ΧΜΘ + ΑΚΘ στον καρκίνο του μαστού

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Ενδείξεις χορήγησης/ Είδος

- ✓**ΧΜΘ**
- ✓**ΟΡΜ**
- ✓**Βιολογική θεραπεία**

Παράγοντες που συνεκτιμώνται

- Βιολογικά χαρακτηριστικά του όγκου
- Στάδιο της νόσου
- Συνοδά νοσήματα
- Ηλικία, ειδικές κατηγορίες (π.χ. κύηση)
- Βούληση της ασθενούς

1. Ενδείξεις Επικουρικής ΧΜΘ

NCCN guidelines

- T >1 cm
- Grade 3
- N +
- ER –
- C-erbB2 (+)

NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2013. Available at www.nccn.com

ESMO guidelines

Clinicopathological features	Relative indications for chemoendocrine therapy	Factors not useful for decision	Relative indications for endocrine therapy alone
ER and PgR	Lower ER and PgR level		Higher ER and PgR level
Histological grade	Grade 3	Grade 2	Grade 1
Proliferation*	High (ki-67 >30%)	Intermediate	Low (ki-67 <15%)
Nodes	≥4 involved nodes	1–3 involved nodes	Node negative
PVI	extensive PVI		No extensive PVI
pT size	>5 cm	2.1–5 cm	≤2 cm
Patient preference	Use all available treatments		Avoid chemotherapy-related side effects
Multigene assays Gene signature	High score	Intermediate score	Low score

Cardoso F, et al. Ann Oncol 2012;23:vii11-9.

Γονιδιακές Υπογραφές

- Oncotype Dx™
- MammaPrint(®)
- Genomic Grade Index
- PAM50 (ROR-S)
- Breast Cancer Index
- EndoPredict

EGAPP κριτήρια

Annals of Oncology 24: 647–654, 2013
doi:10.1093/annonc/mds645
Published online 20 January 2013

Utility of prognostic genomic tests in breast cancer practice: The IMPAKT 2012 Working Group Consensus Statement†

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Background: We critically evaluated the available evidence on genomic tests in breast cancer to define their prognostic ability and likelihood to determine treatment benefit.
Design: Independent evaluation of six genomic tests [Oncotype Dx™, MammaPrint®, Genomic Grade Index, PAM50 (ROR-S), Breast Cancer Index, and EndoPredict] was carried out by a panel of experts in three parameters: analytical validity, clinical validity, and clinical utility based on the principles of the EGAPP criteria.

Panel statements: The majority of the working group members found the available evidence on the analytical and clinical validity of Oncotype Dx™ and MammaPrint® to be convincing. None of the genomic tests demonstrated robust evidence of clinical utility: it was not clear from the current evidence that modifying treatment decisions based on the results of a given genomic test could result in improving clinical outcome.
Conclusions: The IMPAKT 2012 Working Group proposed the following recommendations: (i) a need to develop models that integrate clinicopathologic factors along with genomic tests; (ii) demonstration of clinical utility should be made in the context of a prospective randomized trial; and (iii) the creation of registries for patients who are subjected to genomic testing in the daily practice.

Key words: breast cancer, genomic signatures, prediction, prognosis

Είδος επικουρικής ΧΜΘ

- Ανθρακυκλίνες
- Ταξάνες
- Ανθρακυκλίνες + Ταξάνες
- CMF

- Η χρήση ΧΜΘ σχημάτων βασισμένων στις ανθρακυκλίνες συστήνεται για τις περισσότερες ασθενείς & ειδικά για τις ασθενείς με HER2 + νόσο.
- Οι ταξάνες φαίνεται ότι είναι ιδιαίτερα αποτελεσματικές σε ασθενείς με ER-αρνητική ή HER2-θετική νόσο .
- Ο συνδυασμός CMF πρέπει να χορηγείται σε ασθενείς χαμηλού κινδύνου για υποτροπή. Οι βασιζόμενοι σε ανθρακυκλίνη συνδυασμοί γενικά υπερτερούν του CMF.
- Η χορήγηση εντατικοποιημένων ΧΜΘ σχημάτων (+ G-CSF) είναι υπέρτερη των συμβατικών σχημάτων.

Aebi S, et al. Ann Oncol 2011; (Suppl 6):12-24.
NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2013. Available at www.nccn.com

EFFECTS OF CHEMOTHERAPY AND HORMONAL THERAPY FOR EARLY BREAST CANCER ON RECURRENCE AND 15-YEAR SURVIVAL: AN OVERVIEW OF THE RANDOMISED TRIALS

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

Lancet 365:1687-1717, 2005

- Τα αποτελέσματα της μελέτης προήλθαν από τη μετα-ανάλυση 194 τυχαιοποιημένων μελετών συμπληρωματικής αγωγής (14.000 ασθενείς)
- Η ΧΜΘ με ανθρακυκλίνη (FAC ή FEC) για περίπου 6 μήνες ελάττωσε τη θνητότητα στα 15 έτη κατά 38% σε ασθενείς <50 ετών και κατά 20% σε γυναίκες >50 ετών.
- Το όφελος ήταν ανεξάρτητο από την έκφραση HR, των υπολοίπων χαρακτηριστικών του όγκου και από τη χορήγηση ή όχι ταμοξιφένης.
- Τα βασιζόμενα σε ανθρακυκλίνες σχήματα ήταν σημαντικά υπέρτερα του CMF τόσο στη μείωση των υποτροπών (2p=0.0001) όσο και στη μείωση της θνησιμότητας (2p<0.00001).

Intergroup Study 0102

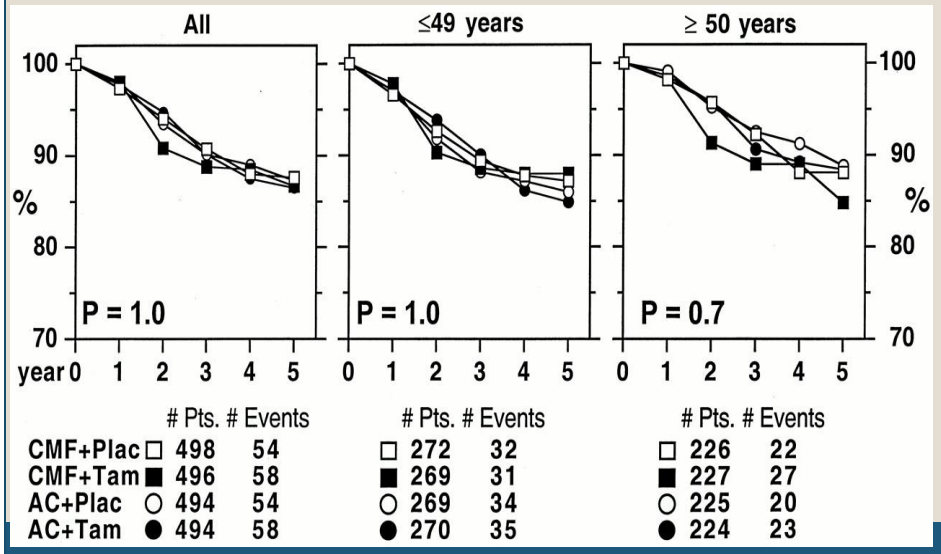
Hutchins L et al. Proc Am Soc Clin Oncol 17a: 1a, 1998

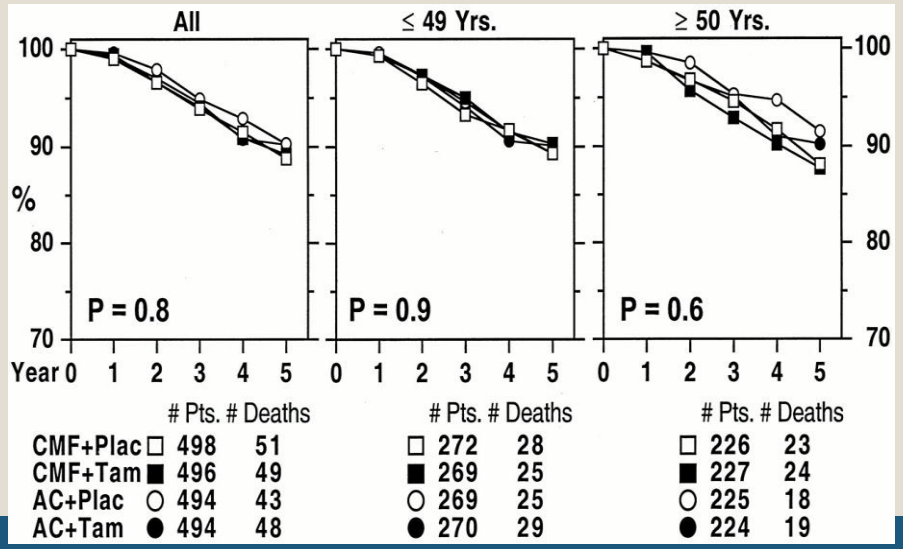
- Μελετήθηκαν 2.631 ασθενείς με Ν- νόσο, στις οποίες χορηγήθηκαν είτε 6 κύκλοι CAF είτε 6 κύκλοι CMF.
- Το CAF ήταν οριακά υπέρτερο του CMF ως προς τη συνολική επιβίωση και το DFS.
- Το CAF ήταν περισσότερο τοξικό.

NSABP B-23

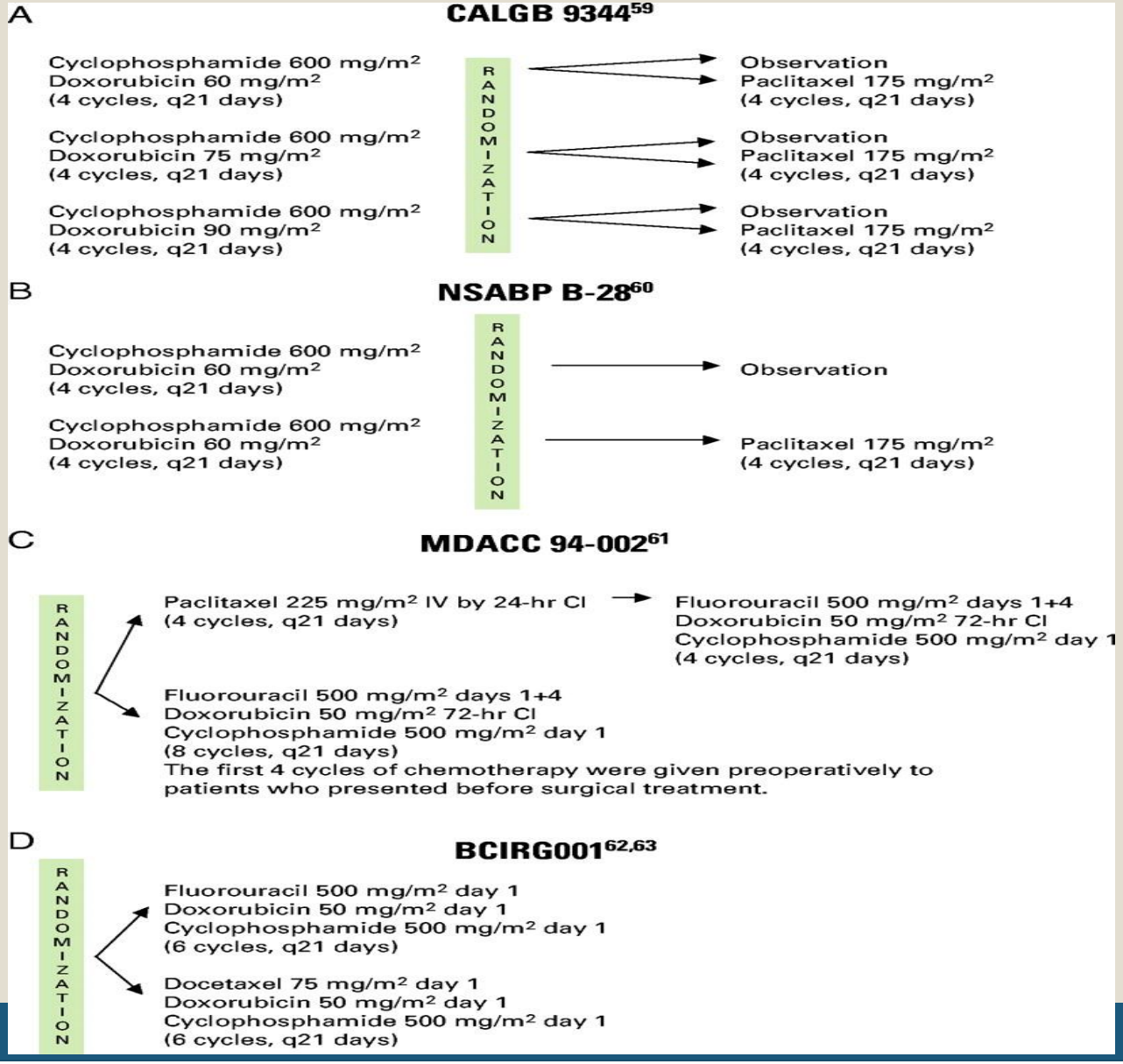
Fisher B et al. J Clin Oncol 19: 931-942, 2001

- Μελετήθηκαν 2008 ασθενείς με Ν- νόσο και HR-
- Στόχοι της μελέτης ήταν (α) να συγκριθεί ο συνδυασμός δοξορουμπικίνης και κυκλο-φωσφαμίδης (AC) με το συνδυασμό CMF και (β) να εξετασθεί η δράση της ταμοξιφένης, όταν συγχορηγείται με ΧΜΘ.
- Δεν διαπιστώθηκαν διαφορές ως προς τη συνολική επιβίωση και το DFS στην 5ετία.





