Titolo ed autore:

Il trattamento chirurgico del tumore primitivo in stadio IV d'esordio

Unit of Investigative Clinical Oncology
Istituto di Candiolo (IRCCS)

Il punto di vista dell'oncologo"

- Differently from locoregional disease, surgery of the primary tumor is not a priority in patients with stage IV disease

"As in previous studies, a surprisingly large number of women who present with metastatic breast cancer and an intact primary tumor underwent definitive local therapy"
Bafford et al, Breast Cancer Res Treat 2009; 115, 7

Impact of increased sensitivity of imaging modalities

- An estimated 15-20% of patients initially diagnosed with operable disease are found to have metastatic disease if PET is systematically used (mostly patients with intermediate or high-risk breast cancer)

Rush-Port, Ann Surg Oncol;13:677, 2006
Klaeser, Ann Oncol;18:1329, 2007

Is “De Novo st. IV prognostically worse than recurring stage IV?

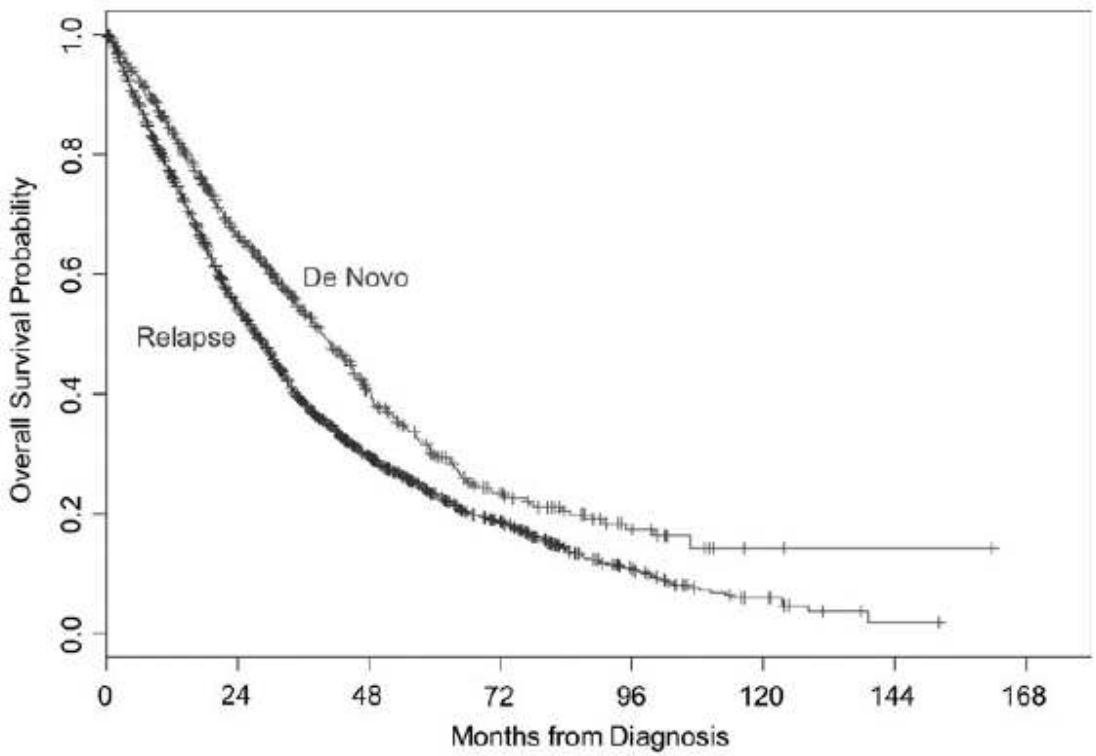
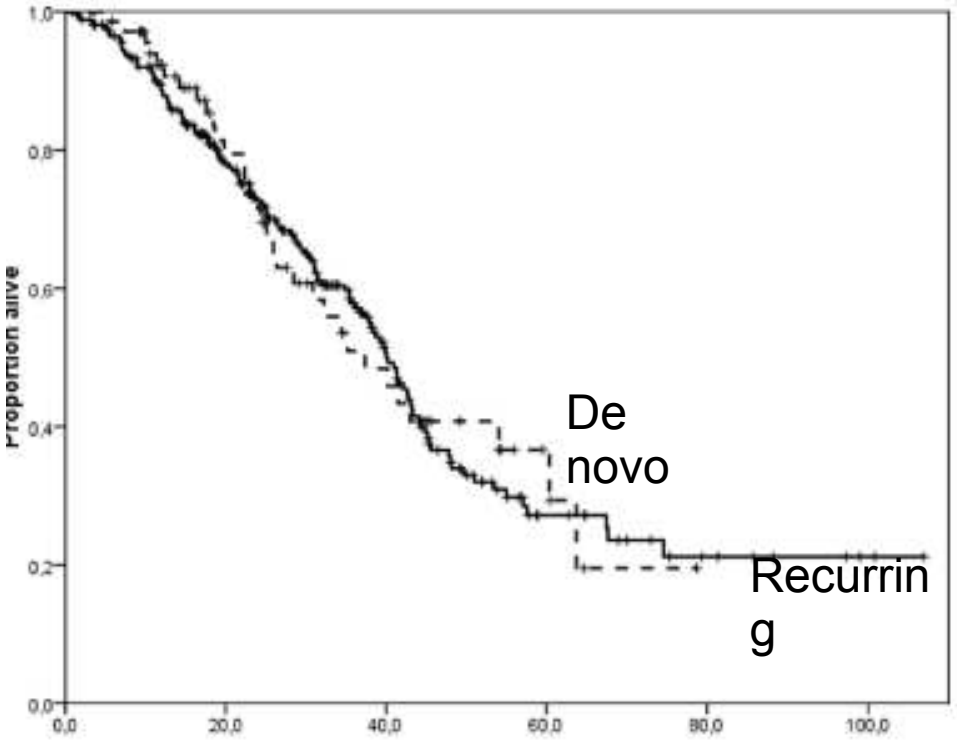


