



Preoperative Therapy: an Overview

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Terminology*

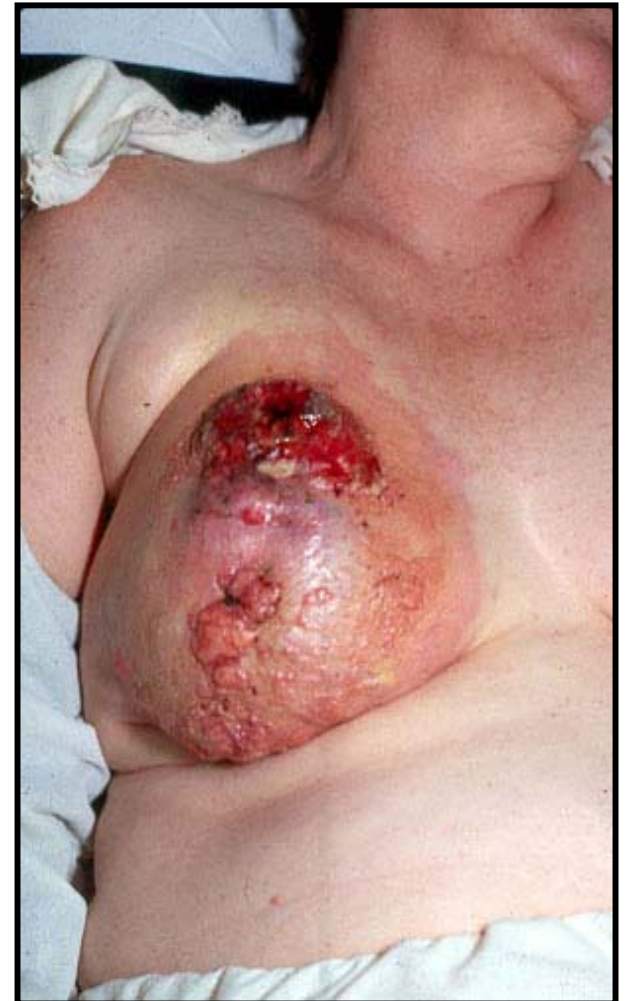
- Adjuvant therapy
- Neo-adjuvant chemotherapy Frei
- Basal chemotherapy Dunphy
- Induction chemotherapy Holland
- Primary chemotherapy DeVita
- Preoperative therapy Anon.

*Wood WC. Neoadjuvant Therapy, in Adjuvant Therapy of Breast Cancer, Henderson IC, Ed. Kluwer Academic Pub, 1992.



Origin of Preoperative Therapy

- To shrink inoperable cancers to allow surgical extirpation
- Endocrine therapy used initially
- Then cytotoxic chemo



Preoperative Rx





Preoperative Rx for Locally Advanced

Agents	N	%Resp	Surv	Author
FAC-CMF	174	87%	26%/10y	Hortobagyi
AV-CMF	277		23%/10y	Valagussa
AC-MLF	75	91%	73%/3y	Ragaz
VTMFAP	98	91%	77%/3y	Jacquillat
CAFV	170	48%		Namer

Wood WC, Neoadjuvant chemotherapy in Adjuvant Therapy of Breast Ca, Henderson IC Ed., Kluwer Academic, 1992



Preoperative Therapy for Locally Advanced and Inflammatory Breast Cancer

- Never prospectively compared to other methods
- 25% and more survivals at 10 years far superior to historical experience in this population
- Response directly related to survival in these series
- Outcome of response vs. selecting biologically more favorable tumors for both response and survival?



Original Rationale for Preoperative Therapy In Stage II BC

- Bonadonna introduced preoperative therapy for Stage II breast cancer to allow BCT
- Second putative advantage was to hasten treatment of micro-metastases, eliminating them prior to the growth spurt after removal of the primary, described in experimental tumor systems



Results of Surgery and Cyclophosphamide on Rat Shay Chloroleukemia

Treatment	Remaining Free of Disease
Surgery only	10%
Cyclophosphamide only	30%
CycloP Post-op days 0 & 1	50%
CycloP Pre-op days -8 & -7	90%

Brock N. Strahlentherapie 1959;41:347-354.