Ο ρόλος των ταξανών (Δεκαετία ’90)



Η ωφέλεια από τις ταξάνες

- CALGB 9344: DFS, OS
- NSABP B-28: DFS, ~~OS~~
- MD Anderson: DFS, OS
- BCIRG 001: DFS, OS
- PACS 01: DFS, OS
- NSABP B-27: ~~DFS~~, ~~OS~~
- ECOG 2197: ~~DFS~~, ~~OS~~
- INT 1199: DFS, OS

ΜΕΤΑ-ΑΝΑΛΥΣΗ:

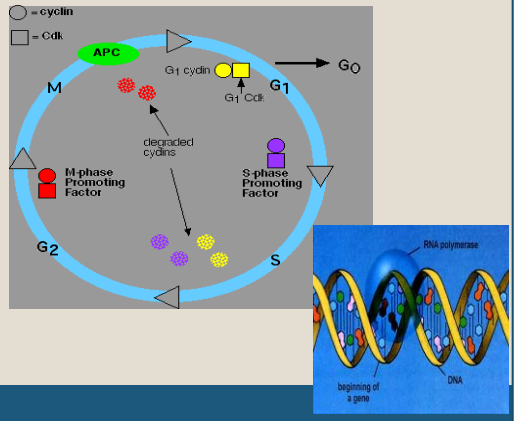
13 μελέτες (22.903 ασθενείς) απόλυτο όφελος 5ετία (DFS: 5%, OS: 3%)

Συχνότερα χημειοθεραπευτικά σχήματα (που δεν περιλαμβάνουν τη χρήση Herceptin)

Προτεινόμενα ΧΜΘ σχήματα σε HER2 – αρνητική νόσο [II, A]		
ΧΜΘ	**Δόση**	**Κύκλοι**
TAC	Docetaxel 75 mg/m² iv ημέρα 1 Doxorubicin 50 mg/m² iv ημέρα 1 Cyclophosphamide 500 mg/m² iv ημέρα 1	21 μέρες x 6 κύκλοι
Dose dense AC→ paclitaxel κάθε 2 εβδομάδες	Doxorubicin 60 mg/m² i.v. ημέρα 1 Cyclophosphamide 600 mg/m² iv ημέρα 1 ↓ Paclitaxel 175 mg/m² iv ημέρα 1	14 μέρες x 4 κύκλοι ↓ 14 μέρες x 4 κύκλοι
AC → paclitaxel εβδομαδιαία	Doxorubicin 60 mg/m² iv ημέρα 1 Cyclophosphamide 600 mg/m² iv ημέρα 1 ↓ Paclitaxel 80 mg/m² iv ημέρα 1	21 μέρες x 4 κύκλοι ↓ Εβδομαδιαία για 12 εβδ
TC	Docetaxel 75 mg/m² iv ημέρα 1 Cyclophosphamide 600 mg/m² iv ημέρα 1	21 μέρες x 4 κύκλοι
AC	Doxorubicin 60 mg/m² iv day 1 Cyclophosphamide 600 mg/m² iv ημέρα 1	21 μέρες x 4 κύκλοι

Άλλα ΧΜΘ σχήματα σε HER2 – αρνητική νόσο [II, B]		
ΧΜΘ σχήμα	**Δόσεις**	**Κύκλοι**
FAC	Cyclophosphamide 500 mg/m² iv day 1 Doxorubicin 50 mg/m² iv day 1 5-Fluorouracil 500 mg/m² iv day 1 & 8	21 days x 6 cycles
CAF	Cyclophosphamide 100 mg/m² iv day 1 Doxorubicin 30 mg/m² iv day 1 & 8 5-Fluorouracil 500 mg/m² iv day 1 & 8	28 days x 6 cycles
FEC/ CEF	5-Fluorouracil 500 mg/m² iv day 1 & 8 Epirubicin 60 mg/m² iv day 1 & 8 Cyclophosphamide 75 mg/m² per os day 1-14	28 days x 6 cycles
CMF	Cyclophosphamide 100 mg/m² per os day 1-14 Methotraxate 40 mg/m² iv day 1 & 8 5-Fluorouracil 600 mg/m² iv day 1 & 8	28 days x 6 cycles
AC→ docetaxel	Doxorubicin 60 mg/m² iv day 1 Cyclophosphamide 600 mg/m² iv day 1 ↓ Docetaxel 100 mg/m² iv day 1	21 days x 4 cycles ↓ 21 days x 4 cycles

Άλλα ΧΜΘ σχήματα σε HER2 – αρνητική νόσο [II, B]		
ΧΜΘ	**Δόσεις**	**Κύκλοι**
EC	Epirubicin 100 mg/m² iv day 1 Cyclophosphamide 830 mg/m² iv day 1	21 days x 8 cycles
Doxorubicin → paclitaxel→ cyclophosphamide	Doxorubicin 60 mg/m² iv day 1 ↓ Paclitaxel 175 mg/m² iv day 1 ↓ Cyclophosphamide 600 mg/m² iv day 1 With filgastrim support	14 days x 4 cycles ↓ 14 days x 4 cycles ↓ 14 days x 4 cycles
FEC → docetaxel	5-Fluorouracil 500 mg/m² iv day 1 Epirubicin 100 mg/m² iv day 1 Cyclophosphamide 500 mg/m² iv day 1 ↓ Docitaxel 100 mg/m² iv day 1	21 days x 3 cycles ↓ 21 days x 3 cycles
FEC → paclitaxel weekly	5-Fluorouracil 600 mg/m² iv day 1 Epirubicin 90 mg/m² iv day 1 Cyclophosphamide 600 mg/m² iv day 1 ↓ Paclitaxel 100 mg/m² iv day 1	21 days x 4 cycles ↓ Weekly x 8 cycles



Συχνότερα χημειοθεραπευτικά σχήματα (που περιλαμβάνουν τη χρήση Herceptin)

Προτεινόμενα ΧΜΘ σχήματα σε HER2 – θετική νόσο [II, A]		
ΧΜΘ	**Δόσεις**	**Κύκλοι**
AC→ paclitaxel + trastuzumab	Doxorubicin 60 mg/m^2 iv day 1 Cyclophosphamide 600 mg/m^2 iv day 1 ↓ Paclitaxel 80 mg/m^2 iv day 1 Trastuzumab 4 mg/kg iv with first dose of paclitaxel ↓ Trastuzumab 2 mg/kg iv (as an alternative, trastuzumab 6 mg/kg every 3 weeks)	21 days x 4 cycles ↓ Weekly x 12 cycles ↓ Weekly to complete 1 year
Dose dense AC→ paclitaxel + trastuzumab	Doxorubicin 60 mg/m^2 iv day 1 Cyclophosphamide 600 mg/m^2 iv day 1 ↓ Paclitaxel 175 mg/m^2 iv day 1 Trastuzumab 4 mg/kg iv with first dose of paclitaxel ↓ Trastuzumab 2 mg/kg iv (as an alternative, trastuzumab 6 mg/kg every 3 weeks)	14 days x 4 cycles ↓ 14 days x 4 cycles ↓ Weekly to complete 1 year

Προτεινόμενα ΧΜΘ σχήματα σε HER2 –θετική νόσο [II, A] (συνέχεια)		
Regimens	**Doses**	**Schedule**
TCH	Docetaxel 75 mg/m^2 iv day 1 Carboplatin 6AUC iv day 1 Trastuzumab 4 mg/kg iv day 1 (loading dose), afterwards 2 mg/kg iv ↓ Trastuzumab 6 mg/kg iv	21 days x 6 cycles Every 7 days and at the end of chemo for 1 year every 21 days.

Άλλα ΧΜΘ σχήματα σε HER2 θετική νόσο [II, B]		
ΧΜΘ	**Δόσεις**	**Κύκλοι**
Docetaxel + trastuzumab→ FEC	Docetaxel 100 mg/m^2 iv day 1 Trastuzumab 4 mg/kg iv (with first dose of docetaxel) ↓ Trastuzumab 2 mg/kg iv ↓ 5-Fluorouracil 600 mg/m^2 iv day 1 Epirubicin 60 mg/m^2 iv day 1 Cyclophosphamide 600 mg/m^2 iv day 1	21 days x 4 cycles ↓ Weekly to complete 9 weeks ↓ 21 days x 3 cycles
AC→ Docetaxel + trastuzumab	Doxorubicin 60 mg/m^2 iv day 1 Cyclophosphamide 600 mg/m^2 iv day 1 ↓ Docetaxel 100 mg/m^2 iv day 1 Trastuzumab 4 mg/kg iv week 1 ↓ Trastuzumab 2 mg/kg iv ↓ Trastuzumab 6mg/kg iv	21 days x 4 cycles ↓ 21 days x 4 cycles Week 1 ↓ Weekly for 11weeks ↓ Every 21 days to complete 1 year

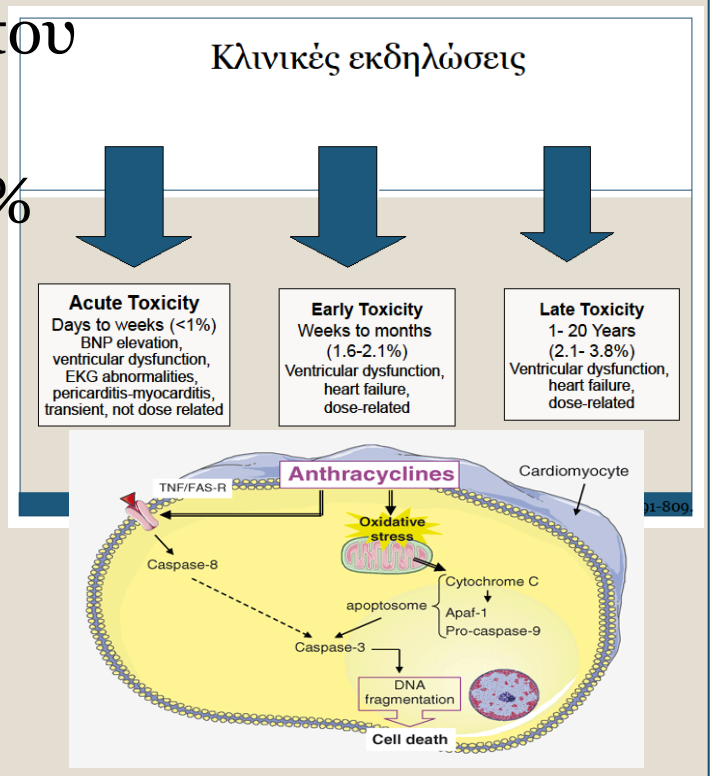
Συνοδά νοσήματα (1)

- Καρδιοτοξικότητα από ανθρακυκλίνες

✓ Αναδρομική μελέτη: 3941 ασθενείς που έλαβαν δοξορουβικίνη

✓ Συνολική επίπτωση heart failure 2.2%

✓ ισχυρά δοσοεξαρτώμενη



Cumulative Dose	Heart Failure
<400 mg/m²	0.14%
~400 mg/m²	3%
~550 mg/m²	7%
~700 mg/m²	18%

Shevchuk OO, et al. Exp Oncol 2012;34:314-22.
Volkova M, Russell R 3rd. Curr Cardiol Rev 2011;7:214-20.
Petrelli F, et al. Breast Cancer Res Treat 2012;135:335-46.
Octavia Y, et al. J Mol Cell Cardiol 2012;52:1213-25.

Συνοδά νοσήματα (2)

- Ψυχιατρικά νοσήματα → αποφυγή χορήγησης ταξανών (λόγω συγχορήγησης κορτιζόνης)
- Νευροπάθεια → αποφυγή χορήγησης ταξανών
- Διαταραχή ηπατικής βιοχημίας → τροποποίηση δόσης
- Διαταραχή νεφρικής λειτουργίας → τροποποίηση δόσης
- Λήψη αντιπηκτικής αγωγής → τροποποίηση δόσης
- Συνοδά νοσήματα με ↓ προσδόκιμο ζωής

Kintzel et al, Cancer Treat Rev 1995;21:33-64
Gelman et al, J Clin Oncol 1984;2:1406-14
Hurria et al, Cancer Control 2007;14:32-43

Γηριατρικές κλίμακες

- Comprehensive geriatric assessment
- Activities of daily living
- Instrumenal activities of daily living
- VES-13

(Λειτουργική κατάσταση, συνοδά νοσήματα, γνωστική κατάσταση, συναισθηματική κατάσταση, γηριατρικά σύνδρομα, διατροφική κατάσταση, πολυφαρμακία, κοινωνικοί παράγοντες)

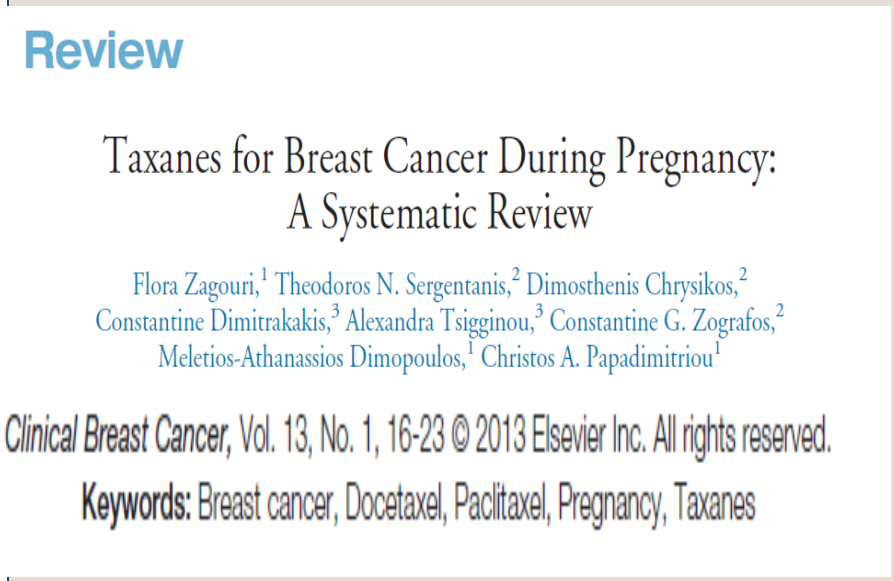
Ειδικές ομάδες- Ηλικιωμένοι ασθενείς

- Μετά την ηλικία των 70 ετών πρέπει να καθορίζεται η βιολογική ηλικία με γηριατρικές κλίμακες.

- Old and fit → ίδια ΧΜΘ
- Frail → καθόλου ΧΜΘ
- Vulnerable → τροποποίηση δόσης ΧΜΘ

Ειδικές ομάδες- Κύηση

- Ανθρακυκλίνες → standard of care
- CMF → όχι
- Ταξάνες → ναι (πρόσφατα)
- trastuzumab → μετά τον τοκετό

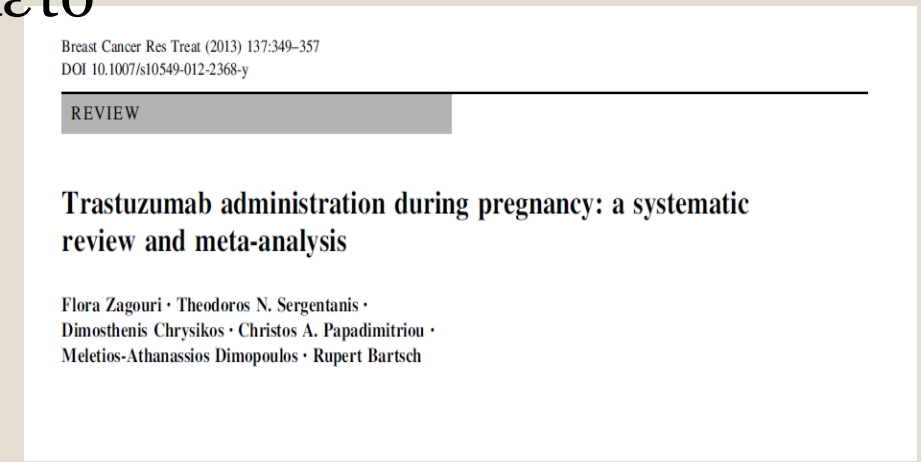

Review

Taxanes for Breast Cancer During Pregnancy: A Systematic Review

Flora Zagouri,[1] Theodoros N. Sergentanis,[2] Dimosthenis Chrysikos,[2] Constantine Dimitrakakis,[3] Alexandra Tsigginou,[3] Constantine G. Zografos,[2] Meletios-Athanassios Dimopoulos,[1] Christos A. Papadimitriou[1]

Clinical Breast Cancer, Vol. 13, No. 1, 16-23

Keywords: Breast cancer, Docetaxel, Paclitaxel, Pregnancy, Taxanes


Breast Cancer Res Treat (2013) 137:349–357
DOI 10.1007/s10549-012-2368-y

REVIEW

Trastuzumab administration during pregnancy: a systematic review and meta-analysis

Flora Zagouri · Theodoros N. Sergentanis · Dimosthenis Chrysikos · Christos A. Papadimitriou · Meletios-Athanassios Dimopoulos · Rupert Bartsch

Zagouri F, et al. Breast Cancer Res Treat 2013;137:349-57.
Zagouri F, et al. Oncology 2012;83:234-8.
Zagouri F, et al. Clin Breast Cancer 2013;13:16-23.
Zagouri F, et al. J Thorac Dis 2013;5:S62-7.
Zagouri F, et al. Obstet Gynecol 2013;121:337-43.

