

Neoadjuvant Therapy in Endocrine Responsive HER2 Negative Breast Cancer

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- **Why neoadjuvant therapy?**
- **Inoperable or desires breast conservation**
- **If patient desires breast conservation needs MRI**
- **If trying to conserve breast then needs a marker inserted into the tumour**

What about the axilla?

- If nodes positive but you get a complete pathological response then will you still perform axillary clearance?
- If no, SLN biopsy after neoadjuvant treatment.
- Complete pathological response much lower in ER+ patients

What about the axilla?

- **Axillary USS, core any suspicious nodes if positive axillary clearance after neoadjuvant therapy**
- **If negative SLN biopsy prior to commencing neoadjuvant treatment**

SLN Biopsy Prior to Therapy

- **Disadvantages**
- **Two operations**
- **Potentially delays start of chemotherapy**
- **Advantages**
- **No effects of therapy eg. fibrosis**
- **Higher identification rate**
- **Lower false negative rate**



Overcoming Prejudice Against Neoadjuvant Endocrine Therapy

- **Postmenopausal ER+ disease**
 - Endocrine therapy provides two-to-threefold more protection from relapse and death from breast cancer than chemotherapy
- **Low toxicity**
 - Older patients who are not suitable for chemotherapy
 - Comorbid conditions
 - Patient choice

Selection for Neoadjuvant Therapy: Endocrine vs Chemotherapy?

- **Significantly lower pCR rate with neoadjuvant chemotherapy in ER+ tumors than in ER– tumors (5.0% vs 20.6%, $P<0.001$)¹**
- **Patients with ER-rich tumors are optimal candidates for neoadjuvant endocrine therapy²**
- **Increasing evidence that patients with ER-rich tumors may derive minimal or no benefit from neoadjuvant chemotherapy³**

pCR = pathologic complete response.