Downstaging Operable Breast Cancer

National Tumor Institute of Milan

Gianni Bonadonna

94 with resectable tumors >3cm diameter

Treated with CMF or CAF preoperatively

Converted 87% to BCT



Bonadonna's Observation

- Response to preoperative chemotherapy predicted prognosis [also Jacquillat, Namer, and Hortobagyi]
- Cause, or biologic staging?
- Only randomized trials would answer



NSABP Protocol B-18

Operable Breast Cancer

Stratification
Age
Clinical Tumor Size
Clinical Nodal Status

Operation

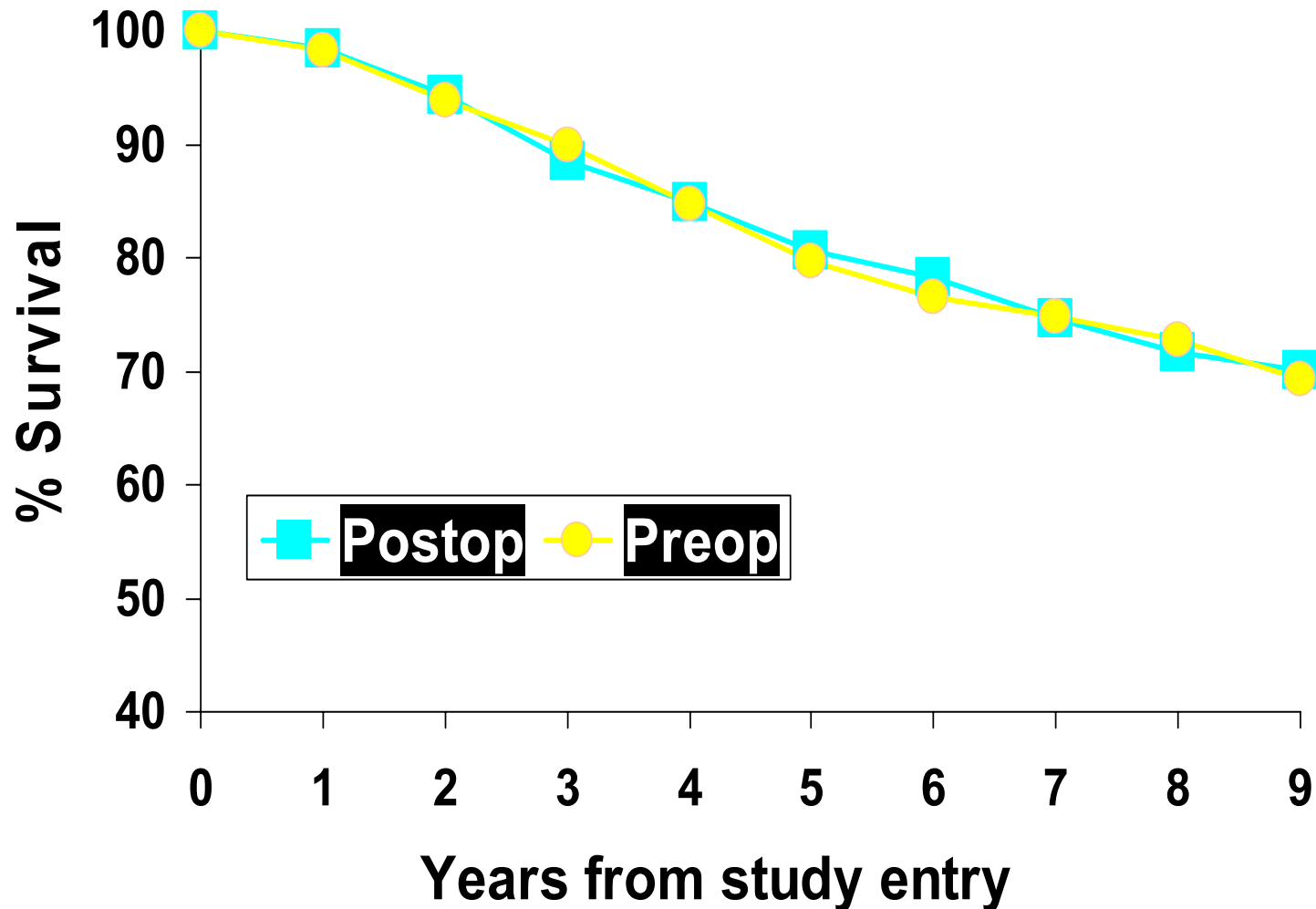
AC x 4
+ TAM if \geq 50 yrs

AC x 4
+ TAM if \geq 50 yrs

Operation



NSABP B-18: Overall Survival Nine Year Update



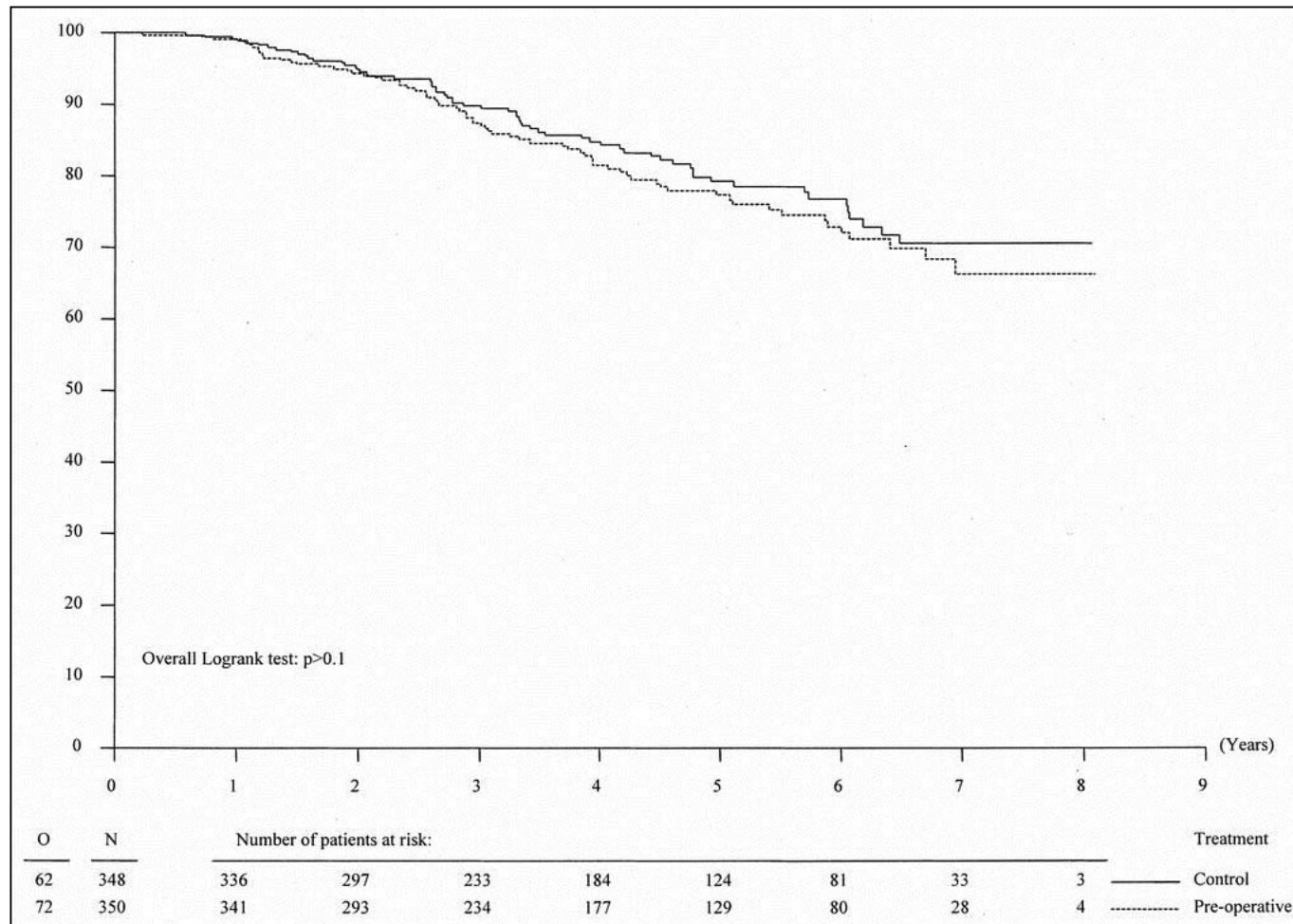


Lessons of B-18

- No survival advantage from preoperative timing of chemotherapy
- No survival disadvantage from leaving tumor in place with preoperative chemotherapy



