

# Role of Neoadjuvant chemotherapy in breast conservative surgery

المستجدات الحديثة في علاج أورام الثدي

2023-12-4

# OBJECTIVES

- NSABP
- NEOADJUVANT CHEMOTHERAPY
- EFFECT ON BREAST CONSERVATIVE SURGERY
- Targeted therapy approved in Iraq for metastatic breast cancer
- CLINICAL CASE
- (MULTIDISPLINARY TEAM APPROACH AND FOLLOWING THE GUIDELINES)

# NSABP<sup>®</sup>

*National Surgical Adjuvant Breast and Bowel Project*

**PARTNERS IN CANCER RESEARCH**

- National Surgical Adjuvant Breast and Bowel Project

it is a clinical trials cooperative group supported since its inception by the National Cancer Institute (NCI)

More than 50 year history of designing and conducting clinical trials that have changed the way breast cancer treated (ex: breast conservative surgery, tamoxifen use in breast cancer)

# Neoadjuvant Chemotherapy

## NSABP 18

Results: 1,523 patient 1988-1993, operable breast cancer. All patient received lumpectomy with axillary dissection or modified radical mastectomy. All patient received Tamoxifen for 5 years.

Primary object:

1. Evaluate Disease Free Survival (DFS)
2. Evaluate Overall Survival (OS)

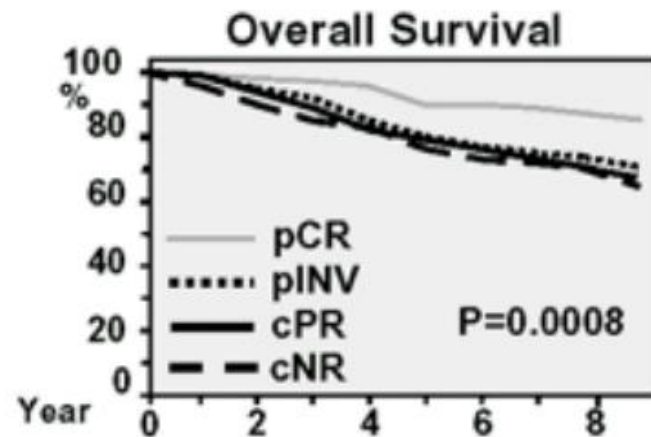
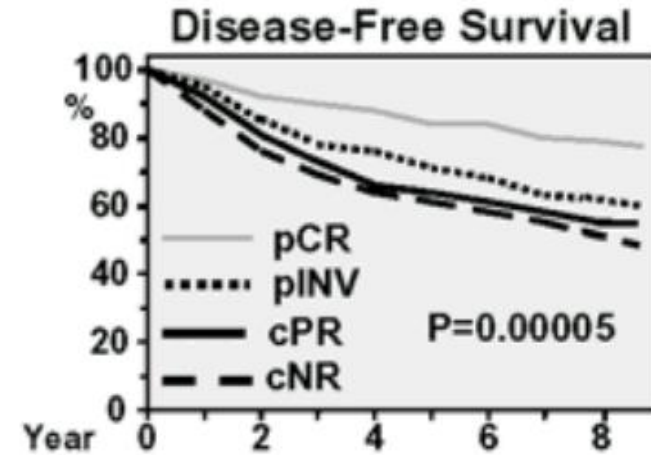
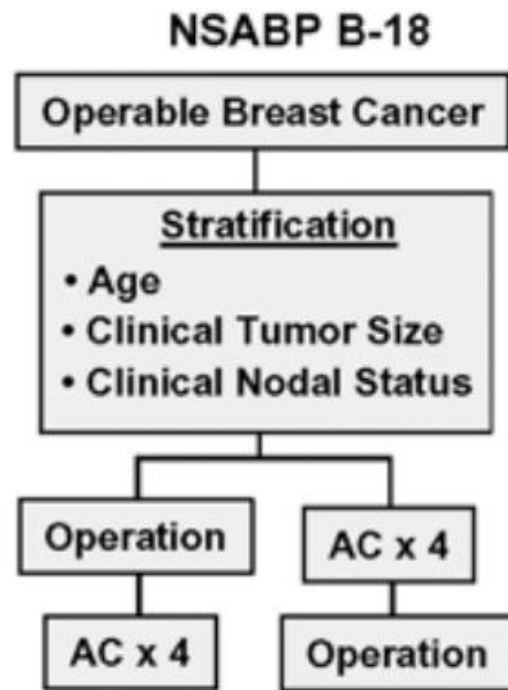
# Neoadjuvant Chemotherapy NSABP 18

Secondary Goals:

1. Evaluate clinical and pathologic response.
2. Downstage positive axillary lymph nodes
3. Convert to BCS.

# Neoadjuvant Chemotherapy

## NSABP 18



# Neoadjuvant Chemotherapy NSABP 18

Pathologic response is predictive of survival

	<b>DFS</b>	<b>p value</b>	<b>OS</b>	<b>p value</b>
pCR	75%	0.00005	85%	0.00008
pINV	58%		73%	

Results are independent of age, nodal status, or tumor size.

