FONDAZIONE AIOM
UNITI PER VINCERE IL CANCRO
Associazione Italiana di Oncologia Medica

Tumore al seno avanzato: dove è arrivata la ricerca scientifica

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PRESIDIO OSPEDALIERO ACCREDITATO - REGIONE VENETO

Sacro Cuore Don Calabria
CCC
Cancer Care Center
Negrar - Verona
Cancer Care Center
Numero Verde
800 143 143
Numero per la Cura del Tumore

TUMORE AL SENO METASTATICO

CHI:

Età media 54 anni

30% di età inferiore ai 45 anni

40% occupata fuori casa

Maggioranza sposata

50% madri di figli minorenni

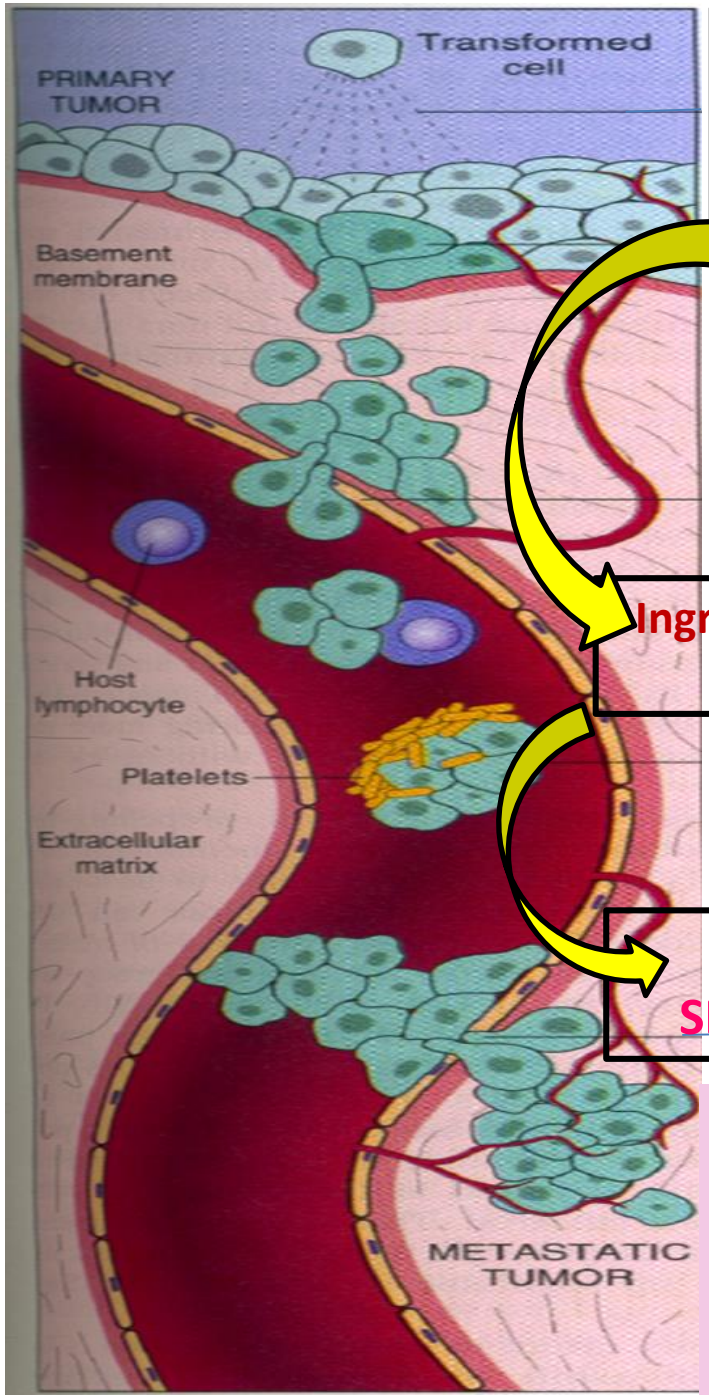
CON:

Vita affettiva

Vita relazionale

Vita familiare

Da una ricerca di GFK-Eurisko per Europa Donna



CARCINOMA PRIMITIVO
Insieme di cellule originate da una singola cellula con danni genetici

Malattia sistemica fin dall'inizio (cellule predestinate a metastatizzare)

Proliferazione incontrollata
Resistenza all'apoptosi
Ridotta adesione ad altre cellule o al tessuto
Aumentata motilità
Capacità di angiogenesi

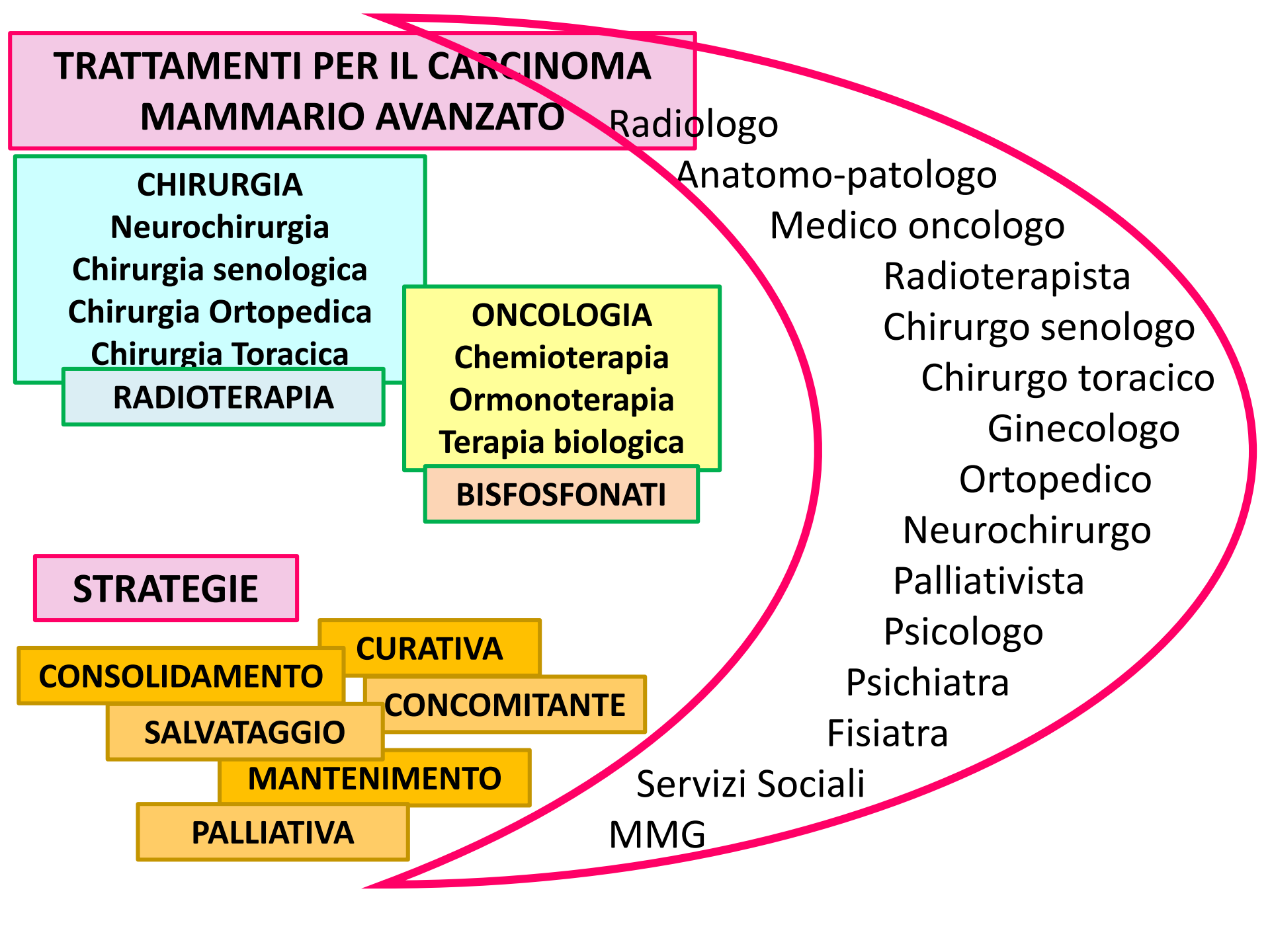
Ingresso nei vasi e sopravvivenza in circolo (emboli neoplastici)

Fuoriuscita dal circolo e deposito in altri organi/apparati
Crescita di cellule incontrollata

CARCINOMA MAMMARIO SECONDARIO o METASTATICO

Nel tempo incorrono ulteriori mutazioni genetiche acquisendo caratteristiche diverse dal tumore primitivo

Teoria delle metastasi dormienti – MICROMETASTASI presenti all'esordio non clinicamente rilevabili anche per decenni dopo la rimozione del tumore primario


TRATTAMENTI PER IL CARCINOMA MAMMARIO AVANZATO
CHIRURGIA
Neurochirurgia
Chirurgia senologica
Chirurgia Ortopedica
Chirurgia Toracica
RADIOTERAPIA
ONCOLOGIA
Chemioterapia
Ormonoterapia
Terapia biologica
BISFOSFONATI
STRATEGIE
CURATIVA
CONSOLIDAMENTO
CONCOMITANTE
SALVATAGGIO
MANTENIMENTO
PALLIATIVA
Radiologo
Anatomo-patologo
Medico oncologo
Radioterapista
Chirurgo senologo
Chirurgo toracico
Ginecologo
Ortopedico
Neurochirurgo
Palliativista
Psicologo
Psichiatra
Fisiatra
Servizi Sociali
MMG

TRATTAMENTO NEL CARCINOMA MAMMARIO AVANZATO: MODALITA' DI SCELTA e SCOPI

Età
Comorbidità
Condizioni cliniche generali
Performance status

Intervallo libero di malattia
Caratteristiche immunofenotipiche del tumore
Trattamenti precedenti
Sedi ed estensione della malattia metastatica

SCELTA DELLA PAZIENTE

Controllare i sintomi
Rallentare o bloccare la progressione della malattia
Prolungare la durata della vita
Migliorare la qualità di vita

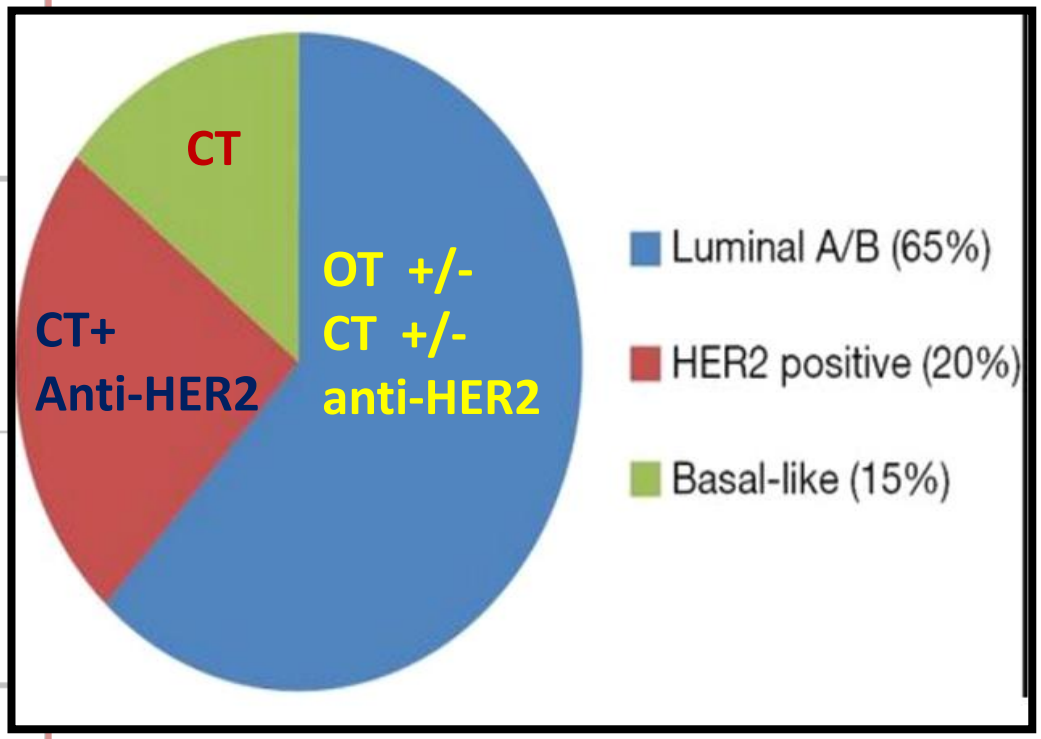
TRASFORMARE LA MALATTIA METASTATICA DA "SEMPRE LETALE" A "PATOLOGIA PREVALENTEMENTE CRONICIZZABILE"

CARCINOMA MAMMARIO: CLASSIFICAZIONE SECONDO FATTORI PREDITTIVI

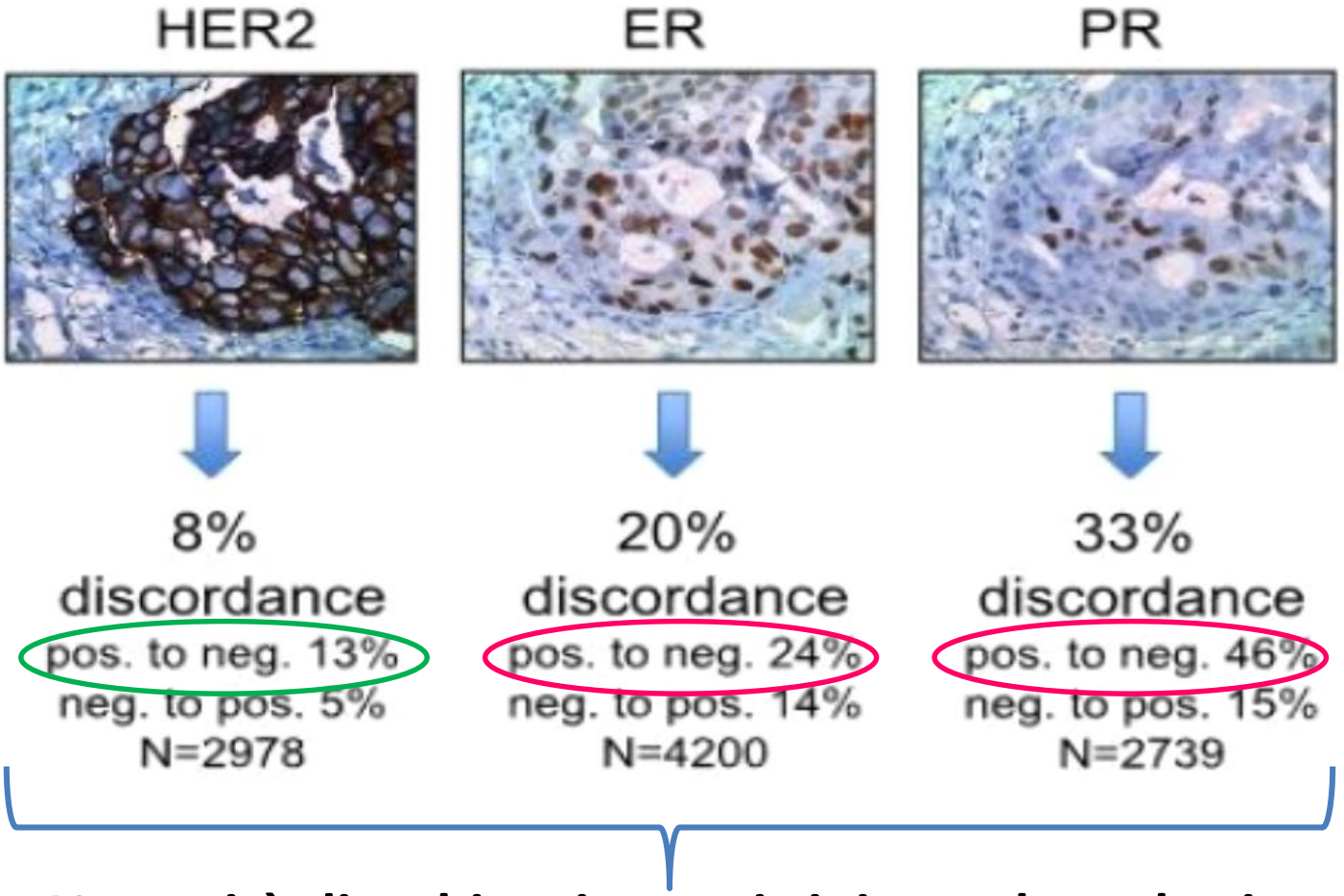
"DIFFERENTI MALATTIE"