EORTC 10902



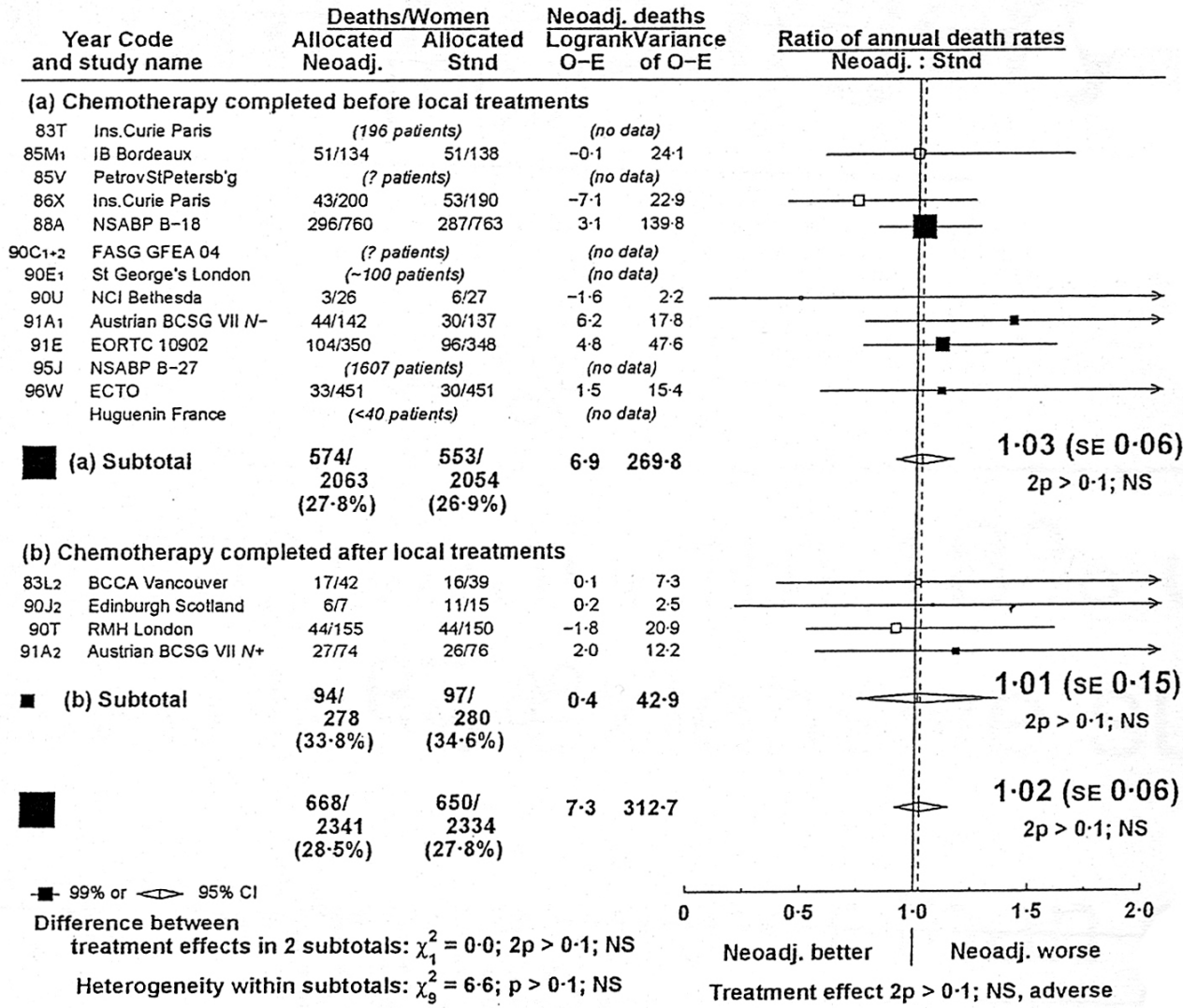


Lessons from EBCTCG Overview*

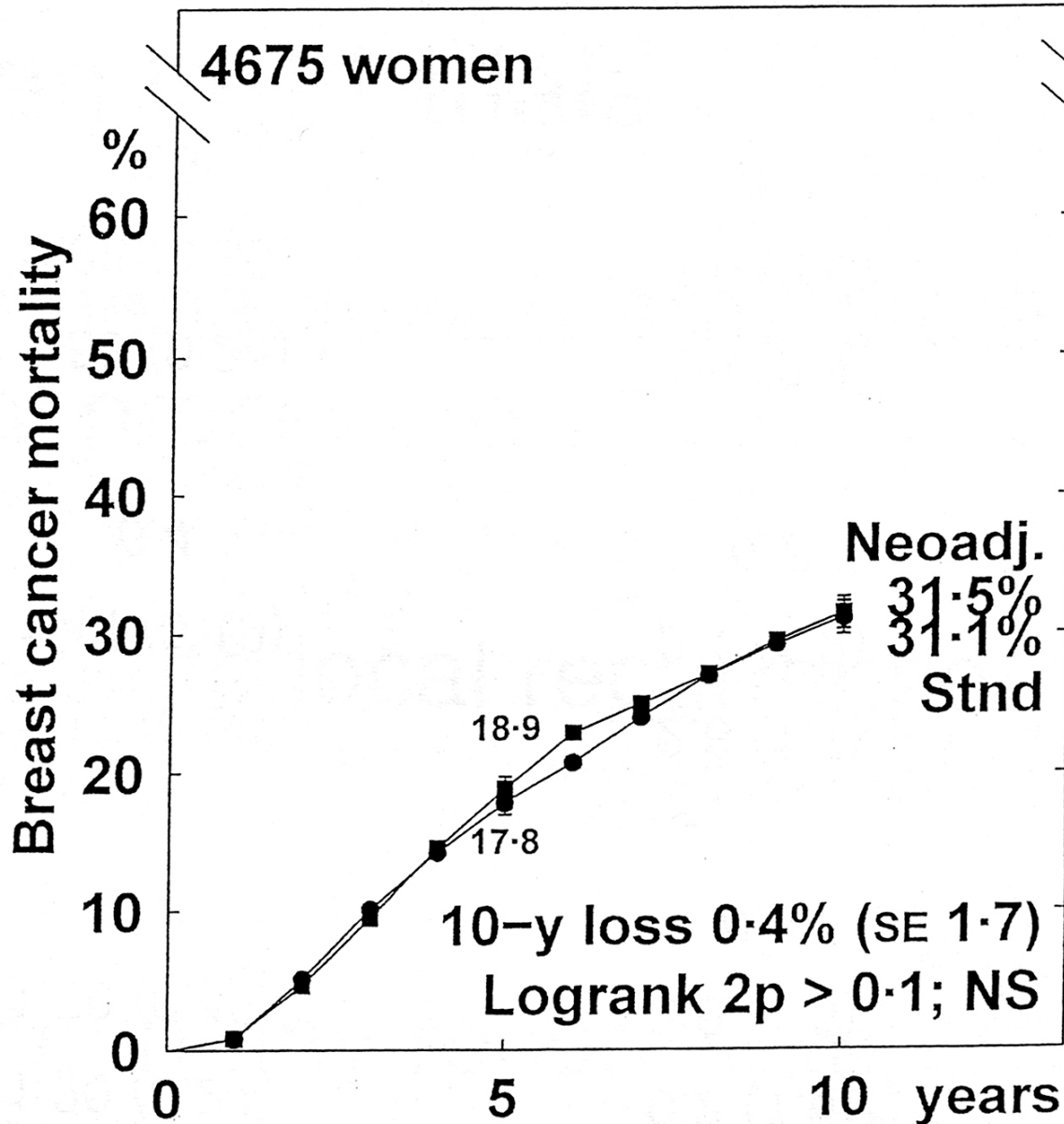
- 11 Randomized trials 1983-91, 4675 women
- Preoperative arm 18% fewer mastectomies
 - Preoperative arm 3% more in-breast recurrences, yr 5
 - No significant difference in any recurrence, breast cancer mortality, or death by year 10