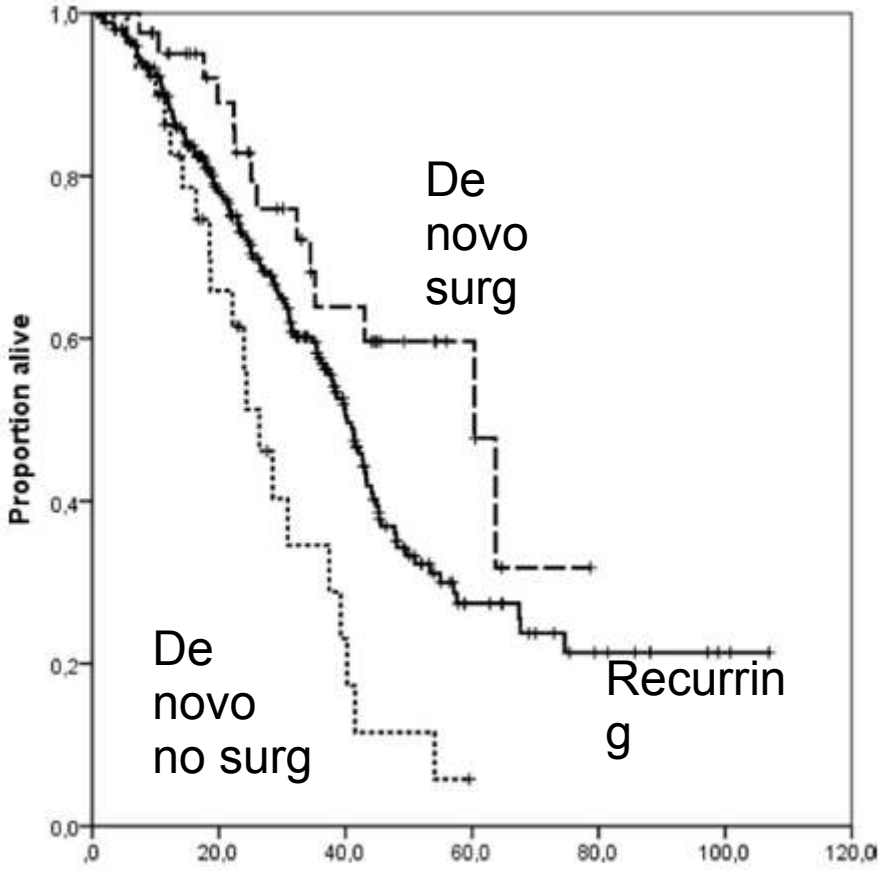
Figure 1. Kaplan–Meier curves illustrating overall survival for patients with *de novo* stage IV versus relapsed disease.

Davood et al, Ann Oncol 2010

What about HER2 positive patients?



Overall survival



Overall survival

V. Rossi et al. / The Breast 23 (2014) 44e49

Impact of locoregional treatment in patients with stage IV disease:

Authors	Number of patients in study	Period of diagnosis	Setting	Primary surgery	Median overall survival (months)	*P* value, surgery versus no surgery (log-rank test)
Bafford et al. [14]	147	1998–2005	Hospital-based	Yes: 61	42	0.093
				No: 86	28	
Ruiterkamp et al. [13]	728	1993–2004	Population-based	Yes: 288	31	<0.0001
				No: 440	14	
Leung et al. [15]	157	1990–2000	Hospital-based	Yes: 52	25	0.06
				No: 105	13	0.004
Cady et al. [16]	622	1970–2002	Hospital-based	Yes: 234	33	<0.0001
				No: 388	18	
Blanchard et al. [12]	395	1973–1991	Other	Yes: 242	27.1	<0.0001
				No: 153	16.8	
Fields et al. [11]	409	1996–2005	Hospital-based	Yes: 187	26.8	<0.0001
				No: 222	12.6	
Gnerlich et al. [10]	9734	1988–2003	Population-based	Yes: 4578	36 and 18	<0.001 (36 vs. 21)
				No: 5156	2 and 7	<0.001 (18 vs. 7)
Rapiti et al. [9]	300	1977–1996	Population-based	Yes, unknown margins: 33	12%	0.0002
				Yes, positive margins: 33	16%	
				Yes, negative margins: 61	27%	
				No: 173	12%	
Babiera et al. [8]	224	1997–2002	Hospital-based	Yes, partial mastectomy: 39	32.1	0.091
				Yes, total mastectomy: 43	(whole group)	
				No: 142		
Khan et al. [7]	16023	1990–1993	Population-based	Yes, partial mastectomy: 3513	26.9	<0.0001
				Yes, total mastectomy: 5649	31.9	
				No: 6861	19.3	

