

PREOPERATIVE THERAPY IN INVASIVE BREAST CANCER

Reviewing the State of the Science and Exploring New Research Directions

Pre-operative cooperative group trials Considerations for further research

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Disclaimer

Considerations for further research

- What is the problem we are trying to solve?
- What are we doing today?
- Immediate next steps
- The BIG picture

“Personalized Medicine”

Tailoring therapy

Right treatment to the Right person

Goals for Breast Cancer Therapy

- No recurrence of the cancer
- No evidence of having had breast cancer
- No evidence of having had treatment for breast cancer
- No acute toxicity of the therapy
- No late sequelae of the therapy

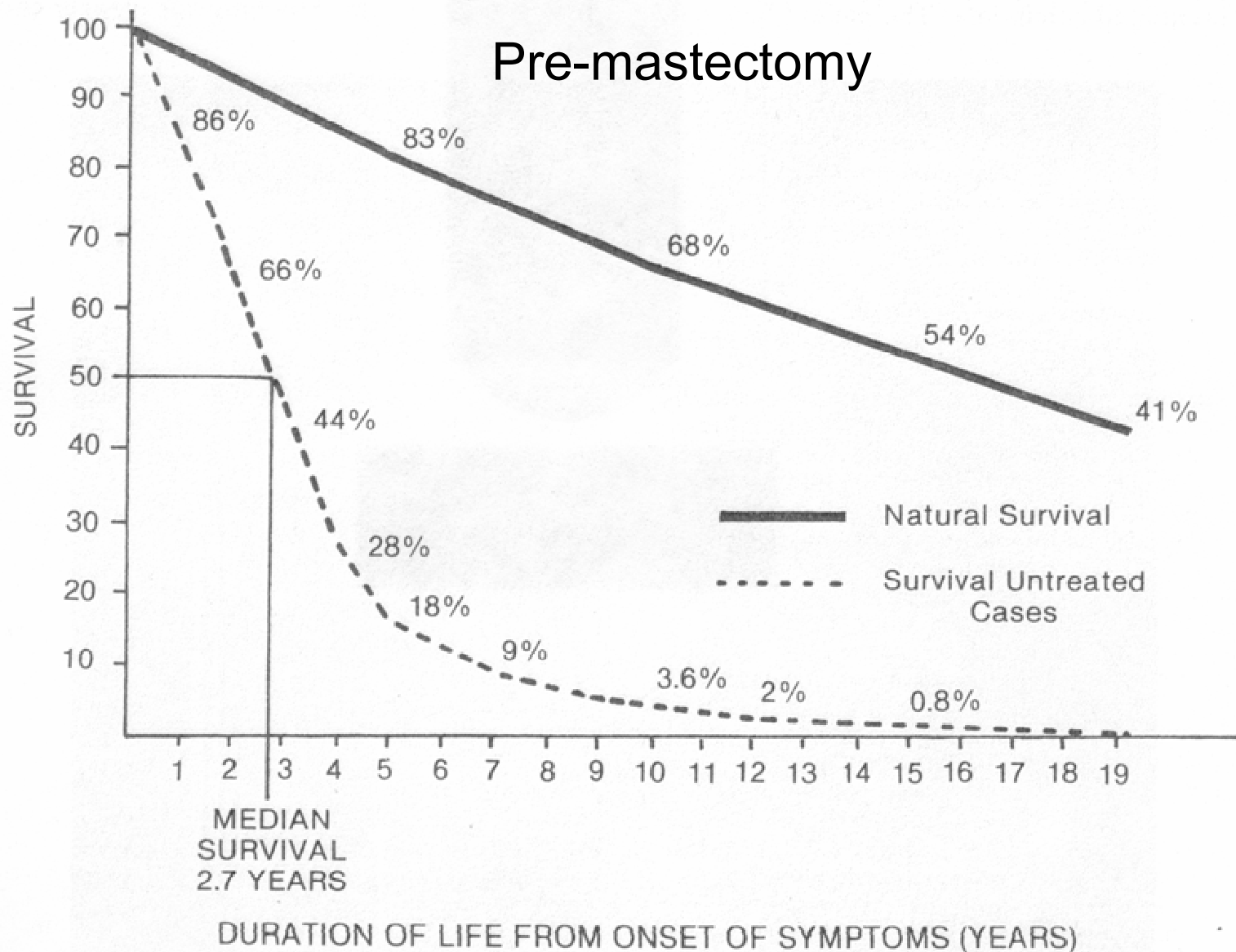


Chart 41-3. Length of survival in 250 patients with untreated breast carcinoma—Middlesex Hospital, 1805 to 1933 (Bloom).ep

