Ideal neo-adjuvant Chemotherapy in breast ca

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When is neo-adjuvant Chemo required?

- Locally advanced breast ca:
  - Breast conservative surgery is intended but not possible
  - Mastectomy is intended but not possible
- Early information on tumor response
- Reduce mortality from breast ca

Useful features

- Age
- ER/PR/HER 2 status
- Tumour grade 1 – 3
- Ki 67

Which Chemo?

- Anthracycline based chemo:
  - AC
  - FAC/FEC etc
- Taxane based chemo:
  - AC – T
- Herceptin
- Endocrine therapy

ANTHRACYCLINE BASED CHEMO

- Backbone of breast ca treatment for many years
- Which pts: - younger pts
  - normal heart(EF% >/=55)
  - luminal B
  - triple negative
  - HER2 +
  - co-morbidities

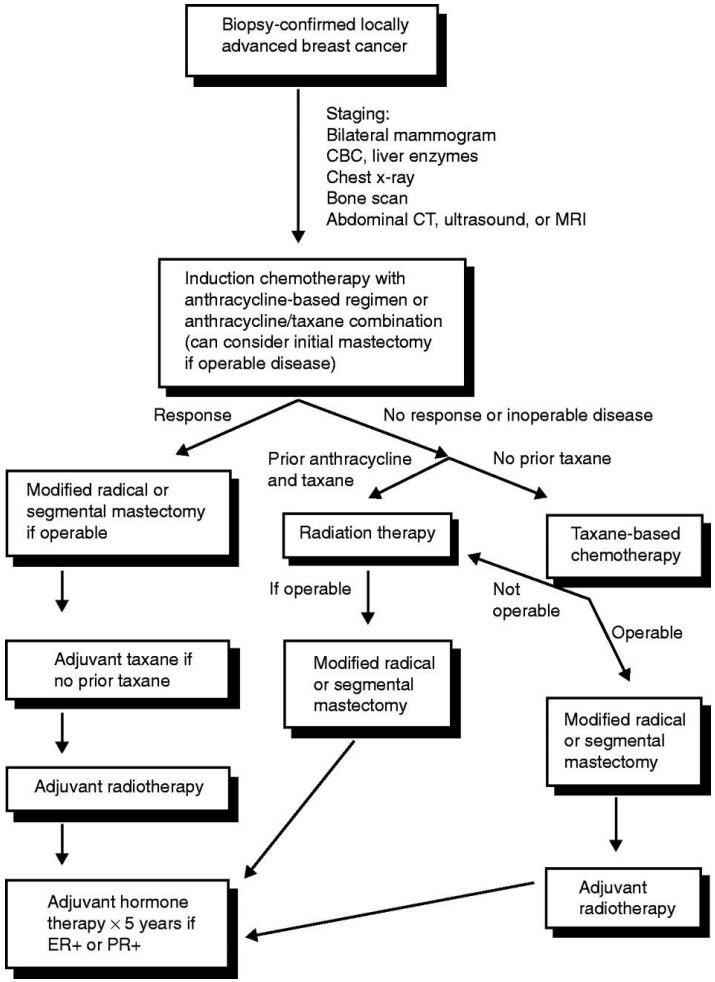
Combination

- FAC – MD Anderson reported 10 yr results in 1989
  - 1% cardiotoxicity
  - 62% survival- stg 2
  - 40% survival – stg 3
  - this was confirmed as good adjuvant treatment
  - It is also used in neoadjuvant settings