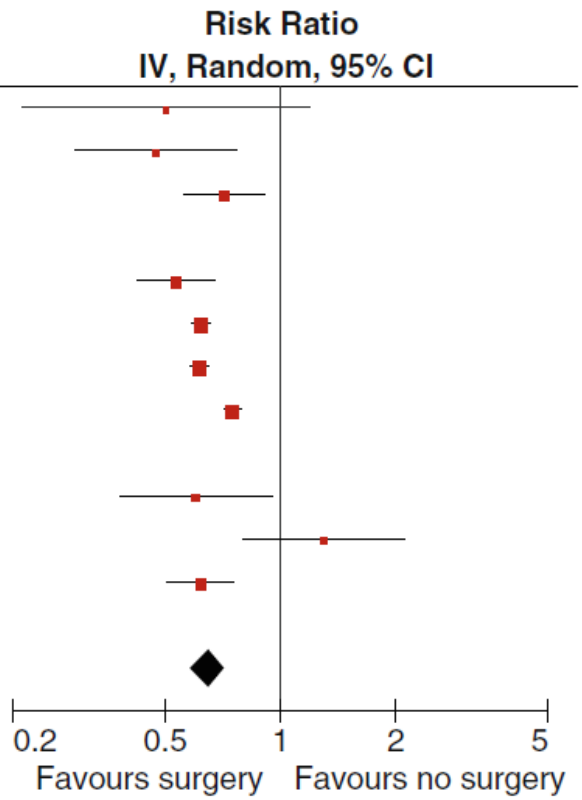
Ruiterkamp et al, Breast Cancer Res Treat;120:9, 2010

Pooled analysis of retrospective studies

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Babiera et al. 2006	-0.69	0.44	1.3%	0.50 [0.21, 1.19]
Bafford et al. 2009	-0.75	0.25	3.5%	0.47 [0.29, 0.77]
Blanchard et al. 2007	-0.34	0.124	9.4%	0.71 [0.56, 0.91]
Cady 2008	0	0		Not estimable
Fields 2007	-0.63	0.119	9.8%	0.53 [0.42, 0.67]
Gnerlich 2007	-0.48	0.029	19.0%	0.62 [0.58, 0.65]
Khan 2002 (1)	-0.49	0.029	19.0%	0.61 [0.58, 0.65]
Khan 2002 (2)	-0.29	0.027	19.1%	0.75 [0.71, 0.79]
Leung 2009	0	0		Not estimable
Rapiti 2006 (1)	-0.51	0.234	3.9%	0.60 [0.38, 0.95]
Rapiti 2006 (2)	0.26	0.246	3.6%	1.30 [0.80, 2.10]
Ruiterkamp 2009	-0.48	0.102	11.3%	0.62 [0.51, 0.76]
Total (95% CI)			**100.0%**	**0.65 [0.59, 0.72]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 47.04$, df = 9 ($P < 0.00001$); $I^2 = 81\%$

Test for overall effect: $Z = 8.38$ ($P < 0.00001$)



Ruiterkamp et al, Breast Cancer Res Treat;120:9, 2010

Overall survival: significant covariates

Author	HR	Significant Covariates
Bafford, 2009	0.47*	Liver metastasis, CNS metastasis, ER, HER2
Ruiterkamp, 2009	0.62*	Age, number of metastatic sites, systemic treatment
Leung, 2009	N.S.	Chemotherapy
Blanchard, 2007	0.71*	Number of metastatic sites, ER and PgR status
Fields, 2007	0.53	Visceral metastases, bone metastases
Rapiti, 2006	0.6* 1.3	Age, N status, visceral metastasis, CNS metastasis, hormonal treatent, margin status
Barbiera, 2006	0.50*	Number of metastatic sites, HER2 status
Khan, 2002	0.61 0.75*	Number of metastatic sites, soft-tissue metastasis (vs visceral), chemotherapy, hormonal therapy, surgical margins