# Neoadjuvant Chemotherapy

## NSABP 18

### Results:

1. No difference in DFS or OS when comparing neoadjuvant to adjuvant chemotherapy.
2. For the neoadjuvant group 36% of patients had a cCR and 43% cPR for a total of 79% were downstaged. Only 3% had progression of disease.
3. Patient who had a pCR had a better DFS and OS compared to pPR. Response is predictor of prognosis, independent of receptor status, grade, and other biomarkers
4. 16% of patient downstaged the positive axillary lymph nodes.
5. Patients receiving neoadjuvant chemotherapy is more likely to have BCS. 67% vs.60% (p=0.002)



# Neoadjuvant Chemotherapy NSABP 27

Evaluate Docetaxol in the neoadjuvant setting after 4 cycles of Adriamycin and Cytosan

- ❖ Opened in 1995, closed in 2000.
- ❖ Accrued 2,411 patients.

# Neoadjuvant Chemotherapy NSABP 27

Primary goal:

1. Evaluate the worth of giving Docetaxol (Taxol) in the preoperative setting after 4 cycles of AC, compared to AC alone.
2. Evaluate DFS and OS

# Neoadjuvant Chemotherapy

## NSABP 27

Secondary goal:

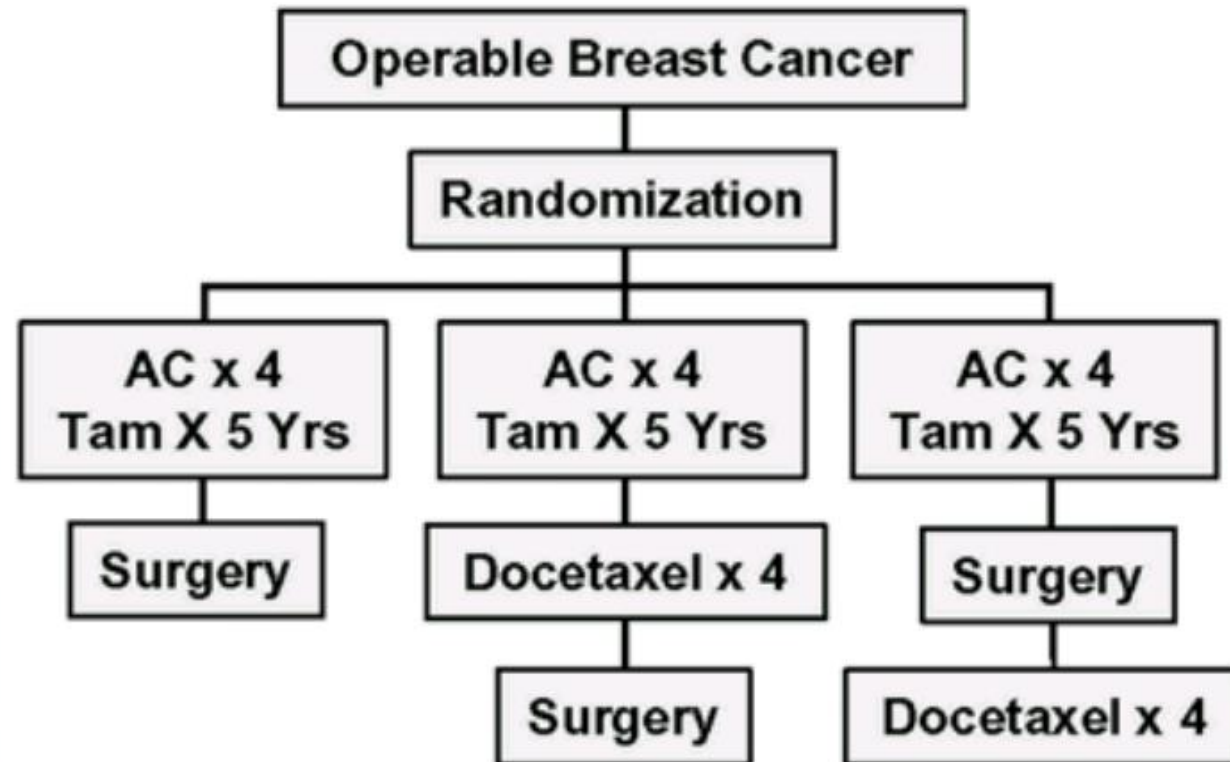
1. Preoperative Docetaxol after 4 cycles of AC improve pCR, axillary nodal status, increase BCS
2. For patient who receive preoperative AC alone, did postoperative Docetaxol improve DFS and OS for patient with residual invasive cancer (pINV).