"TRATTAMENTI DIVERSI"

Subtype	These tumors tend to be*	Prevalence (approximate)
Luminal A	ER+ and/or PR+, HER2-, low Ki67	40%
Luminal B	ER+ and/or PR+, HER2+ (or HER2- with high Ki67)	20%
Triple negative/basal-like	ER-, PR-, HER2-	15-20%
HER2 type	ER-, PR-, HER2+	10-15%



CAMBIAMENTO DEI FATTORI PREDITTIVI TRA IL TUMORE MAMARIO PRIMITIVO E IL TUMORE MAMMARIO METASTATICO



Necessità di re-biopsiare e ri-tipizzare la malattia

Aurilio et al, EJC 2015

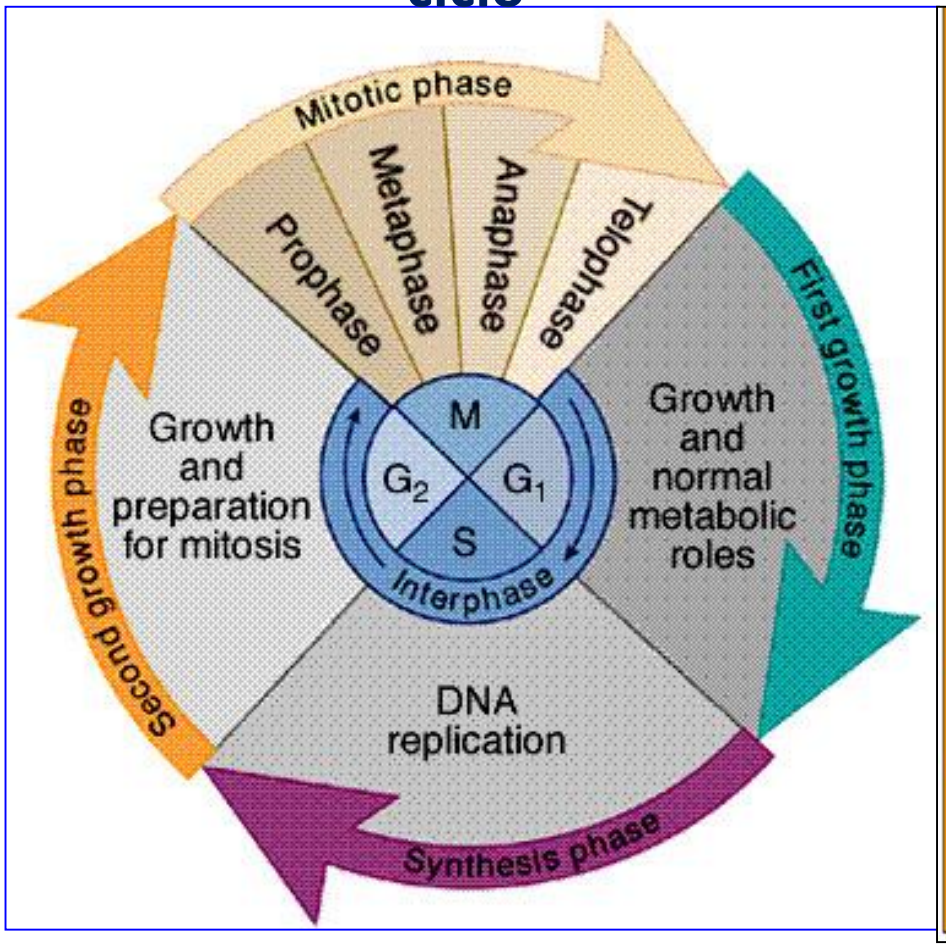
FARMACI CHEMIOTERAPICI

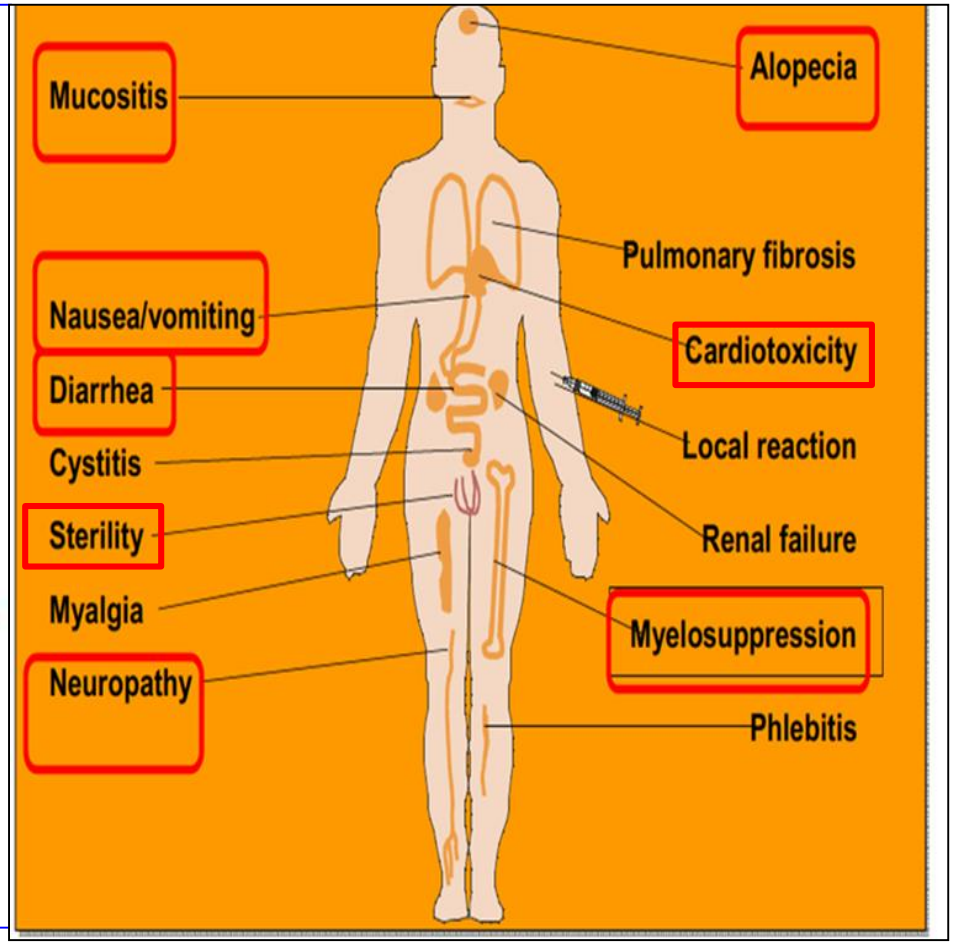
Meccanismo d'azione

interferiscono con i processi di proliferazione di tutte le cellule in ciclo

Tossicità

scarsa selettività agiscono su tutte le cellule incluse quelle non neoplastiche





Preferred single agents:

Anthracyclines

- Doxorubicin
- Pegylated liposomal doxorubicin

Taxanes

- Paclitaxel

Anti-metabolites

- Capecitabine
- Gemcitabine

Other microtubule inhibitors

- Vinorelbine
- Eribulin

Other single agents:

- Cyclophosphamide
- Carboplatin
- Docetaxel
- Albumin-bound paclitaxel
- Cisplatin
- Epirubicin
- Ixabepilone

Chemotherapy combinations:

- CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)
- FEC (fluorouracil/epirubicin/cyclophosphamide)
- AC (doxorubicin/cyclophosphamide)
- EC (epirubicin/cyclophosphamide)
- CMF (cyclophosphamide/methotrexate/fluorouracil)
- Docetaxel/capecitabine
- GT (gemcitabine/paclitaxel)
- Gemcitabine/carboplatin
- Paclitaxel/bevacizumab[3]

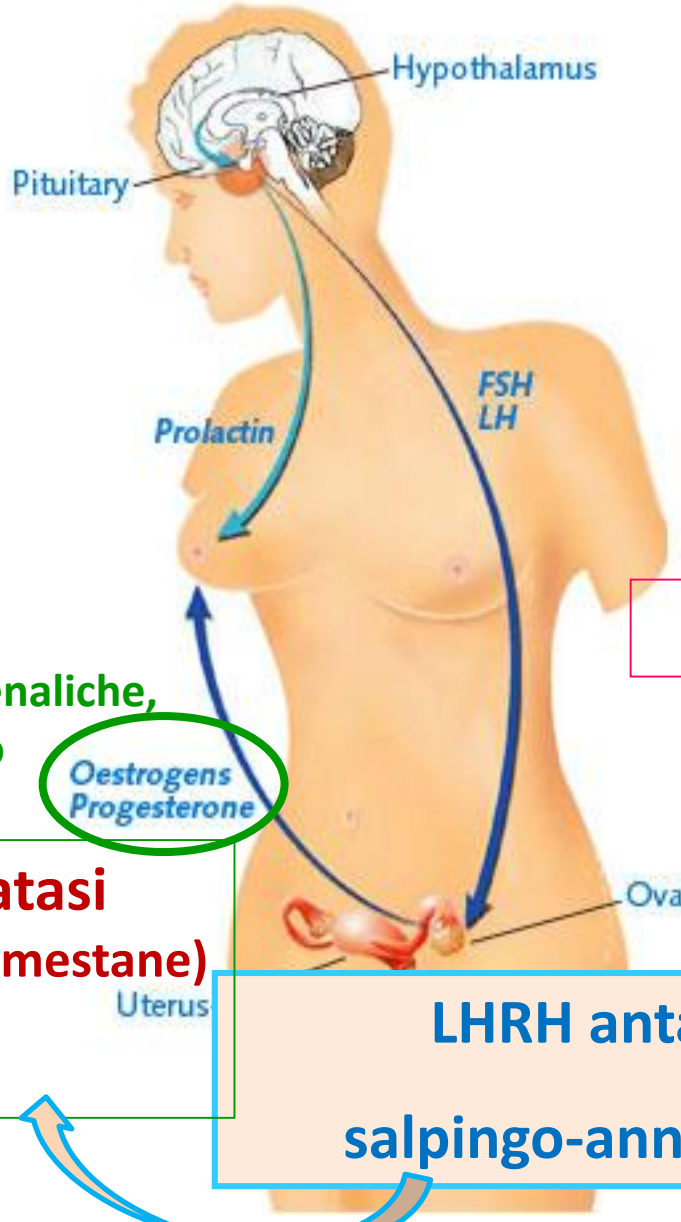
«TARGET» THERAPY

- Farmaci diretti contro uno specifico bersaglio molecolare espresso sulle cellule tumorali
- Azione selettiva e specifica verso le cellule tumorali
- Possibile utilizzo in concomitanza di chemioterapia e/o radioterapia

«TAILORED» THERAPY

ORMONOTERAPIA

POST-MENOPAUSA



PRE-MENOPAUSA

Tamoxifene

Fegato, ghiandole surrenaliche, tessuto adiposo

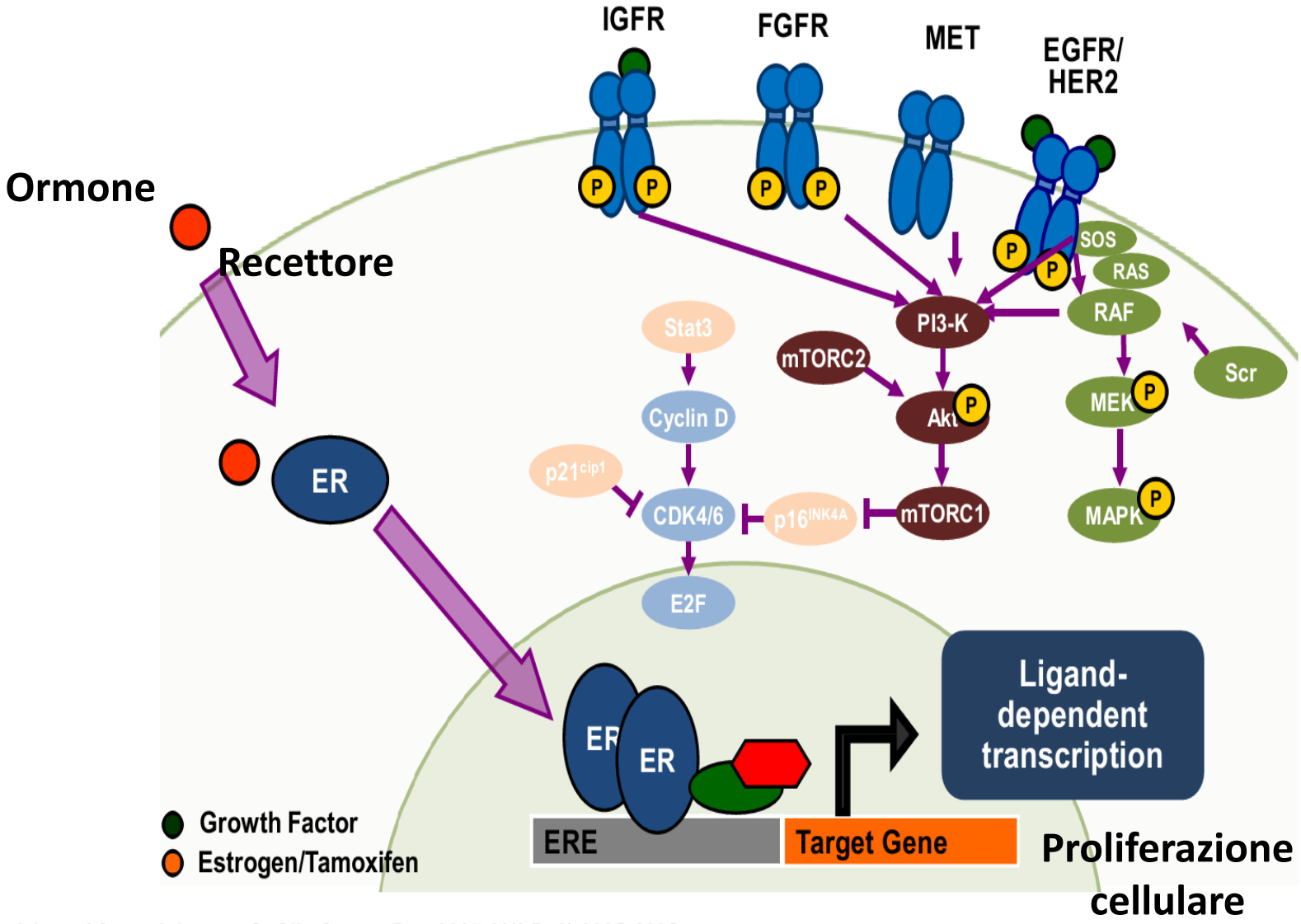
Inibitori dell'aromatasi
(letrozolo, anastrozolo, exemestane)