Clinical data regarding locoregional treatment in stage IV breast cancer

- Possible sources of bias

Survival of untreated breast cancer

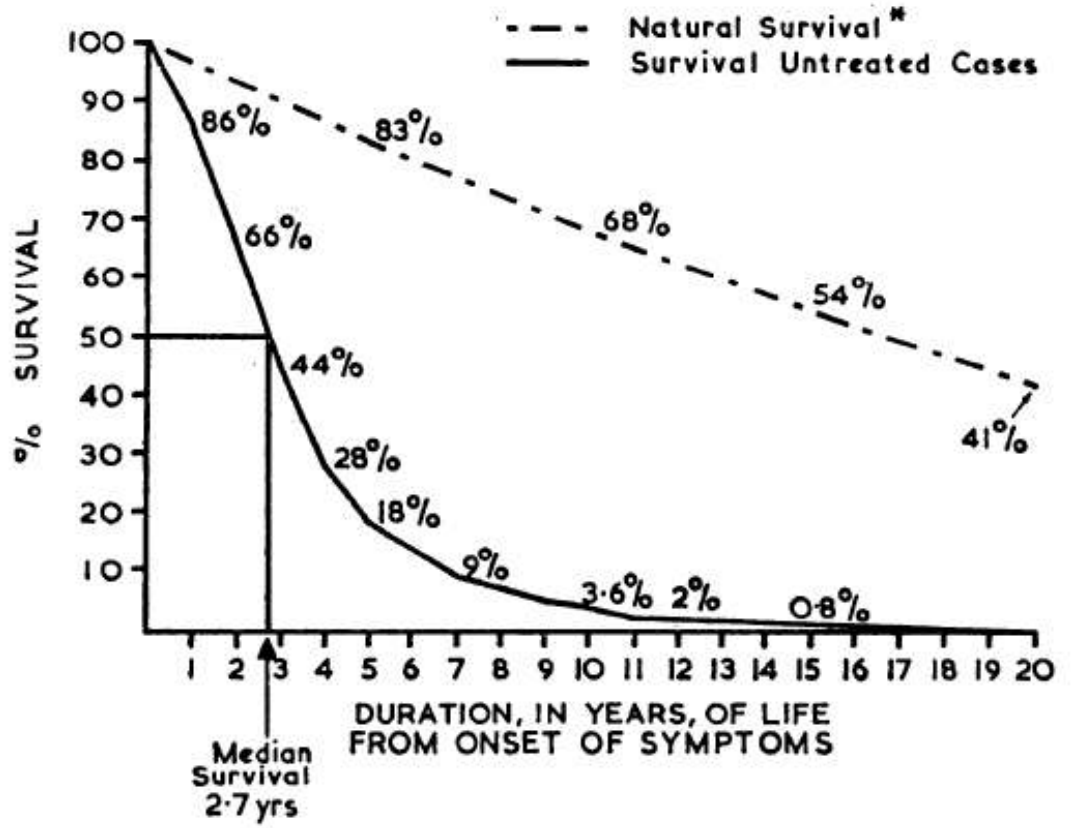


FIG. 1.—Survival of untreated breast cancer. Middlesex Hospital, 1805-1933 (250 cases). *See Appendix.

Bloom et al, BMJ 2;213, 1967

Impact of patient selection on clinical outcomes

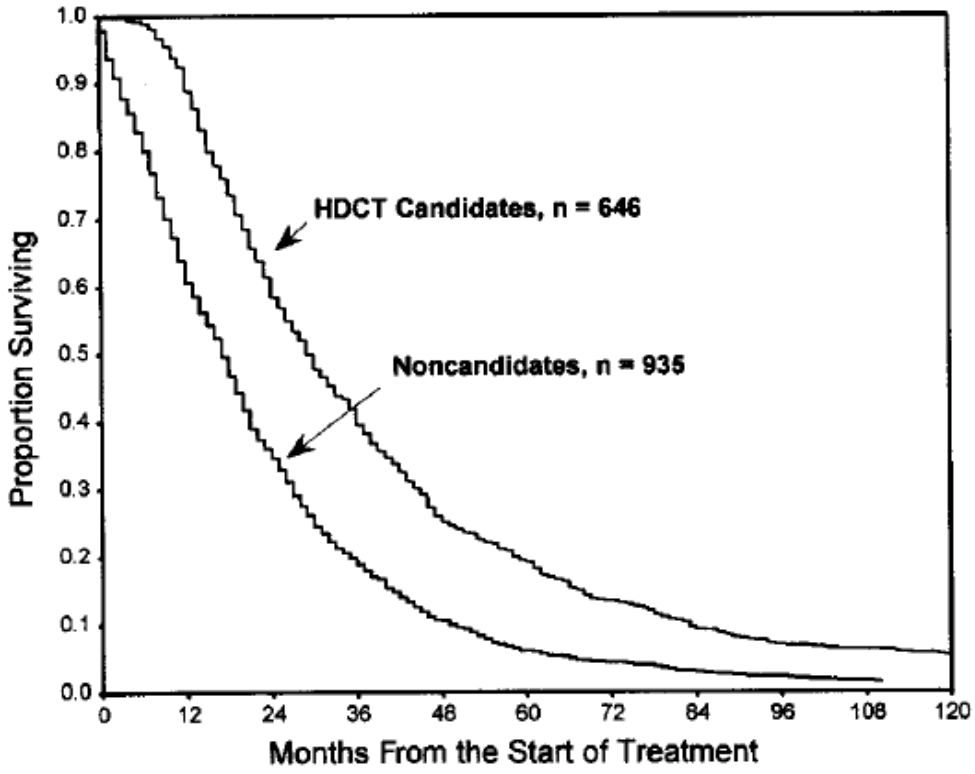
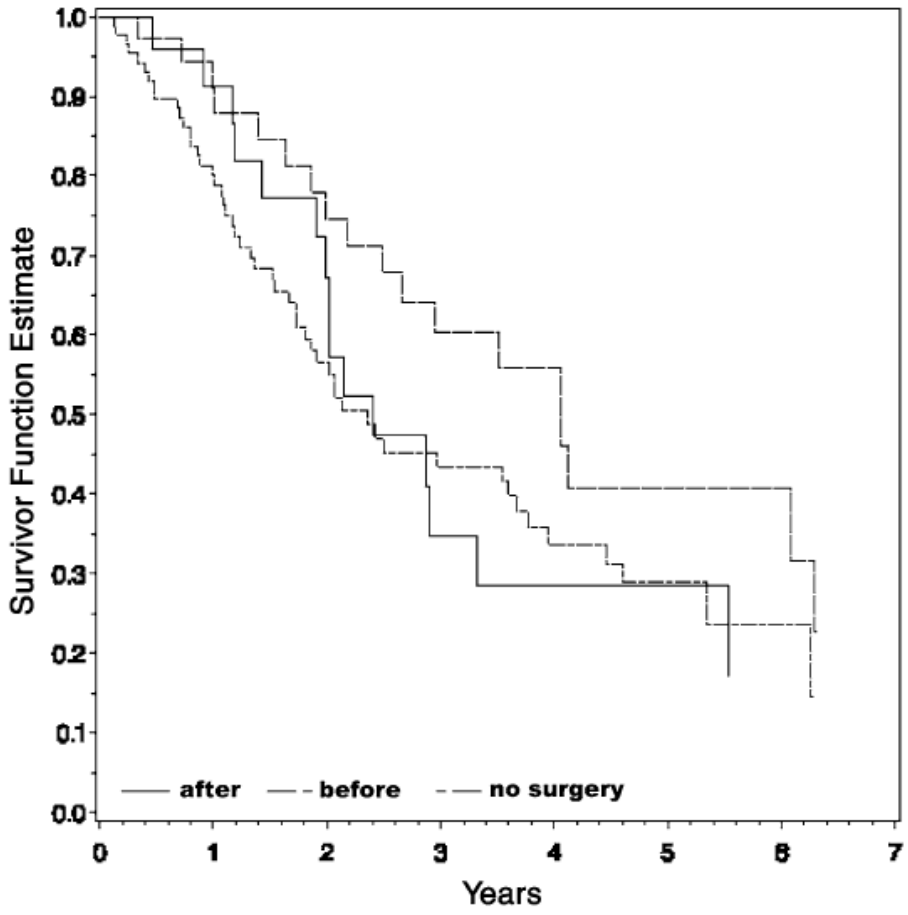