# Neoadjuvant Chemotherapy

## NSABP 27

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### NSABP B-27



# NSABP 27

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	cCR	P value	Overall cCR+cPR	P value	pCR	P value
AC>T	65.4%	0.001	91.1%	0.001	25.6%	<0.001
AC	40.4%		85.7%		13.7%	

# Neoadjuvant Chemotherapy NSABP 27

	<b>BCS</b>	<b>p value</b>	<b>Node Neg</b>	<b>p value</b>
AC	61.45	0.7	50.7%	>0.01
AC>T	63.1%		75.8%	

BCS is in contrast to NSAPB 18

DSF and OS data not published

Prediction for survival with biomarkers not published

# Neoadjuvant Chemotherapy

Take home points from NASBP 18 and 27

- ❖ The response to chemotherapy is predictive of DFS and OS.
- ❖ The response to chemotherapy can be used as an immediate endpoint in testing new chemotherapy or target agents.
- ❖ Evaluate biomarkers for predicting prognosis, ER, PR, grade, Ki-67, Her-2, P53, and others.
- ❖ Serial monitoring of biomarkers may provide insight into the nature and function of these markers. Example the Ki-67 or hormonal receptor status may change with neoadjuvant chemotherapy.

# Neoadjuvant Chemotherapy

- ❖ Improved evaluation of mechanism of action with evaluation of treated cancer cells.
- ❖ Provide information for regarding need for additional chemotherapy (e.g., anthracyclines) or postmastectomy radiation.
- ❖ Evaluate predictors of response, Oncotype DX, Mammaprint and breast MRI.
- ❖ Downstage patients to allow BCS and lesser axillary surgery.
- ❖ Objective tumor response for high risk patients.



# Neoadjuvant Chemotherapy

Consider Neoadjuvant chemotherapy for all breast cancer that are high risk for LRR and metastatic disease.

# Neoadjuvant Chemotherapy

1. Breast cancers larger than 2.5 CM.
2. Triple negative breast cancers larger than 5mm
3. Her-2 positive breast cancers larger than 5mm
4. Core needle or FNA positive axillary lymph nodes.
5. Any T3 or T4 breast cancer
6. All inflammatory breast cancers.

# Neoadjuvant chemotherapy in breast cancer

**MAIN INDICATIONS :**

- i) STAGE III A-B or T<sub>3-4</sub>**
- ii) Inflammatory breast cancer**
- iii) Involvement of ipsilateral supra- or infraclavicular LNs**

**SECONDARY INDICATIONS :**

- i) Desire for breast –conservation after biopsy or lumpectomy**
- ii) Medical contraindications to surgery**
- iii) Pregnant women with breast cancer (> 2<sup>nd</sup> trimester)**

**RECOMMENDED REGIMENS:**

- i) Anthracycline – based chemotherapy (x 4 cycles)**
- ii) Taxanes or trastuzumab (look promise but need further investigation)**

# Neoadjuvant Hormonal Therapy

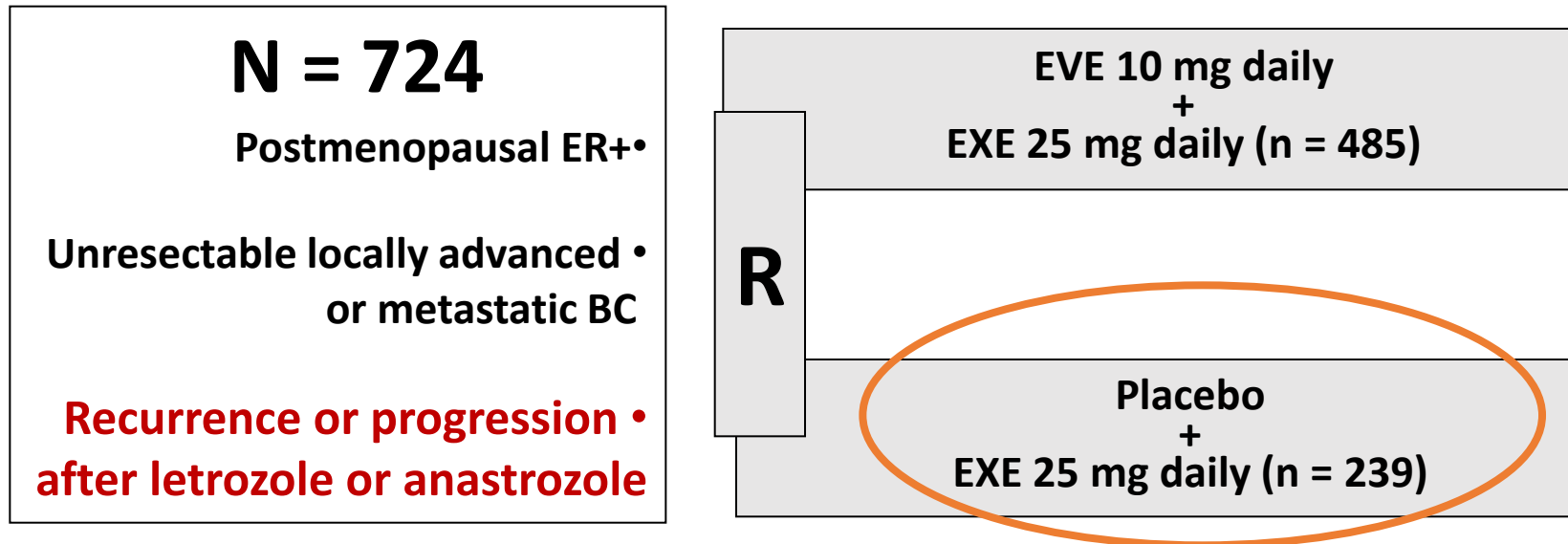
Questions for future and ongoing clinical trials

1. Efficacy of neoadjuvant hormonal therapy in pre and postmenopausal women. Currently multiple trials are open using Tamoxifen, Letrozole, and Anastrozole.
2. NSABP recently opened NSABP-N-SAS-BC06
3. Alliance and CALGB recently open a DCIS trial and hormonal therapy.
4. Is surgery indicated for women who have a cCR on breast MRI. Is radiation sufficient treatment?