Ενημέρωση ασθενούς- Βούληση ασθενούς

- Απώλεια μαλλιών/ τοξικότητα

Makubate B, et al. Br J Cancer 2013;108:1515-24.
Font R, et al. Br J Cancer 2012;107:1249-56.
Huiart L, Ferdynus C, Giorgi R. Breast Cancer Res Treat 2013;138:325-8.

- Μελλοντική κύηση: διατήρηση ωοθηκικής λειτουργίας

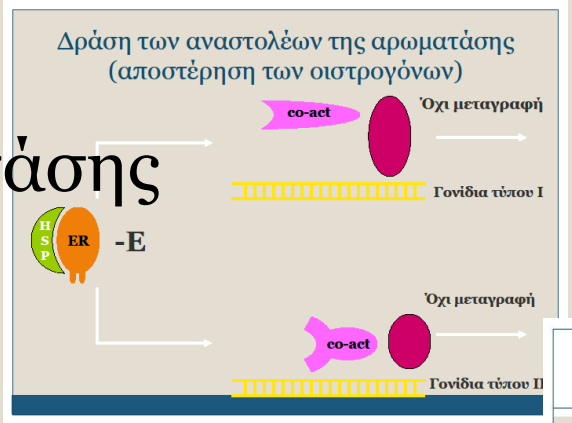
Zagouri F, et al. Obstet Gynecol 2013;121:1235-40.

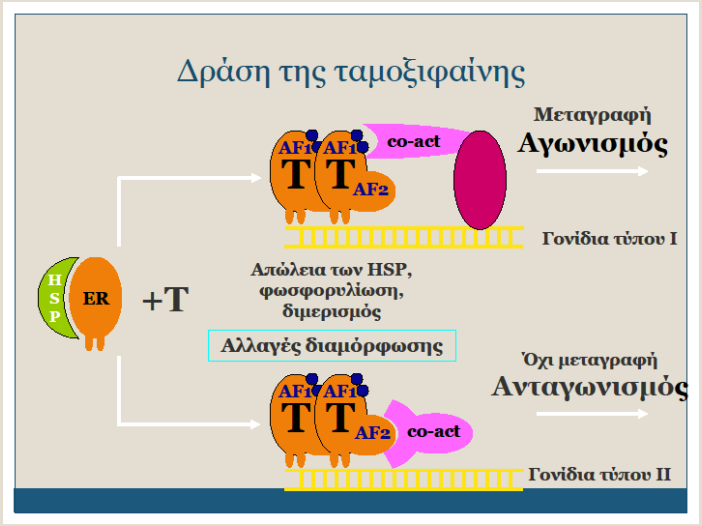
- Κίνδυνος / όφελος από λήψη επικουρικής θεραπείας

Barcenas CH, et al. Oncologist 2012;17:303-11
Sedjo RL, Devine S. Breast Cancer Res Treat 2011;125:191-200.

2. Ενδείξεις χορήγησης επικουρικής ΟΡΜ

- >1% IHC έκφραση ER ή/και PR
  - ✓ Ταμοξιφαίνη
  - ✓ Αναστολείς αρωματάσης





Aebi S, et al. Ann Oncol 2011; (Suppl 6):12-24.
NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2013. Available at www.nccn.com

Είδος επικουρικής ΟΡΜ

- Προεμμηνοπαυσιακές ασθενείς→
- Ταμοξιφαίνη για 10 έτη (LOE I)
- διακοπή έμμηνου ρύσεως για 2-3 έτη (γοσερελίνη, τριπτορελίνη, λευπρορελίνη) (LOE III)

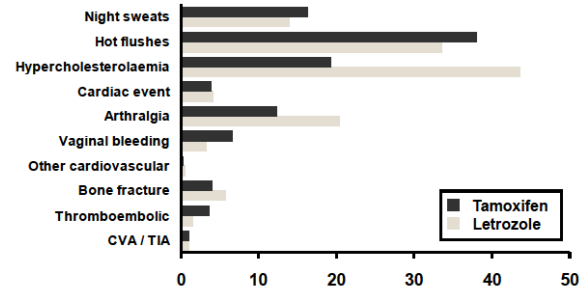
- Μετεμμηνοπαυσιακές ασθενείς → αναστολείς αρωματάσης για 5 έτη ± 5 έτη ΟΡΜ (LOE IIB)
- Αναστραζόλη
- Λετροζόλη
- Εξεμεστάνη

Aebi S, et al. Ann Oncol 2011; (Suppl 6):12-24.
NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2013. Available at www.nccn.com

Συνοδά νοσήματα

- Οστεοπόρωση
- Αρθραλγίες
- Θρομβοεμβολικά συμβάματα

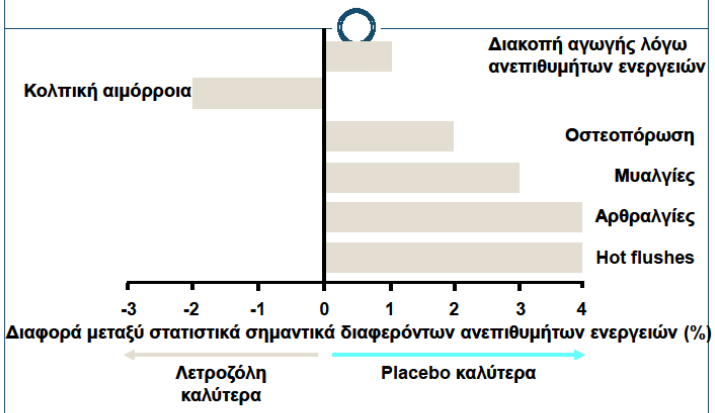
BIG 1-98 adverse events



BIG, Breast International Group
CVA, cerebrovascular accident
TIA, transient ischaemic attack

The BIG 1-98 Collaborative Group. NEJM 2005

MA.17 Ανάλυση ασφάλειας



Goss PE et al. J Natl Cancer Inst 2005

IES Ανεπιθύμητες ενέργειες

	Επίπτωση οποιουδήποτε βαθμού(%)	
	Εξεμεστάνη	Ταμοξιφένη
Οπτικές διαταραχές	7.4	5.7
Οστεοπόρωση	7.4	5.7
Αρθραλγίες	5.4	3.6
Διάρροιες	4.3	2.3
Θρομβοεμβολική νόσος	1.3	2.4
Κράμπες	2.8	4.4
Κολπική αιμόρροια	4.0	5.5
Άλλα γυναικολογικά ενοχλήματα	5.8	9.0

IES, Intergroup Exemestane Study

Coombes RC et al. N Engl J Med 2004

Ειδικές ομάδες

- Ανδρικός Ca μαστού
  - ✓ ταμοξιφαίνη: standard of care

Br J Cancer. 2013 Jun 11;108(11):2259-63. doi: 10.1038/bjc.2013.255. Epub 2013 May 30.

Aromatase inhibitors with or without gonadotropin-releasing hormone analogue in metastatic male breast cancer: a case series.

Zagouri F, Sergentanis TN, Koutoulidis V, Sparber C, Steger GG, Dubsky P, Zografos GC, Psaltopoulou T, Gnant M, Dimopoulos MA, Bartsch R.

F. Zagouri[1], T. N. Sergentanis[2], D. Chrysikos[2], E. Zografos[2], M. Rudas[1], G. Steger[1], G. Zografos[2] & R. Bartsch[1]

Fulvestrant and male breast cancer: a case series

Annals of Oncology

Volume 24 | No. 1 | January 2013

- Κύηση
  - ✓ όχι ορμονοθεραπεία

REVIEW ARTICLE

Challenges in managing breast cancer during pregnancy

Flora Zagouri[1,2], Theodora Psaltopoulou[3], Constantine Dimitrakakis[4], Rupert Bartsch[2], Meletios-Athanassios Dimopoulos[1]

[1]Department of Clinical Therapeutics, Alexandra Hospital, Medical School, University of Athens, Athens, Greece; [2]Comprehensive Cancer Center Vienna, Department of Medicine I/Division of Oncology, Medical University of Vienna, Austria; [3]Department of Hygiene, Epidemiology and Medical Statistics, Medical School, University of Athens, Athens, Greece; [4]Department of Obstetrics and Gynaecology, Medical School, University of Athens, Athens, Greece

Βούληση ασθενούς- συμμόρφωση με τη λήψη ΟΡΜ

Breast Cancer Res Treat (2011) 125:191–200
DOI 10.1007/s10549-010-0952-6

EPIDEMIOLOGY

Predictors of non-adherence to aromatase inhibitors among commercially insured women with breast cancer

Rebecca L. Sedjo · Scott Devine

British Journal of Cancer (2008) 99, 1763 – 1768

www.bjcancer.com

Cohort study examining tamoxifen adherence and its relationship to mortality in women with breast cancer

C McCowan*[,1], J Shearer[2], PT Donnan[1], JA Dewar[2], M Crilly[3], AM Thompson[4] and TP Fahey[1,5]

[1]Division of Community Health Sciences, University of Dundee, MacKenzie Building, Kirsty Semple Way, Dundee DD2 4BF, UK; [2]Department of Radiotherapy and Oncology, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK; [3]Department of Public Health, University of Aberdeen, School of Medicine, Polwarth Building, Aberdeen AB25 2ZD, UK; [4]Department of Surgery and Molecular Oncology, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK; [5]Department of General Practice, Royal College of Surgeons in Ireland, 120 St Stephens Green, Dublin 2, Ireland

Clinical Studies

BJC

FULL PAPER

British Journal of Cancer (2013) 109, 1172–1180 | doi: 10.1038/bjc.2013.464

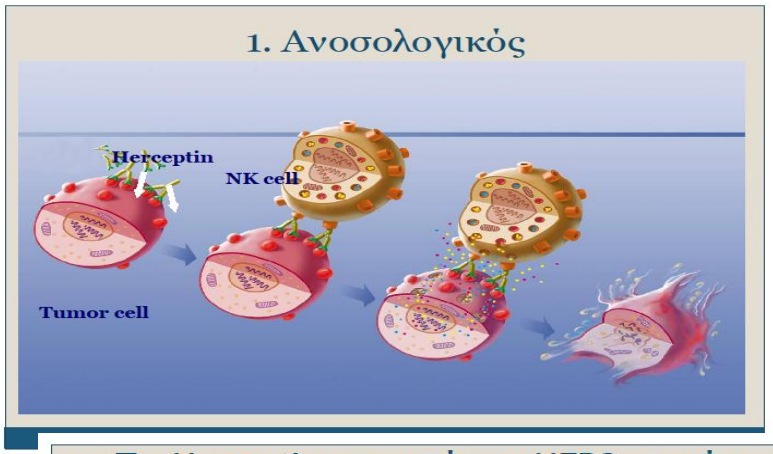
Keywords: tamoxifen; breast cancer; adherence; cost-effectiveness; QALYs

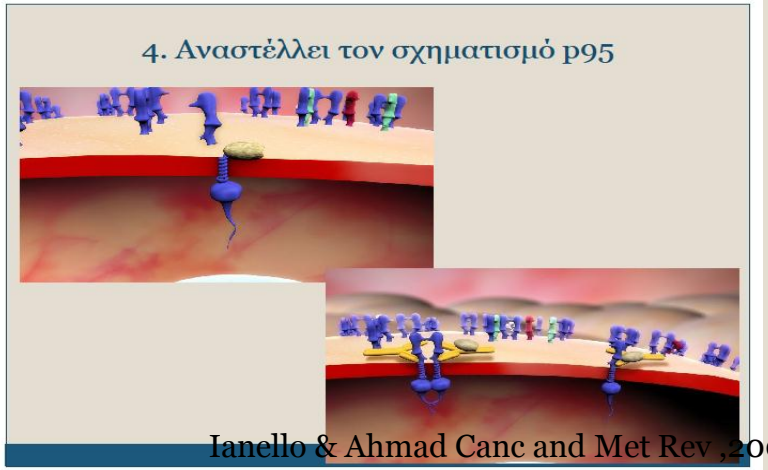
The value of high adherence to tamoxifen in women with breast cancer: a community-based cohort study

C McCowan*[,1], S Wang[2], A M Thompson[3], B Makubate[4] and D J Petrie[5]