Fulvestrant

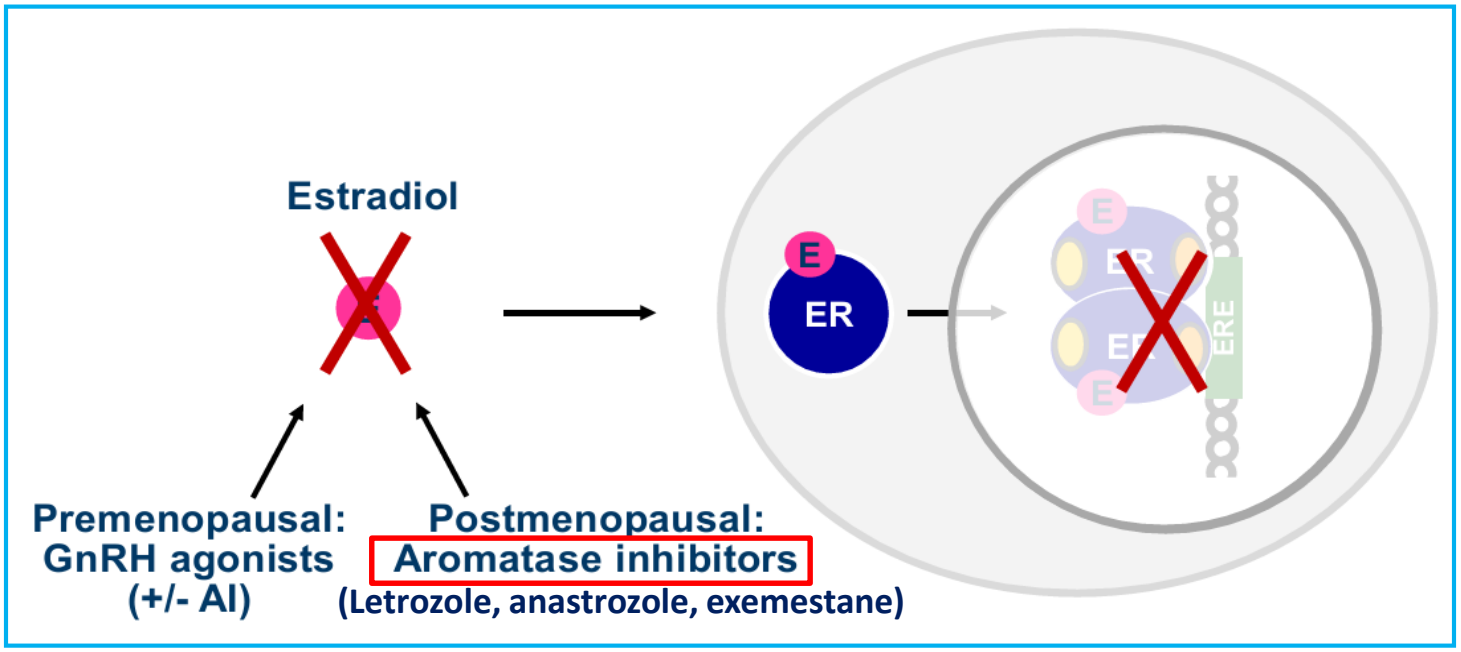
LHRH antagonisti/

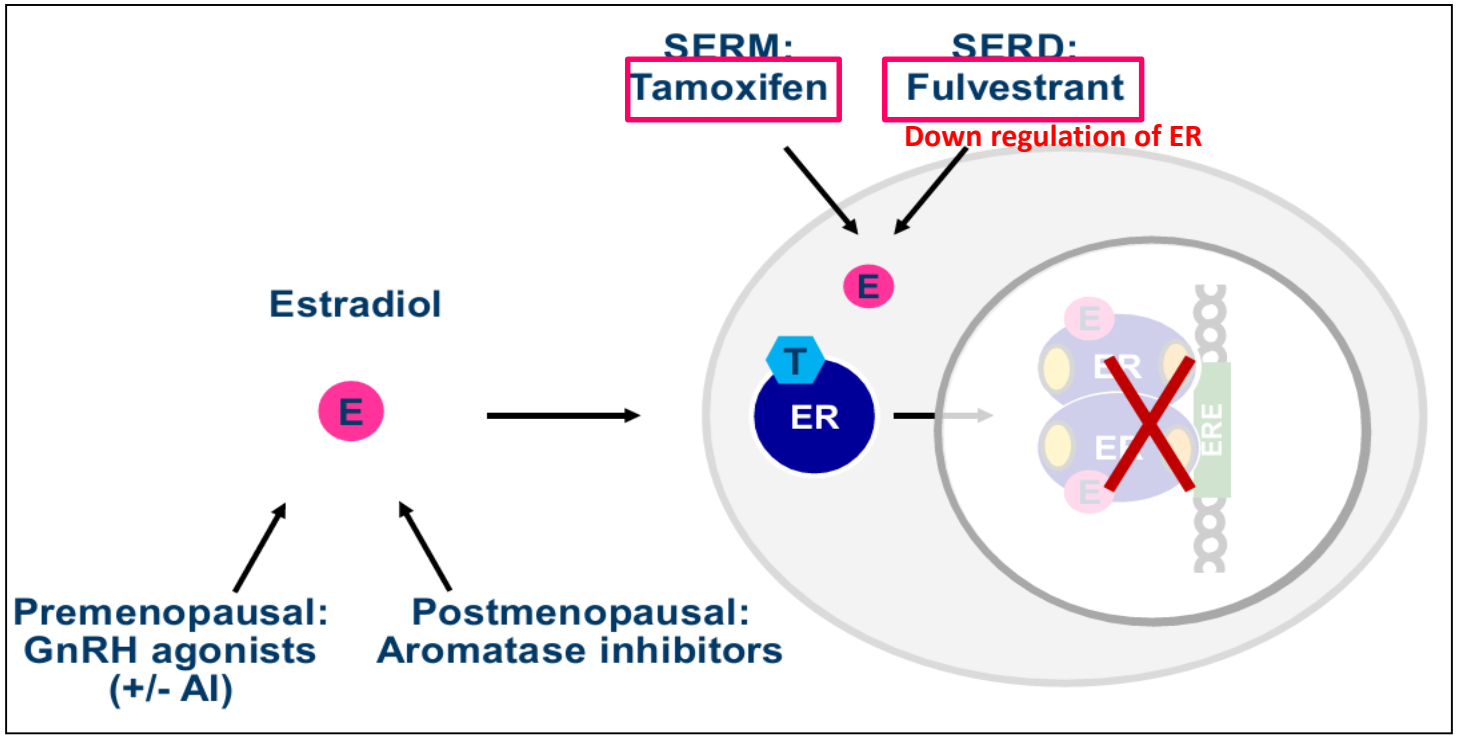
salpingo-annessiectomia

ER-Signaling and Cellular Signaling Network



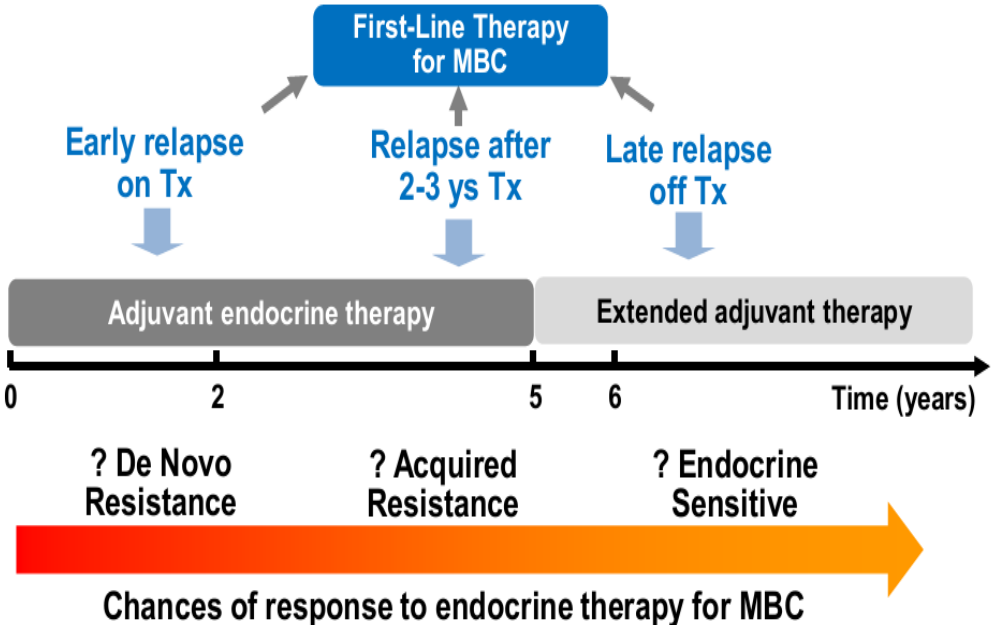
Adapted from: Johnston S. *Clin Cancer Res*. 2005;11(2 Pt 2):889S-899S.





MECCANISMI D'AZIONE DELLA TERAPIA ENDOCRINA NEL CARCINOMA MAMMARIO

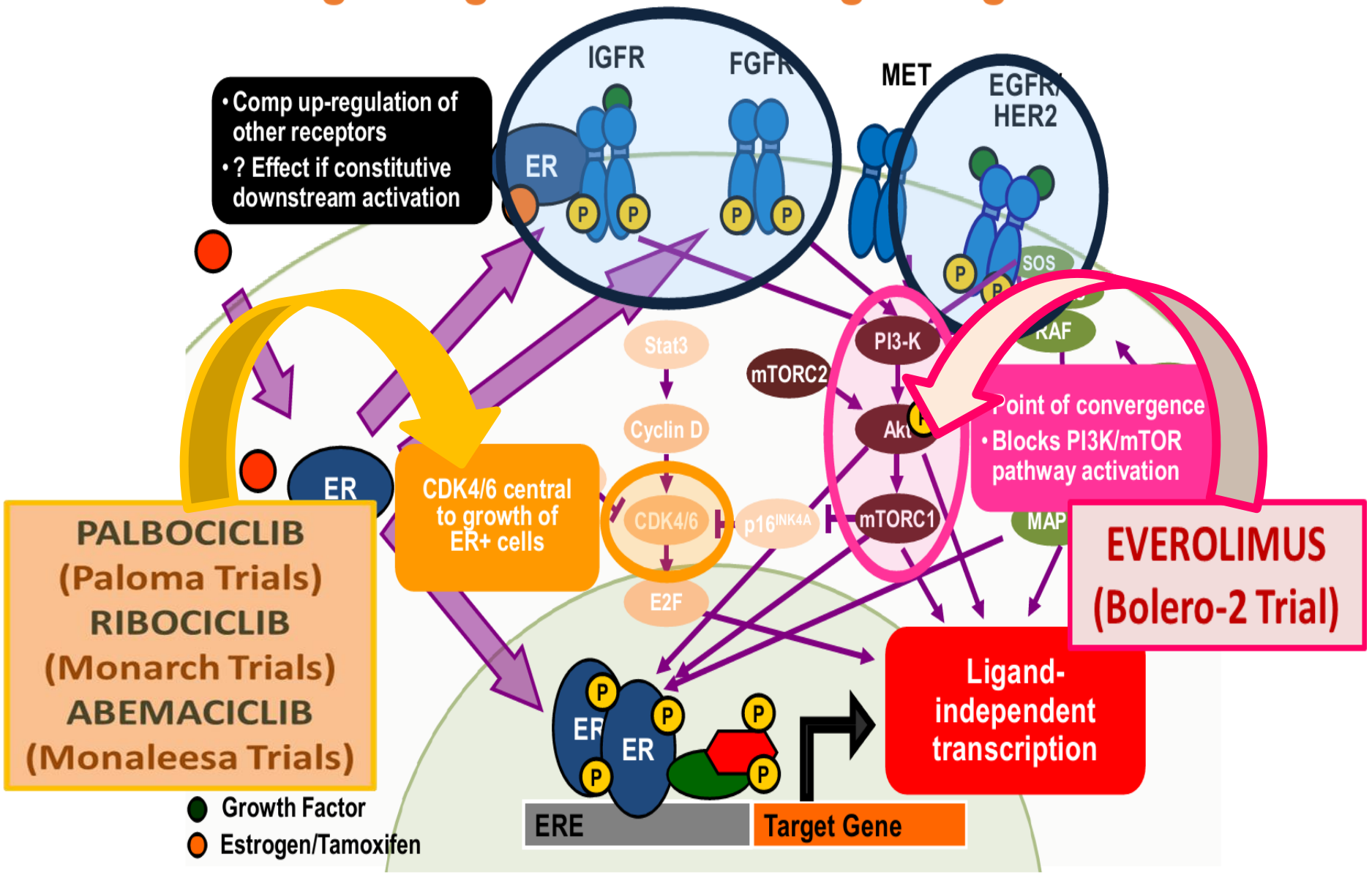
Defining Endocrine Sensitivity/Resistance With Adjuvant Treatment



MECCANISMI DI RESISTENZA ALLA TERAPIA ORMONALE NEL CARCINOMA MAMMARIO METASTATICO RECETTORE ORMONALE POSITIVO

TARGET THERAPY?

ER-Signaling and Cellular Signaling Network



Adapted from: Johnston S. *Clin Cancer Res*. 2005;11(2 Pt 2):889S-899S.

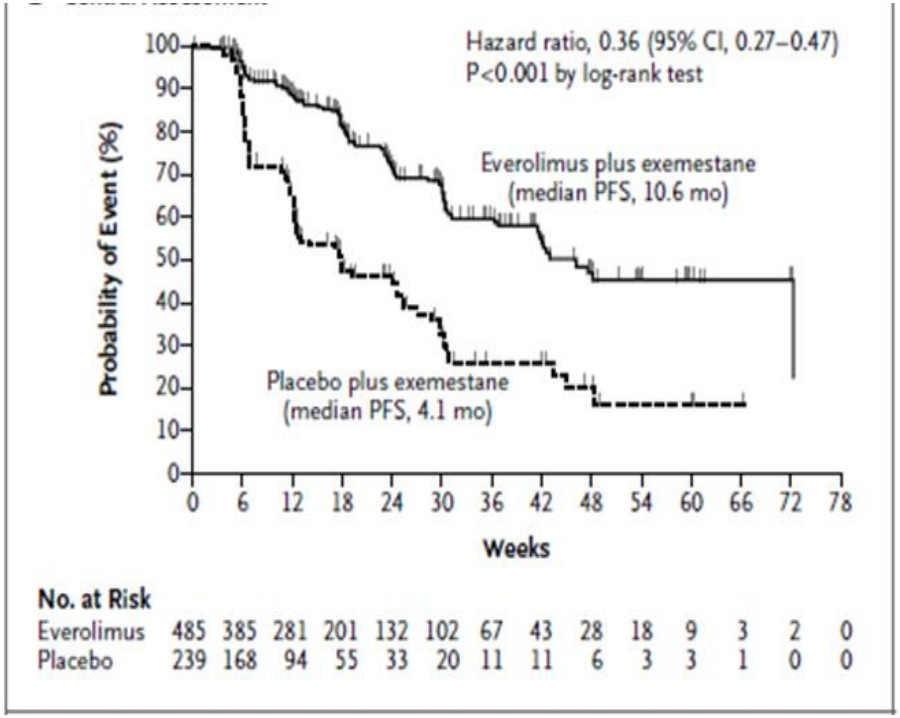
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Everolimus in Postmenopausal Hormone-Receptor–Positive Advanced Breast Cancer

José Baselga, M.D., Ph.D., Mario Campone, M.D., Ph.D., Martine Piccart, M.D., Ph.D., Howard A. Burris III, M.D., Hope S. Rugo, M.D., Tarek Sahmoud, M.D., Ph.D., Shinzaburo Noguchi, M.D., Michael Gnant, M.D., Kathleen I. Pritchard, M.D., Fabienne Lebrun, M.D., J. Thaddeus Beck, M.D., Yoshinori Ito, M.D., Denise Yardley, M.D., Ines Deleu, M.D., Alejandra Perez, M.D., Thomas Bachelot, M.D., Ph.D., Luc Vittori, M.Sc., Zhiying Xu, Ph.D., Pabak Mukhopadhyay, Ph.D., David Lebwohl, M.D., and Gabriel N. Hortobagyi, M.D.