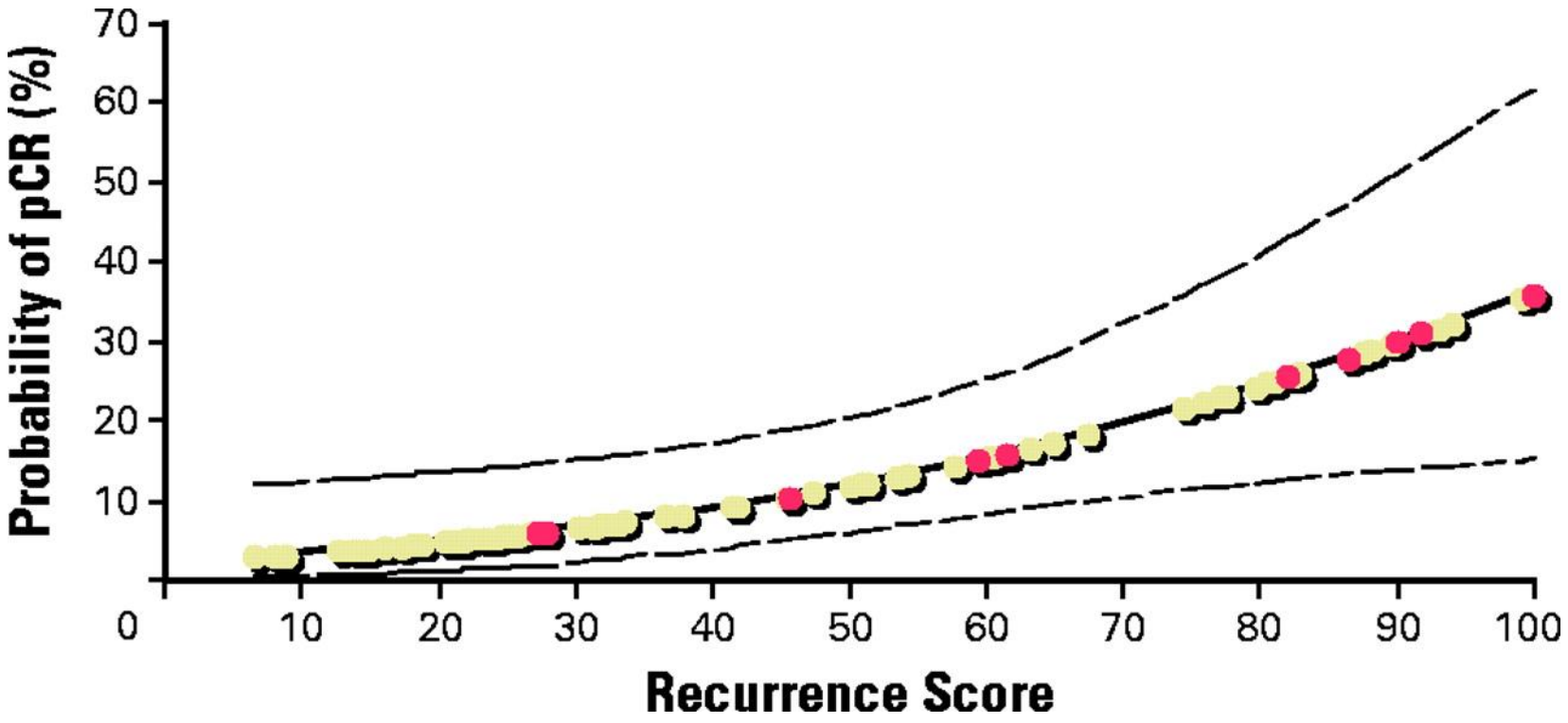
NEOADJUVANT FAC/FEC

- First used in 1970s in a multimodality treatment
- Primary aim was to down-size T3/4 tumor, making it operable
- Recently, it is used for both cosmetic and survival benefit
- Any chemotherapy that is used in adjuvant setting can be used in Neoadjuvant setting

Treatment algorithm for locally advanced breast cancer.



Probablity of pathologic complete response (pCR) as a function of Recurrence Score in the Instituto Nazionale Tumori–Milan (Italy) cohort.



Gianni L et al. JCO 2005;23:7265-7277

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NSABP B-18

- Effects of Preoperative Chemotherapy on the Outcome of Women With Operable Breast Cancer

- AC: Fisher at el(NSABP B-18), in 1998 showed same benefit when AC was used as either neoadjuvant or adjuvant