3. Ενδείξεις επικουρικής βιολογικής θεραπείας

- HER2 (+) → Trastuzumab





Ianello & Ahmad Canc and Met Rev ,2005

Clynes et al Nat Med 2000

Gennari et al, Clin Cancer Res 2004

Repka et al, Clin Cancer Res 2003

Κατευθυντήριες οδηγίες στην επικουρική θεραπεία HER2 όγκων

Trastuzumab recommended across international guidelines

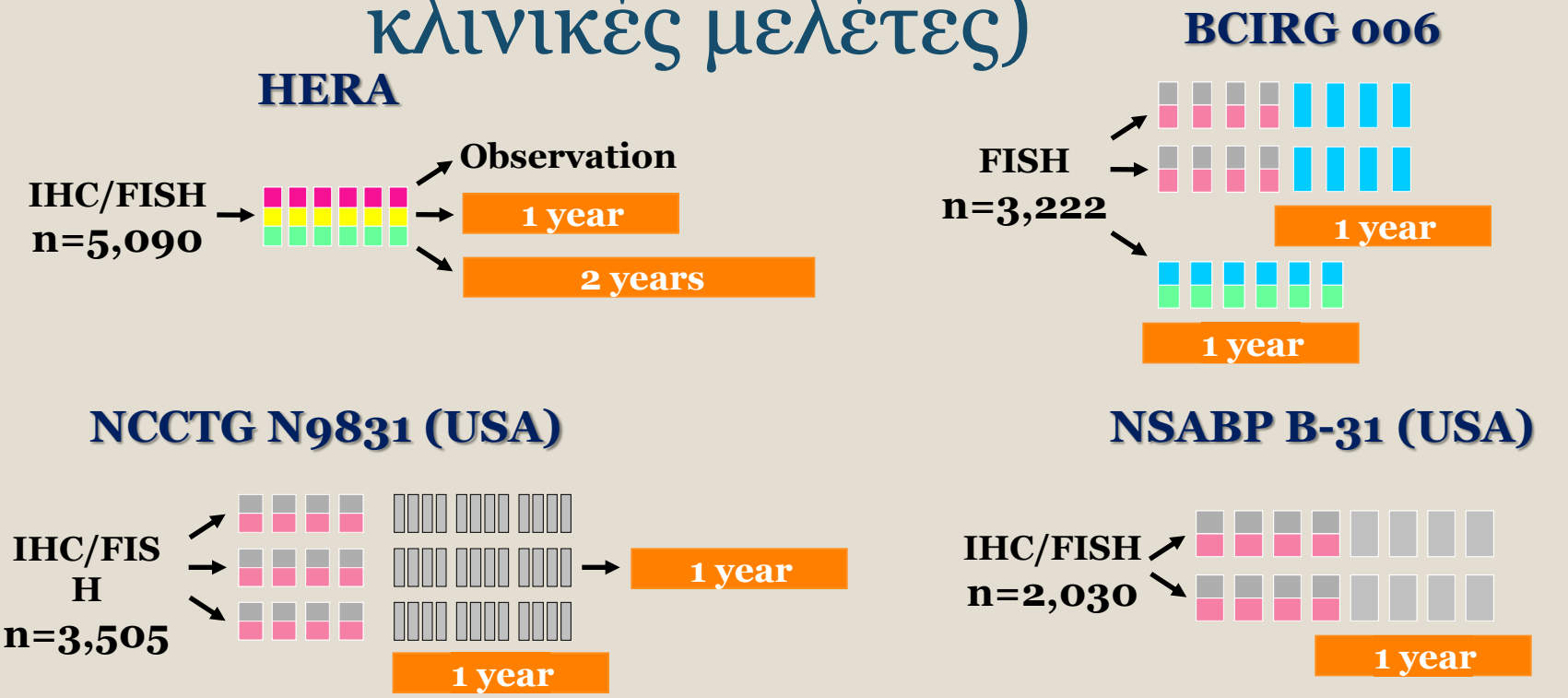
	Adjuvant therapy	Recommended patient groups	Administration with chemotherapy
St. Gallen[1]	**1 year of trastuzumab**	• HER2-positive tumours ≥1 cm • HER2-positive node-negative tumours 0.5–1.0 cm (pT1b) • Excludes: HER2-positive node-negative tumours 0.1–0.5 cm (pT1a)	• Preferred: concurrent use of trastuzumab with chemotherapy • Acceptable: sequential use of trastuzumab with chemotherapy
ESMO[2]	**1 year of trastuzumab**	• HER2-positive tumours ≥1 cm • Use of trastuzumab should be discussed with patients with small node-negative HER2-positive breast cancers	• Trastuzumab may be started in parallel with a taxane • Trastuzumab should not be given concurrently with an anthracycline outside the context of a clinical trial
NCCN[3]	**1 year of trastuzumab**	• Category 1 recommendation: patients with HER2-positive tumours ≥1 cm • Category 2A recommendation: patients with HER2-positive node-negative tumours 0.6–1.0 cm • (HER2-positive node-negative pT1a or pT1b tumours: use of trastuzumab to be based on individual benefit:risk)	• Preferred: AC followed by concurrent administration of trastuzumab with taxane • Preferred: TCH • Acceptable: chemotherapy followed by trastuzumab sequentially

Goldhirsch A, *et al*. *Ann Oncol* 2011; 22:1736-1747.

Aebi S, et al. *Ann Oncol* 2011; 22 (Suppl. 6):vi12-vi24.

NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2013. Available at: www.nccn.org

Επικουρική θεραπεία με trastuzumab (>13,000 ασθενείς με 4 μεγάλες κλινικές μελέτες)

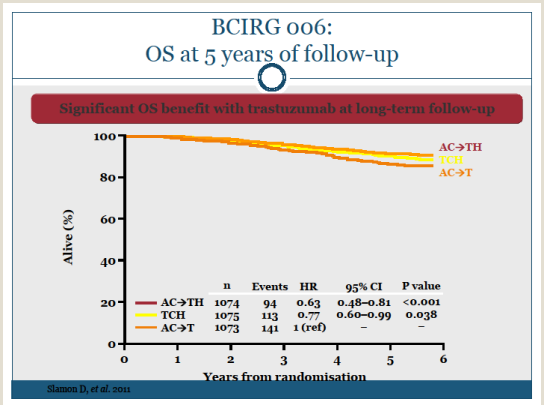


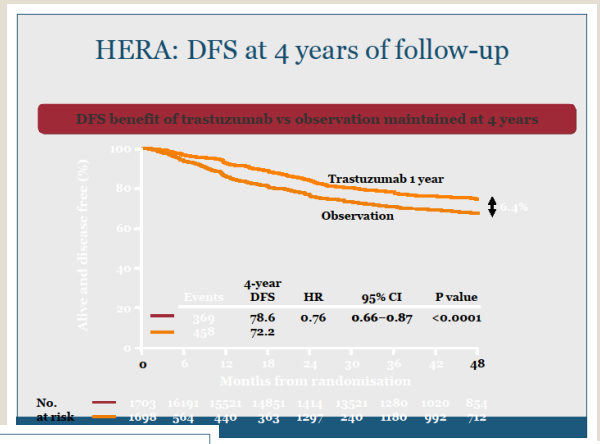
Piccart-Gebhart MJ et al. N Engl J Med 2005; 353: 1659-1672.

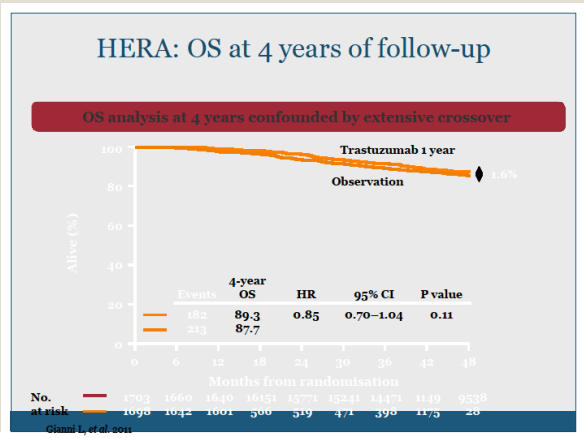
Romond EH et al. N Engl J Med 2005; 353: 1673-1684.

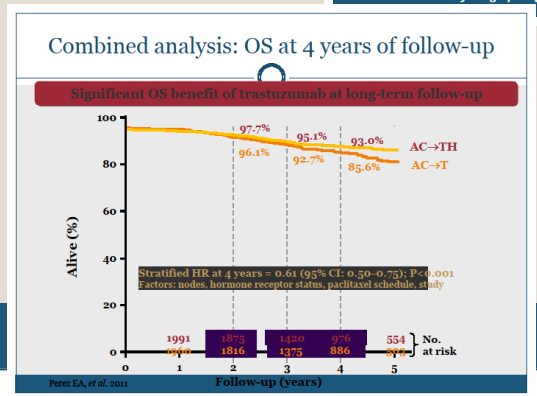
Αποτελεσματικότητα trastuzumab

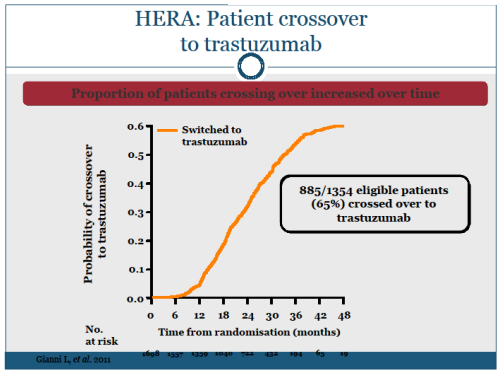
1. Μειώνει τον κίνδυνο τοπικής υποτροπής κατά 52%
2. Μειώνει τον κίνδυνο απομακρυσμένης μετάστασης κατά 53%
3. Στατιστικά σημαντική διαφορά στην 5ετή επιβίωση με όφελος 33%.



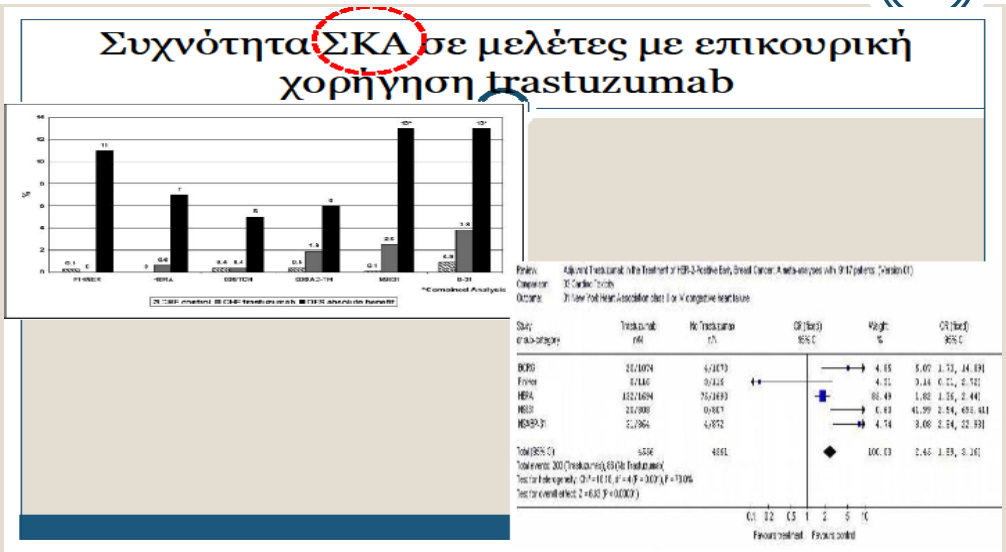


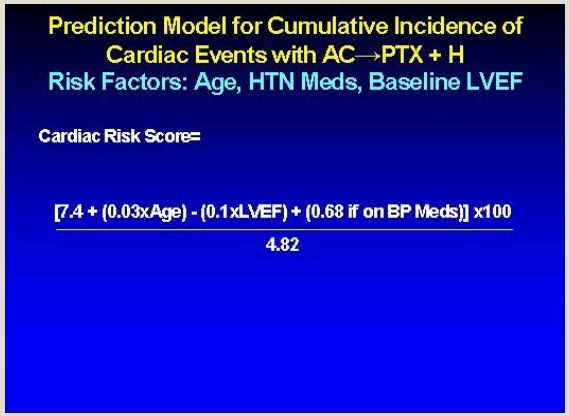






Καρδιοτοξικότητα- trastuzumab





- Ηλικία ≥ 60 ετών
- Αρτηριακή υπέρταση
- Καρδιολογικά νοσήματα
- Performance Status
- Προηγούμενη θεραπεία με ανθρακυκλίνες
- Συνυπάρχουσα νοσηρότητα
- Baseline LVEF
- Γενετικοί Πολυμορφισμοί *HER2 [Ile655Val]*

Rastogi et al, ASCO 2007

Bird BR, Swain SM. Clin Cancer Res 2008;14:14-24.

Επικουρική ΑΚΘ

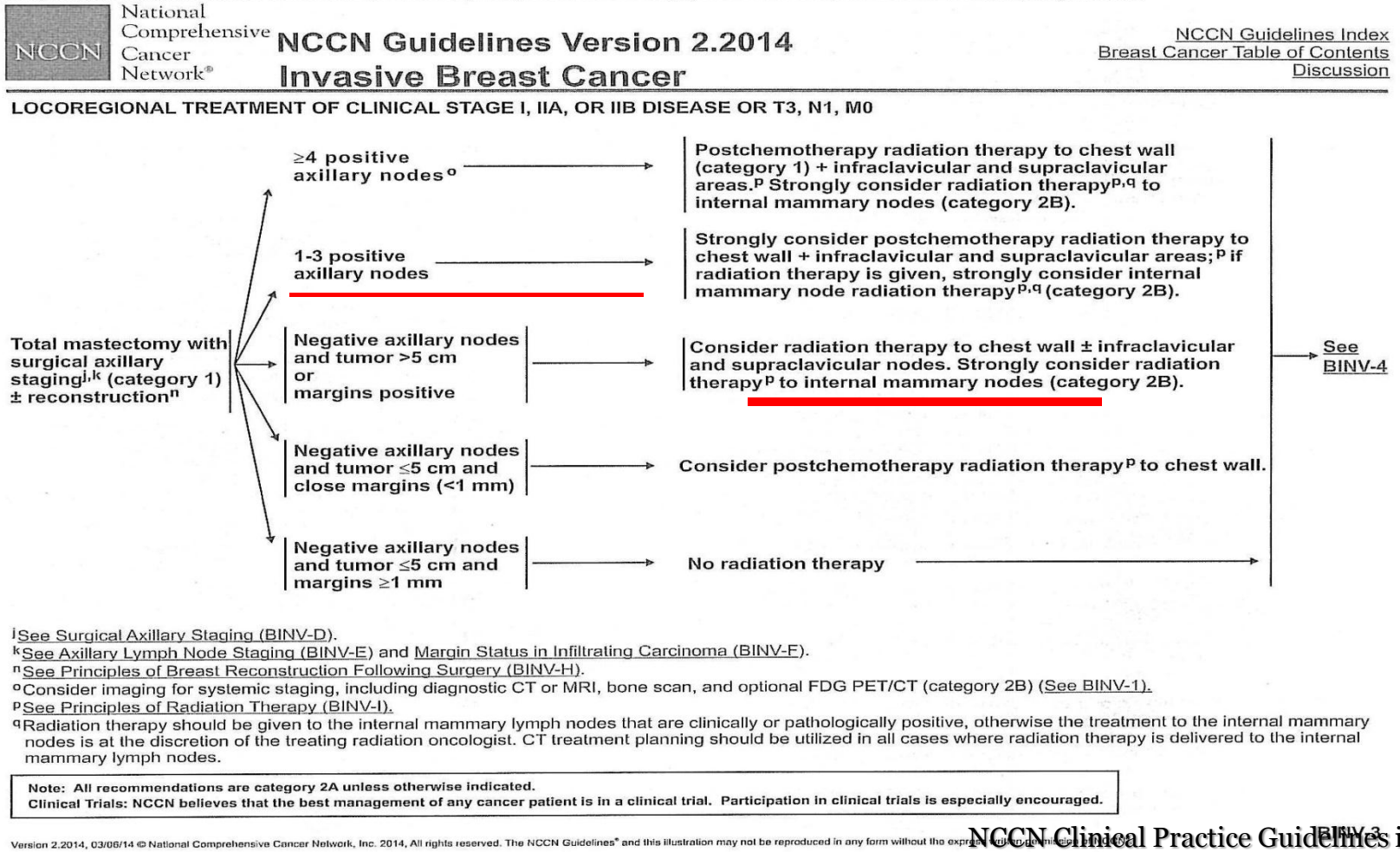
- ESMO

radiation after mastectomy: PMRT in node-positive patients reduces the local recurrence risk fourfold, which translates into 5% reduction in 15-year breast cancer mortality [48]. It is always recommended for patients with positive deep margins and four or more positive axillary nodes [I, A], and is indicated for patients with T3–T4 tumours independent of the nodal status [II, B]. The evidence supporting the use of PMRT for patients with one to three positive axillary lymph nodes is at least as strong as for patients with more involved lymph nodes, however less accepted [20, 49]. It should, however, be considered, especially in the presence of additional risk factors such as young age, vascular invasion and a low number of examined axillary lymph nodes. The value of PMRT in such patients is being investigated in clinical trials.

regional irradiation: Most older randomised trials have used large comprehensive locoregional RT encompassing the chest wall and all regional lymph nodes. Therefore, although clinically

Senkus E, et al. Ann Oncol 2013;24:vii7-23.