N ENGL J MED 366;6 NEJM.ORG FEBRUARY 9, 2012



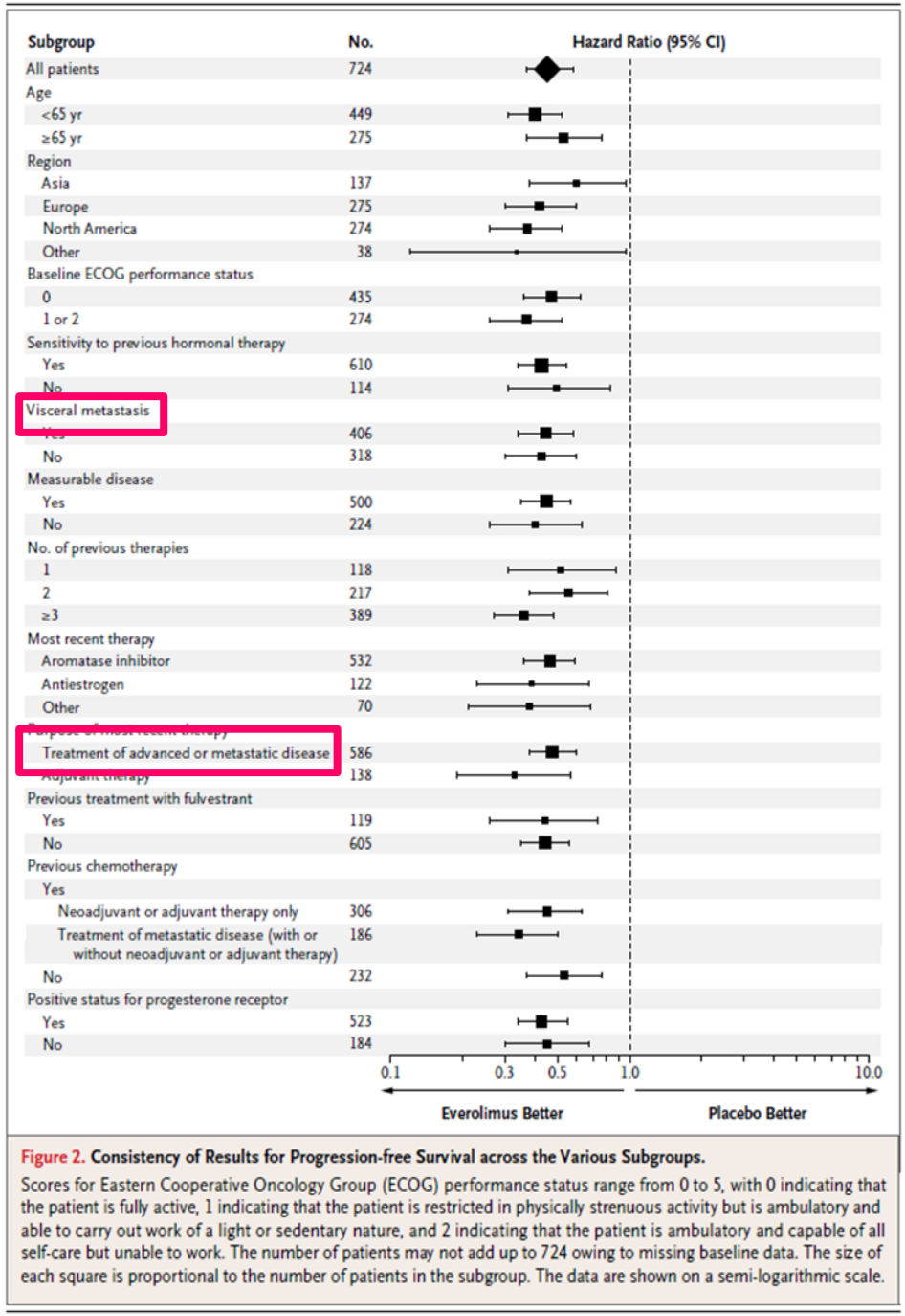


Figure 2. Consistency of Results for Progression-free Survival across the Various Subgroups.

Scores for Eastern Cooperative Oncology Group (ECOG) performance status range from 0 to 5, with 0 indicating that the patient is fully active, 1 indicating that the patient is restricted in physically strenuous activity but is ambulatory and able to carry out work of a light or sedentary nature, and 2 indicating that the patient is ambulatory and capable of all self-care but unable to work. The number of patients may not add up to 724 owing to missing baseline data. The size of each square is proportional to the number of patients in the subgroup. The data are shown on a semi-logarithmic scale.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 17, 2016 VOL. 375 NO. 20

Palbociclib and Letrozole in Advanced Breast Cancer

...m, M.D., Ph.D.,
...e, M.D.,
...M.D., Ph.D.,

Lancet Oncol 2016; 17: 425–39

Articles

Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial

Massimo Cristofanilli*, Nicholas C Turner*, Igor Bondarenko, Jungsil Ro, Seock-Ah Im, Norikazu Masuda, Marco Colleoni, Angela DeMichele, Sherene Loi, Sunil Verma, Hiroji Iwata, Nadia Harbeck, Ke Zhang, Kathy Puyana Theall, Yuqiu Jiang, Cynthia Huang Bartlett, Maria Koehler, Denn...

Updated Results From MONALEESA-2, a Phase 3 Trial of First-line Ribociclib + Letrozole in Hormone Receptor-Positive (HR+), HER2-Negative (HER2–), Advanced Breast Cancer (ABC)

Abstract 1038

Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Paluch-Shimon S, Campone M, Petrakova K, Blackwell KL, Winer EP, Janni W, Verma S, Conte PF, Arteaga CL,

MONARCH 2: Abemaciclib in Combination With Fulvestrant in Patients With HR+/HER2- Advanced Breast Cancer Who Progressed on Endocrine Therapy

Abstract 1000

Sledge GW, Toi M, Neven P, Sohn J, Inoue K, Pivot XB, Burdaeva ON, Okera M, Masuda N, Kaufman PA, Koh HA, Grischke E-M, Frenzel M, Lin Y, Barriga S, Smith IC, Bourayou N, Llombart A

MOLECOLE DISPONIBILI NELLA PRATICA CLINICA (up date aprile 2018

	FDA (USA)	EMA (EUROPE)	AIFA (ITALY)
Everolimus (2012)	X	X	X
Palbociclib	X	X	X
Ribociclib	X	X	/
Abemaciclib	X	/	/

MODALITA' DI ASSUNZIONE

Everolimus (AFINITOR): per os, somministrazione giornaliera continua.

Palbociclib (IBRANCE), **Ribociclib**: per os, 3 settimane su 4/mese, in un'unica somministrazione giornaliera, combinati con inibitore dell'aromatasi «letrozolo» e, solo Palbociclib, anche con «Fulvestrant».

Abemaciclib (solo in studi clinici): per os, somministrazione giornaliera continua.

CDK 4 and 6 Inhibitors for the Treatment of HR-Positive, HER2-Negative Breast Cancer

Setting	Trial	Arm	Median PFS (mo)	Hazard Ratio (95% CI)
Endocrine sensitive No prior systemic treatment for advanced disease	PALOMA-2[a]	**Palbociclib** + letrozole	**24.8**	0.58 (0.46, 0.72); $P < .001$
		placebo + letrozole	14.5	
	MONALEESA-2[b,c]	**Ribociclib** + letrozole	**25.3**	0.57 (0.46, 0.70); $P = 9.63 \times 10^{-8}$
		placebo + letrozole	16.0	
	MONARCH-3[d,e]	**Abemaciclib** + anastrozole/letrozole	**Not reached**	0.54 (0.41, 0.72); $P = .000021$
		placebo + anastrozole/letrozole	14.7	
Endocrine resistant Relapse or disease progression on prior endocrine therapy	PALOMA-3[f,g]*	**Palbociclib** + fulvestrant	**11.2**	0.50 (0.40, 0.62); $P < .0001$
		placebo + fulvestrant	4.6	
	MONARCH-2[h]**	**Abemaciclib** + fulvestrant	**16.4**	0.55 (0.45, 0.68); $P < .001$
		placebo + fulvestrant	9.3	

*Disease progression while on or within 12 months after completion of adjuvant endocrine therapy, or while on or within 1 month after endocrine therapy in the advanced setting; 1 prior line of CT allowed

**Disease progression while on or within 12 months after completion of adjuvant endocrine therapy or while on first line endocrine therapy for metastatic disease

a. Finn RS, et al. *N Engl J Med*. 2016;375:1925-1936. b. Kisqali (ribociclib) PI. c. Hortobagyi G, et al. ASCO 2017; Abstract 1038. d. Di Leo A, et al. ESMO 2017. Abstract 2360. e. Goetz et al. *J Clin Oncol*. 2017;35:3638-3646. f. Ibrance (palbociclib) PI. g. Turner N, et al. SABCS 2016. Abstract P4-22-06. h. Sledge GW Jr, et al. *J Clin Oncol*. 2017;35:2875-2884.

Table 2. Adverse Events Irrespective of Relationship to Study Treatment (with at Least 10% Incidence in the Everolimus–Exemestane Group).

Adverse Event	Everolimus and Exemestane (N=482)			Placebo and Exemestane (N=238)		
	Any Event	Grade 3 Event	Grade 4 Event	Any Event	Grade 3 Event	Grade 4 Event
	percent					
Stomatitis	56	8	0	11	1	0
Rash	36	1	0	6	0	0
Fatigue	33	3	<1	26	1	0
Diarrhea	30	2	<1	16	1	0
Decreased appetite	29	1	0	10	0	0
Nausea	27	<1	<1	27	1	0
Cough	22	1	0	11	0	0
Dysgeusia	21	<1	0	5	0	0
Headache	19	<1	0	13	0	0
Decreased weight	19	1	0	5	0	0
Dyspnea	18	4	0	9	1	<1
Arthralgia	16	1	0	16	0	0
Anemia	16	5	1	4	<1	<1
Epistaxis	15	0	0	1	0	0
Vomiting	14	<1	<1	11	<1	0
Peripheral edema	14	1	0	6	<1	0
Pyrexia	14	<1	0	6	<1	0
Aspartate aminotransferase level increased	13	3	<1	6	1	0
Constipation	13	<1	0	11	<1	0
Hyperglycemia	13	4	<1	2	<1	0
Pneumonitis	12	3	0	0	0	0
Thrombocytopenia	12	2	1	<1	0	<1
Asthenia	12	2	0	3	0	0
Alanine aminotransferase level increased	11	3	<1	3	2	0
Pruritus	11	<1	0	3	0	0
Insomnia	11	<1	0	8	0	0
Back pain	11	0	0	8	1	0

Hematological AEs are higher with CDK 4/6 inhibitors compared to endocrine therapy alone. The incidence of febrile neutropenia is low (<2%)

	Palbociclib[a]		Ribociclib[b]		Abemaciclib[c,d]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Neutropenia, %	79.5	56.1/10.4	74.3	49.7/9.6	87.7	22.3/4.6

Non-hematological AEs are higher in all trials with CDK 4 and 6 inhibitors, compared to endocrine therapy alone[a-d]

- Mostly grade 1 and 2; rarely grade 3
- Nausea, vomiting, fatigue
- Alopecia: 15% to 30%, rarely above grade 1
- Diarrhea: frequent with abemaciclib, 9% grade 3/4

Other AEs with CD4/6 inhibitors

Liver enzyme elevation with ribociclib and abemaciclib[a-c]

- AST/ALT: 4%-7%, grade 3/4

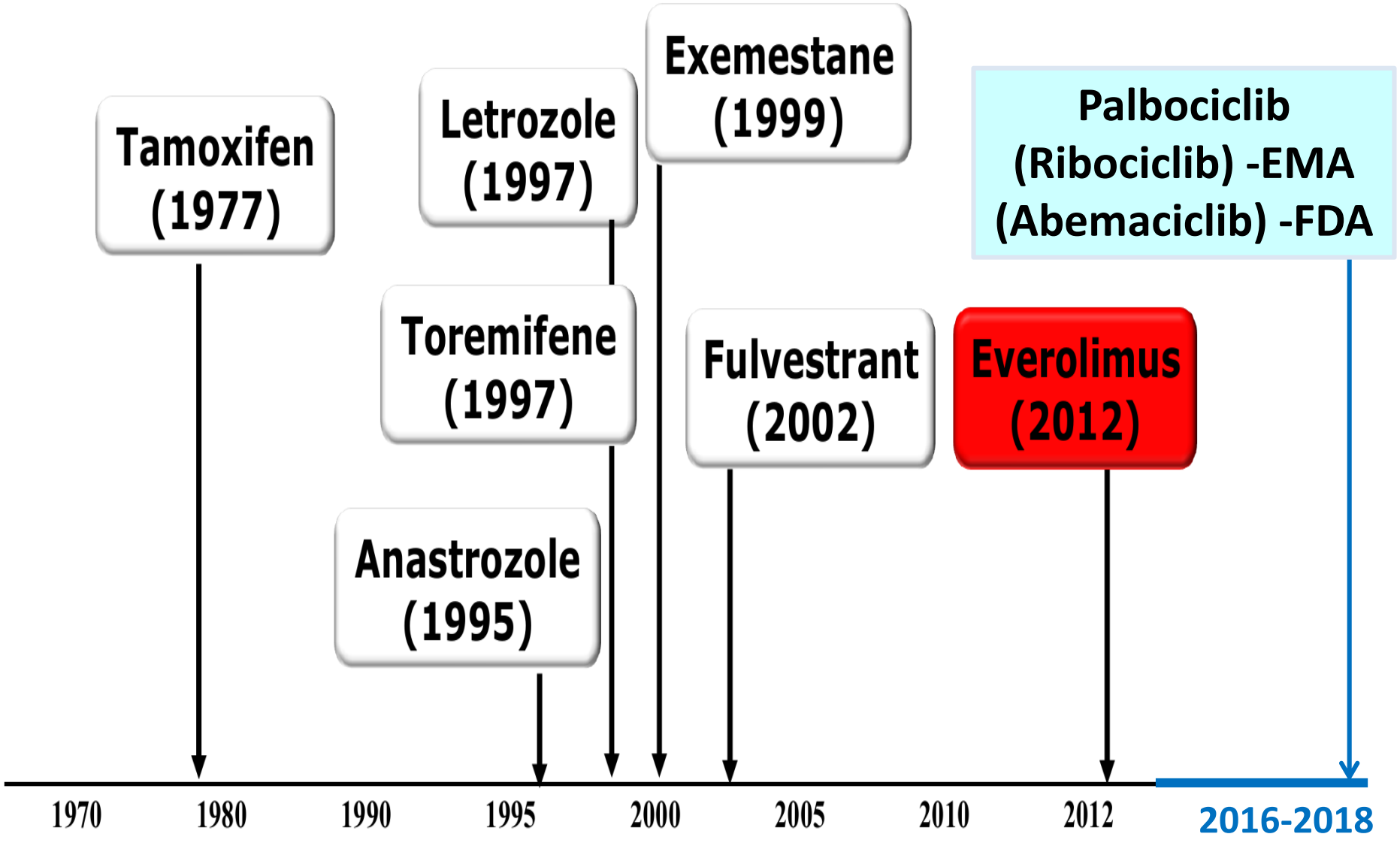
Blood creatinine with abemaciclib[b,c]

- 10% to 20% with abemaciclib, rarely grade 3

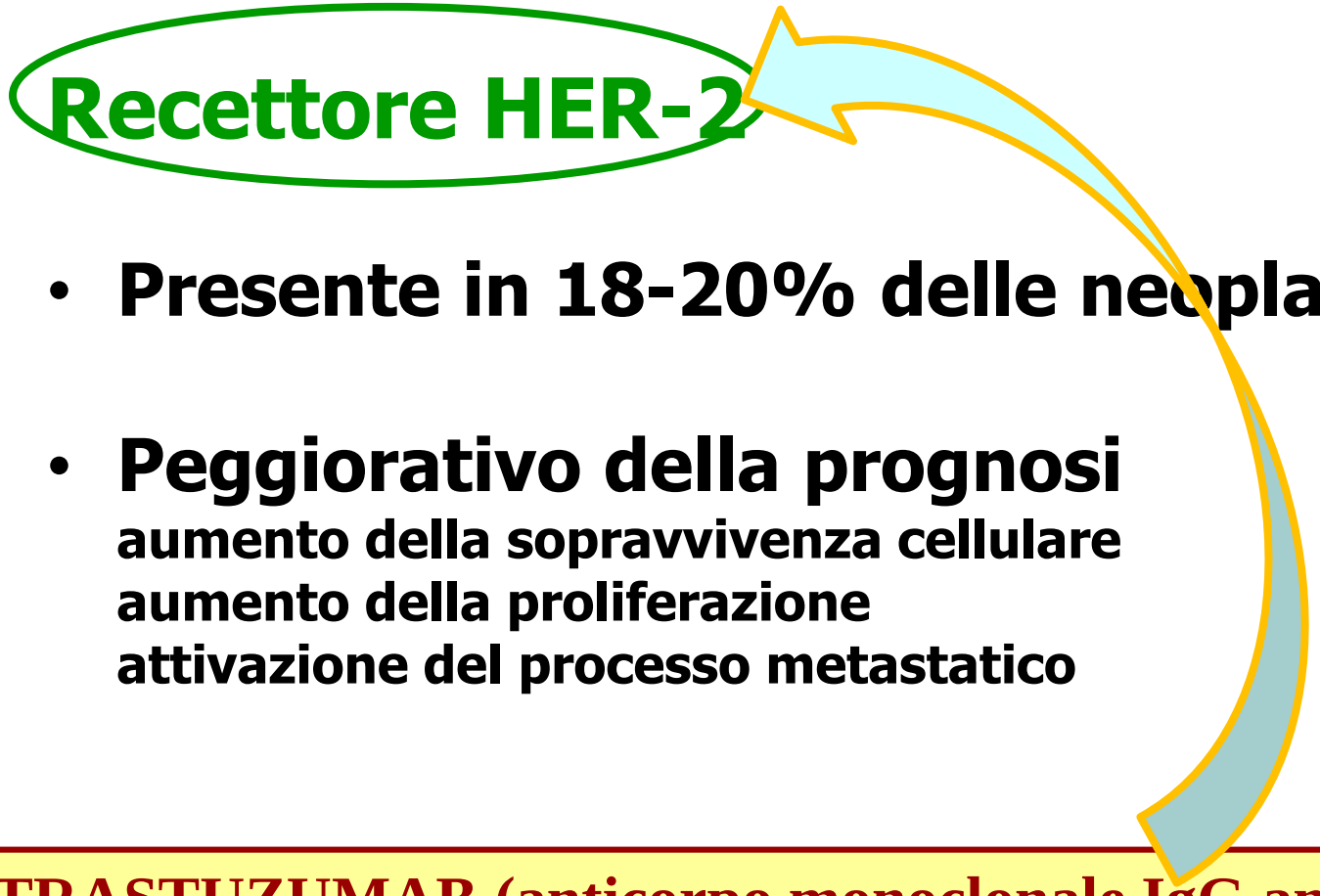
QTc interval prolongation with ribociclib[a]

