Neoadjuvant Therapy for Breast Cancer

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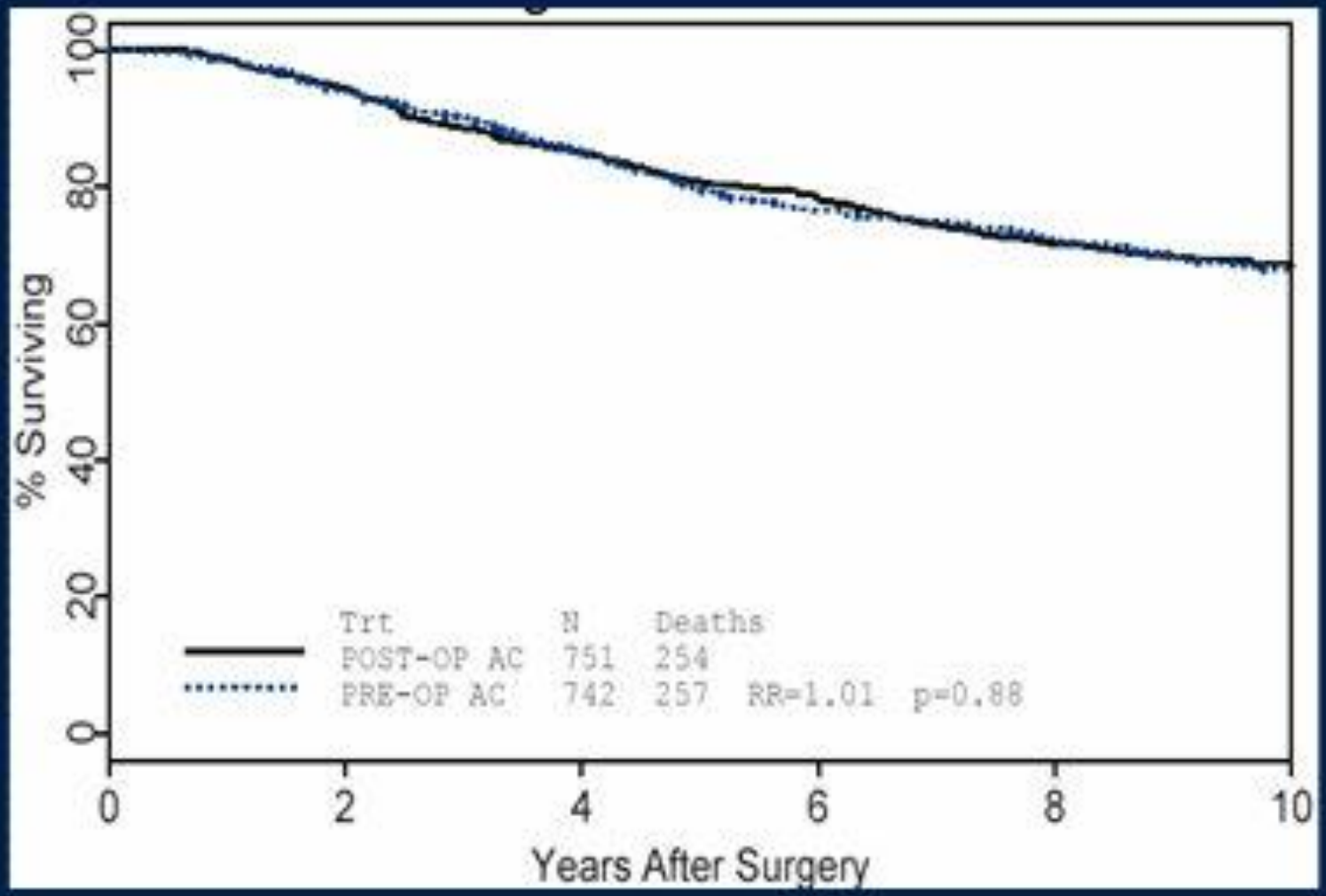
Neoadjuvant Therapy in Clinical Practice

- Prolong Survival (DFS and OS)
- Decrease invasiveness of surgical therapy
  - Breast: Change to breast conservation
  - Axilla: Omission of Axillary dissection?
  - Improved cosmesis?
- Gain prognostic information
- Allow for adjustment of treatment for non-responders ?