Incremental benefit

chemoTx + antiER + targeted

Each incremental step assumed that no pt is cured with the previous step

mastectomy

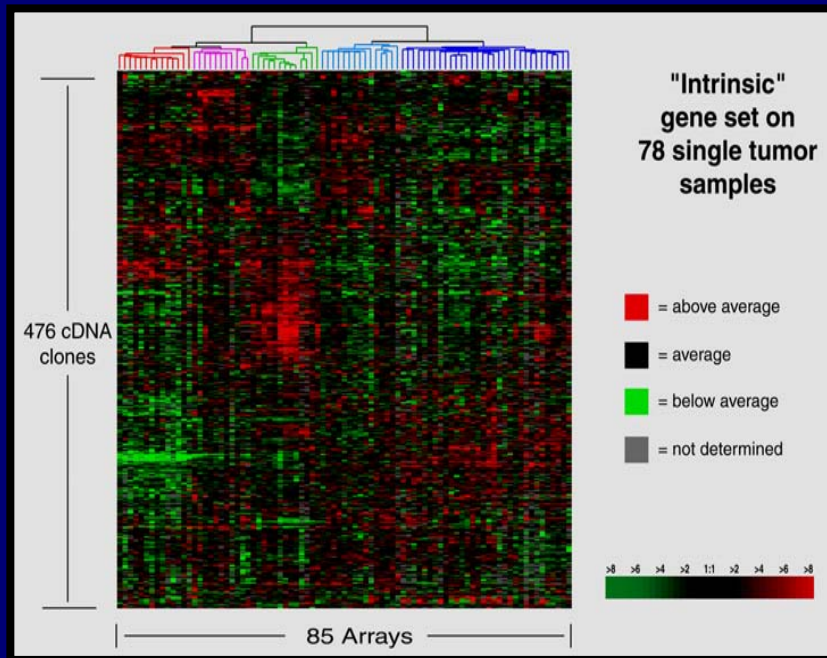
No surgery

- Significant overtreatment
- Necessity to conduct large trials to demonstrate small benefit

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Molecular Profiling



- Address subtype specific questions
- Select therapies for future research
- Discovery of “targets”