- 3% grade 2
- 0.3% grade 3 (>500 ms prolongation)

PIETRE MILIARI DELLA TERAPIA DEL CARCINOMA MAMMARIO ORMONOSENSIBILE



TERAPIE ANTI HER-2



- **Presente in 18-20% delle neoplasie**
- **Peggiorativo della prognosi**
  aumento della sopravvivenza cellulare
  aumento della proliferazione
  attivazione del processo metastatico

TRASTUZUMAB (anticorpo monoclonale IgG antigene-specifico)

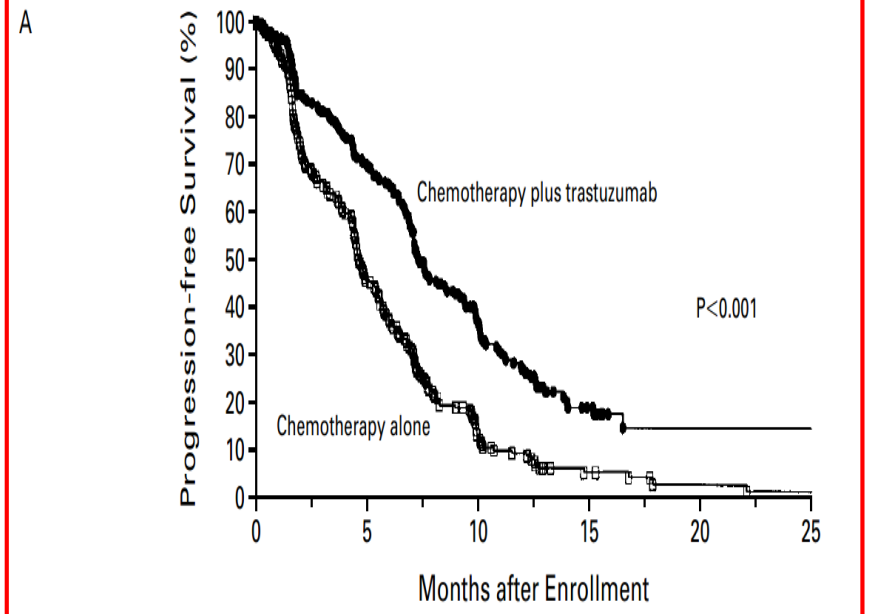
Agente bersaglio contro HER2

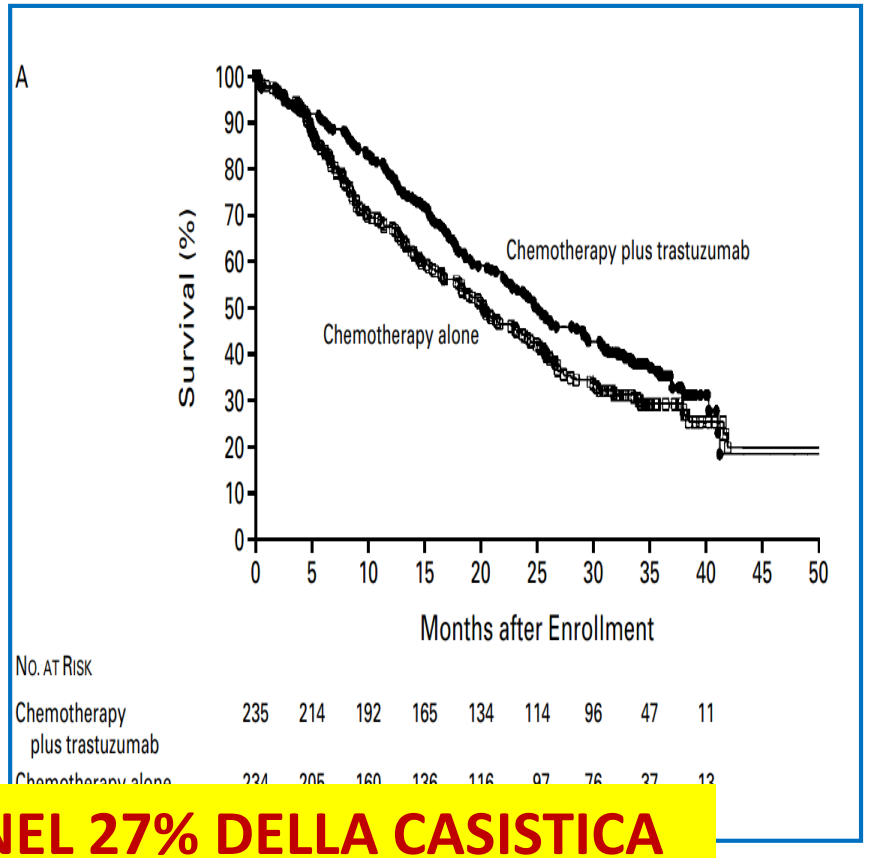
The New England Journal of Medicine

VOLUME 344 MARCH 15, 2001 NUMBER 11

USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2

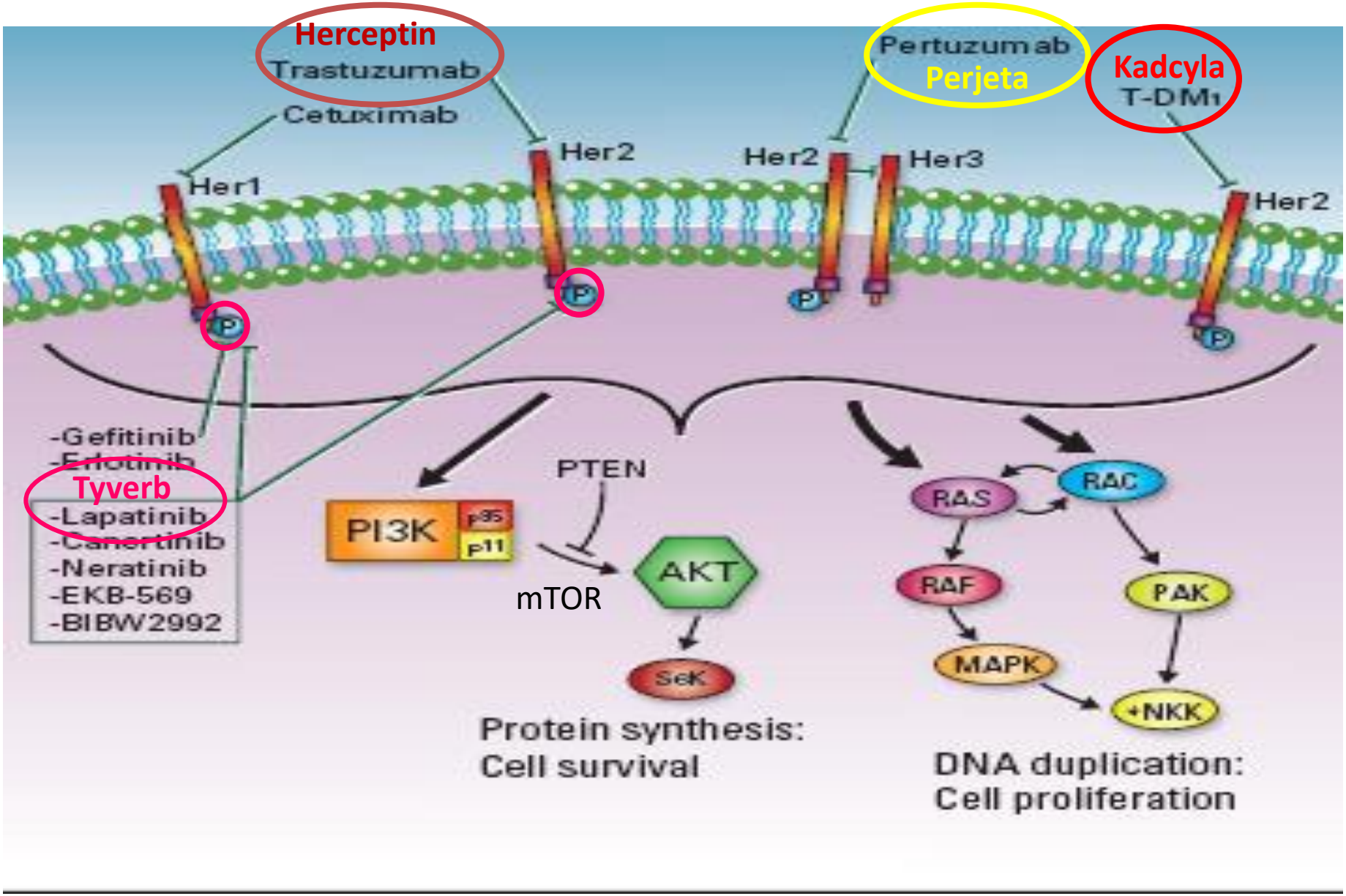
DENNIS J. SLAMON, M.D., PH.D., BRIAN LEYLAND-JONES, M.D., STEVEN SHAK, M.D., HANK FUCHS, M.D., VIRGINIA PATON, PHARM.D., ALEX BAJAMONDE, PH.D., THOMAS FLEMING, PH.D., WOLFGANG EIERMANN, M.D., JANET WOLTER, M.D., MARK PEGRAM, M.D., JOSE BASELGA, M.D., AND LARRY NORTON, M.D.*





DISFUNZIONE CARDIACA NEL 27% DELLA CASISTICA

TERAPIE BERSAGLIO NEL CARCINOMA MAMMARIO HER2 POSITIVO



EMILIA STUDY

HER2-positive LABC or MBC (N=980)

- Prior taxane and trastuzumab
- Progression on metastatic treatment or within 6 months of adjuvant treatment

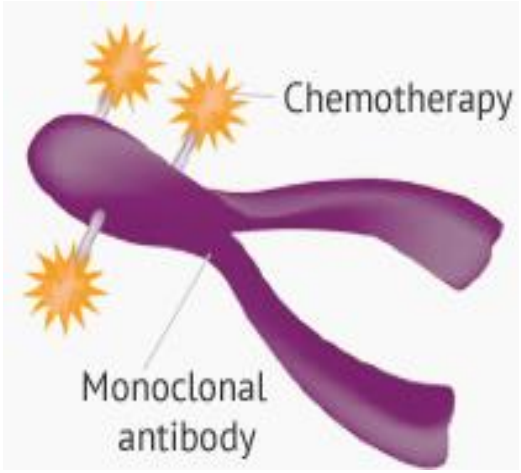
1:1

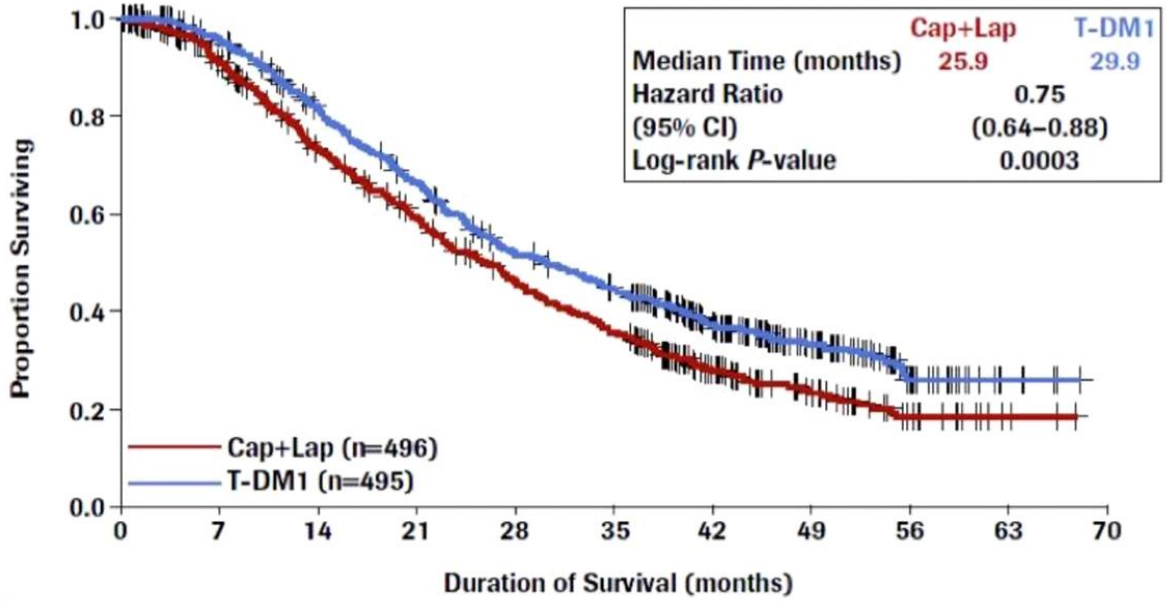
T-DM1
3.6 mg/kg q3w IV

→ PD

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

→ PD





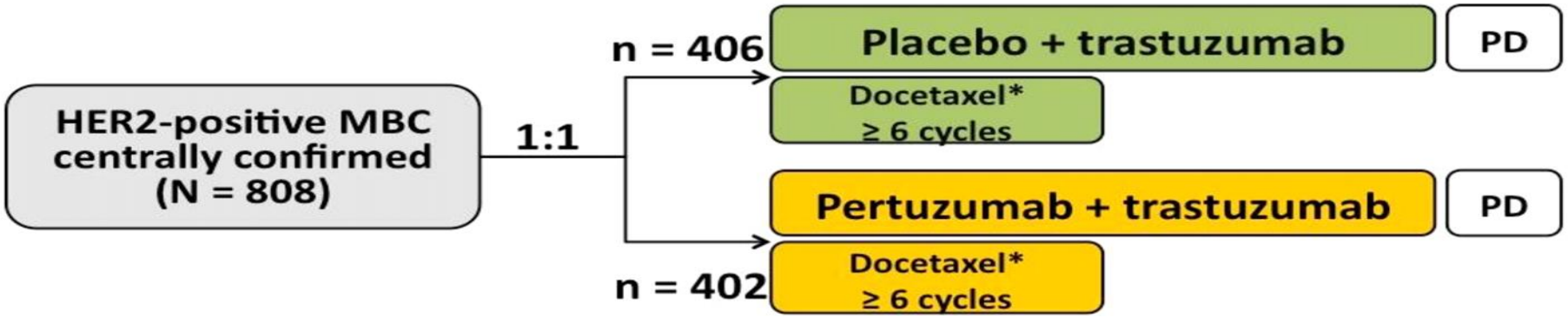
Number at Risk:

Cap+Lap	496	418	326	258	195	153	82	48	19	3	0
T-DM1	495	451	374	302	231	194	127	68	23	5	0

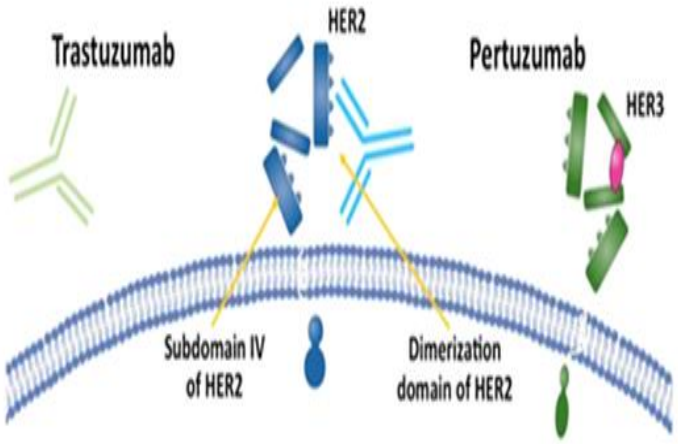
Cap+Lap, capecitabine plus lapatinib; CI, confidence interval; T-DM1, trastuzumab emtansine.