 - Primary operable breast ca

 - Conclusion: pre-operative AC is as effective as post-operative AC

- More lumpectomies are done
- Response correlates with outcomes

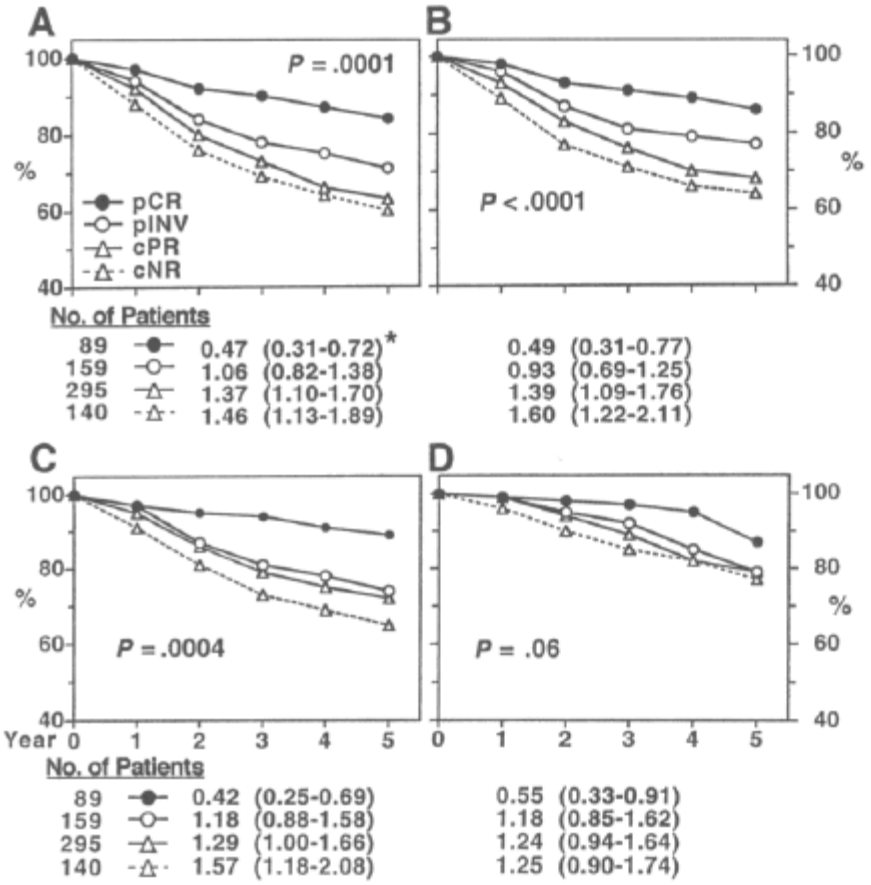

Fig 5. Comparison of pathologic and clinical breast tumor response in patients who received preoperative AC with regard to (A) DFS, (B) RFS, (C) DDFS, and (D) survival rates. *Relative risk (95% CI).

Table 7. Association Between Breast Tumor Response and Pathologic Nodal Status After Preoperative Therapy

Breast Tumor Response	No. of Patients	Pathologic Nodal Status, %					
		Negative	Positive	1-3	4-9	≥ 10	Unknown
pCR	89	87	13	8	6	0	0
pINV	159	62	37	25	9	3	1
cPR	295	56	44	27	14	3	< 1
cNR	140	47	52	29	15	9	< 1

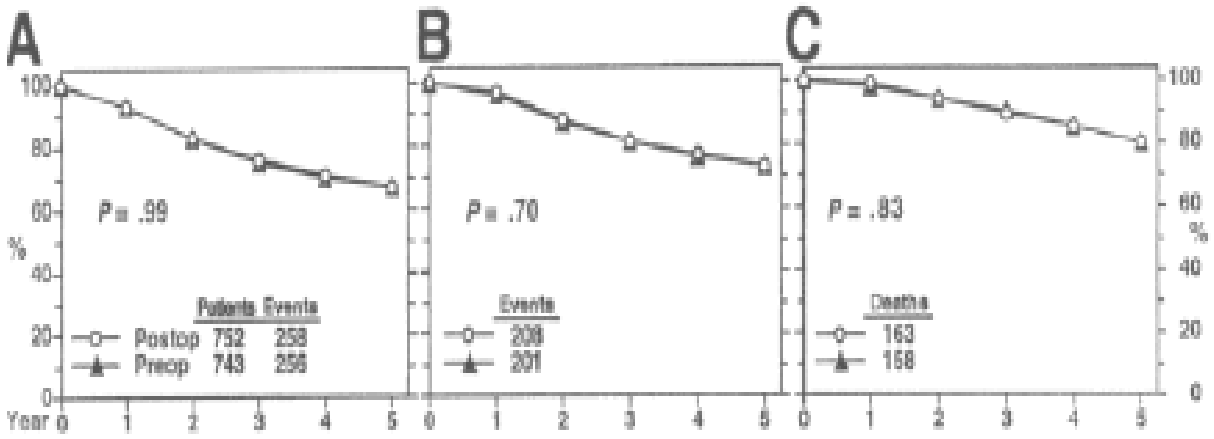

Fig 2. Comparison of outcome between patients who received postoperative versus preoperative AC therapy. (A) DFS; (B) DDFS; (C) survival.