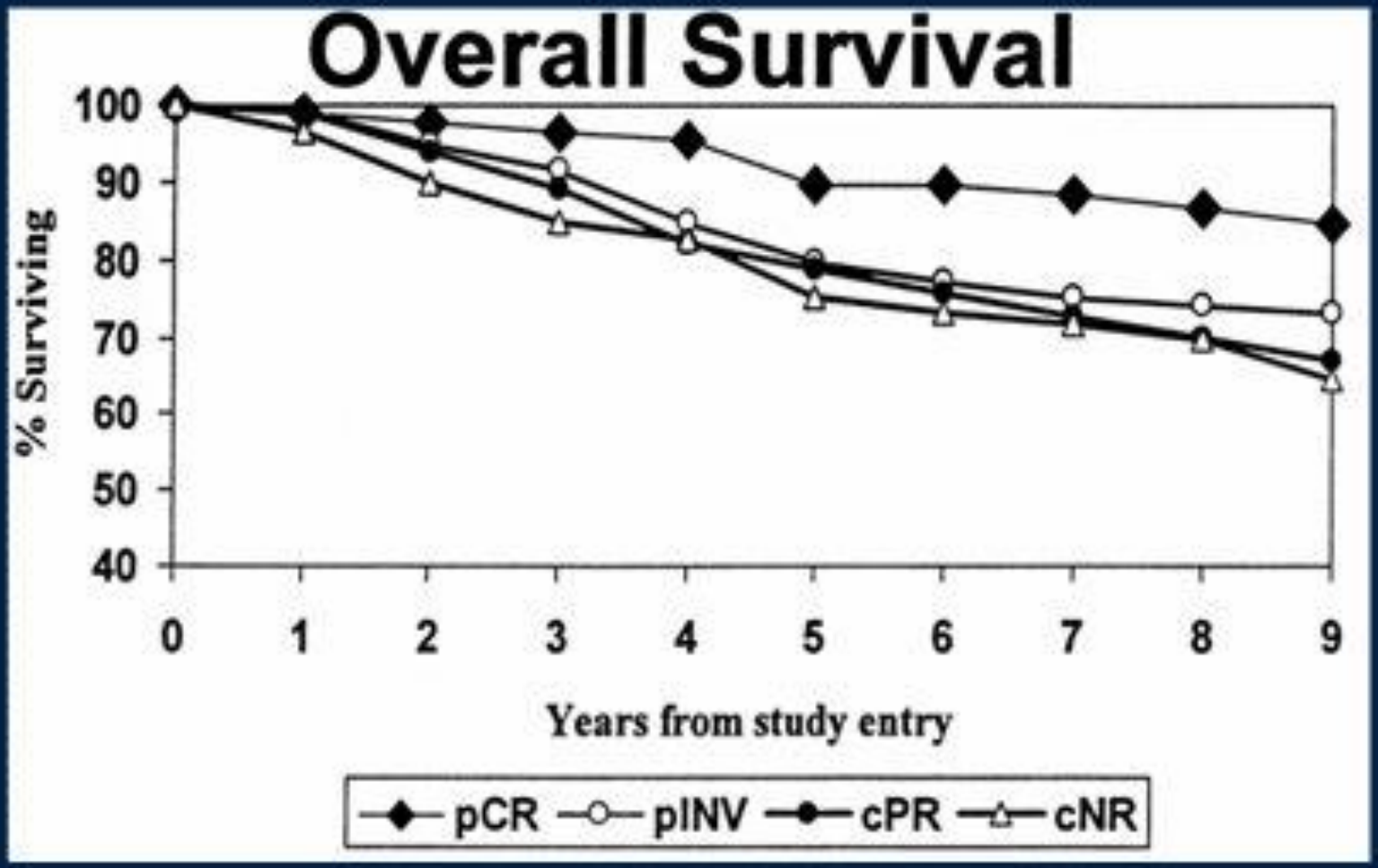
Neoadjuvant Therapy in Research

- Identification of molecular predictors of response
- Identification of pharmacodynamic markers
- Examination of drug effects on targets by serial biopsy
- Rapid identification and comparison of new systemic treatments