Fig 2. OS rates in the potential HDCT candidates and noncandidates. All patients were treated on the same doxorubicin-containing standard-dose chemotherapy protocols in a single institution. The median follow-up is greater than 14 years.

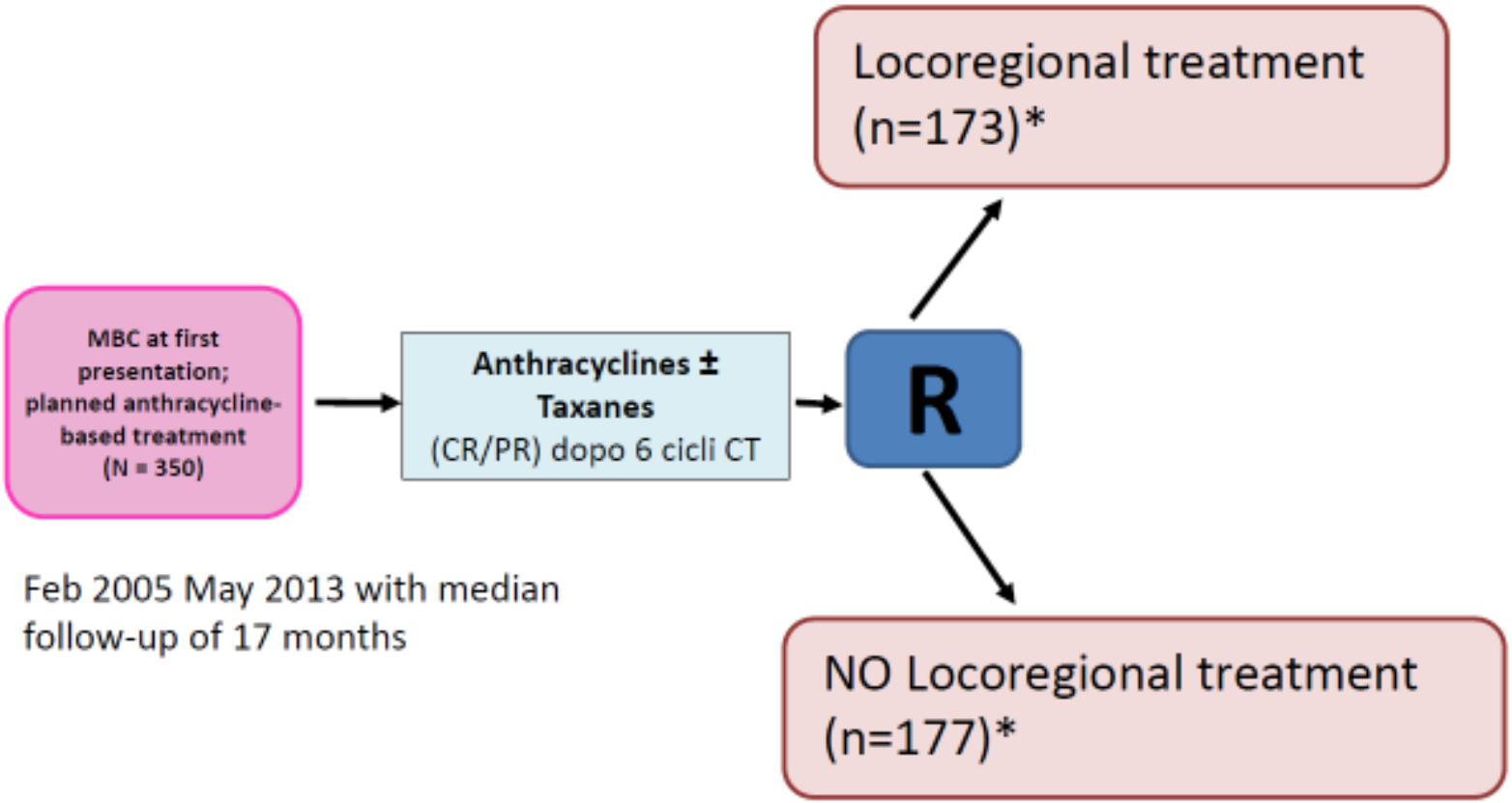
Rahman et al, J Clin Oncol 15:3171, 1997