# targeted therapy approved by MOH for advanced breast cancer

- Everolimus (afinitor): m TOR inhibitor
- Trastuzumab (Herceptin) :Her 2/ neu inhibitor
- Fulvestrant : estrogen receptor downregulator

# BOLERO-2 (Ph III): Everolimus in Advanced BC



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

## Endpoints

**Primary:** PFS (local assessment) •

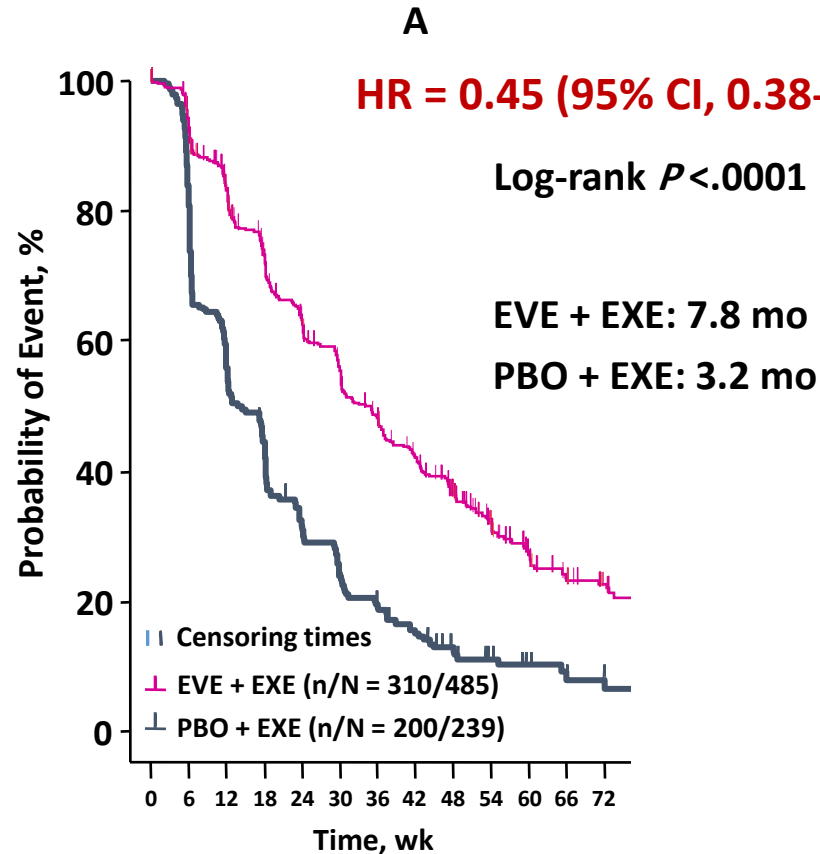
**Secondary:** OS, ORR, QOL, safety, bone markers, PK •