B-18: Overall Survival



B-18: Response and Prognosis



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Neoadjuvant Therapy - Indications

- **BHGI guidelines for resource restricted countries**
  - **Neoadjuvant therapy for LABC (T3 & 4, any T and N2/3)**
  - **Anthracyclin containing regimens mainstay**
  - **Neoadjuvant hormonal therapy for elderly acceptable** (El Saghir at al, Cancer 2008;113(8 suppl):2315
- **Contraindications:**
  - **Clinical: T1N0**
  - **Pathology:**
    - **Pure classic lobular ca**
    - **Tubular ca**
    - **Mucinous ca**
    - **Inf. papillary ca**
  - **Molecular Profiling: Low Risk Tumors**
  - **Other?**

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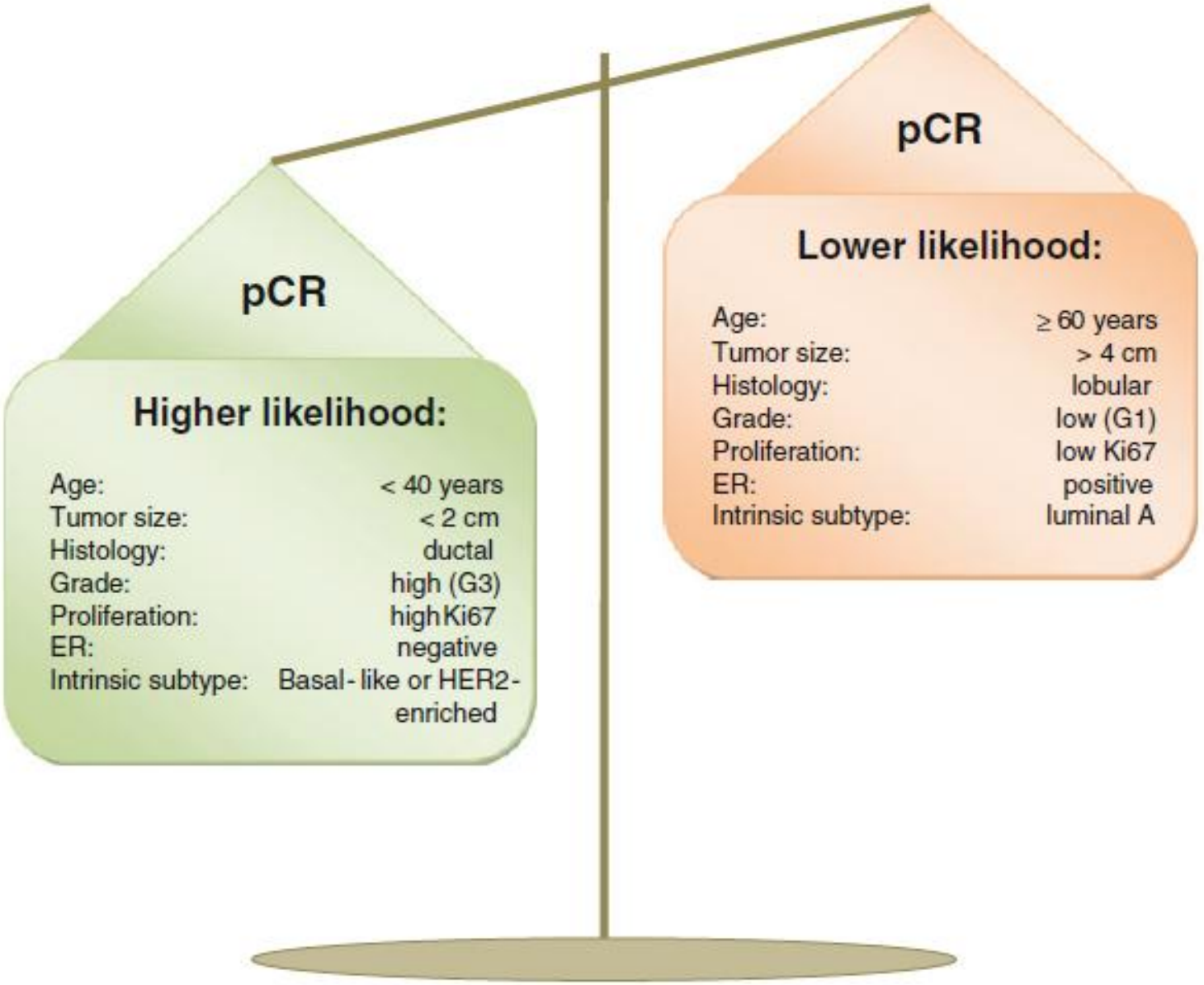