1. Buzdar et al. *Breast Cancer Res Treat.* 2003;82(suppl 1):S69. Abstract 302.

2. Dixon et al. *Eur J Cancer.* 2002;38:2214.

3. Gianni et al. *J Clin Oncol.* 2005; 23:7265.

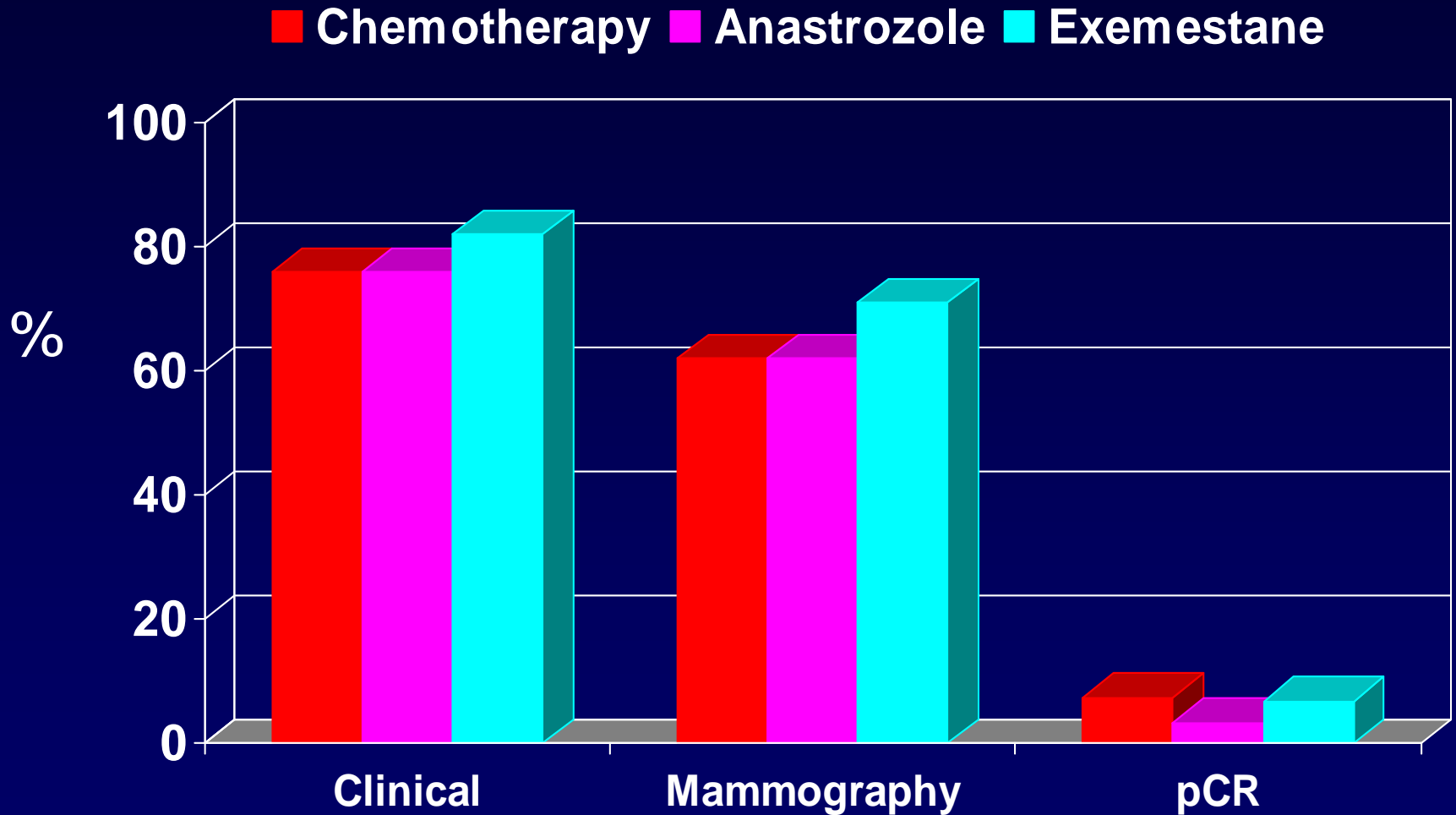
Neoadjuvant Endocrine vs Chemotherapy

- **121 Postmenopausal women**
- **ER+ and/or PgR+ large operable and LABC**
- **Randomised to chemo or hormone therapy**
- **Median ages: 69 y Chemo; 67 y hormone therapy**
- **Chemo: doxorubicin + paclitaxel q3w × 4 (n=62) or
Anastrozole 1 mg or exemestane 25 mg for
3 months (n=59)**

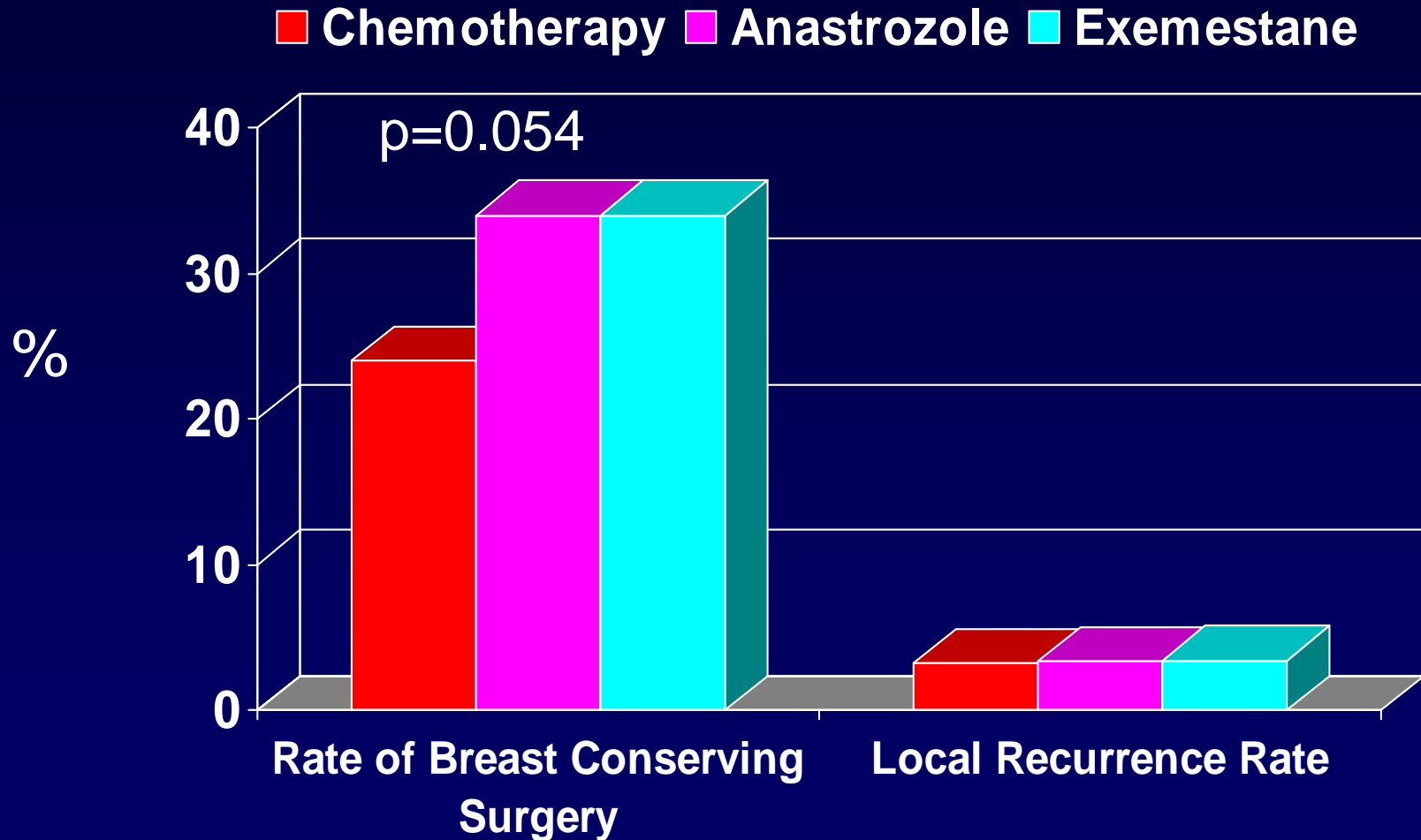
PgR = progesterone receptor; LABC = locally advanced breast cancer.