Table 2. First Reported Site of Treatment Failure

Event	Postoperative, % (n = 752)	Preoperative, % (n = 743)	Total, % (n = 1,495)
IBTR*	5.8	7.9	6.9
Other local	2.4	2.7	2.5
Regional	3.2	3.0	3.1
Distant	16.8	16.2	16.5
Second cancers†	2.3	2.3	2.3
Contralateral breast cancer	2.3	2.6	2.4
Dead, NED	2.5	1.2	1.9
Inoperable‡	1.5	1.2	1.3
Total first events	34.3	34.5	34.4
Alive, event free	65.7	65.5	65.6

Abbreviation: NED, no evidence of disease.

*Ipsilateral breast tumor recurrence after lumpectomy: percentage based on 450 patients in the postoperative and 504 in the preoperative lumpectomy-treated groups.

†Except contralateral breast cancer.

‡Clinically inoperable, gross residual disease.

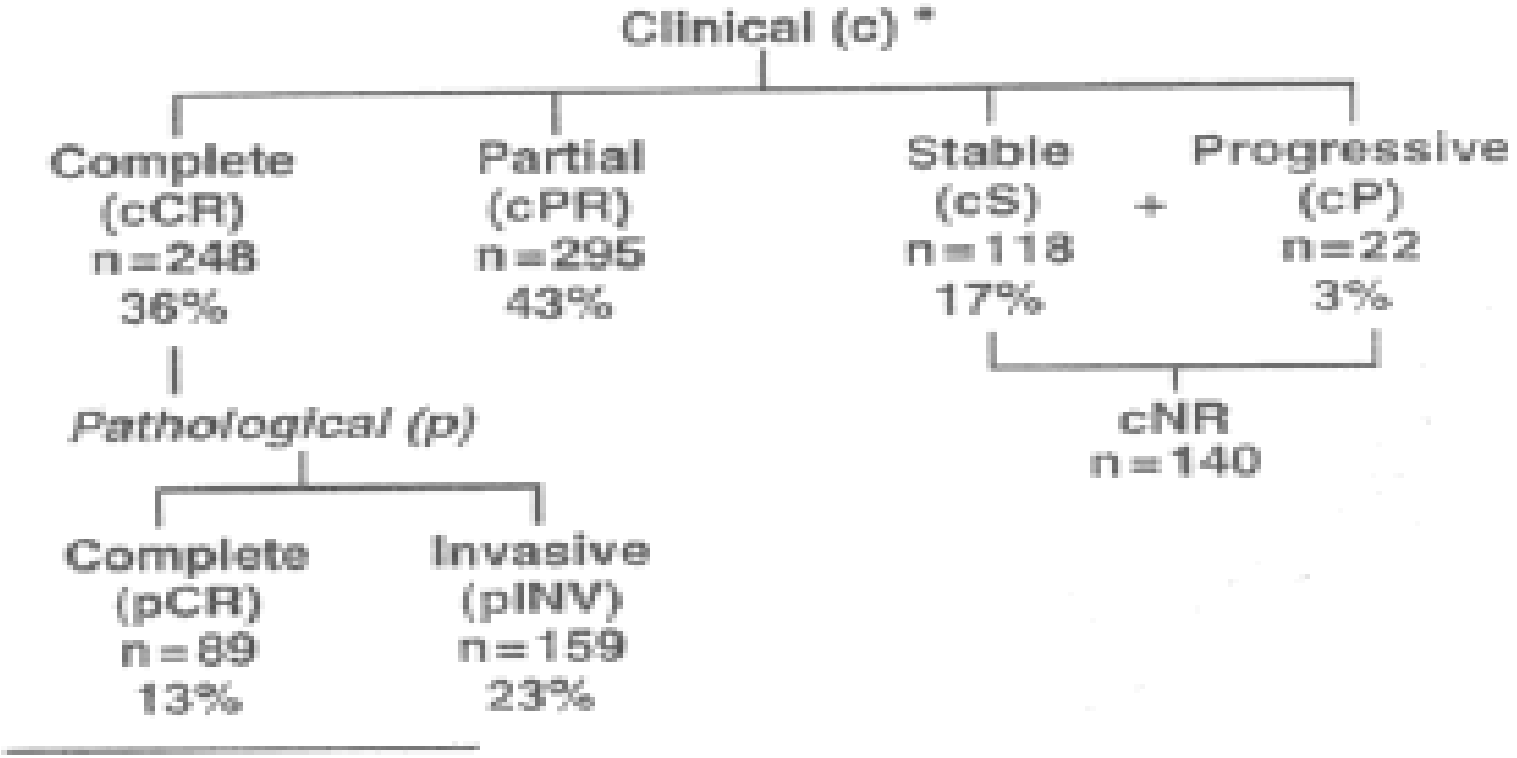

Fig 1. Magnitude of the clinical and pathologic response of primary breast tumors to preoperative chemotherapy. * 683 patients.