Kaufmann M et al, Ann Surg Oncol 2012, 19: 1508

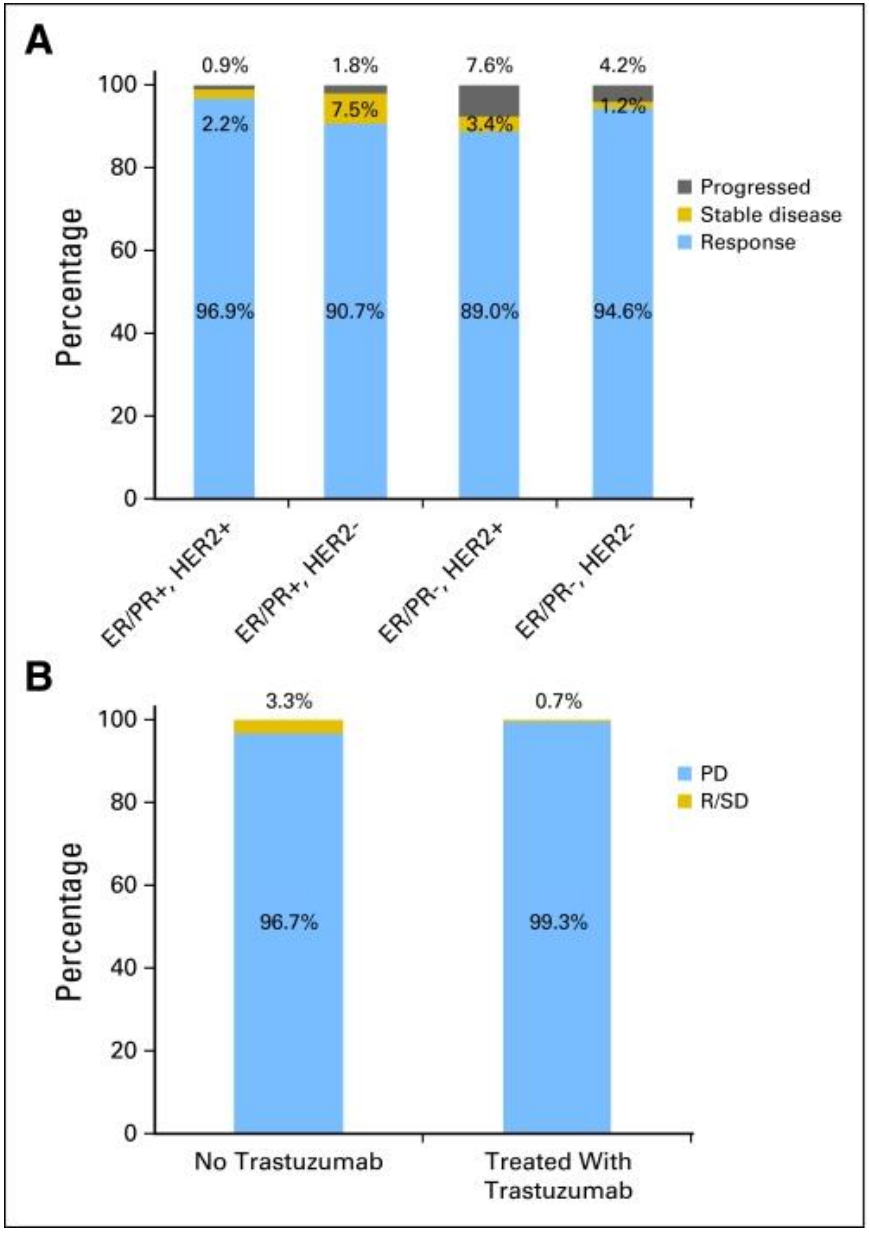
Progressive Disease

- African patients
- Larger tumors
- Higher grade
- HR –
- High Ki 67

Claudle AS et al, J Clin Oncol. 2010 April 10; 28(11): 1821