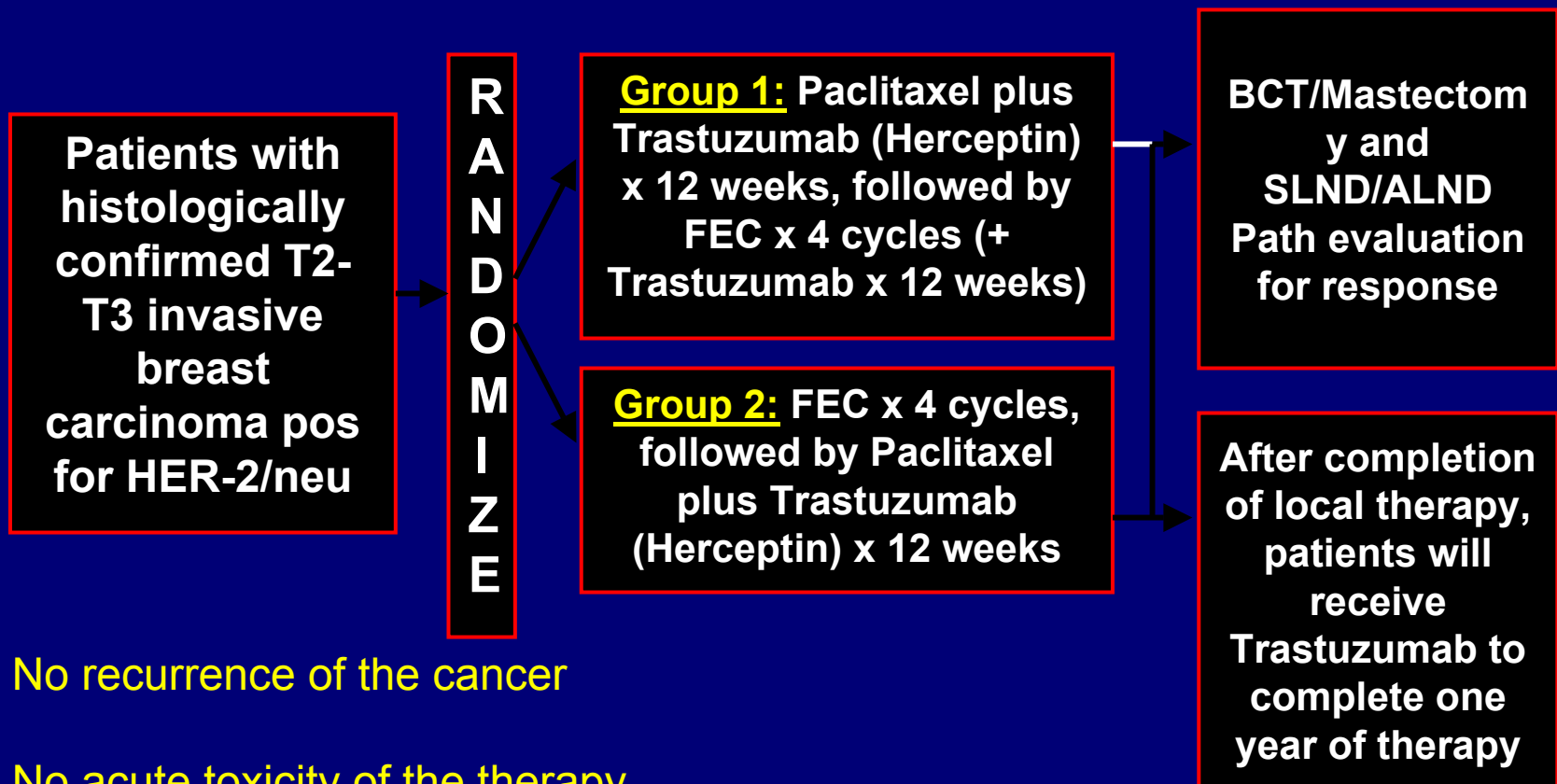
ACOSOG Z1031



No recurrence of the cancer

No acute toxicity of the therapy
No late sequelae of the therapy

ACOSOG Z1041: HER-2 Concurrent chemotherapy and targeted therapy

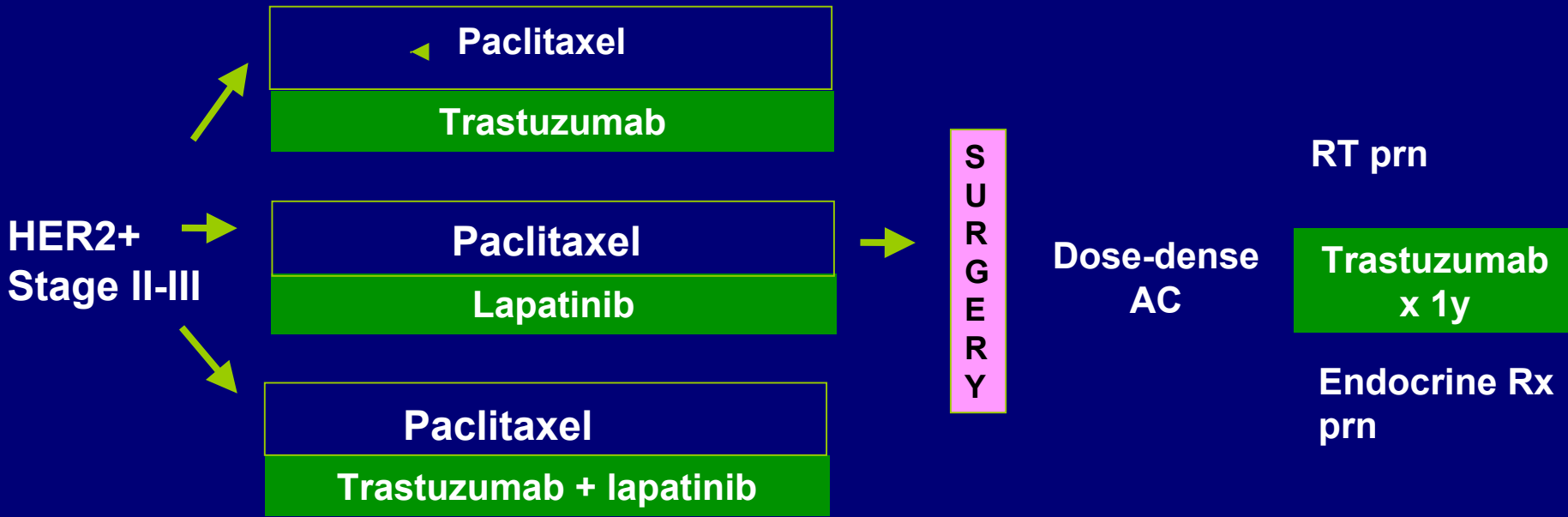


No recurrence of the cancer

No acute toxicity of the therapy

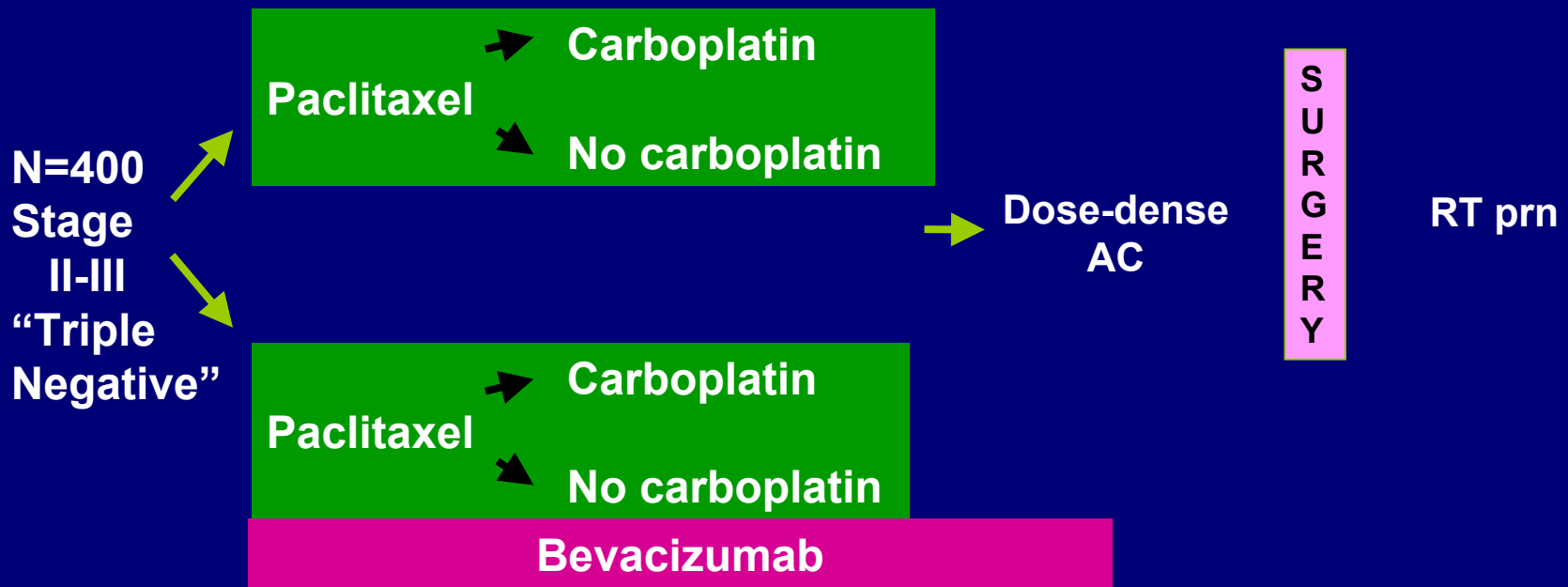
No late sequelae of the therapy

CALGB HER-2 blockade



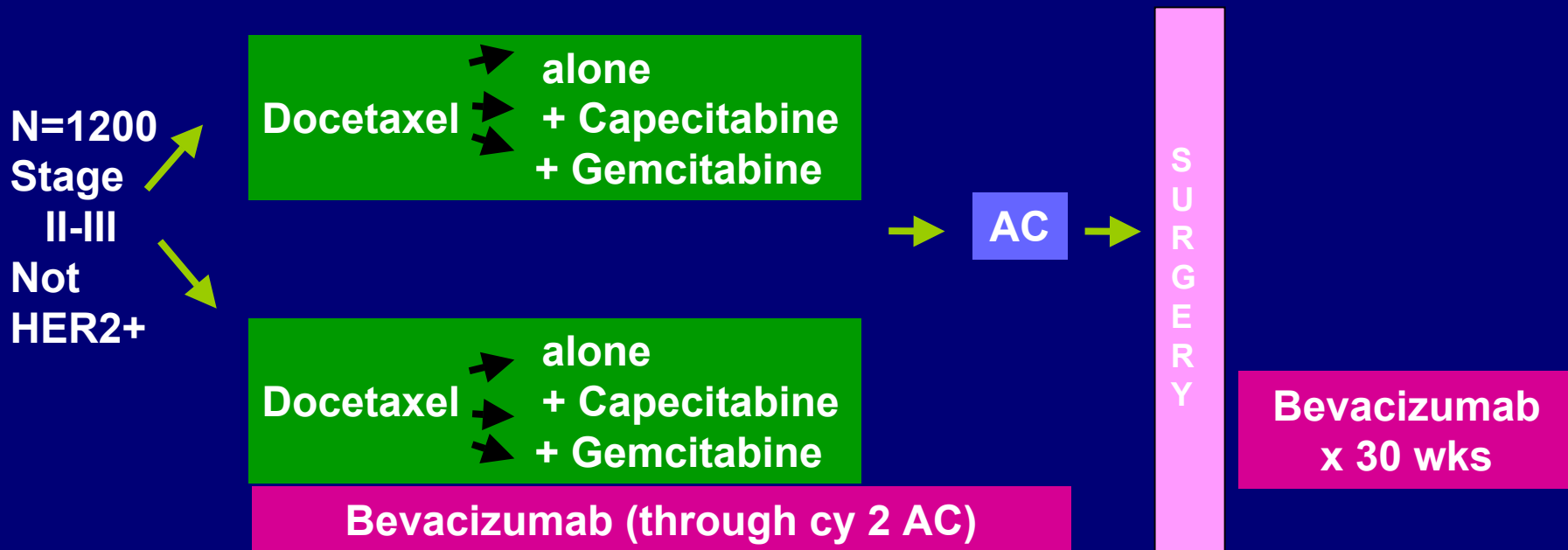
No recurrence of the cancer

TRIPLE NEG- DNA damage



No recurrence of the cancer

Antiangiogenesis: combination of chemotherapy and biologic

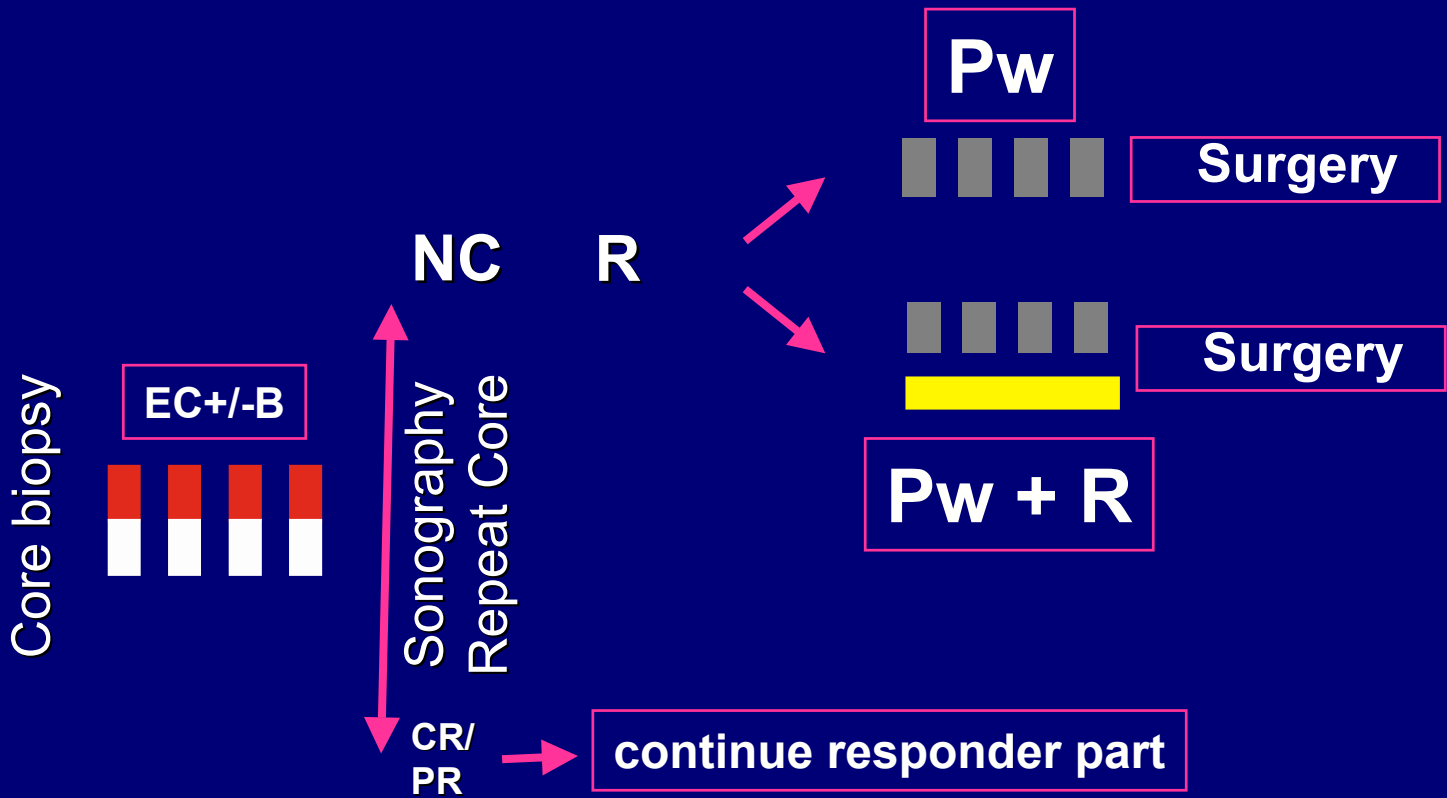


No recurrence of the cancer



Can early response drive therapy?

No recurrence of the cancer



N=540 Her 2 neg. Non-responder