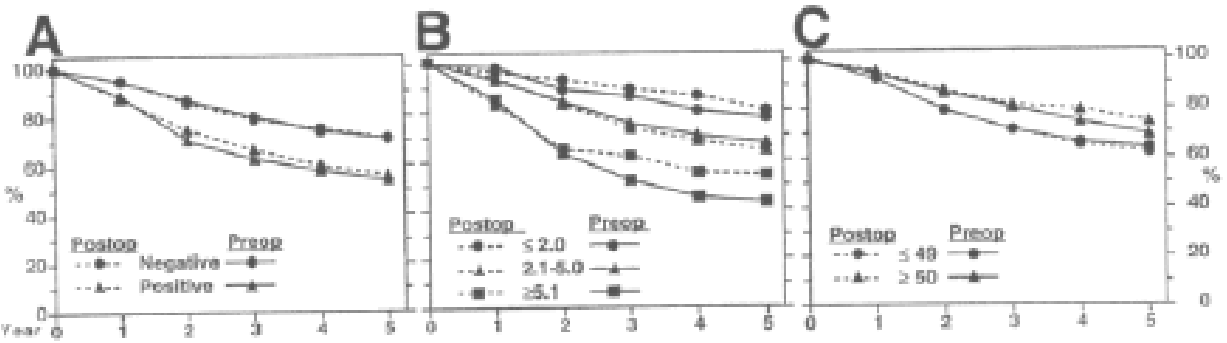

Fig 3. Effect of (A) clinical nodal status, (B) clinical tumor size (cm), and (C) age (years) on DFS rates of patients who received either postoperative or preoperative AC therapy.

New Generation

- AC –T: Sparano at el (ECOG), in 2008 published results showing better outcome of wkly paclitaxel compared to taxotere in adjuvant settings
- Other studies have shown equivalent outcomes
- Currently, any pt who is a high risk of relapse is given AC – T(P/T) in Adjuvant/neoadjuvant setting.

Non Anthracycline based

- CMF: Anthracycline based chemo have been shown to be better than CMF
  - Should be used in Pts with contra-indications for Anthracyclines

- TC: Doxetaxel/Carboplatin
  - TNBC
  - HER2 + in Combination with Trastuzumab
  - ER/PR neg
  - BRCA-1?

Byrski at el in 2010 reported on BRCA1 PTS

Table 2.
Treatment and Response to Different Chemotherapy Regimens

Regimen	No. of Patients Treated	No. of pCRs	% pCRs
CMF	14	1	7
AC	23	5	22
FAC	28	6	21
AT	25	2	8
Cisplatin	12	10	83

- George ML at el, showed in a small study btwn 1991 and 1995 that CMF used as neoadjuvant in large operable breast ca makes lumpectomy possible

- 38 pts elligible
- 22 pts agreed to neoadjuvant chemo
- 15(68%) pts avoided mastectomy
- 3(14%) CR, 13(60%) PR
- 42% Refused neoadjuvant and received mastectomy +/- RT/Adj chemo
- 3 yrs follow up – no differences in OS, distant and local recurrences

TC combination

- Chang at el evaluated:

 - pCR/cCR/ after neoadj TC

 - Locally advanced breast ca

 - 3 subtypes: TNBC

ER/PR +ve, HER 2 neg

HER2 +ve, ER/PR neg

- 74 pts
- 11 TNBC, 33 ER/PR +ve HER 2neg, 30 HER 2 +ve
- 4 cycles of TC preop and 4 cycles postop
- Herceptin given to HER2 +ve preop and post op

	TNBC	ER/PR +ve	HER2 +ve	
cCR	45,4%	40,6%	50%	
pCR	54,6%	19,4%	24,1%	

- No significant differences in OS and RFS
- TNBC and HER2 +ve pts had better pCR on TC and TC + trastuzumab(herceptin)

- Trastuzumab(herceptin):
  - HER 2+ pts
  - Combined with AC – TH, TCH
  - Cardiac monitoring mandatory
  - Avoid in pts with EF% < 55 or in pts with decrease of EF by >10 – 15%
  - Duration – 1 yr

- Endocrine therapy:
  - Pts with ER/PR +ve breast ca
  - Aromatase inhibotors are recommended in postmenopausal pts
  - Tamoxifen in premenopausal pts
  - HER 2 neg

Summary

- All pts with locally advanced breast ca can benefit from neoadjuvant chemo
- Stage < II has not proven to benefit from noeadjuvant chemo
- Herceptin and endocrine therapy should be used in HER 2+ve and ER/PR +ve pts respectively
- Neoadjuvant chemotherapy is the same as adjuvant chemo.