Response as per tumor characteristics

- 1928 patients
- 91% response
- Predictors of progression:
  - African Americans
  - Disease load:
    - T stage
    - Nodal load
  - Tumor IHC



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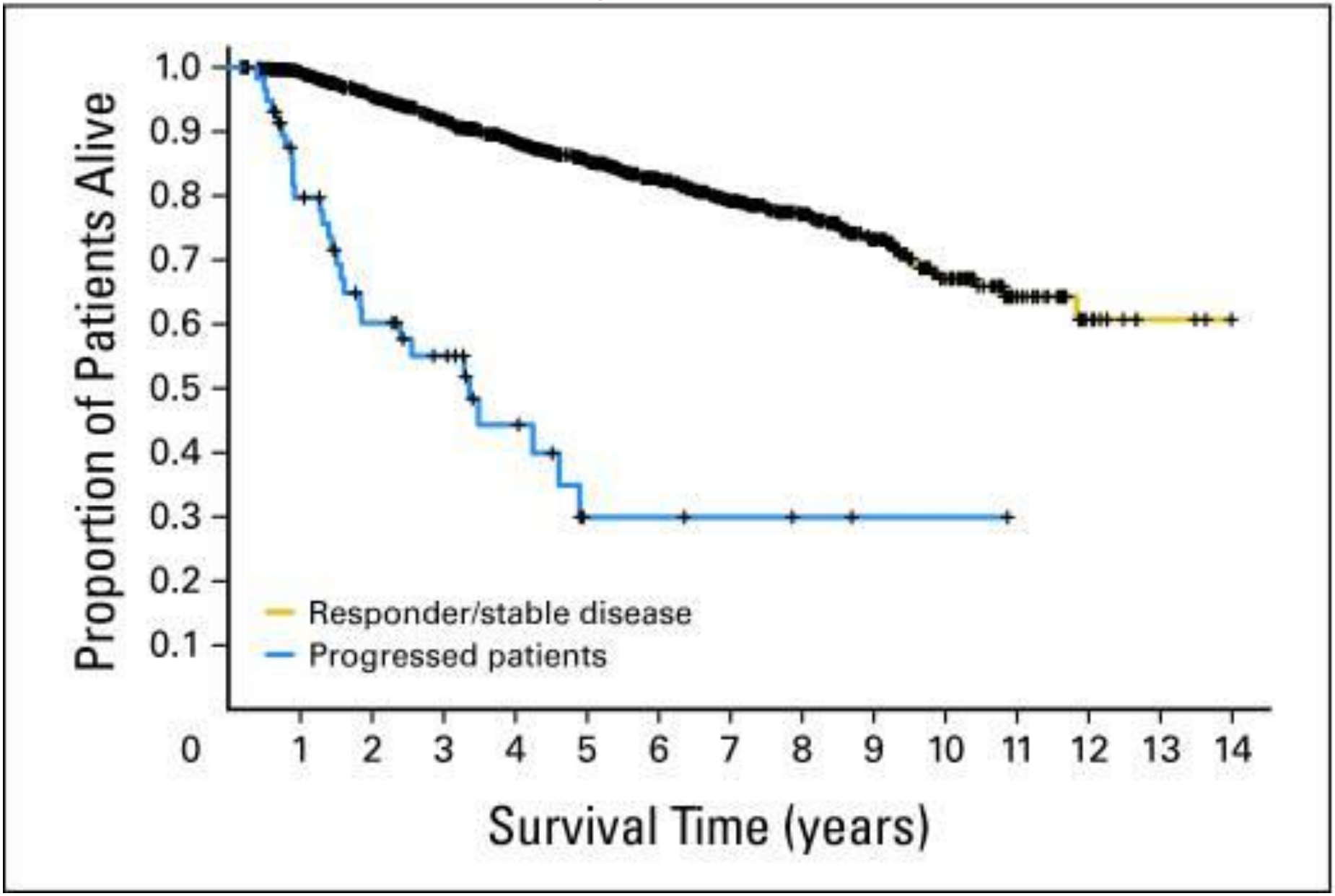