Επικουρική ΑΚΘ



NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 2.2014. Available at www.nccn.com

APBI (Accelerated partial breast irradiation)

- ESMO

for APBI [46]. Nevertheless, APBI might be considered an acceptable treatment option in patients at least 50 years old with unicentric, unifocal, node-negative, non-lobular breast cancer up to 3 cm in size without the presence of an extensive intraductal component or lymphovascular invasion, and with negative margins of at least 2 mm [III, C] [47].

Senkus E, et al. Ann Oncol 2013;24:vii7-23.

- NCCN

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

LES OF RADIATION THERAPY

reast Radiation:
efinition includes the majority of the breast tissue, and is e by both clinical assessment and CT-based treatment . A uniform dose distribution and minimal normal tissue re the goals and can be accomplished using compensators wedges, forward planning using segments, intensity- ed radiation therapy (IMRT), respiratory gating, or prone ng. The breast should receive a dose of 45-50 Gy in 1.8-2 Gy on, or 42.5 Gy at 2.66 Gy per fraction. A boost to the tumor commended in patients at higher risk (age <50 and high- sease). This can be achieved with brachytherapy or electron photon fields. Typical doses are 10-16 Gy at 2 Gy/fx. All dose s are given 5 days per week.

all Radiation (including breast reconstruction):
et includes the ipsilateral chest wall, mastectomy scar, and es where possible. Depending on whether the patient has onstructed or not, several techniques using photons and/or s are appropriate. CT-based treatment planning is ged in order to identify lung and heart volumes, and minimize e of these organs. Special consideration should be given to f bolus material when photon fields are used, to ensure the e is adequate.

Otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where radiation therapy is delivered to the internal mammary lymph node field.

Accelerated Partial Breast Irradiation (APBI):
Preliminary studies of APBI suggest that rates of local control in selected patients with early-stage breast cancer may be comparable to those treated with standard whole breast RT. However, compared to standard whole breast radiation, several recent studies document an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing. Patients are encouraged to participate in clinical trials. If not trial eligible, per the consensus statement from the American Society for Radiation Oncology (ASTRO), patients who may be suitable for APBI are women 60 y and older who are not carriers of *BRCA 1/2* mutation treated with primary surgery for a unifocal T1N0 ER-positive cancer. Histology should be infiltrating ductal or a favorable ductal subtype and not associated with EIC or LCIS, and margins should be negative. Thirty-four Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is prescribed to the

Θεραπεία Μεταστατικής νόσου

- **luminal subtype**
- **HER2+**
- **TRIPLE NEGATIVE**

- Προτιμώνται οι θεραπευτικές επιλογές με τη μικρότερη τοξικότητα.
- Προτιμάται η μονοθεραπεία, εκτός από τις περιπτώσεις ύπαρξης απειλητικών για τη ζωή μεταστάσεων.
- Η ΧΜΘ 1ης γραμμής μπορεί να συνεχίζεται μέχρι την επίτευξη μεγίστης αποτελεσματικότητας, απαγορευτικής τοξικότητας ή προόδου νόσου.
- Οστικές μεταστάσεις: Χορήγηση ζολανδρενικού οξέος, ή denosumab. Μέχρι και μετά τα 2 έτη εφόσον το προσδόκιμο επιβίωσης είναι > 3 μήνες και δεν υπάρχει τοξικότητα.

- Ενδείξεις διακοπής ΧΜΘ:

- 1. Αποτυχία να επιτευχθεί ανταπόκριση του όγκου σε 3 συνεχόμενα ΧΜΘ σχήματα
- 2. ECOG performance status ≤ 3.

Luminal subtype

a. Αναστολείς αρωματάσης
b. ταμοξιφαίνη
c. φουλβεστράνη
d. mTOR αναστολείς

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NCCN Guidelines Version 1.2012
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Staging, Discussion

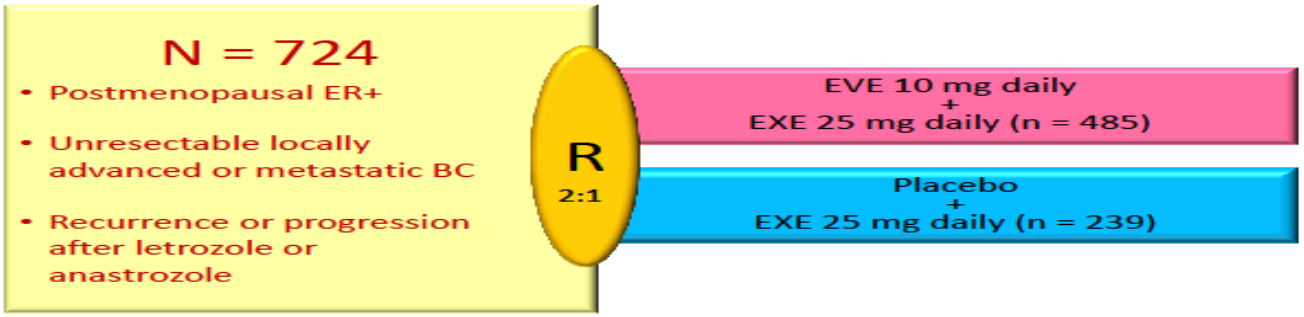
FOLLOW-UP THERAPY FOR ENDOCRINE TREATMENT OF RECURRENT OR STAGE IV DISEASE

Fulvestrant

- Postmenopausal women
- Blocks the estrogen receptor
- Administered intramuscularly once per month
- Side effects: hot flashes, headache, back pain, GI, all generally mild

Αναστολείς του mTOR

BOLERO-2: Everolimus σε προχωρημένο Ca μαστού



Stratification: Sensitivity to prior hormone therapy and presence of visceral metastases

Endpoints

- **Primary**: PFS (local assessment)
- **Secondary**: OS, ORR, QOL, safety, bone markers, PK

BC = breast cancer; ER+ = estrogen receptor-positive; EVE = everolimus; EXE = exemestane; ORR, overall response rate; OS = overall survival; PFS = progression-free survival; PK = pharmacokinetics; QOL = quality of life.

1

Gynecologic Oncology 127 (2012) 662–672

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review

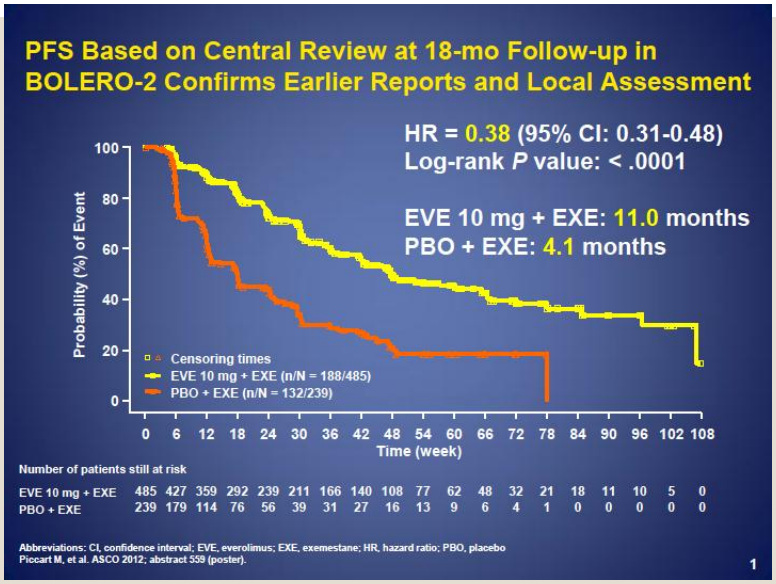
mTOR inhibitors in breast cancer: A systematic review

Flora Zagouri [a,*], Theodoros N. Sergentanis [b], Dimosthenis Chrysikos [b], Martin Filipits [a], Rupert Bartsch [a]

[a] Comprehensive Cancer Center Vienna, Department of Medicine I/Division of Oncology, Medical University of Vienna, Austria
[b] 1st Propaedeutic Surgical Dept, Hippocrateion Hospital, University of Athens, Athens, Greece

Αποτελεσματικότητα BOLERO-2

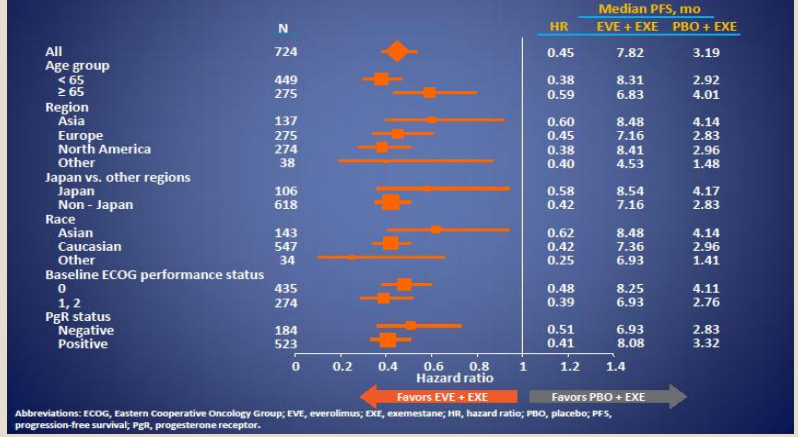
PFS Based on Central Review at 18-mo Follow-up in BOLERO-2 Confirms Earlier Reports and Local Assessment



Abbreviations: CI, confidence interval; EVE, everolimus; EXE, exemestane; HR, hazard ratio; PBO, placebo
Piccart M, et al. ASCO 2012; abstract 559 (poster).

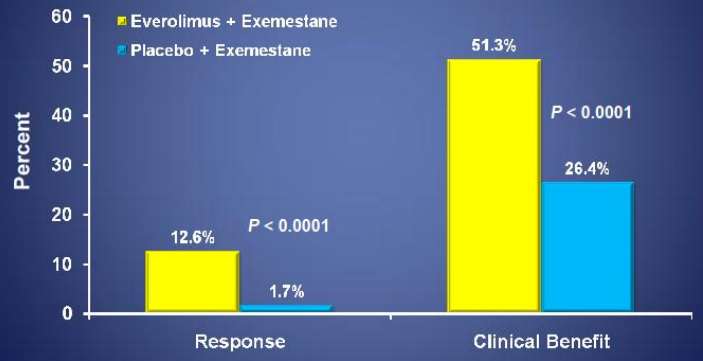
1

PFS subgroup analysis: patient characteristics and hormone receptor status.



Abbreviations: ECOG, Eastern Cooperative Oncology Group; EVE, everolimus; EXE, exemestane; HR, hazard ratio; PBO, placebo; PFS, progression-free survival; PgR, progesterone receptor.

BOLERO-2 (18 mo f/up): Response Rates & Clinical Benefit Were Significantly Higher in the Everolimus Arm



Piccart M, et al. ASCO 2012; abstract 559 (poster).

1

BOLERO-2 (18 mo f/up): Overall Survival Was Numerically Better With Everolimus

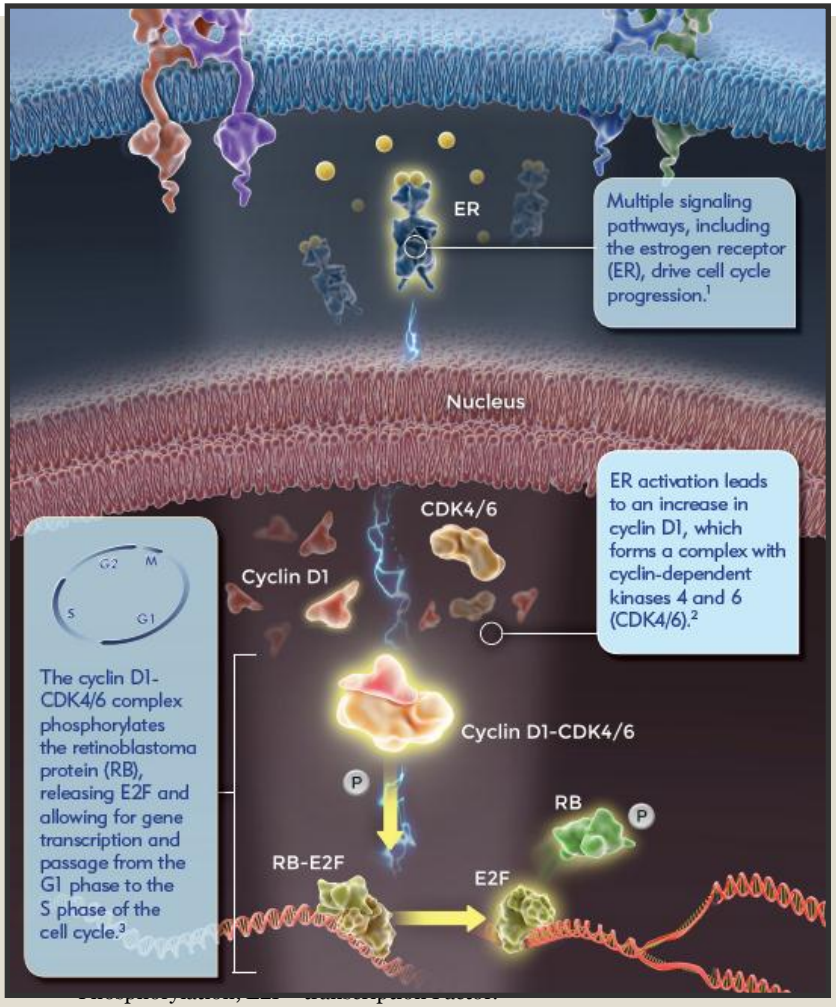
	PFS Interim[1] (7 mo follow-up)	PFS Update[2] (12 mo follow-up)	PFS Final[3] (18 mo update)
Cut-off Date	11-Feb-2011	8-Jul-2011	15-Dec-2011
OS events (EVE vs PBO%)	83 (10.6 vs 13.0%)	137 (17.3 vs 22.7%)	200 (25.4 vs 32.2%)
Δ OS events	2.4%	5.4%	6.8%

Abbreviations: EVE, everolimus; mo, month; OS, overall survival; PBO, placebo; PFS, progression-free survival; vs, versus.
Baselga J, et al. *N Engl J Med.* 2012;366(6):520-529.
Hortobagyi G, et al. SABCS 2011; abstract S3-7 (oral).
Piccart M, et al. ASCO 2012; abstract 559 (poster).