- Neoadjuvant chemo: part of it can be given pre-op and the other part post-op
- pCR correlate with DFS and OS

THANK YOU

References

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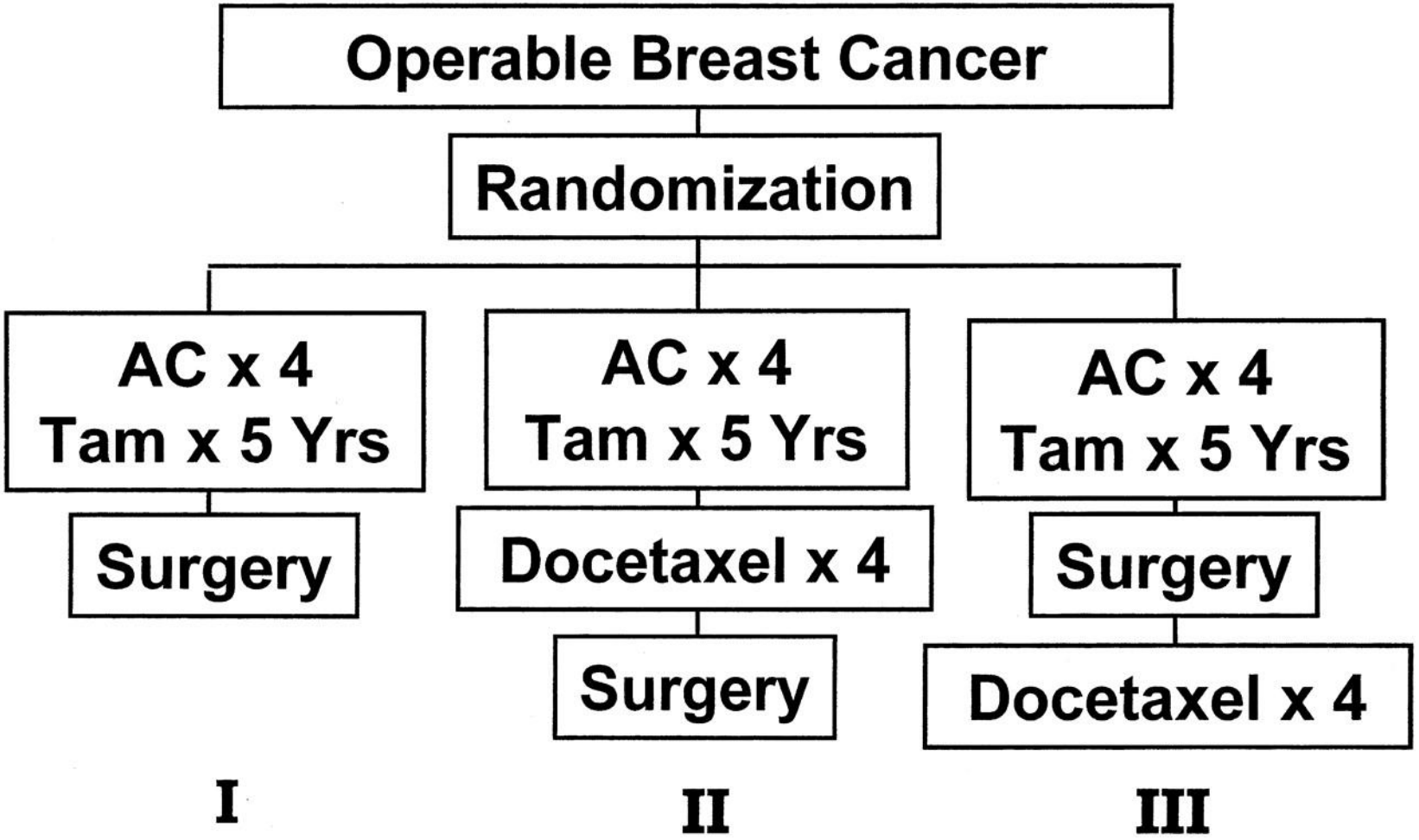
Schema for National Surgical Adjuvant Breast and Bowel Protocol B-27.



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