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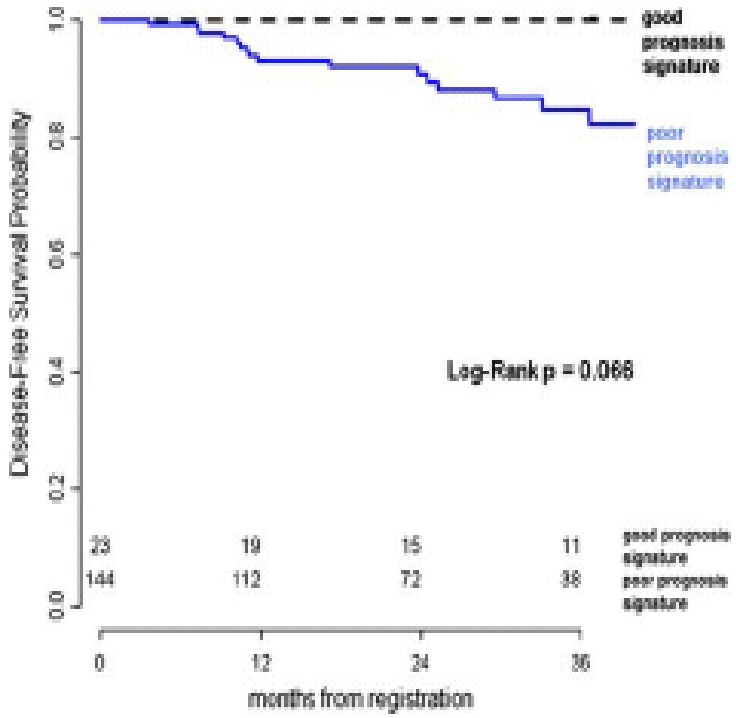
Claudle AS et al, J Clin Oncol. 2010 April 10; 28(11): 1821