*Oxford, September 7, 2006, NOT FINAL DATA, TENTATIVE RESULTS

Neoadjuvant chemotherapy ANY DEATH



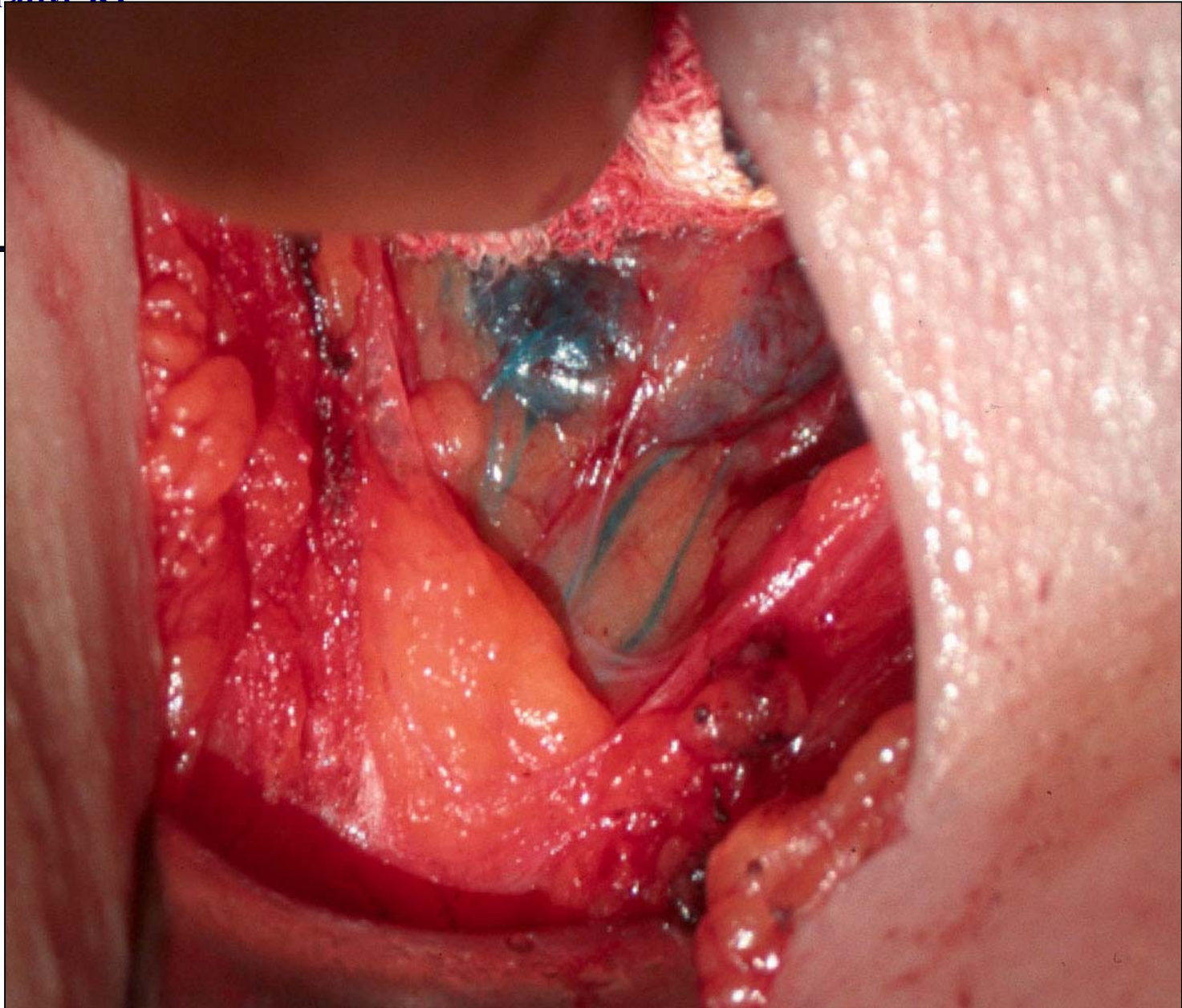
Neoadjuvant chemotherapy BREAST CANCER MORTALITY