Pw = weekly Paclitaxel
R = Rad 001

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Coordinated Global Efforts



Incorporate Specimen Collection SOPs

- **To promote and ensure proper collection of high-quality research specimen such that each patient diagnosed with breast cancer can have a reliable, interpretable molecular diagnosis.**
- **To provide a known baseline of standardization of specimen collection and handling procedure, to the extent possible, such that more global biomarker analysis across studies is possible.**
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- **To promote specimen collection that would allow for future technologies, particularly in the molecular arena, to be applied to specimens for research.**

Incorporate Specimen Collection SOPs

- Prospective validation of predictive factors in “retrospective” clinical trials

STandardized definitions for **Efficacy End Points** in **NEO**-Adjuvant Breast Cancer Trials (**STEEP**)

- Malignant cells undetectable in breast and lymph nodes
- Invasive tumor undetectable in breast and lymph nodes (DCIS allowed)
- Invasive disease absent in breast
- Total or near total therapeutic effect in the primary tumor and evidence of therapeutic effect in lymph nodes, no metastasis

THE BIG Picture

- How will we get from pCR to changing practice?

Pre- or post- SLNB

- How can we answer this question?

Confirming Surrogates in prospective studies of clinical outcome

- Over-interpretation of early results
 - Will we be able to confirm high response rates in triple negative disease
- Should we “nest” the neoadjuvant studies?
 - “Less” selection bias, concurrent validation possible, more “robust” diagnostics

What if you do not get a pCR?

- Residual risk strategies
 - Problem of more of the same?
 - Systemic therapies?
 - Local therapies?

Proposed Randomized Trial for Post Preoperative Therapy

Standard Neoadjuvant Chemotherapy

Residual Invasive Breast Cancer

Targeted

Chemotherapy

Chemotherapy

Targeted

Inflammatory Breast Cancer

- **How do we study a rare disease**
 - **More basic science-incentives?**
 - **Registries?**
 - **International randomized trials?**

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Partnerships
Academia, Industry, Government,
Advocacy