# BOLERO-2: Final Analysis of Progression-Free Survival

18-mo follow-up

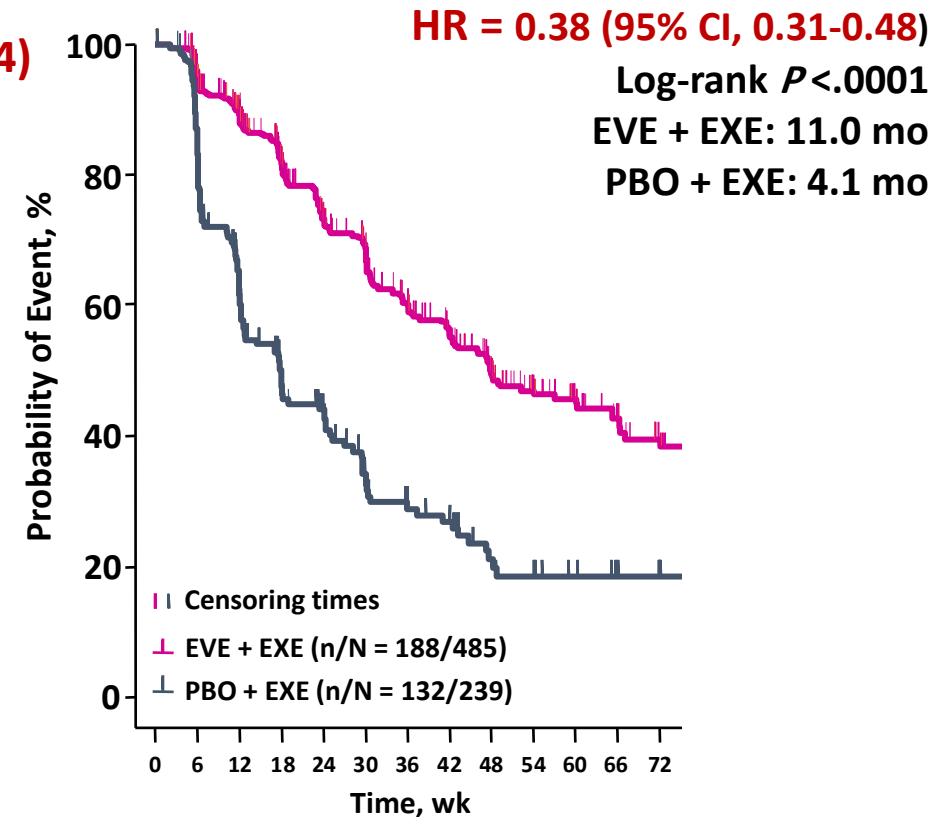
Local Assessment

Central Assessment



Patients at risk

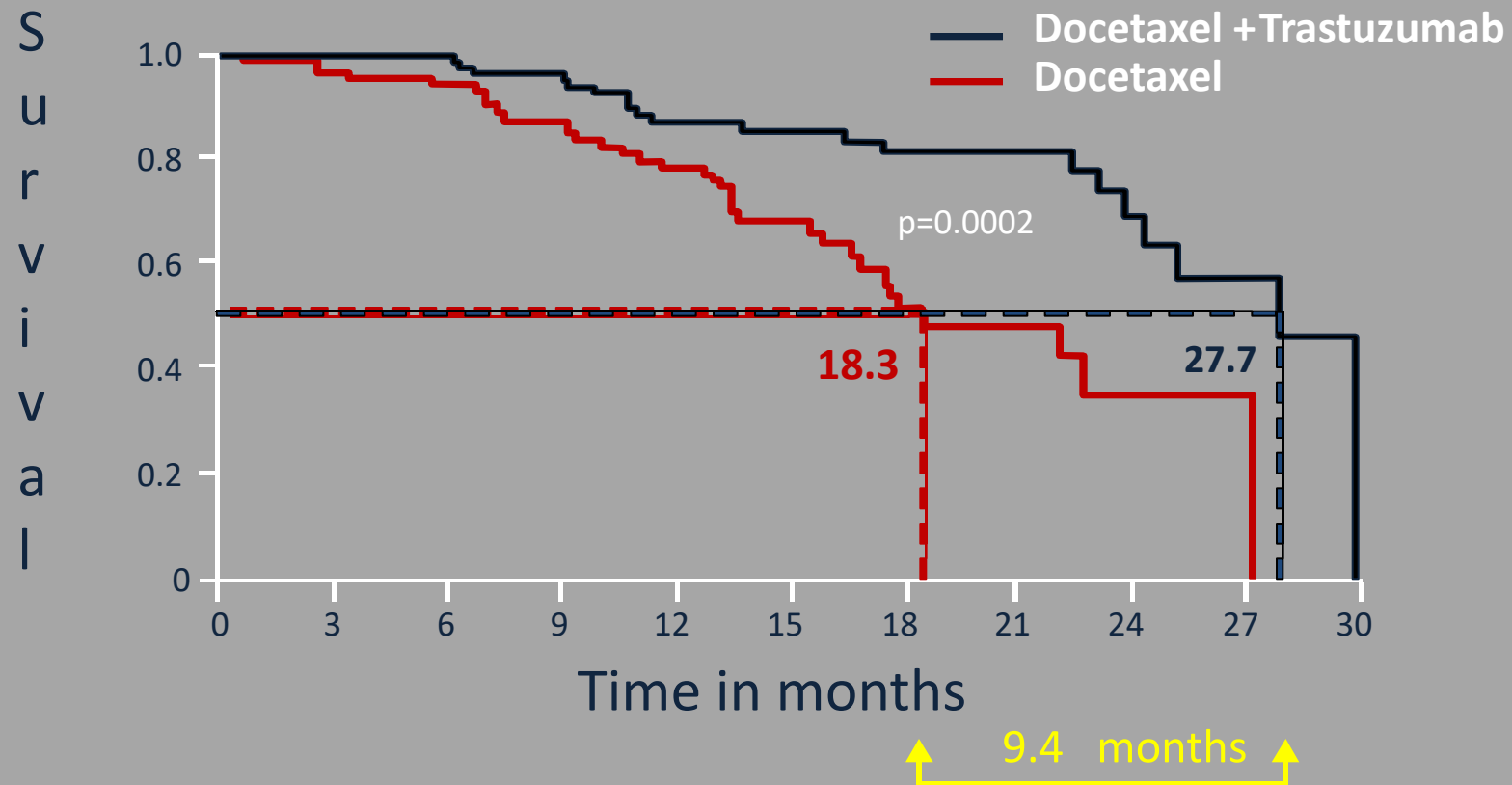
EVE + EXE	485	436	366	304	257	221	185	158	124	91	66	50	35
PBO + EXE	239	190	132	96	67	50	39	30	21	15	10	8	5



EVE + EXE	485	427	359	292	239	211	166	140	108	77	62	48	32
PBO + EXE	239	179	114	76	56	39	31	27	16	13	9	6	4

mo, months.