Neoadjuvant Therapy
Molecular Profiling

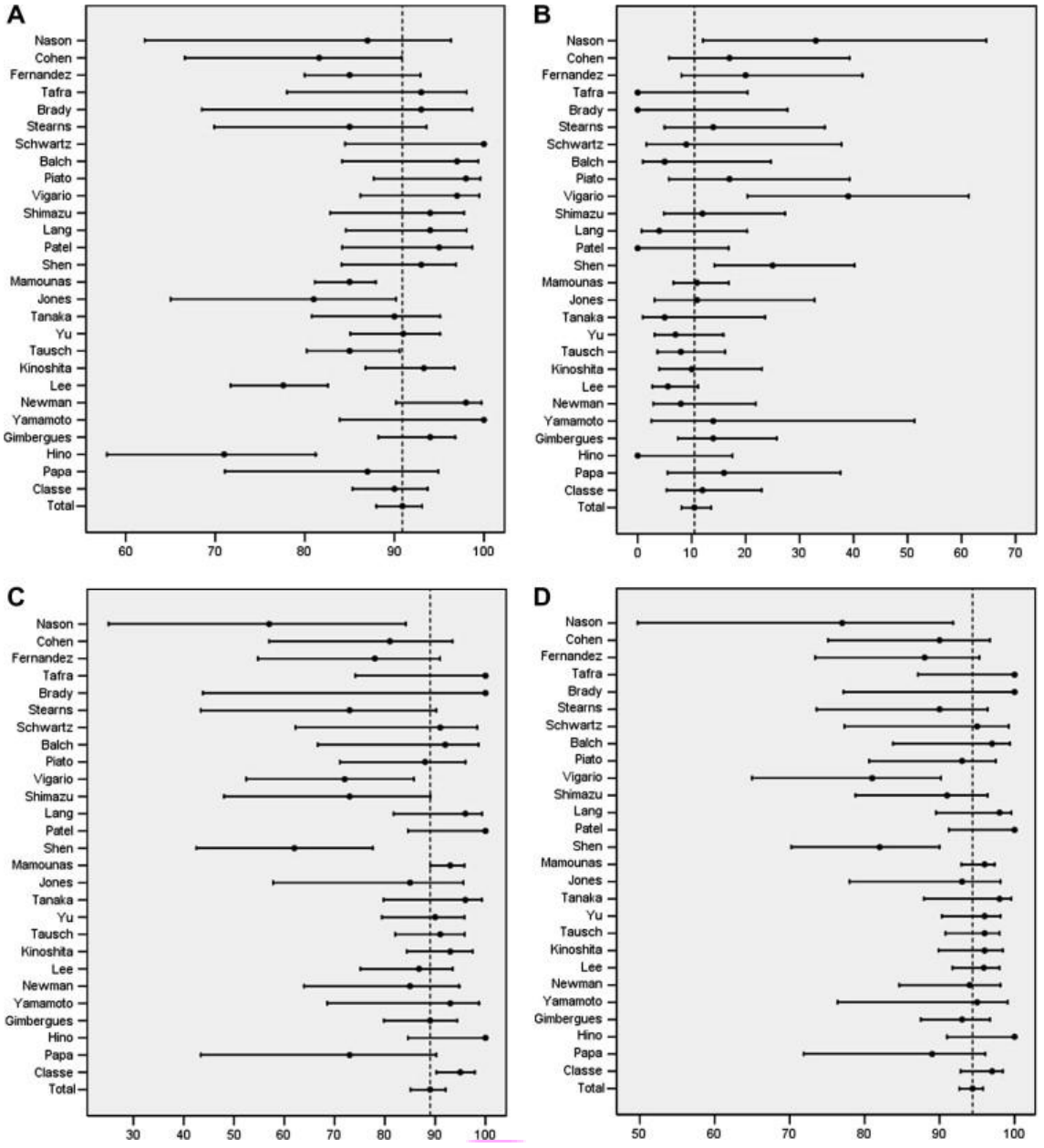
- 167 patients stage II and III disease
- 144 poor prognosis, 23 good prognosis
- CR as surrogate marker
  - CR Good prognosis 9%
  - CR Poor prognosis ER+ 32%
  - CR Triple – 50%
- Much more benefit of chemotherapy for poor prognosis patients



Straver ME et al, Breast Cancer Res Treat 2009, Jan 29

Forest plots of SN identification rate (A), false-negative rate (B), negative predictive value (C) and accuracy (D) of an SN biopsy following neoadjuvant chemotherapy in 2148 breast cancer patients

(Carolien HM et al, EJC December 2009, 45(18) 3124)



