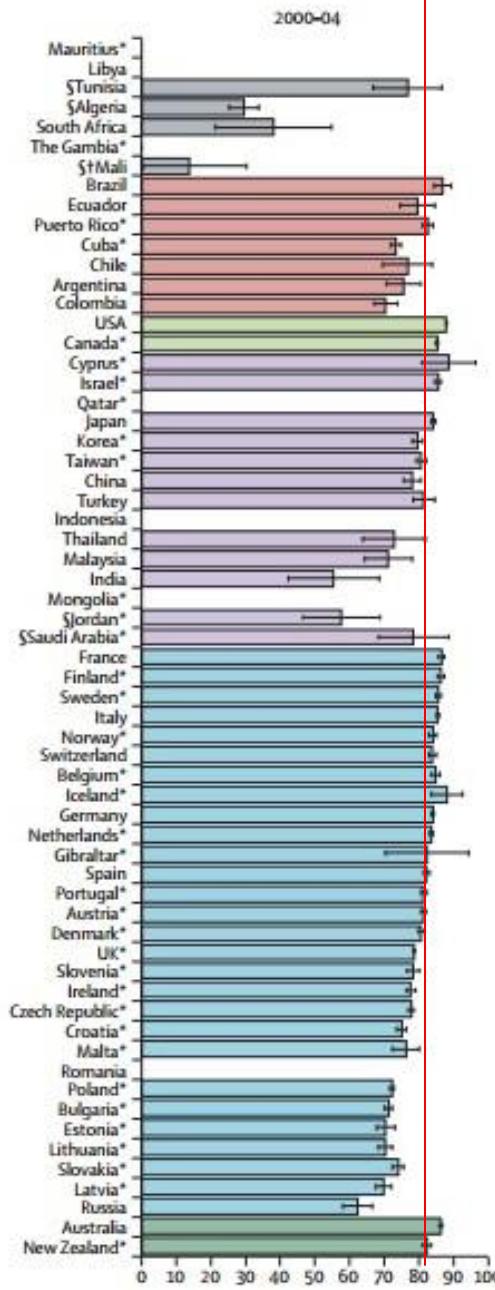
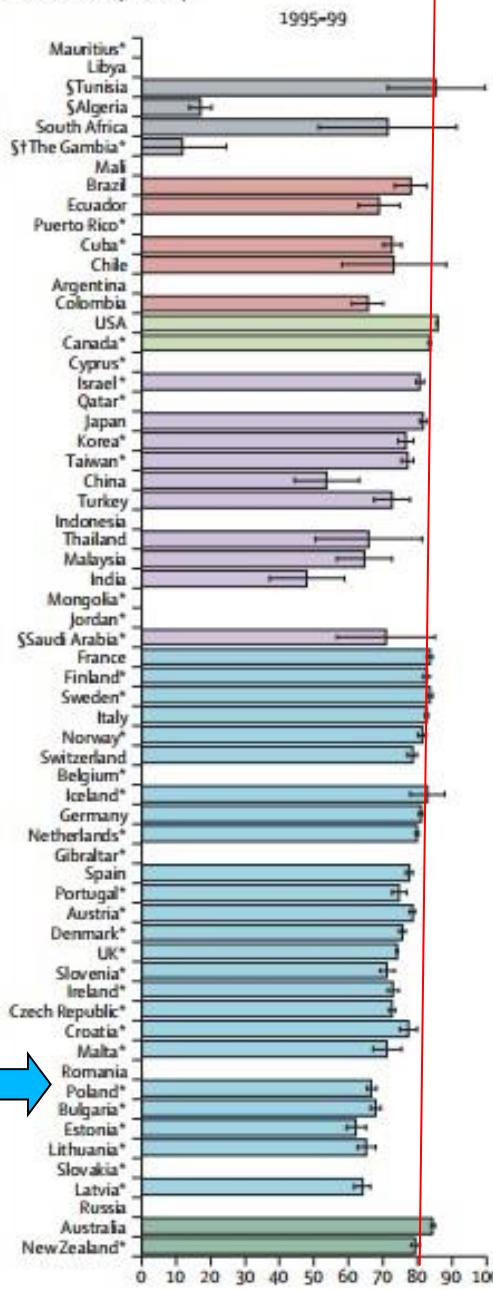


Neoadjuvant and adjuvant trastuzumab in patients with HER2-positive locally advanced breast cancer (NOAH): follow-up of a randomised controlled superiority trial with a parallel HER2-negative cohort