# Trastuzumab-Significantly Improved Overall survival In MBC

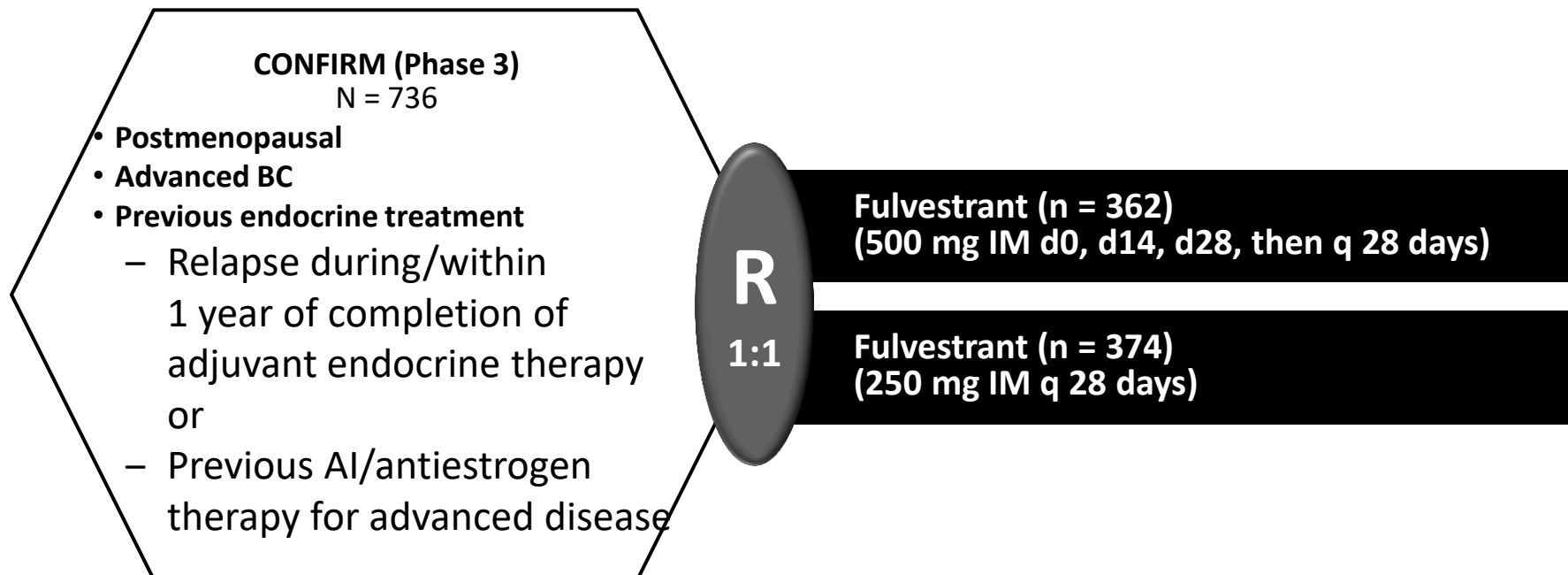




# CONFIRM Trial Design: Fulvestrant 250 mg vs Fulvestrant 500 mg

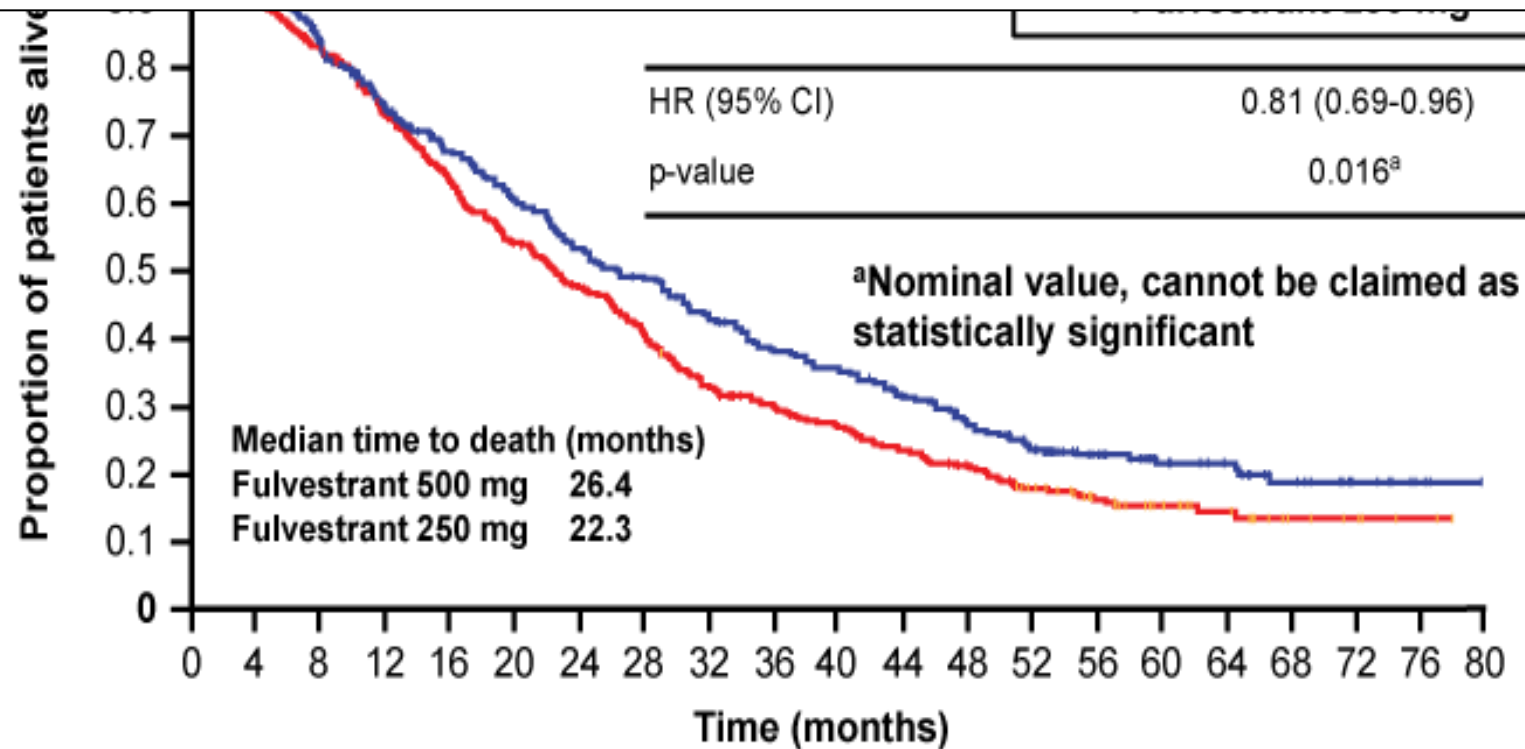
## Key endpoints

- Primary: Progression-free survival (PFS)