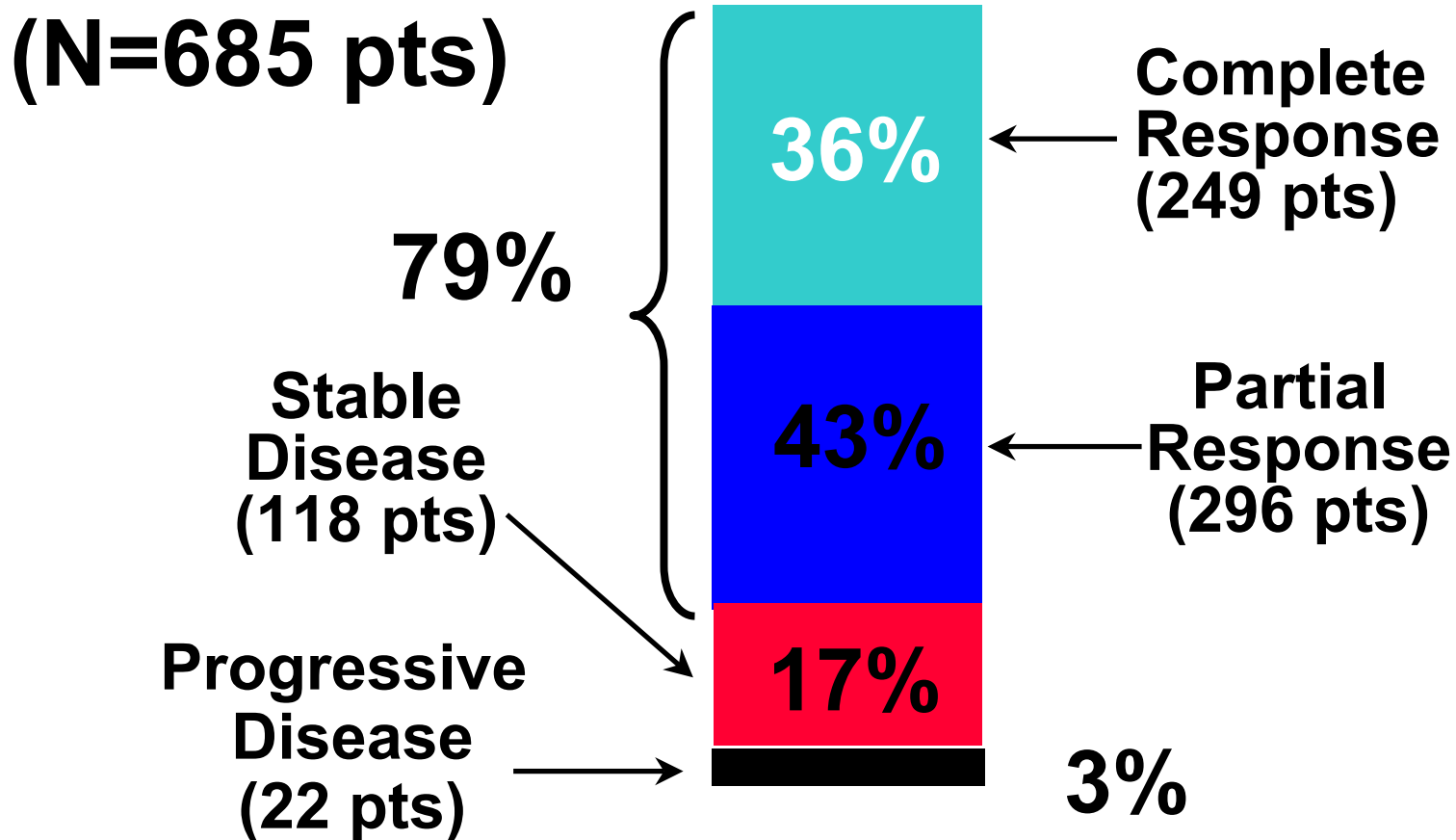
Goals for Breast Cancer Therapy

- 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





Clinical Breast Tumor Response to Preop Chemo





Preoperative Rx





Timing of Systemic Therapy

- Surgery first is an accident of medical history
- Preoperative therapy allows:

Reduction of tumor volume- cosmesis

Identification of tumors resistant to Rx- for trials of other therapies

Trials of biological and other agents- to hasten development of these

Favors tailored therapy- new generation of trials



Who To Get Preoperative Rx?

Anyone who will require the systemic therapy in question with certainty...



No more “One size fits all...”

Finis