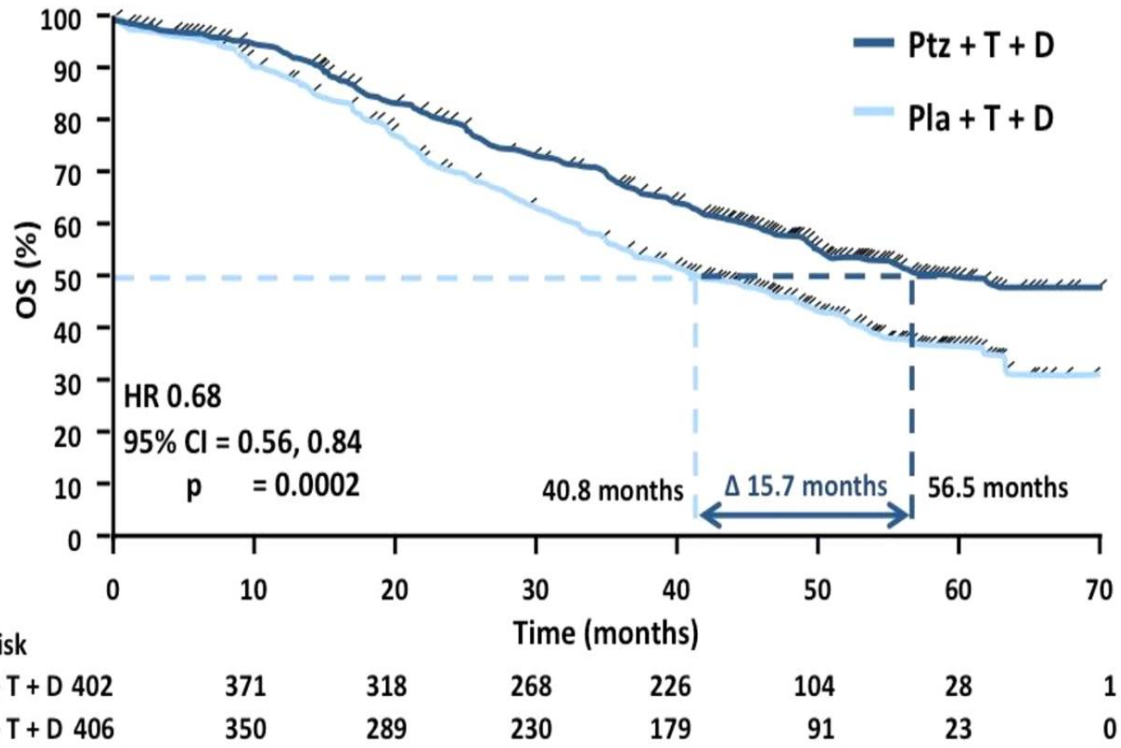
Diéras et al., SABCS 2015.

CLEOPATRA STUDY



Median follow-up 50 months (range 0 – 70 months)





Swain SM, et al. *N Engl J Med.* 2015;372(8):724-734.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lapatinib plus Capecitabine for HER2-Positive Advanced Breast Cancer

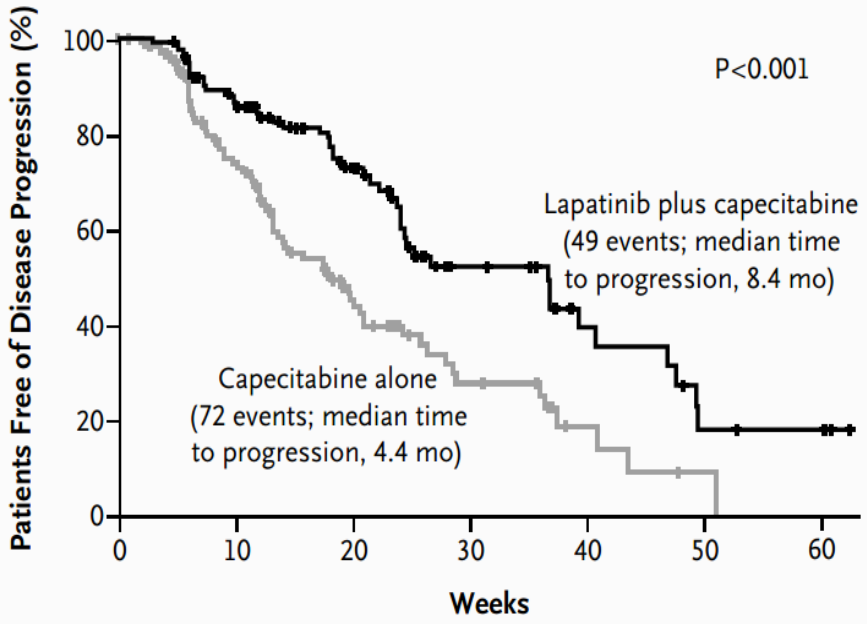
Charles E. Geyer, M.D., John Forster, M.Sc., Deborah Lindquist, M.D., Stephen Chan, M.D., C. Gilles Romieu, M.D., Tadeusz Pienkowski, M.D., Ph.D., Agnieszka Jagiello-Gruszfeld, M.D., John Crown, M.D., Arlene Chan, M.D., Bella Kaufman, M.D., Dimosthenis Skarlos, M.D., Mario Campone, M.D., Neville Davidson, M.D., Mark Berger, M.D., Cristina Oliva, M.D., Stephen D. Rubin, M.D., Steven Stein, M.D., and David Cameron, M.D.

163 Received combination therapy (lapatinib, 1250 mg by mouth/day continuously, plus capecitabine, 2000 mg/m²/day orally on days 1–14 every 3 wk)

vs

161 Received monotherapy (capecitabine, 2500 mg/m²/day orally on days 1–14 every 3 wk)

A



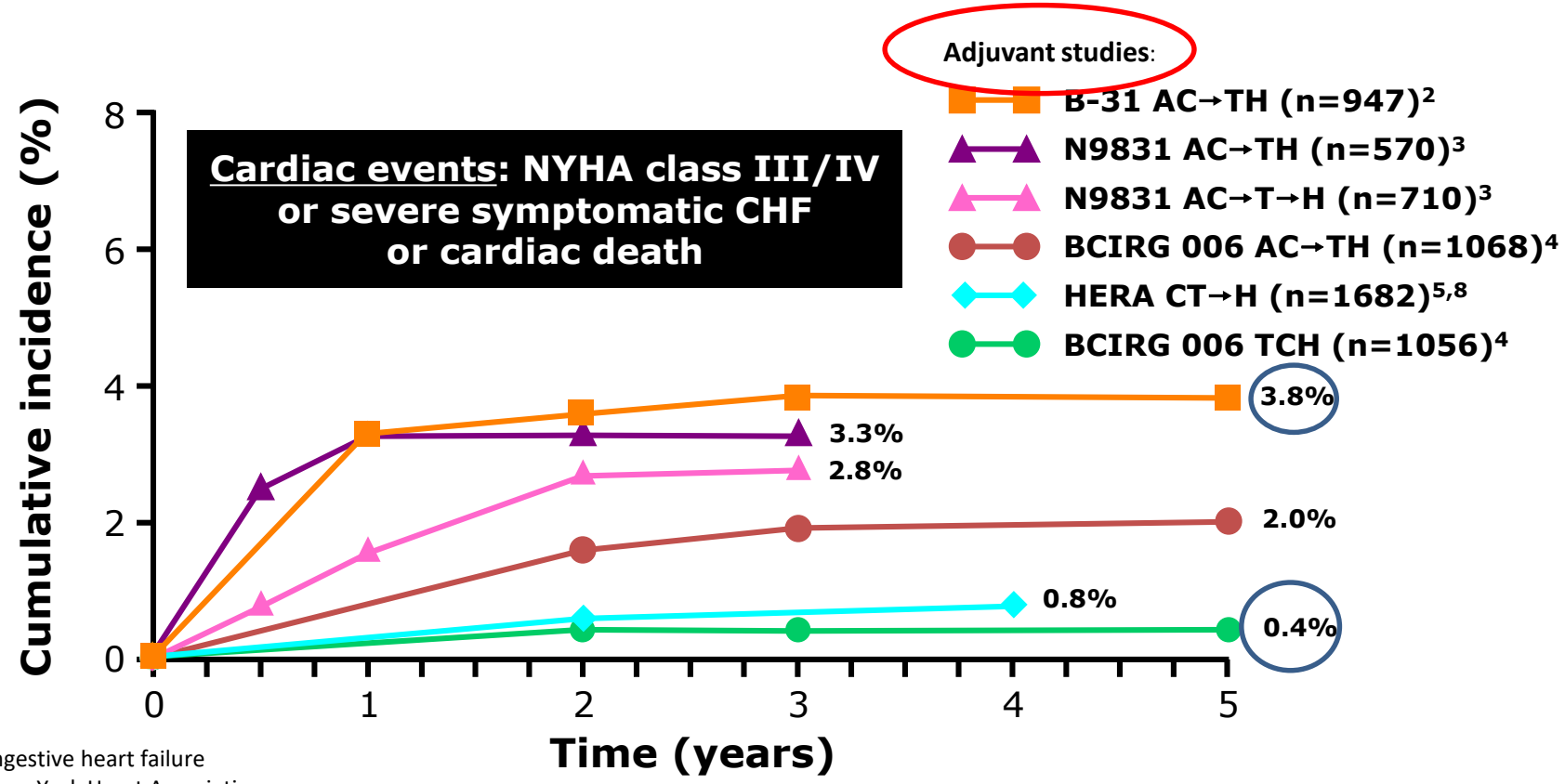
No. at Risk							
Lapatinib plus capecitabine	163	96	52	21	10	4	3
Capecitabine alone	161	78	33	14	4	1	0

COMMON OR SEVERE TOXICITIES OF anti-HER2 BIOLOGIC AGENTS

Anti-HER2 Agent	Common or Serious Grade ¾ Adverse Events
Trastuzumab	Cardiotoxicity Infusion reactions
Lapatinib	Diarrhea Rash
Pertuzumab	Neutropenia Febrile neutropenia Diarrhea Rash
T-DM1	Thrombocytopenia Liver Disfunction (elevate AST/ALT)

Herceptin has a consistent safety profile based on experience in ~1,000,000 patients[1]

- Herceptin is well tolerated with a consistent safety and tolerability profile[2–7]
- Low cumulative incidence of cardiac events after long-term follow-up[2–7]



CHF, congestive heart failure
NYHA, New York Heart Association

1. PSUR 03/2011; 2. Rastogi P, *et al.* 2007; 3. Perez EA, *et al.* 2008; 4. Slamon D, *et al.* 2011
5. Procter M, *et al.* 2010; 6. Gianni L, *et al.* 2011; 7. Perez EA, *et al.* 2011; 8. Suter T, *et al.* 2007

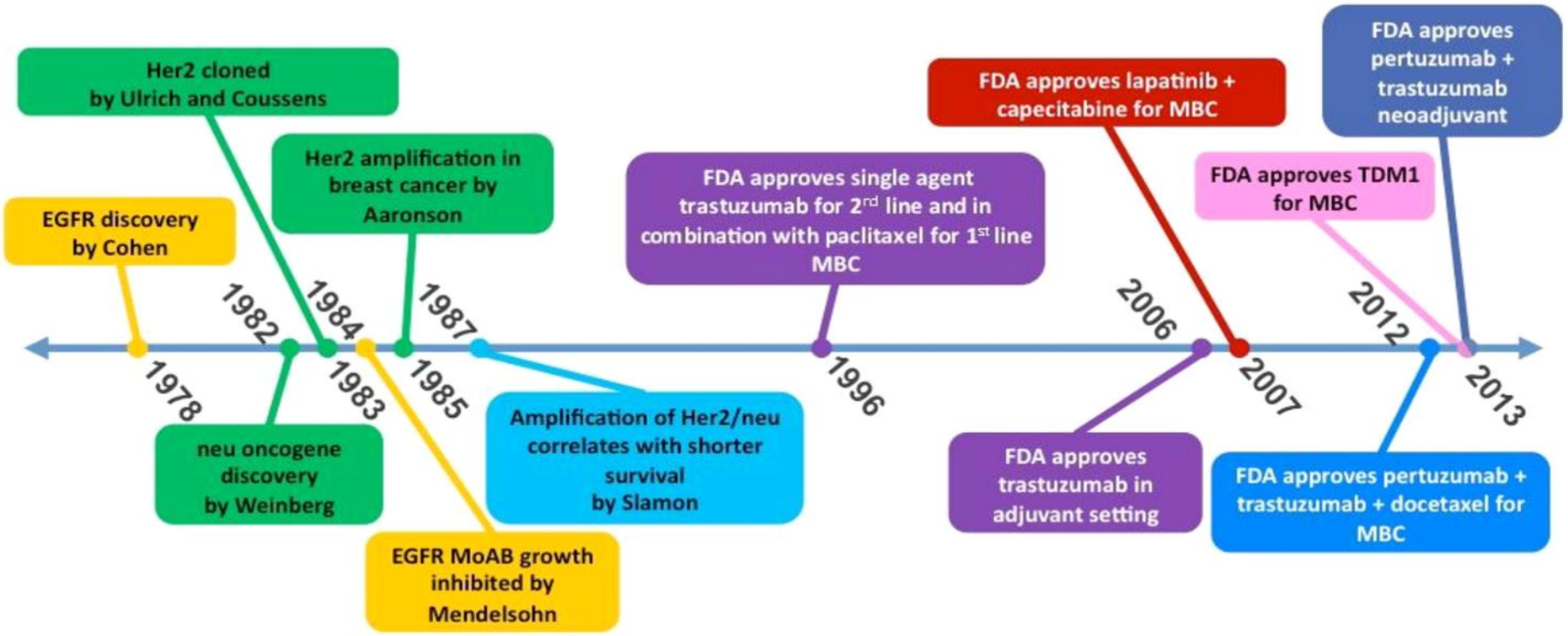
Cardiac Dysfunction

CARDIAC EVENTS IDENTIFIED IN «EMILIA study» (metastatic setting)

	Cap + Lap	T-DM1
Cardiac dysfunction AEs,[a] n (%)	(n=488)	(n=490)
All grades	15 (3.1)	9 (1.8)
Grade 3	2 (0.4)	1 (0.2)
Lowest post-baseline LVEF value, n (%)	(n=461)	(n=482)
≥45%	454 (98.5)	476 (98.8)
≥40 to <45%	4 (0.9)	3 (0.6)
<40%	3 (0.7)	3 (0.6)
LVEF <50% and ≥15-point decrease from baseline, n (%)	(n=445) 7 (1.6)	(n=481) 8 (1.7)