Surgery before or after the diagnosis of synchronus metastases: stage migration



Bafford, Breast Cancer Res Treat;115:7,

Randomized trial



Badwe et al Lancet Oncol 2015; 16: 1380–88

Surgical outcomes

	Locoregional treatment group (n=173)	No locoregional treatment (n=177)
Surgery		
Modified radical mastectomy	125 (72%)	1 (1%)
Breast-conserving surgery	40 (23%)	NA
No surgery	8 (5%)	176 (99%)
Palliative surgery upon progression	1 (1%)	18 (10%)
Radiotherapy		
Chest wall and breast with supraclavicular fossa	119 (69%)	NA
Chest wall alone	19 (11%)	NA
No radiotherapy	8 (5%)	NA
Not known	27 (16%)	..

NA=not done.

Table 4: Details of locoregional treatment

Badwe et al Lancet Oncol 2015; 16: 1380–88

Overall suvival

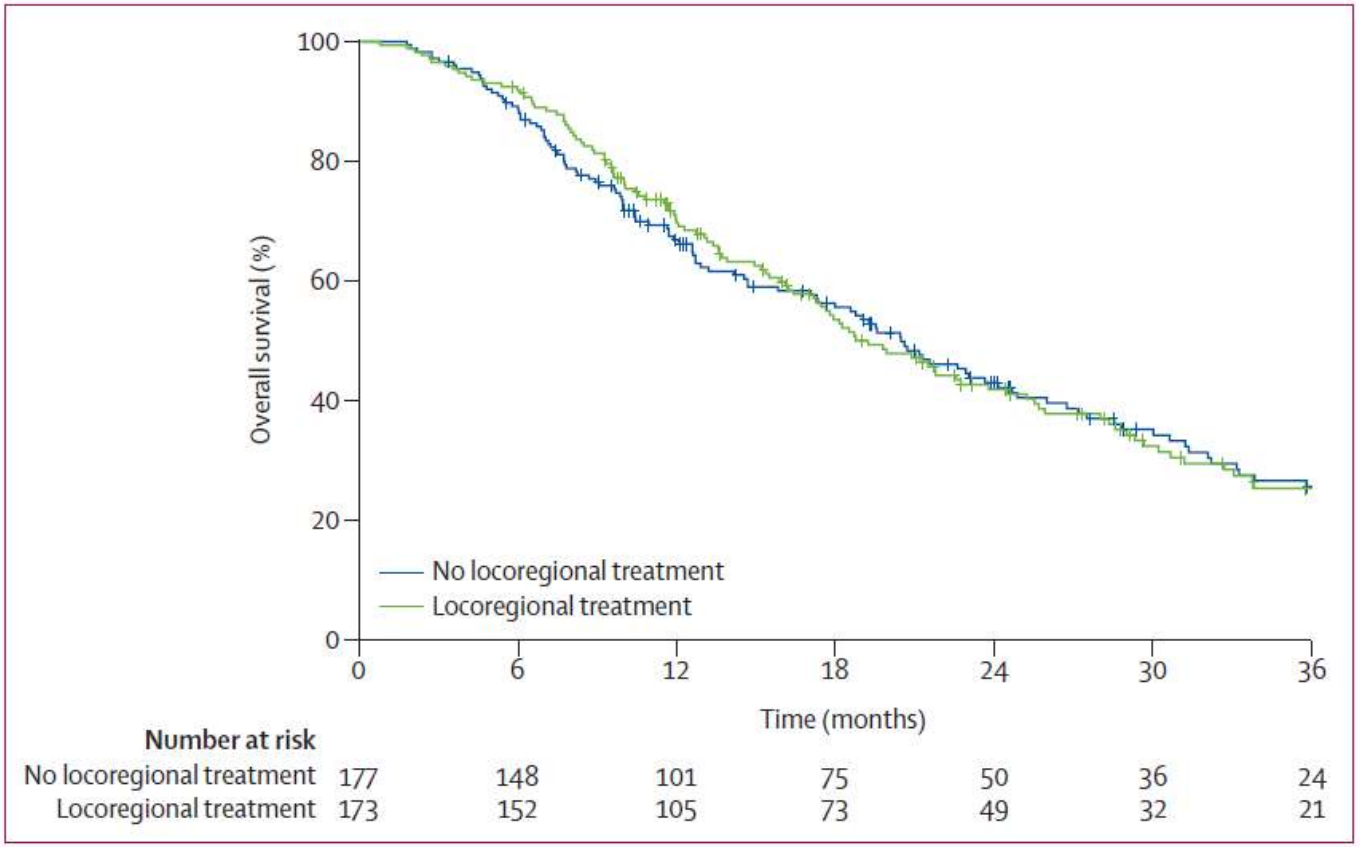
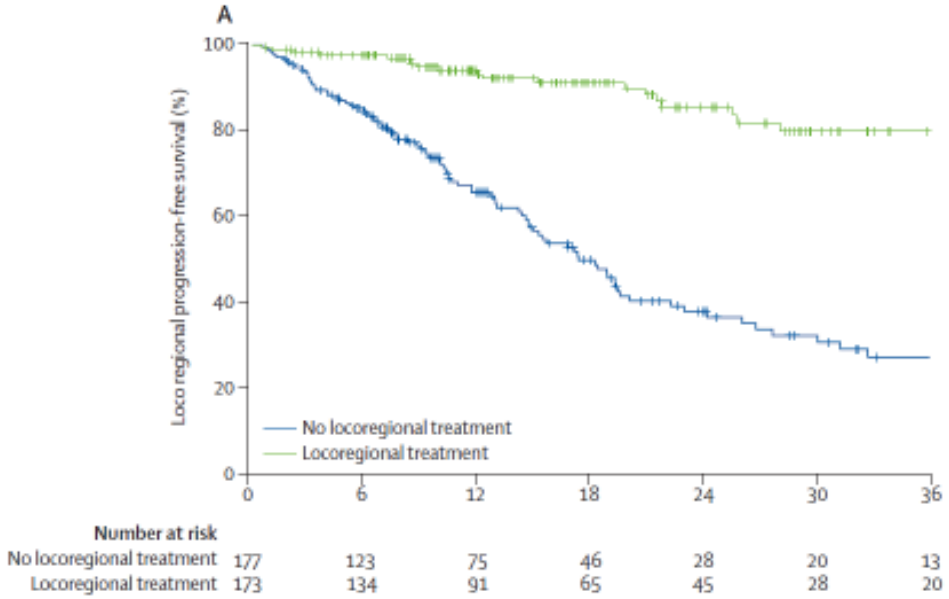