- Secondary: Objective response (OR), clinical benefit rate (CBR), duration of clinical benefit (DOCB), quality of life (QoL), tolerability, overall survival (OS)



# CONFIRM Study : OS Fulvestrant HD (500) vs. LD (250): Second Line (AI-R)

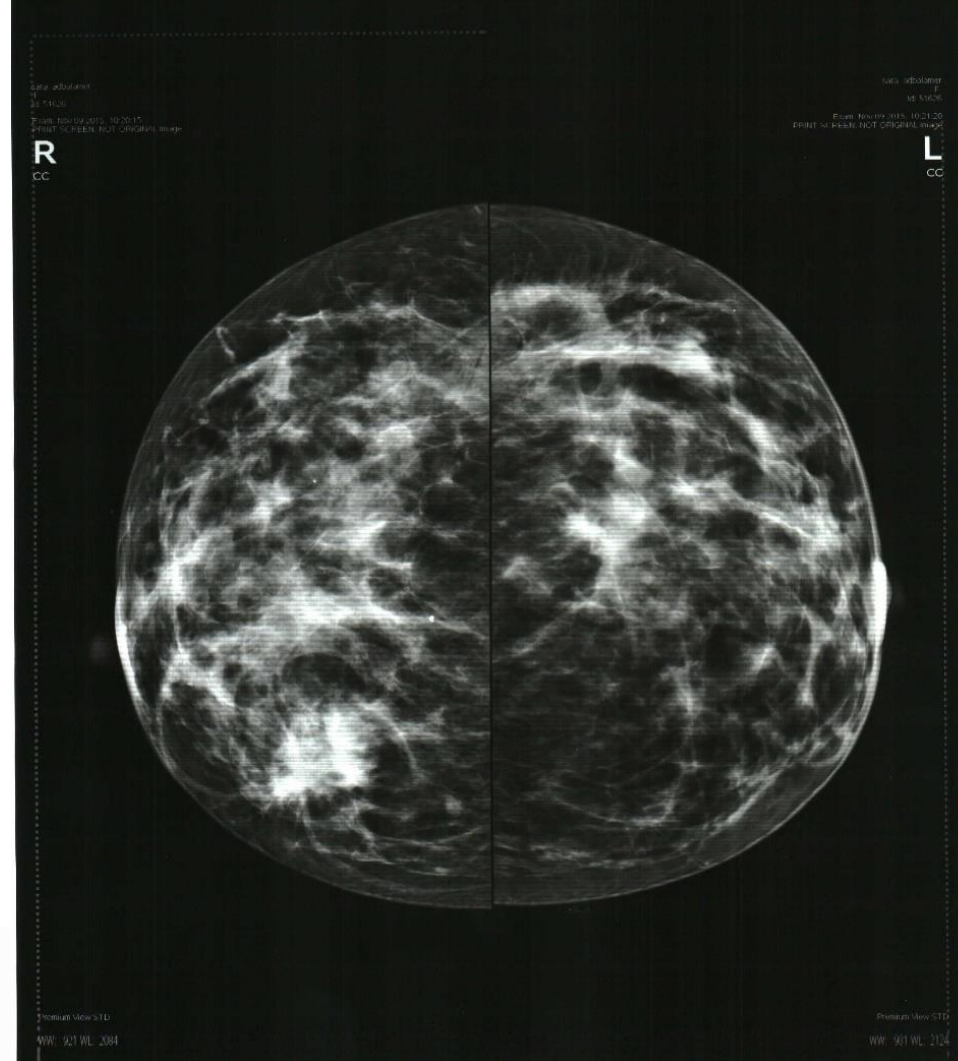
On the basis of these results, FDA approved Fulvestrant HD in HR+ MBC