1

Synergistic Potential of Dual Inhibition in HR+ BC

CDKs: LY2835219, LEE011, palbociclib

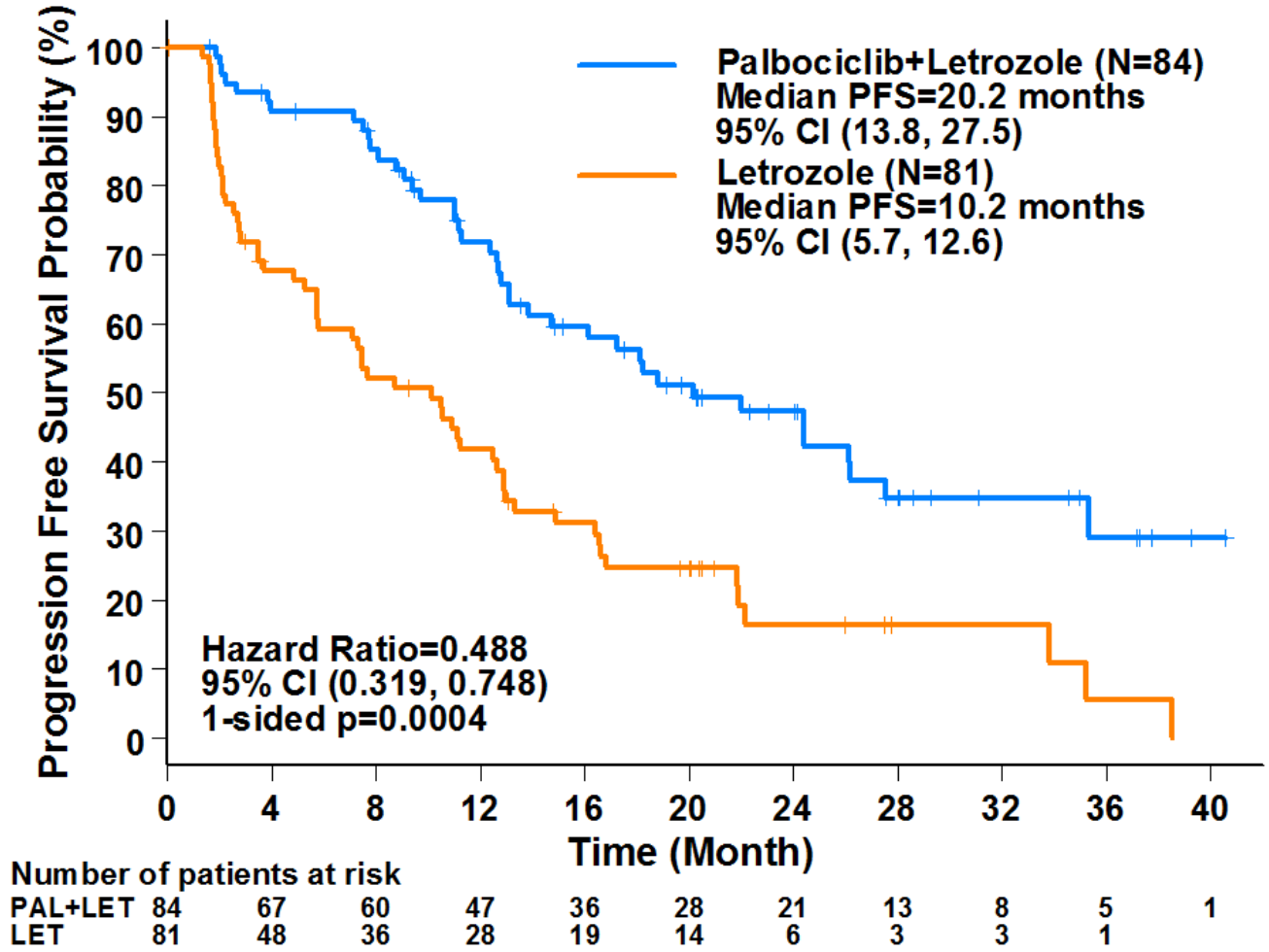


In ER+ breast cancer, estrogen signaling increases the activity of the cyclinD1-CDK4/6-RB pathway, resulting in a loss of proliferative control[4,6]

In preclinical models, the dual inhibition of CDK4/6 and ER has been found to be synergistic[6]

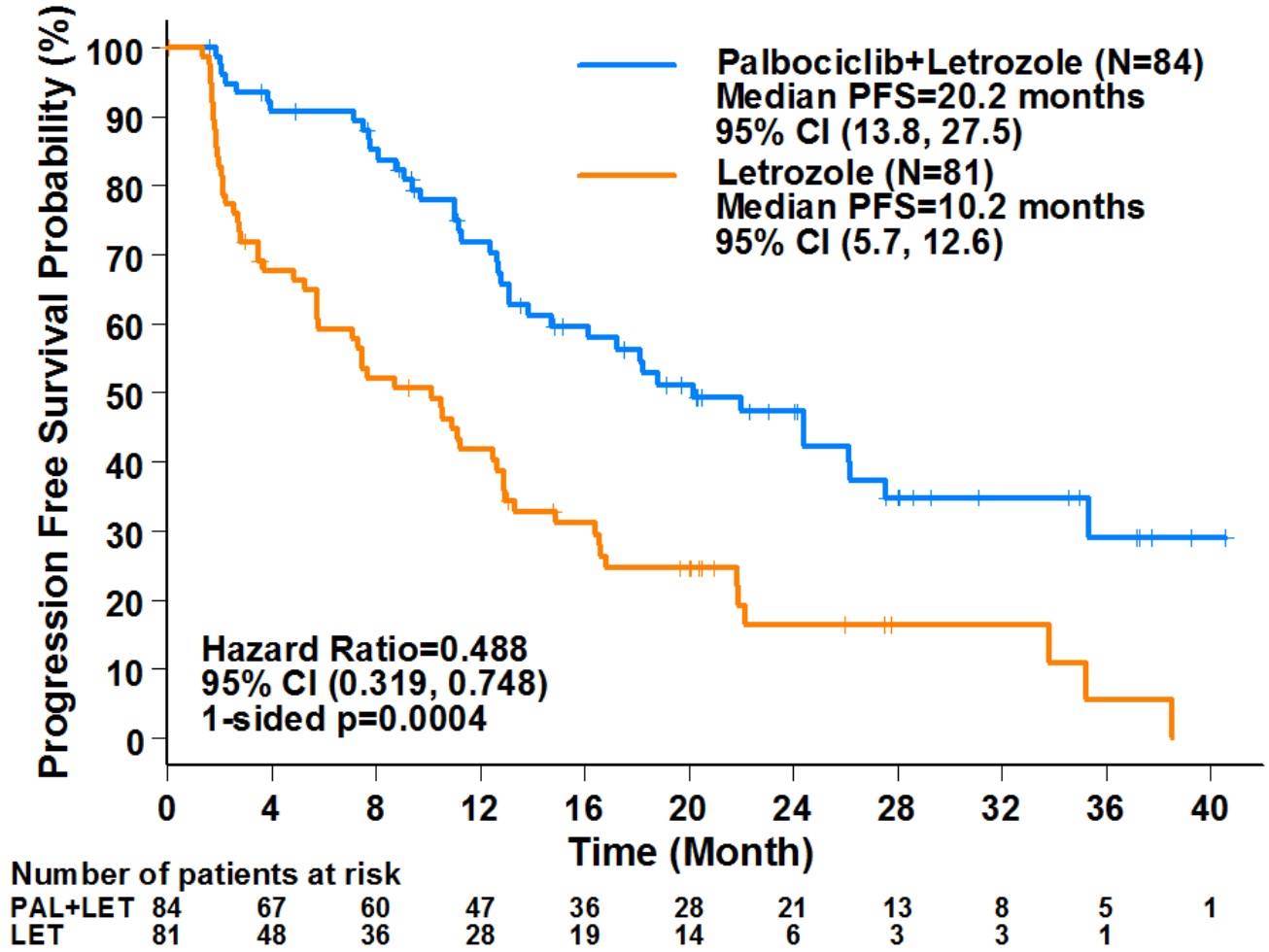
Ref:1. Lukas J, Bartkova J, Bartek J. *Mol Cell Biol.* 1996;16(12):6917-6925; 2. Prall OWJ, Saroevic B, Musgrove EA, Watts CK, Sutherland RL. *J Biol Chem.* 1997;272(16):10882-10894; 3. Ji J-Y, Dyson NJ. In: Enders GH, ed. *Cell Cycle Deregulation in Cancer.* New York, NY: Humana Press; 2010:23-42; 4. Rocoa A, Farolfi A, Bravoccini S, Schirone A, Amadori D. *Expert Opin Pharmacother.* 2014;15(3):407-420. 5. Weinberg RA. In: *The Biology of Cancer.* 2nd ed. New York, NY: Garland Science; 2013; 6. Finn RS, Dering J, Conklin D, et al. *Breast Cancer Res.* 2009;11:R77. doi:10.1186/bcr2419

Palbociclib Plus Letrozole Demonstrated Significant PFS Improvement in Advanced Breast Cancer



Finn R, et al. AACR Annual Meeting; April 5-9, 2014; San Diego, CA. Abstract CT101.

Palbociclib Plus Letrozole Demonstrated Significant PFS Improvement in Advanced Breast Cancer



Finn R, et al. AACR Annual Meeting; April 5-9, 2014; San Diego, CA. Abstract CT101.

Palbociclib

Palbociclib in HR+/HER2– BC: Phase 3 Studies

	Metastatic breast cancer			Post-neoadjuvant
Study	**1008 (PALOMA-2)**	**1023 (PALOMA-3)**	**PEARL**	**PENELOPE**
Setting	Endocrine sensitive	Endocrine resistant	Endocrine resistant	High risk
Menopausal status	Post-menopausal	Pre-menopausal + post-menopausal	Post-menopausal	Pre-menopausal + post-menopausal
No. patients	450	417	348	800
Treatment arms	Palbociclib + letrozole vs. placebo + letrozole	Palbociclib + fulvestrant vs. placebo + fulvestrant	Palbociclib + exemestane vs. capecitabine	Palbociclib vs. placebo
Primary endpoint	PFS	PFS	PFS	iDFS

FFPV, first patient first visit; iDFS, invasive disease-free survival; PFS, progression-free survival

HER2+ νόσο

Review

Pertuzumab in Breast Cancer: A Systematic Review

Flora Zagouri,[1,2] Theodoros N. Sergentanis,[3] Dimosthenis Chrysikos,[3] Constantine G. Zografos,[3] Martin Filipits,[1] Rupert Bartsch,[1] Meletios-Athanassios Dimopoulos,[2] Theodora Psaltopoulou[4]

J Clin Oncol. 2013 Mar 20;31(9):1157-63. doi: 10.1200/JCO.2012.44.9694. Epub 2013 Feb 4.

Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer.

Hurvitz SA, Dirix L, Kocsis J, Bianchi GV, Lu J, Vinholes J, Guardino E, Song C, Tong B, Ng V, Chu YW, Perez EA.

Source

University of California, Los Angeles Jonsson Comprehensive Cancer Center and Translational Oncology Research International, Los Angeles, CA, USA.

The Oncologist® New Drug Development and Clinical Pharmacology

Lapatinib for Advanced or Metastatic Breast Cancer

FRANS L. OPDAM,[a,b] HENK-JAN GUCHELAAR,[b] JOS H. BEIJNEN,[c,d] JAN H.M. SCHELLENS[a,d]

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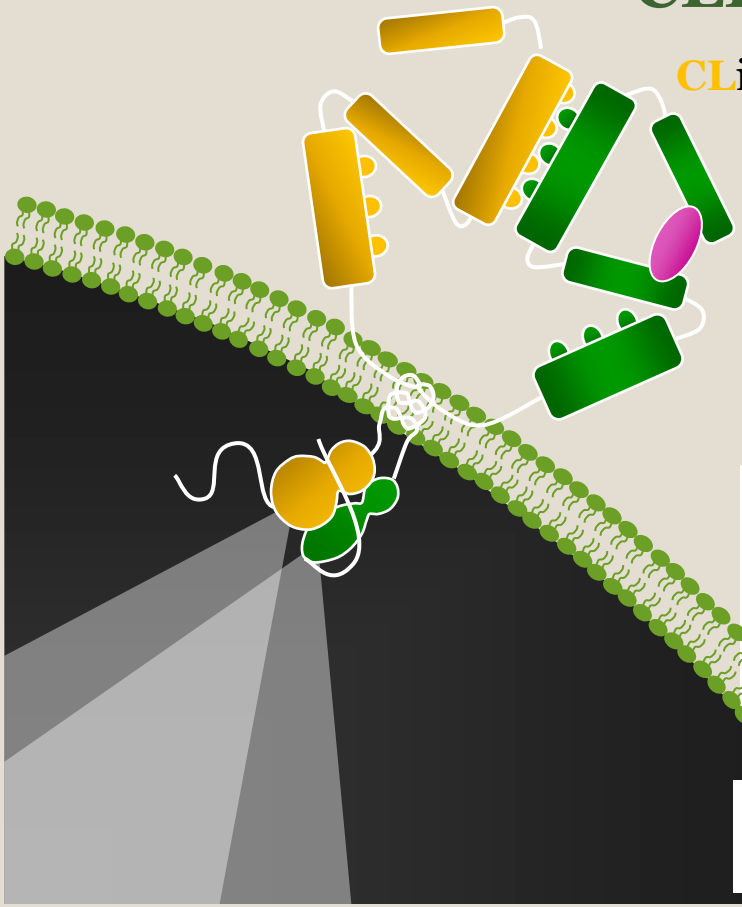
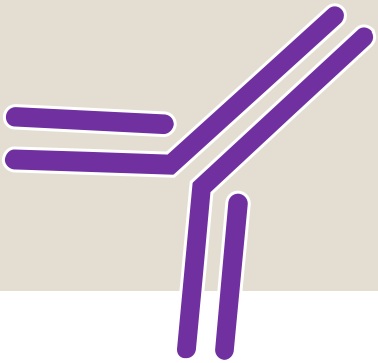
Pertuzumab