Figure 2: Kaplan-Meier plot of overall survival

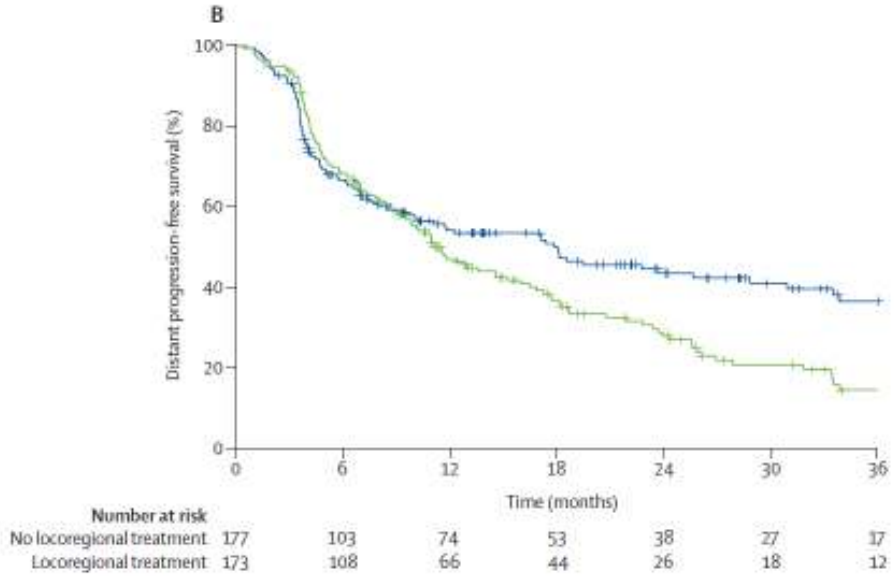
Badwe et al Lancet Oncol 2015; 16: 1380–88