REVERSIBILITY OF CARDIAC ADVERSE EVENTS IN HERA trial

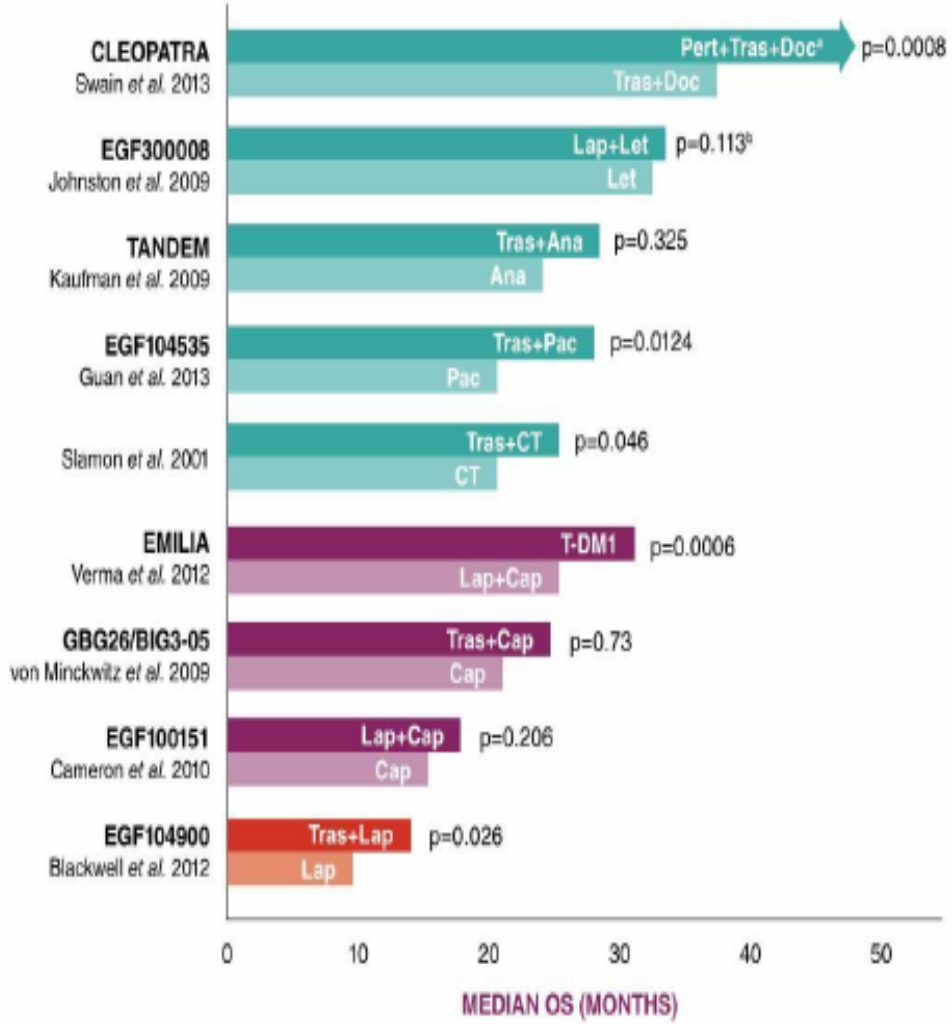
	Recovery (% of patients)	Median Time (days)
Cardiac death	-	-
Severe CHF	**80**	**124**
Symptomatic CHF	**67**	**151**
Confirmed significant LVEF drop	**69**	**192**



Gli agenti terapeutici selettivi sul carcinoma mammario HER2 positivo hanno apportato significative modifiche nella disponibilità di trattamenti specifici e cambiato la storia naturale del carcinoma mammario metastatico HER2 positivo

Selezione dei carcinomi mammari: determinazione di HER2 con metodica immunoistochimica e/o amplicazione genica (FISH, SISH)
Selezione dei pazienti con attenzione alle comorbidità cardiache e programmazione di routinario monitoraggio ecocardiografico

HER 2-Positive MBC Overall Survival



LEGEND

- First-Line
- Second-Line Plus
- Third Line-Plus

ABBREVIATIONS

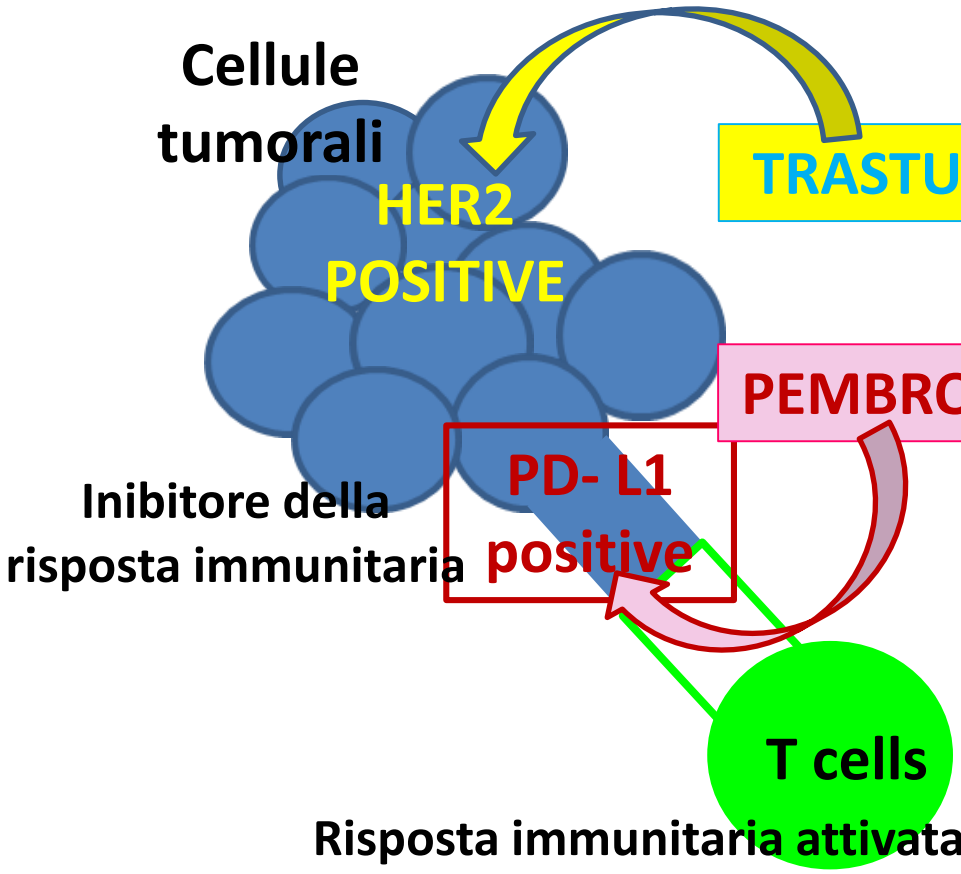
Ana	anastrozole
Cape	capecitabine
CT	chemotherapy
Doc	docetaxel
Lap	lapatinib
Let	letrozole
OS	overall survival
Pac	paclitaxel
Pert	pertuzumab
T-DM1	trastuzumab emtansine
Tras	trastuzumab

Source: Verma et al. The Oncologist 2013

Phase Ib/II study evaluating safety and efficacy of pembrolizumab and trastuzumab in patients with trastuzumab-resistant HER2-positive advanced breast cancer: Results from the PANACEA study

(IBCSG 45-13/BIG 4-13/KEYNOTE-014)

Loi S, et al. SABCS 2017. Abstract GS2-06



ORR: 15-17% in donne con tumori PD-L1 + trattate con pembrolizumab

OS mediana: 16.7 mesi nelle donne con tumore PD-L1 + verso 7 mesi nelle donne con PD-L1-

Conclusione: per le donne **ampiamente pretrattate con farmaci anti-HER2**, il pembrolizumab rappresenta una possibile opzione terapeutica **se il tumore co-esprime anche PDL-1**

CARCINOMA MAMMARIO «TRIPLO NEGATIVO»: RECETTORI ORMONALI NON PRESENTI E HER2 NEGATIVO

SOLO CHEMIOTERAPIA ?

Preferred single agents:

Anthracyclines
- Doxorubicin
- Pegylated liposomal doxorubicin

Taxanes
- Paclitaxel

Anti-metabolites
- Capecitabine
- Gemcitabine

Other microtubule inhibitors
- Vinorelbine
- Eribulin

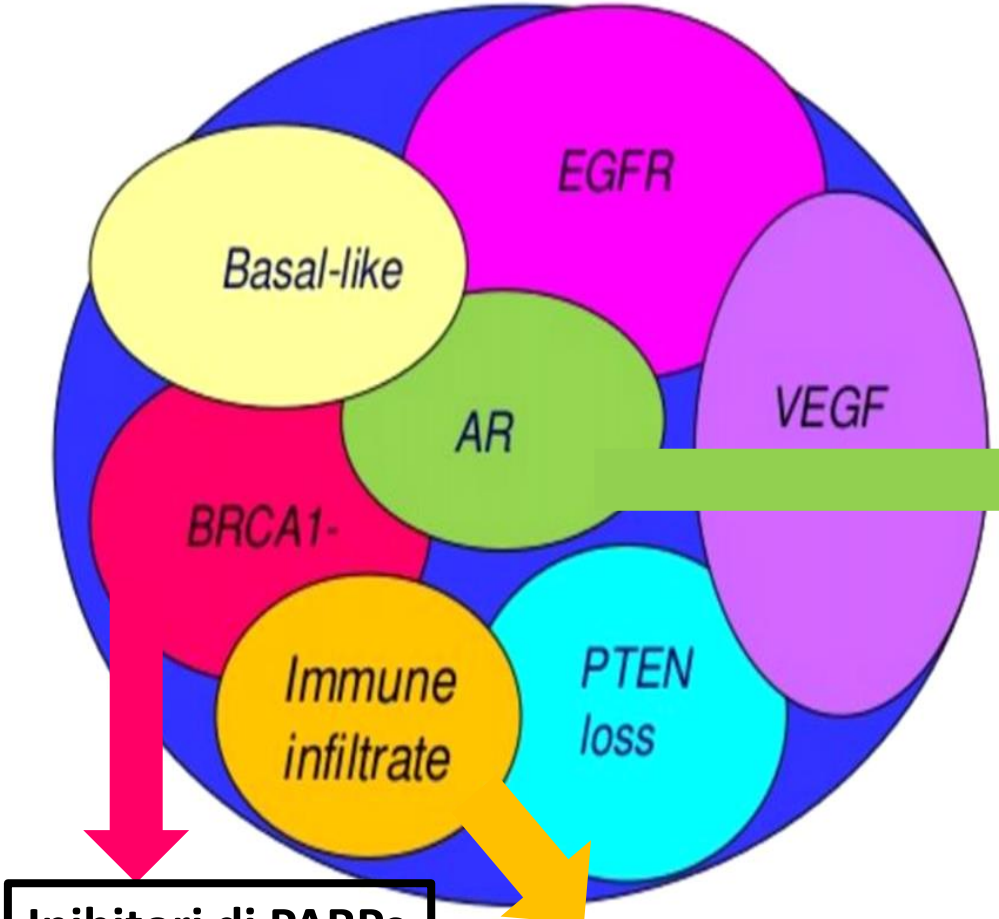
Other single agents:
- Cyclophosphamide
- Carboplatin
- Docetaxel
- Albumin-bound paclitaxel
- Cisplatin
- Epirubicin
- Ixabepilone

Regimen	n	ORR (%)	PFS (months)	Prior Chemo (%)	Disease-free interval (median)
Gemcitabine / Carboplatin[1]	258	30%	4.1	90%	15 mos
1st line	*148*		*4.6*		*15.9 mos*
2nd/3rd line	*110*		*2.9*		*13.8 mos*
Carboplatin or cisplatin[2]	86	30%	3.2	86%	NA
1st line		*32%*			
2nd line		*20%*			
Cisplatin – 1st & 2nd line[3]	58	10%	1.5	83%	15.4 mos

PLATINUM in METASTATIC TNBC

CARCINOMA MAMMARIO «TRIPLO NEGATIVO»: RECETTORI ORMONALI NON PRESENTI E HER2 NEGATIVO

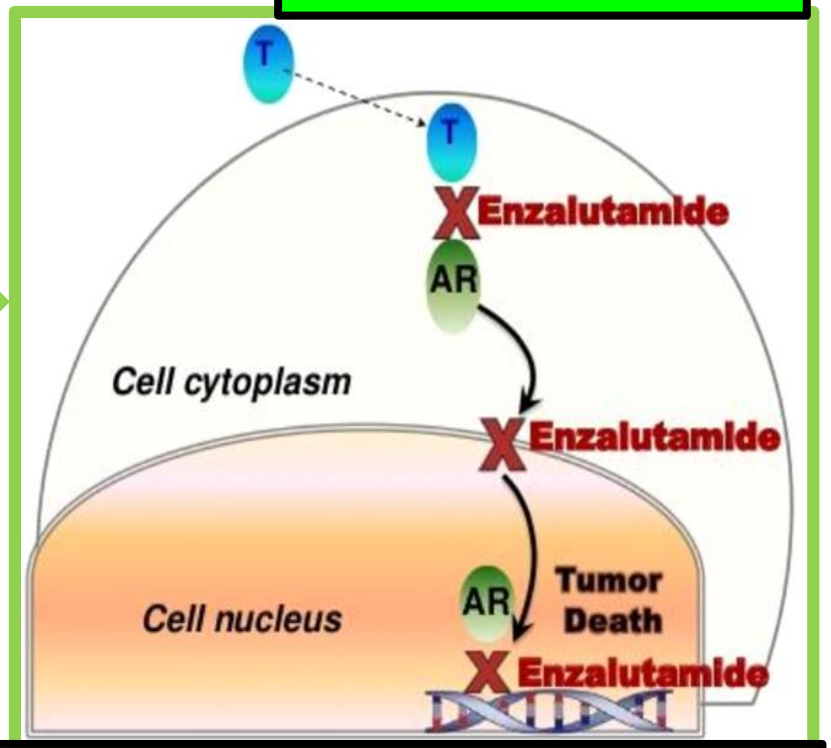
TANTE MALATTIE DIFFERENTI…
TANTI BERSAGLI PER TERAPIE “MIRATE”?