- **CLEOPATRA: A landmark trial**

  CLinical **E**valuation **O**f **P**ertuzumab **A**nd **TRA**stuzumab





Review

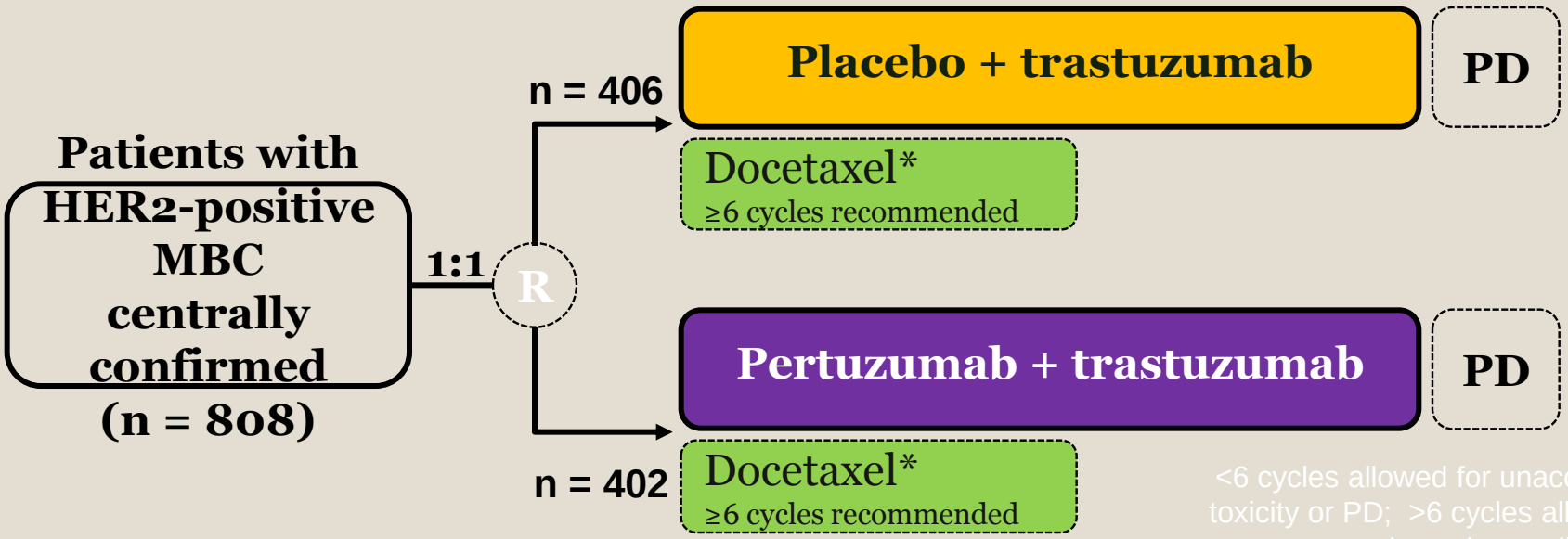
Pertuzumab in Breast Cancer: A Systematic Review

Flora Zagouri,[1,2] Theodoros N. Sergentanis,[3] Dimosthenis Chrysikos,[3] Constantine G. Zografos,[3] Martin Filipits,[1] Rupert Bartsch,[1] Meletios-Athanassios Dimopoulos,[2] Theodora Psaltopoulou[4]

Clinical Breast Cancer, Vol. 13, No. 5, 315-24

Keywords: Breast cancer, Perjeta, Pertuzumab, Systematic review

CLEOPATRA: Phase III trial of trastuzumab plus docetaxel with or without pertuzumab

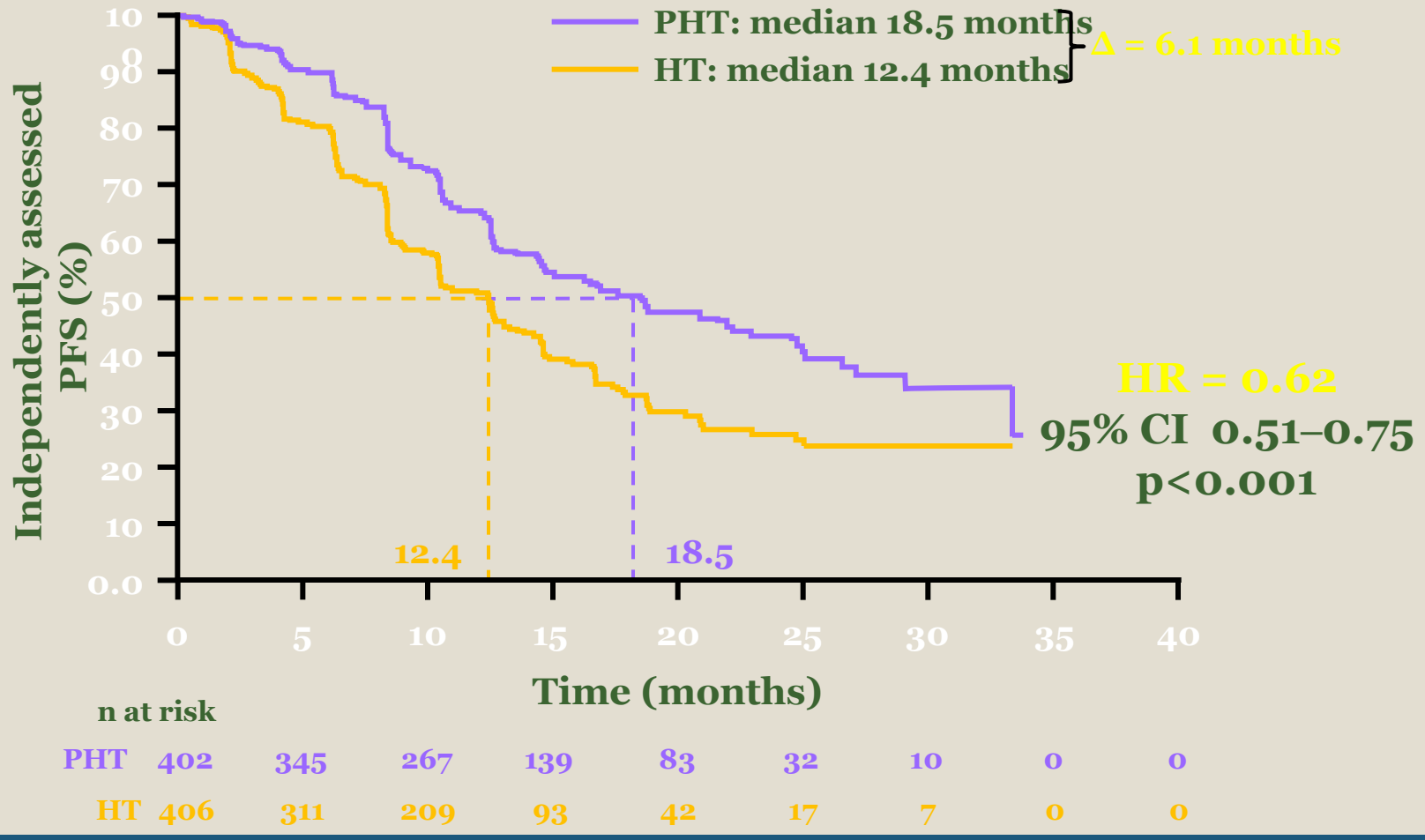


- Randomisation was stratified by geographic region and prior treatment status (neo/adjuvant chemotherapy received or not)
- Study dosing q3w:
  - Pertuzumab/placebo: 840 mg loading dose, 420 mg maintenance
  - Trastuzumab: 8 mg/kg loading dose, 6 mg/kg maintenance
  - Docetaxel: 75 mg/m^2, escalating to 100 mg/m^2 if tolerated

MBC, metastatic breast cancer; PD, progressive disease

Baselga *et al. N Engl J Med* 2012;**366**(2):109-119

CLEOPATRA: significantly prolonged PFS with pertuzumab and trastuzumab



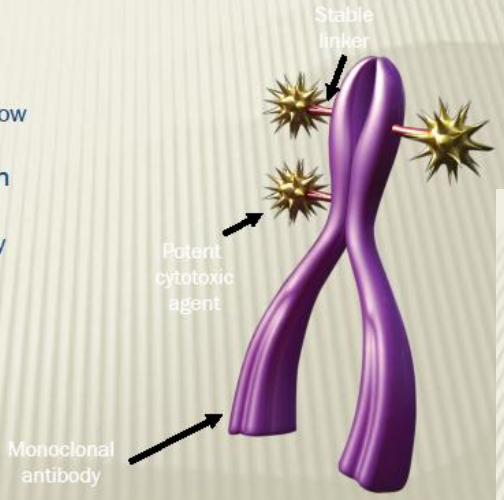
P, pertuzumab; H, trastuzumab; T docetaxel.
PFS, progression-free survival; HR, hazard ratio.

Baselga *et al. N Engl J Med* 2012;**366**(2):109-119

T-DM1

ANTIBODY–DRUG CONJUGATES (ADCS)

- ADCs are designed to target cancer cells while minimising effects on normal tissue
  - Improving the therapeutic window of the cytotoxic component
- An ADC is a unique combination of:
  - A targeted monoclonal antibody (mAb)
  - A stable linker
  - A potent cytotoxic agent



Gerber HP, *et al. MAbs* 2009; **1**:247–25

DM1: *A POTENT CYTOTOXIC AGENT*

- DM1 is a maytansinoid, one of several derivatives of the anti-mitotic drug maytansine[1]
- Maytansinoids are:
  - 24- to 270-fold more potent than paclitaxel[1]
  - 2 to 3 orders of magnitude more potent than doxorubicin[1]
- DM1 inhibits microtubule assembly, leading to apoptosis[1,2]
  - Binds directly to microtubules to inhibit polymerisation, causing cell cycle arrest and cell death[2]

DM = derivative of maytansine

1. Junttila TT, *et al. Breast Cancer Res Treat* 2011; **128**:347–356; 2. Barok M, *et al. Cancer Lett* 2011; **306**:171–179.

EMILIA

The NEW ENGLAND JOURNAL of MEDICINE

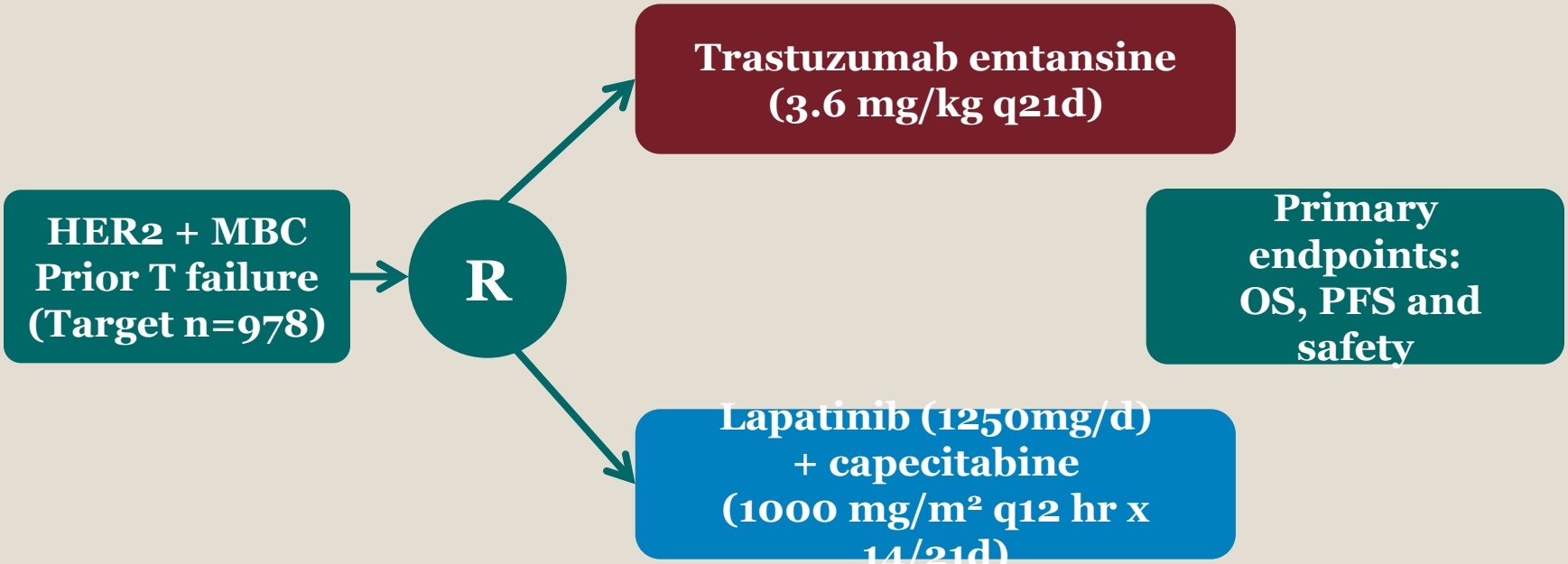
ORIGINAL ARTICLE

Trastuzumab Emtansine for HER2-Positive Advanced Breast Cancer

Sunil Verma, M.D., David Miles, M.D., Luca Gianni, M.D., Ian E. Krop, M.D., Ph.D., Manfred Welslau, M.D., José Baselga, M.D., Ph.D., Mark Pegram, M.D., Do-Youn Oh, M.D., Ph.D., Véronique Diéras, M.D., Ellie Guardino, M.D., Ph.D., Liang Fang, Ph.D., Michael W. Lu, Pharm.D., Steven Olsen, M.D., Ph.D., and Kim Blackwell, M.D., for the EMILIA Study Group