Luca Gianni, Wolfgang Eiermann, Vladimir Semiglazov, Ana Lluch, Sergei Tjulandin, Milvia Zambetti, Angela Moliterni, Federico Vazquez, Mikhail Byakarov, Mikhail Lichinitser, Miguel Angel Climent, Eva Ciruelos, Belen Ojeda, Mauro Mansutti, Alla Bozhok, Domenico Magazzù, Dominik Heinzmann, Jutta Steinseifer, Pinuccia Valagussa, Jose Baselga



Breast cancer (women)

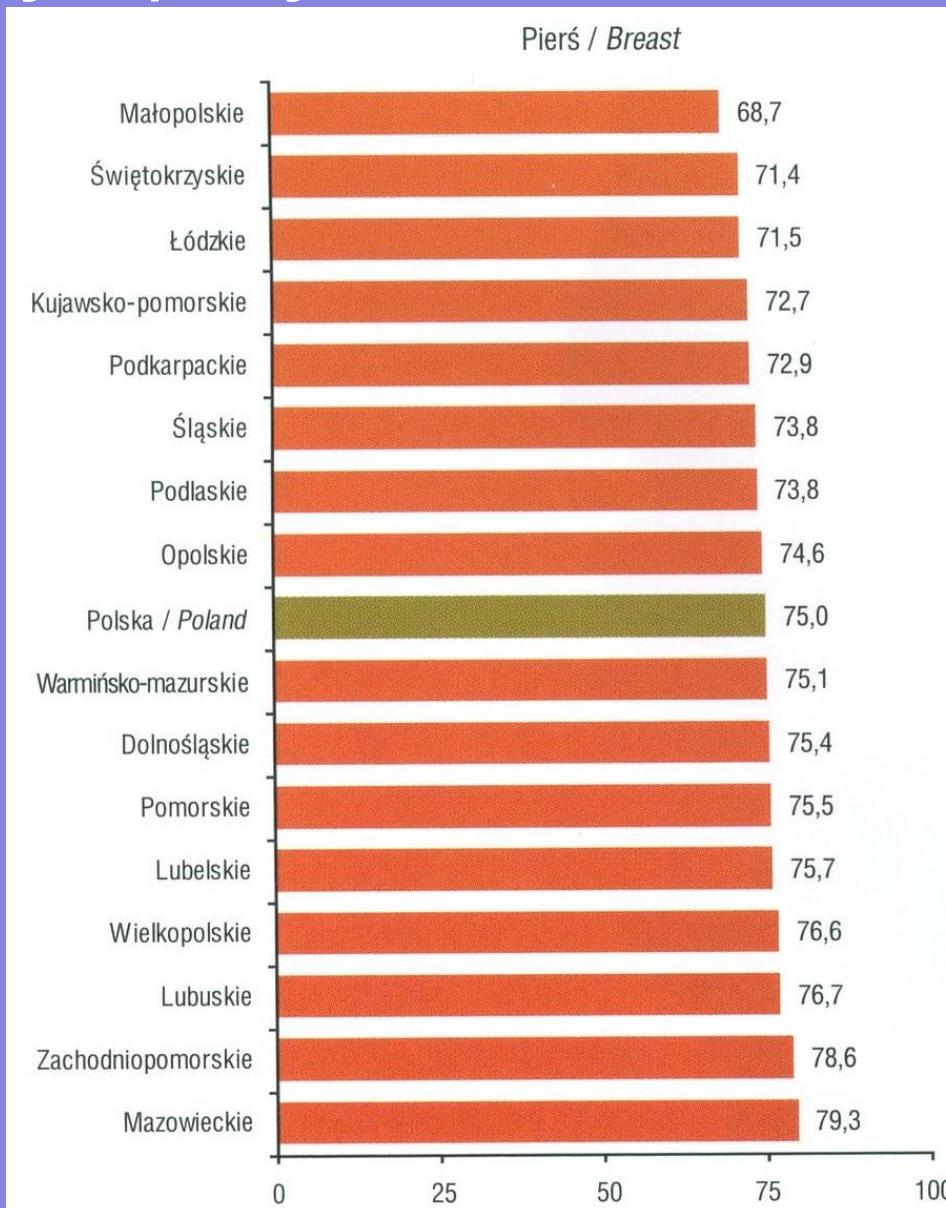


Przeżycia
5-letnie

Lancet

RAK PIERSI PRZEŻYCIA 5-LETNIE

Krajowy Rejestr Nowotworów 2010



NOWY PARADYGMAT SENOLOGII

AUTONOMICZNA DZIEDZINA MEDYCYNY

OPARTA NA ZESPOŁOWYM,
INTERDYSCYPLINARNYM DIAGNOZOWANIU I
LECZENIU CHORYCH

WYMAGAJĄCA ODRĘBNEJ EKONOMIKI
KLINICZEJ OPARTEJ NA PODEJŚCIU
POPULACYJNYM