Semiglazov et al. ASCO, 2004. Abstract 519.

Responses



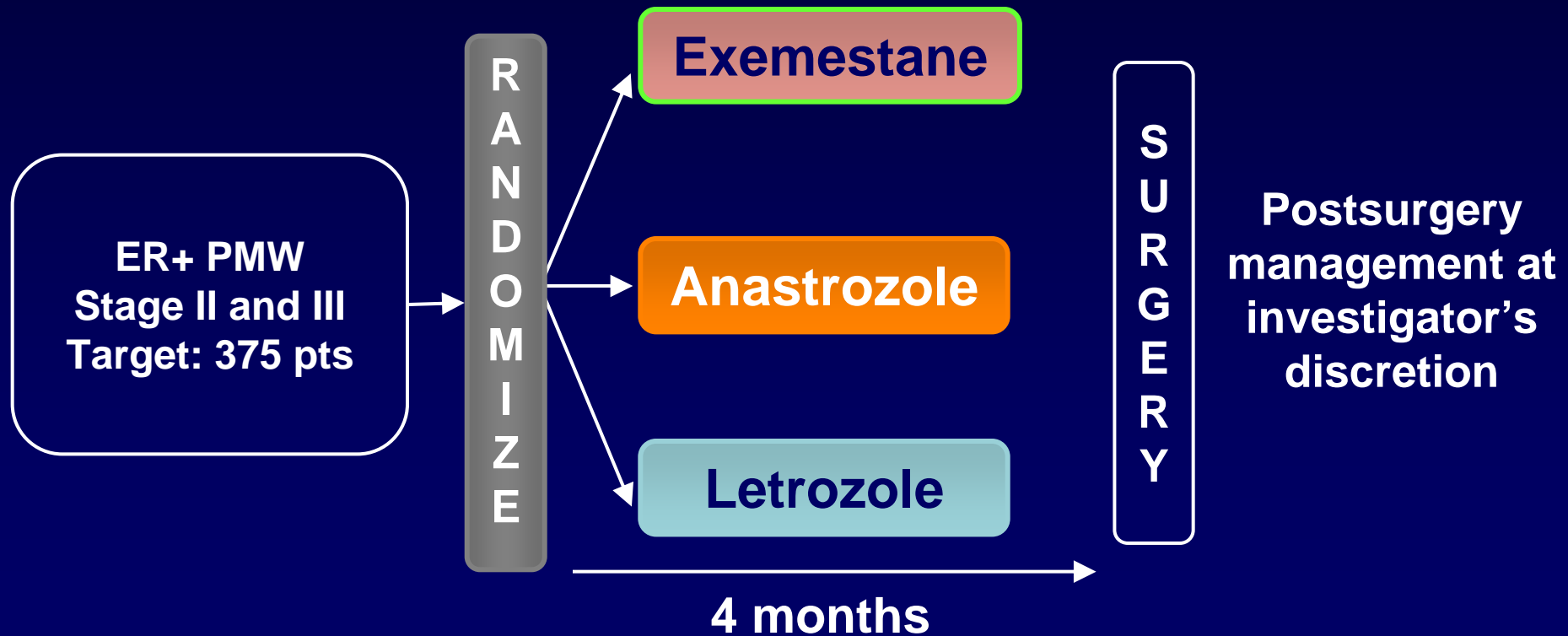
Outcomes



Neoadjuvant Therapy: Patient Selection by ER Status

- Patients with low ER levels are unlikely to respond to neoadjuvant therapy with tamoxifen or oophorectomy
 - Candidates for chemotherapy
- Patients with ER-rich tumors are optimal candidates for neoadjuvant endocrine therapy
 - ≥ 20 fmol/mg protein
 - Histoscore >80 with $>30\%$ ER-positive cells
 - Allred score 6-8

ACOSOG Z1031: Randomized Neoadjuvant AI Protocol



Optimal Duration of Neoadjuvant Letrozole Therapy: Design

- Prospective study to assess whether tumors continue to respond to neoadjuvant letrozole for periods of >3-4 mo
- 142 PMW with large operable or locally advanced, ER+ breast cancer
- After 3 mo treatment, 42 pts had responses but were still unfit for BCS, and treatment was continued
- Clinical tumor volume percent reductions were calculated
 - In first 3 mo, between 3 and 6 mo, and between 6 and 12 mo
 - Allowed assessment of tumor shrinkage over each time period
 - After 12 months 75% of patients underwent breast conservation