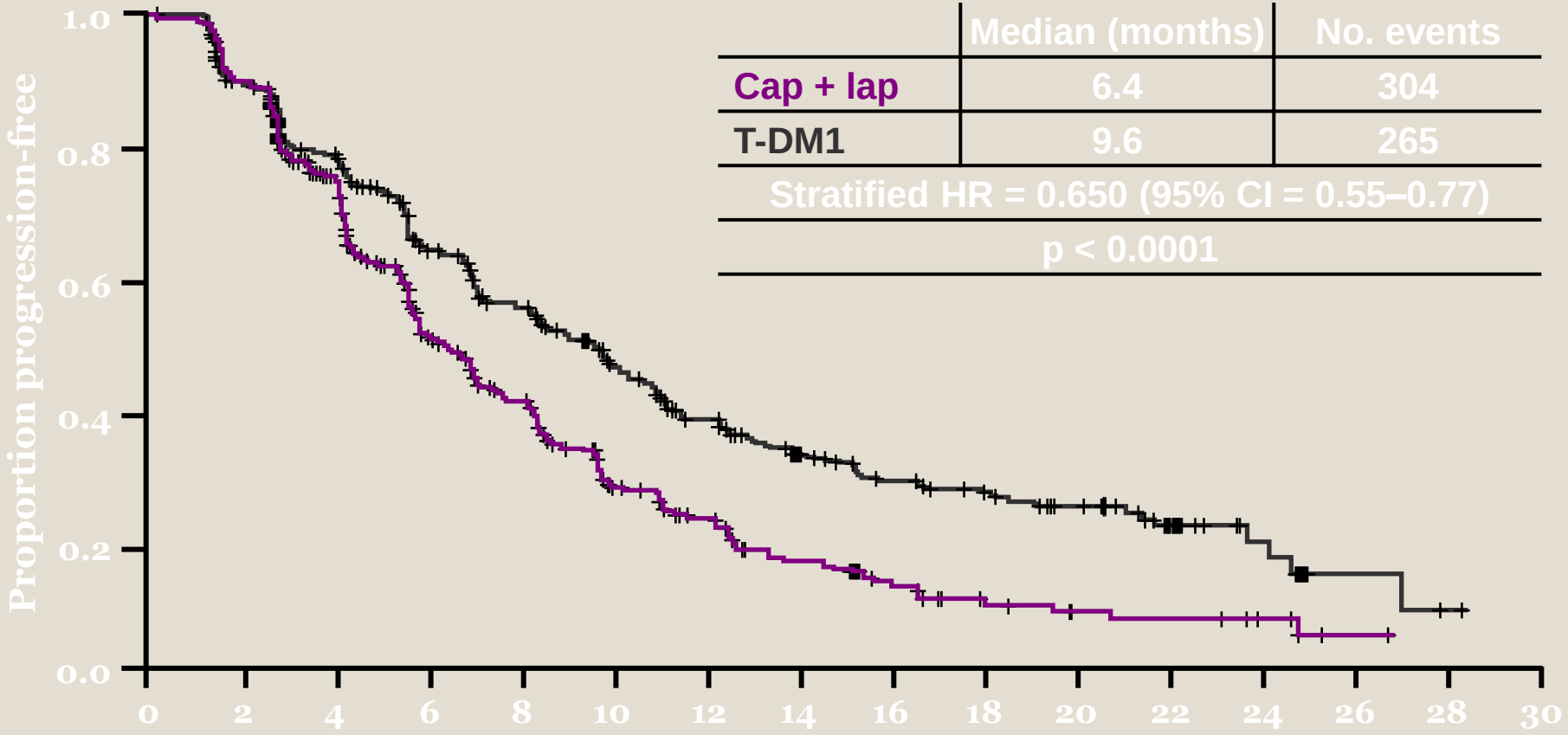
EMILIA – Trastuzumab emtansine *vs* lapatinib + capecitabine in patients progressing after trastuzumab: Study design

- Entry criteria
  - Centrally confirmed HER2+ locally advanced or metastatic, progressive breast cancer
  - Prior taxane and trastuzumab
  - ECOG PS 0–1
- Secondary endpoints
  - ORR and clinical benefit, duration of response
  - Time to symptom progression



Verma et al, N Engl J Med. 2012; 367: 1783-91.

EMILIA: PFS survival by IRF



	Median (months)	No. events
Cap + lap	6.4	304
T-DM1	9.6	265
Stratified HR = 0.650 (95% CI = 0.55–0.77)		
p < 0.0001		

No. at risk by IRF:

Cap + lap	496	404	310	176	129	73	53	35	25	14	9	8	5	1	0	0
T-DM1	495	419	341	236	183	130	101	72	54	44	30	18	9	3	1	0

Unstratified HR = 0.66 (p <0.0001).

CI, confidence interval; HR, hazard ratio; IRF, independent review facility; PFS, progression-free survival.

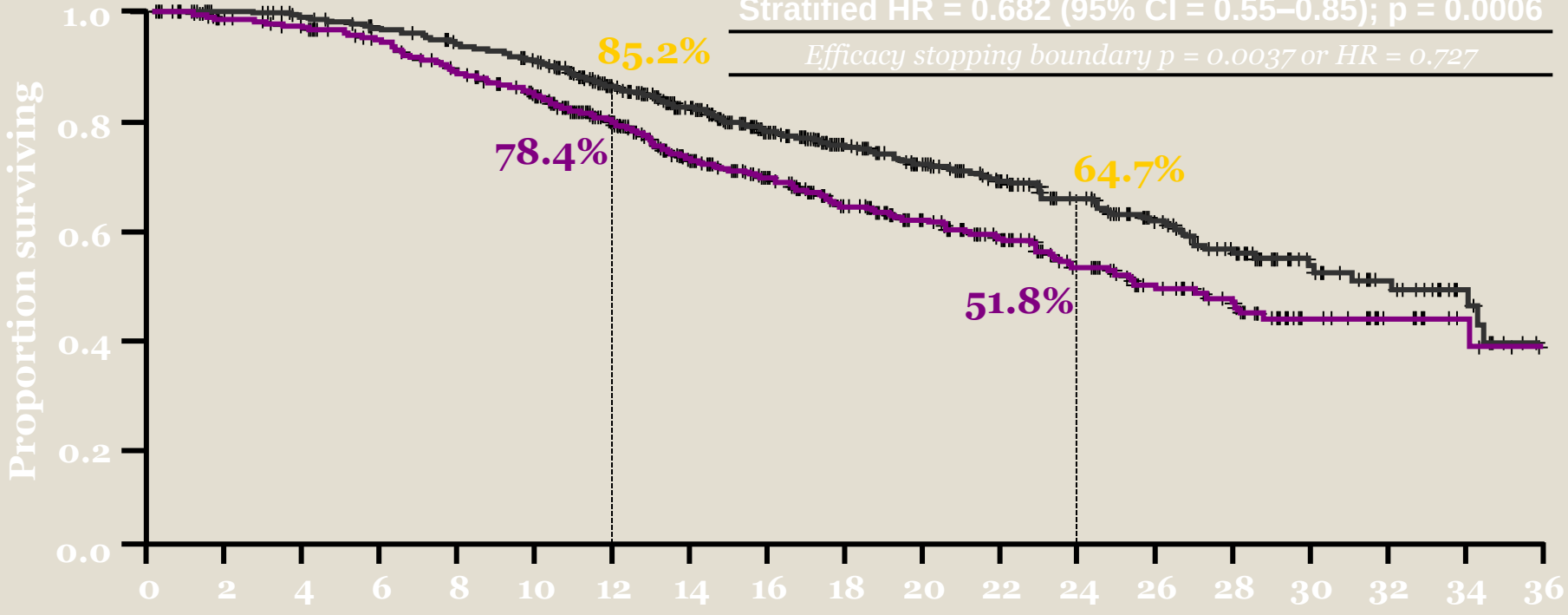
Verma S, *et al. N Engl J Med* 2012; **367**:1783–1791 (supplementary material available with the publication online); Blackwell KL, *et al.* ASCO 2012 (Abstract LBA1; oral presentation).

EMILIA: Overall survival (confirmatory analysis)

	Median (mo)	No. events
Cap + lap	25.1	182
T-DM1	30.9	149

Stratified HR = 0.682 (95% CI = 0.55–0.85); p = 0.0006

Efficacy stopping boundary p = 0.0037 or HR = 0.727



No. at risk:																		
Cap + lap	496	471	453	435	403	368	297	240	204	159	133	110	86	63	45	27	17	7	4
T-DM1	495	485	474	457	439	418	349	293	242	197	164	136	111	86	62	38	28	13	5

Data cut-off July 31, 2012; Unstratified HR = 0.70 (p = 0.0012).

CI, confidence interval; HR, hazard ratio.

Verma S, *et al. N Engl J Med* 2012; **367**:1783–1791 (supplementary material available with the publication online); Verma S, et al. ESMO 2012 (Abstract LBA12; oral presentation).

Triple negative

- ✓Όχι στοχευμένη θεραπεία
- ✓Bevacizumab
- ✓↓ OS
- ✓Μονοθεραπεία
- ✓carboplatin?

Συχνότερα ΧΜΘ σχήματα στη μεταστατική νόσο

PREFERRED CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

PREFERRED CHEMOTHERAPY COMBINATIONS

CAF chemotherapy[1]
- Cyclophosphamide 100 mg/m^2 PO days 1-14
- Doxorubicin 30 mg/m^2 IV days 1 & 8
- 5-Fluorouracil 500 mg/m^2 IV days 1 & 8

Cycled every 28 days.

FAC chemotherapy[2]
- 5-Fluorouracil 500 mg/m^2 IV days 1 & 8 or days 1 & 4
- Doxorubicin 50 mg/m^2 IV day 1
- Cyclophosphamide 500 mg/m^2 IV day 1

Cycled every 21 days.

FEC chemotherapy[3]
- Cyclophosphamide 400 mg/m^2 IV days 1 & 8
- Epirubicin 50 mg/m^2 IV days 1 & 8
- 5-Fluorouracil 500 mg/m^2 IV days 1 & 8

Cycled every 28 days.

AC chemotherapy[4]
- Doxorubicin 60 mg/m^2 IV day 1
- Cyclophosphamide 600 mg/m^2 IV day 1

Cycled every 21 days.

EC chemotherapy[5]
- Epirubicin 75 mg/m^2 IV day 1
- Cyclophosphamide 600 mg/m^2 IV day 1

Cycled every 21 days

AT chemotherapy[6]
- Doxorubicin 60 mg/m^2 IV day 1
- Paclitaxel 125-200 mg/m^2 IV day 1

Cycled every 21 days

AT chemotherapy[7]
- Doxorubicin 50 mg/m^2 IV day 1
- Docetaxel 75 mg/m^2 IV day 1

Cycled every 21 days

CMF chemotherapy[8]
- Cyclophosphamide 100 mg/m^2 PO days 1-14
- Methotrexate 40 mg/m^2 IV days 1 & 8
- 5-Fluorouracil 600 mg/m^2 IV days 1 & 8

Cycled every 28 days.

Docetaxel/capecitabine chemotherapy[9]
- Docetaxel 75 mg/m^2 IV day 1
- Capecitabine 950 mg/m^2 PO twice daily days 1-14

Cycled every 21 days.

GT chemotherapy[10]
- Paclitaxel 175 mg/m^2 IV day 1
- Gemcitabine 1250 mg/m^2 IV days 1 & 8 (following paclitaxel on day 1)

Cycled every 21 days.

OTHER COMBINATIONS

Ixabepilone/capecitabine (category 2B)
- Ixabepilone 40 mg/m^2 IV day 1
- Capecitabine 2000 mg/m^2 PO days 1-14

Cycled every 21 days.

PREFERRED CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

PREFERRED SINGLE AGENTS

Anthracyclines:
Doxorubicin 60-75 mg/m^2 IV day 1[11]
Cycled every 21 days
OR
- Doxorubicin 20 mg/m^2 IV weekly[12]

- Epirubicin 60-90 mg/m^2 IV day 1[13]

Cycled every 21 days.

- Pegylated liposomal encapsulated doxorubicin 50 mg/m^2 IV day 1[14]

Cycled every 28 days.

Taxanes:
- Paclitaxel 175 mg/m^2 IV day 1[15]

Cycled every 21 days.
OR
- Paclitaxel 80 mg/m^2 IV weekly[16]

- Docetaxel 60-100 mg/m^2 IV day 1[17,18]

Cycled every 21 days.
OR
- Docetaxel 40 mg/m^2 IV weekly for 6 wks followed by a 2 week rest, then repeat[19]

- Albumin-bound paclitaxel 100 mg/m^2 or 150 mg/m^2 days 1, 8, and 15 IV[20,21]

Cycled every 28 days.

Albumin-bound paclitaxel 260 mg/m^2 IV[20]
Cycled every 21 days.

Anti-metabolites:
- Capecitabine 1000-1250 mg/m^2 PO twice daily days 1-14[22]

Cycled every 21 days.

- Gemcitabine 800-1200 mg/m^2 IV days 1, 8 & 15[23]

Cycled every 28 days.

Other microtubule inhibitors:
- Vinorelbine 25 mg/m^2 IV weekly[24]
- Eribulin 1.4 mg/m^2 IV days 1, 8

Cycled every 21 days.

OTHER SINGLE AGENTS
- Cyclophosphamide
- Mitoxantrone
- Cisplatin
- Etoposide (PO) (category 2B)
- Vinblastine
- Fluorouracil CI
- Ixabepilone

PREFERRED AGENTS WITH BEVACIZUMAB

Paclitaxel plus bevacizumab[25]
- Paclitaxel 90 mg/m^2 by 1 h IV days 1, 8 & 15
- Bevacizumab 10 mg/kg IV days 1 & 15

Cycled every 28 days.

PREFERRED CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

PREFERRED FIRST-LINE AGENTS WITH TRASTUZUMAB FOR HER2-POSITIVE DISEASE

COMBINATIONS

PCH chemotherapy[26]
- Carboplatin AUC of 6 IV day 1
- Paclitaxel 175 mg/m^2 IV day 1

Cycled every 21 days.

Weekly TCH chemotherapy[27]
- Paclitaxel 80 mg/m^2 IV days 1, 8 & 15
- Carboplatin AUC of 2 IV days 1, 8 & 15

Cycled every 28 days.

SINGLE AGENTS
- Paclitaxel 175 mg/m^2 IV day 1[28]

Cycled every 21 days.
OR
- Paclitaxel 80-90 mg/m^2 IV weekly[29]

- Docetaxel 80 to 100 mg/m^2 IV day 1[30]

Cycled every 21 days
OR
- Docetaxel 35 mg/m^2 IV infusion weekly[31]

- Vinorelbine 25 mg/m^2 IV weekly[32]

- Capecitabine 1000-1250 mg/m^2 PO twice daily days 1-14[33]

Cycled every 21 days

TRASTUZUMAB COMPONENT

Trastuzumab 4 mg/kg IV day 1
Followed by
2 mg/kg IV weekly[28,37]
OR
Trastuzumab 8 mg/kg IV day 1
Followed by
6 mg/kg IV every 3 wks[38]

PREFERRED AGENTS FOR TRASTUZUMAB-EXPOSED HER2-POSITIVE DISEASE

Capecitabine plus lapatinib[34]
- Capecitabine 1000 mg/m^2 PO twice daily Days 1 - 14
- Lapatinib 1250 mg PO daily Days 1-21

Cycled every 21 days

Trastuzumab + other first-line agents

Trastuzumab + capecitabine[35]

Trastuzumab + lapatinib[36]

TRASTUZUMAB COMPONENT

Trastuzumab 4 mg/kg IV day 1
Followed by
2 mg/kg IV weekly[28,37]
OR
Trastuzumab 8 mg/kg IV day 1
Followed by
6 mg/kg IV every 3 wks[38]

Το μέλλον της θεραπείας

- ✓Εξατομίκευση
- ✓Χορήγηση κατάλληλης θεραπείας στον κατάλληλο ασθενή
- ✓Οχι τοξικότητα
- ✓Βέλτιστη αποτελεσματικότητα

✓ΕΝΘΑΡΡΥΝΣΗ ΑΣΘΕΝΩΝ ΝΑ ΣΥΜΜΕΤΕΧΟΥΝ ΣΕ ΚΛΙΝΙΚΕΣ ΜΕΛΕΤΕΣ

Ευχαριστώ για την προσοχή σας…