Inibitori di PARPs

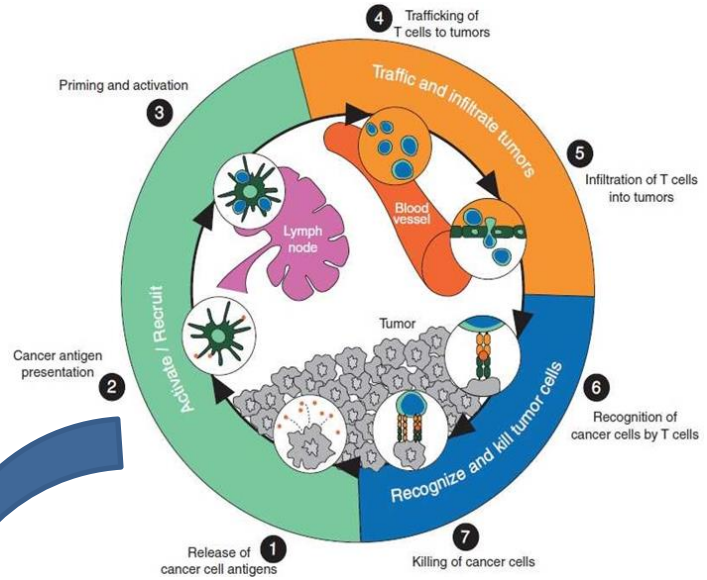
Immunoterapia

ORMONOTERAPIA E TNBC

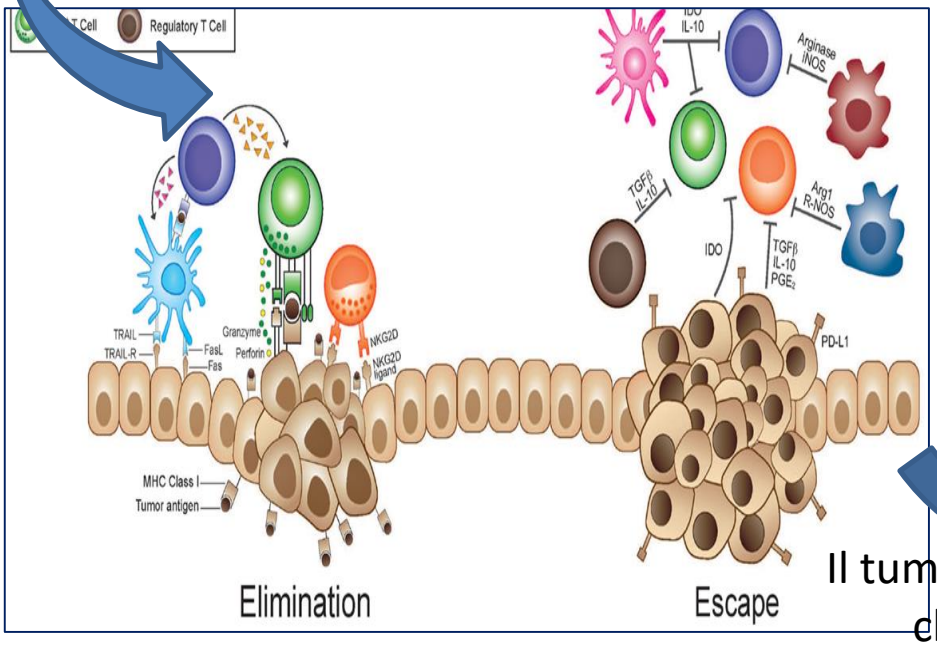


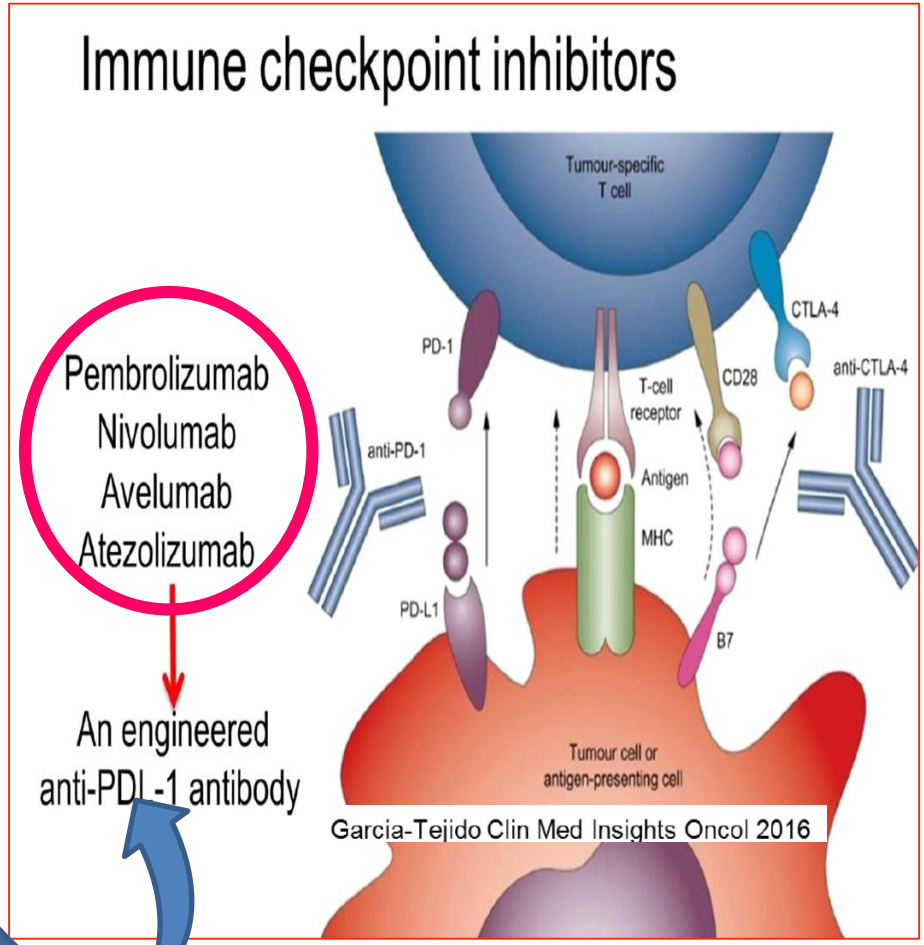
Inibizione del recettore androgeno

TNBC e immunoterapia



Il tumore induce la risposta immunitaria
Aumenta l'infiltrato immunitario





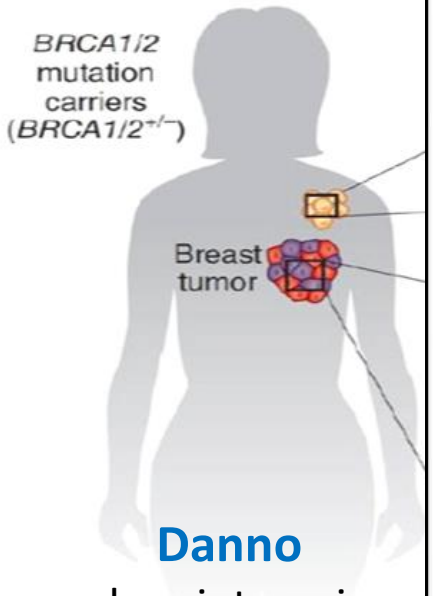
Il tumore presenta alta espressione di PD-L1
che inibisce la risposta immunitaria

TNBC E MUTAZIONE BRCA

80% dei tumori BRCA1 mutati sono TNBC

10% dei TNBC che insorgono in giovane età sono BRCA1 mutato

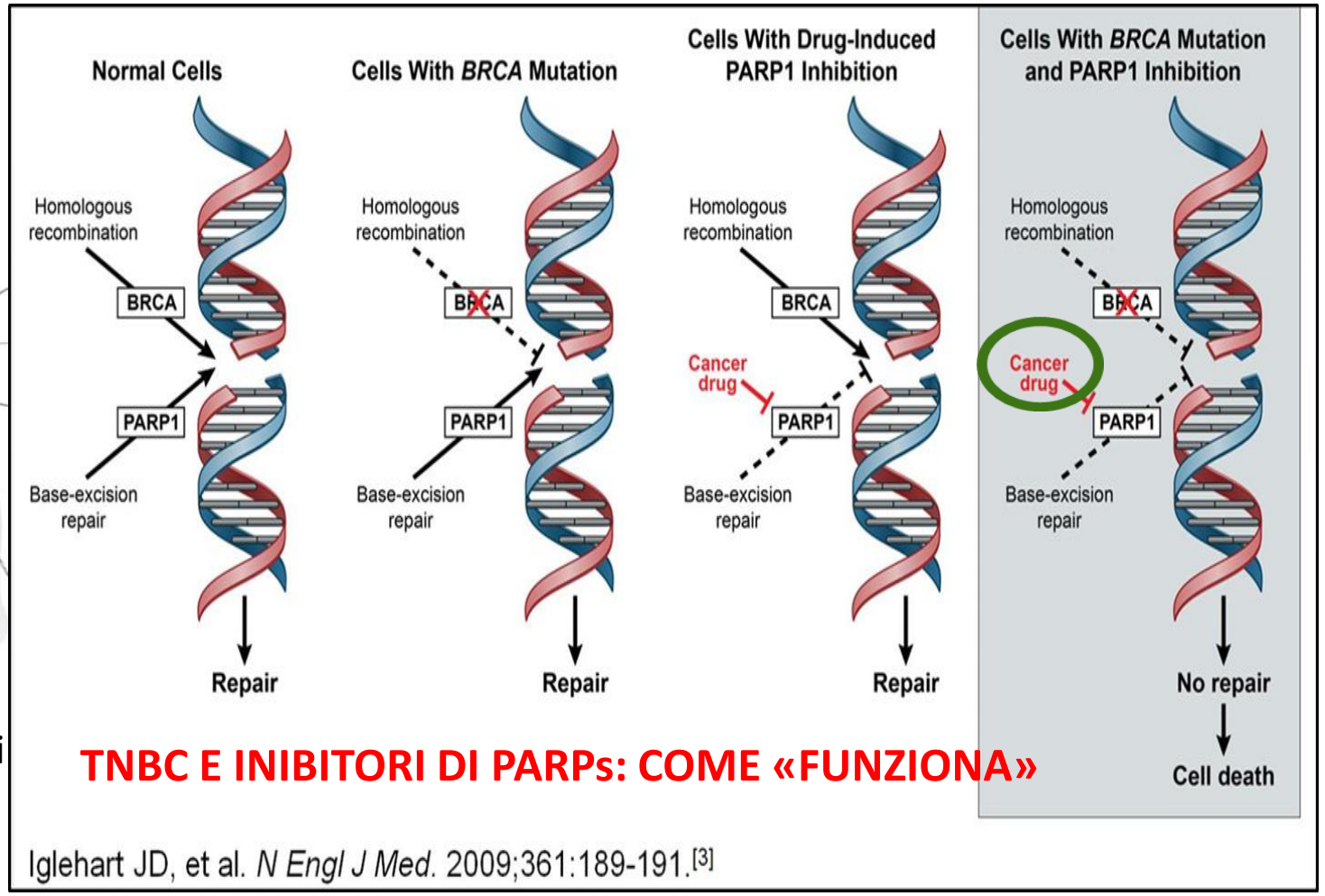
(Breast Cancer Res Treat, July, 2012)



Danno

chemioterapia

radiazioni ionizzanti



TNBC E INIBITORI DI PARPs: COME «FUNZIONA»

Iglehart JD, et al. *N Engl J Med.* 2009;361:189-191.[3]

STUDI CLINICI IN CORSO CON INIBITORI DI PARP NEL CARCINOMA MAMMARIO METASTATICO BRCA-mutato

Agent	Metastatic Breast Cancer
Olaparib*	OlympiAD, phase 3
Niraparib*	BRAVO, phase 2 (BIG, EORTC)
Talazoparib	ABRAZO, phase 2
	EMBRACA, phase 3 (fully accrued)
Rucaparib*	RUBY, phase 2
Veliparib	BROCADE, phase 3

*approvato per il carcinoma ovarico

Olympiad

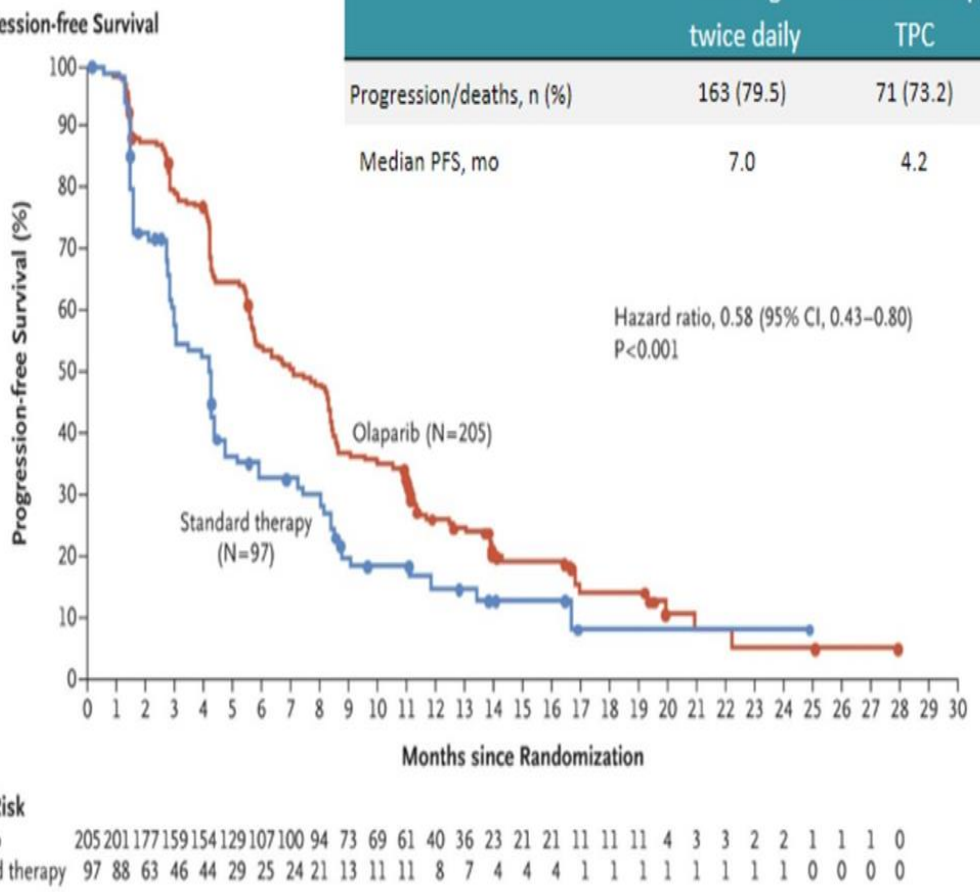
Metastatic breast cancer patients with gBRCA 1/2 mutations suitable for 1st, 2nd, 3rd line chemotherapy TNBC; ER/PgR+ and Her2- (n=310)

2:1

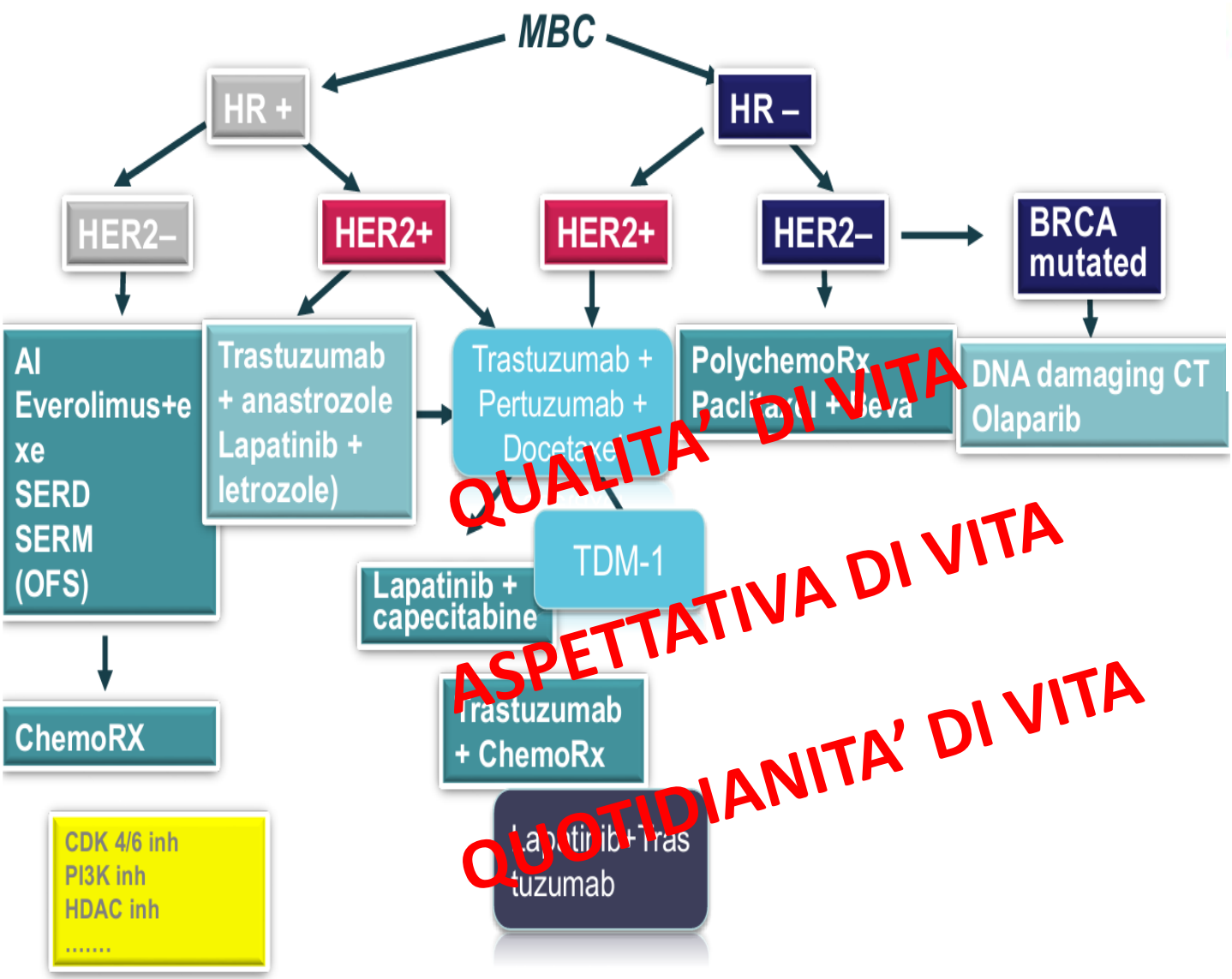
- Olaparib 300mg bd
- Physician's choice: (capecitabine, vinorelbine or eribulin)

Studio di fase III randomizzato, multicentrico
NEJM 2017; 377:1700

	Olaparib 300 mg twice daily	Chemotherapy TPC
Progression/deaths, n (%)	163 (79.5)	71 (73.2)
Median PFS, mo	7.0	4.2



CARCINOMA MAMMARIO METASTATICO: MALATTIA CURABILE?



QUALITA' DI VITA

ASPETTATIVA DI VITA

QUOTIDIANITA' DI VITA

PROTOCOLLI CLINICI PER IL CARCINOMA MAMMARIO AVANZATO

Sacro Cuore Don Calabria
Cancer Care Center
Negrar - Verona
Cancer Care Center
Numero Verde
800 143 143
Numero per la Cura del Tumore