# Clinical case

- S. A. 32 year old female , mother of 4 children
- Presented to the oncologist with mass in ILQ of the right breast
- Examination reveal hard gritty mass about 2 cm in size , mobile with no associated skin or nipple changes, negative axillary
- Patient were send for full evaluation

# *Mammography*



## Mammographic report (bilateral CC and MLO View):

- Density of breast 50%
- There is an ill defined radio dense spiculated mass at R IIQ region disturbing surrounding architecture
- Normal retroareolar nipple region
- Normal skin thickness
- Clear axilla
- Picture of R breast CA
  - RIGHT BIRADS V
  - LEFT BIRADS I

# Breast ultrasound

Age:

24c

Recorder No.:

017c7

## Right breast ultrasound report :

- There is a hypoechoic mass ,irregular outline ,surrounded by desmoplastic reaction at 3 o'clock measure (15x14 ) mm
- Multiple axillary LN with benign criteria
- Left breast CA

**BIRADS V**

Scoring system used by radiologist to evaluate the breast examination by U/S or Mammography as follow:

- BIRADS 0 = non informative (need other modality for diagnosis).
- BIRADS I = normal breast study.
- BIRADS II = benign lesion.
- BIRADS III = benign ( for follow up ).

# True cut tissue biopsy

Report Title: RT. breast mass true cut biopsy

Date of sample:  
Report No.: B 116/15

## Gross:

Multiple pieces of tissue each measuring( 2x0.2) cm, all taken.

## Microscopic:

Section shows features consistent with **invasive ductal carcinoma (NOS ) with desmoplastic reaction.**

# What is missing ?

Sentinel lymph node biopsy  
(negative axilla by ultrasound)

# CT SCAN CHEST AND ABDOMEN

Date: 15.11.2015

Abd & chest CT is done

evidence of Rt. breast mass.

clear lungs

no ph off

no mediastinal l. nodes.

no PDL no metastasis

no liver, spleen, pancreas, no  
lesions

Rt. kidney shows cyst (55x50mm)

no renal size no hydronephrosis  
no stone.

no bony metastasis



# Breast conservative surgery

Patient's name: [Arabic name]

Age: 32 years

Date of referral: 19 /11/2015

Sex: female

Serial no.: 4806 /15

Contact number: 07705888860

Residence: بغداد/المحمودية

## Histopathological Report

### Specimen site and clinical data :

Right breast upper outer quadrantectomy with axillary clearance (for a patient with previously diagnosed as a mammary carcinoma by a true cut biopsy)

### Gross Appearance :

Two labeled containers:

- 1- The right breast upper outer quadrant and axillary tail with its overlying skin flap in a single piece measured 8x5x3.5 cm in size. Cut-sectioning revealed a 2.5 cm whitish firm-hard stellate mass impinging the surgical margin and invading the skin grossly (from which 5 pieces were taken for histopathological study in 3 cassettes as A).
- 2- The axillary tail: multiple pieces of adipose tissue, measured in aggregate about 4x3x2 cm in size, cut-sectioning revealed 16 small lymph-nodes, the largest one measured 1 cm in size while the smallest one measured 0.3 cm in size (from which multiple sections were taken for histopathological study in 2 cassettes as B).

Microscopical Diagnosis :

- Sections from the right breast mass showed features of a **MODERATELY DIFFERENTIATED INFILTRATIVE DUCTAL CARCINOMA**, of NOS (not otherwise specified type) invading the surrounding tissues, on a background of ductal carcinoma insitu of the comedocarcinoma, solid, and cribriform types.
- The mass was tethered with no frank invasion of the overlying skin.
- The surgical margins were tumor free, but the tumor is associated with lymphatic vessels permeation.
- <sup>2/16</sup> **TWO** out of the 16 examined axillary lymph-nodes were **POSITIVELY** involved by **METASTATIC MAMMARY DUCTAL CARCINOMA**.
- The tumor is stage T2N1Mx equivalent to at least stage IIB in the TNM staging system.

*Sincerely yours.....*

- As all investigations are completed pre operatively
- Patient started on adjuvant chemotherapy
- Waiting for the results of IHC

**Thank you**