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Authors	Year	No.	Centers	Timing	Technique	MAP (%)	% FN	% +LN	Recommendation
Breslin *et al*[25]	2000	51	One	After	Mixed	84.3	12	51.2	Yes
Nason *et al*[21]	2000	15	One	After	Mixed	87	22	69.2	No
Haid *et al*[26]	2001	33	One	After	Mixed	88	0	62	Yes
Fernández *et al*[22]	2001	40	One	After	Radiotracer	85	22	40	No
Tafra *et al*[23]	2001	29	Many	After	Mixed	93	0	52	Yes
Stearns *et al*[27]	2002	26	One	After	Dye	88	6	45	Yes
Brady[28]	2002	14	One	After	Dye	93	0	77	Further studies
Miller *et al*[29]	2002	35	One	After	Mixed	86	0	25.7	Yes
Julian *et al*[30]	2002	34	One	After	R/D/Mixed	91.2	0	38.7	Further studies
Reitsamer *et al*[34]	2003	30	One	After	Mixed	86.7	6.7	50	Further studies
Schwartz & Meltzer[35]	2003	21	One	After	Dye	100	9	52	Yes
Balch *et al*[36]	2003	32	One	After	Mixed	97	5	59.3	Further studies
Piato *et al*[37]	2003	42	One	After	Radiotracer	98	17	42.8	Further studies
Aihara *et al*[38]	2004	20	One	After	Dye	85	8	60	Further studies
Bonardi *et al*[39]	2004	102	Two	After	Radiotracer	96	22.5	31.6	Yes
Kang *et al*[40]	2004	80	One	After	R/D/Mixed	76.3	7.3	20	Yes
Patel *et al*[24]	2004	42	One	After	R/D/Mixed	95	0	42	Yes
Shimazu *et al*[41]	2004	47	One	After	Mixed	94	12.1	66	Further studies
Lang *et al*[42]	2004	53	One	After	R/Mixed	94	4	43	Yes
Tio *et al*[43]	2004	89	Two	After	C/Mixed	93.3	5.7	–	Yes
Khan *et al*[44]	2005	33	One	After	Mixed	97	4.5	69	Yes with US
Mamounas *et al*[45]	2005	428	Many	After	R/D/Mixed	84.8	10.7	36.4	Yes
Jones *et al*[46]	2005	36	One	After	Mixed	80.6	11	55	No
		52		Before		100	–	58	Yes
Tanaka *et al*[50]	2006	70	One	After	Dye	90	5	44.2	Yes
Peley *et al*[51]	2006	17	One	After	Radiotracer	59	0	80	No
Lee *et al*[52]	2007	238	One	After	R/D/Mixed	77.6	5.6	69	Yes
Kinoshita[53]	2007	104	One	After	Mixed	93.3	11	33	Yes
Shen *et al*[54]	2007	69	One	After	R/D/Mixed	92.8	25	48.4	No
Newman *et al*[55]	2007	54	One	After	Mixed	98	8.6	66	Yes
Bauerfeind *et al*[56]	2008	92	Many	After	Mixed	96	16.6	32.60	Further studies
Reitsamer *et al*[57]	2008	C:143	Two	After	Mixed	81.1	8.3	–	Yes
		E: 22				77.3	10	–	
Gimbergues *et al*[58]	2008	129	One	After	Radiotracer	93.8	N_0: 0 N_{1-2}: 29.6	46.2	Yes (N_0)
Papa *et al*[60]	2008	31	One	After	Mixed	87	15.8	59.3	No
		58		Before		97	0	64.9	Yes
		28*		Before		100	–	75	Yes
Gomez *et al*[61]	2008	61	Many	After	Mixed	N_0: 100	N_0: 0	N_0: –	Yes (N_0)
		44		Before		N_{1-2}: 80	N_{1-2}: 15	N_{1-2}: 43	

MAP, mapped, detected nodes; FN, false negatives; LN, lymph node; C, chemotherapy; E, endocrine therapy; *, SLN before PST and axillary dissection only in positive SLN; R, radiotracer; D, dye; mixed, radiotracer plus dye; US, ultrasound.

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Pinero et al, Tumori. 2010 Jan-Feb;96(1):17

Questions on Sentinel Nodes

- Assessment axillary nodes
  - Light Microscopy?
  - IHC?
- Omission of axillary dissection?
  - Negative nodes
  - Micro vs macrometastases?
- Radiation therapy to include supraclav. field?

Surgery after Neoadjuvant Therapy

- **Preop Assessment**
  - **Mammography and US**
  - **MRI not supported**
- **Operative management**
  - **Complete removal of all tumor**
  - **Specimen radiography for TE**
  - **Reconstruction as per usual indications**

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