Other outcomes

Locoregional
PFS

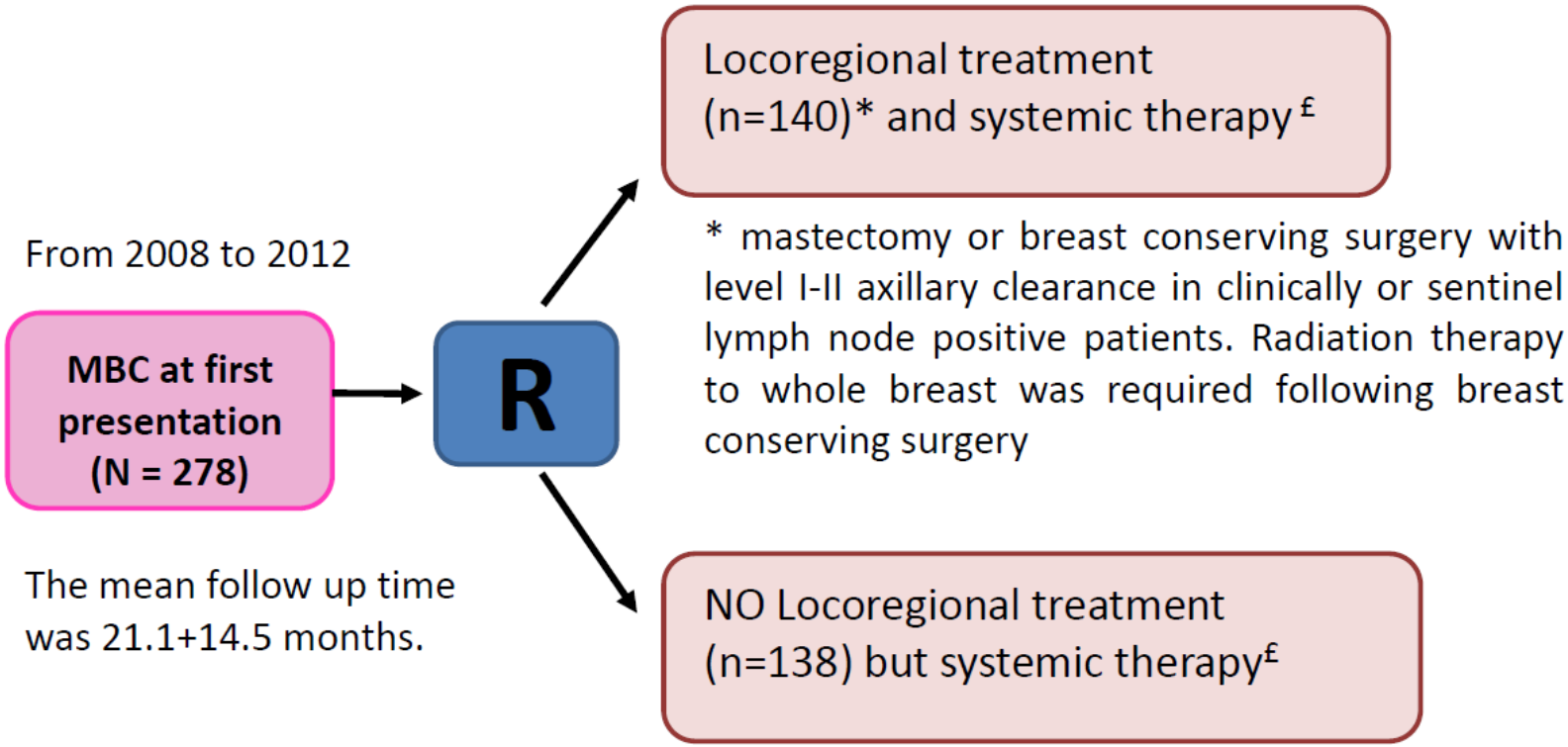


Distant
DFS



Badwe et al Lancet Oncol 2015; 16: 1380–88

Turkish Study

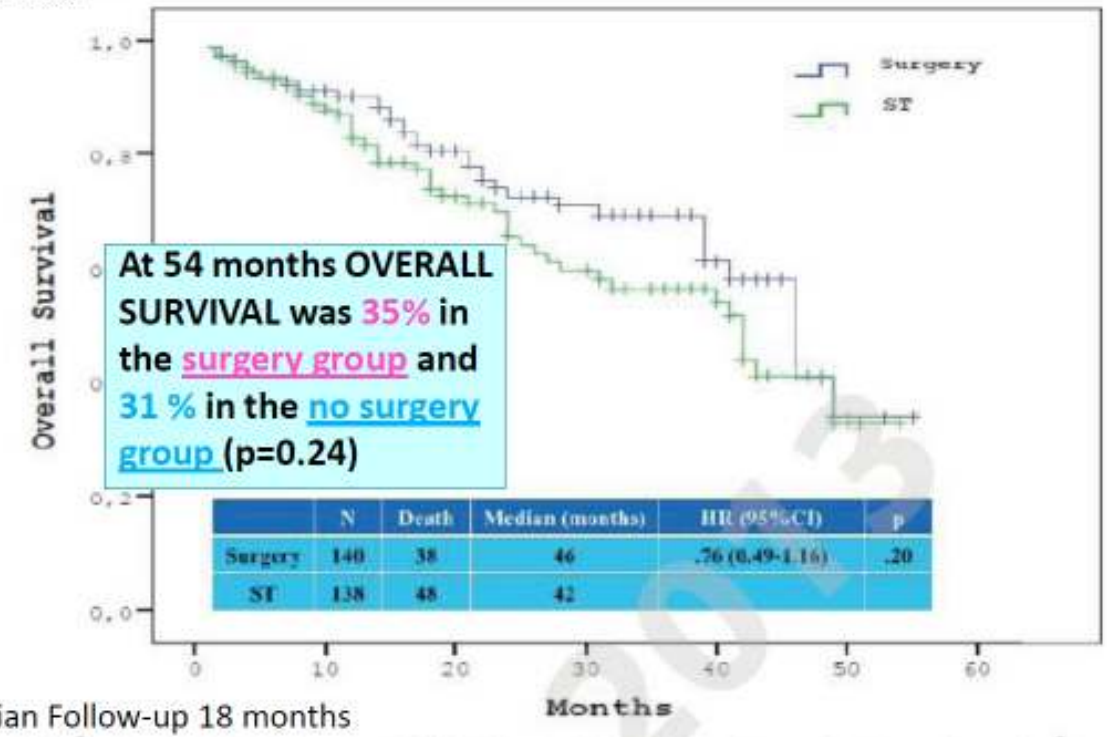


£ systemic therapy of either endocrine treatment or chemotherapy (plus trastuzumab for HER2 +) was given to all patients

No overall advantage, but…

SAN ANTONIO BREAST CANCER SYMPOSIUM

OVERALL SURVIVAL



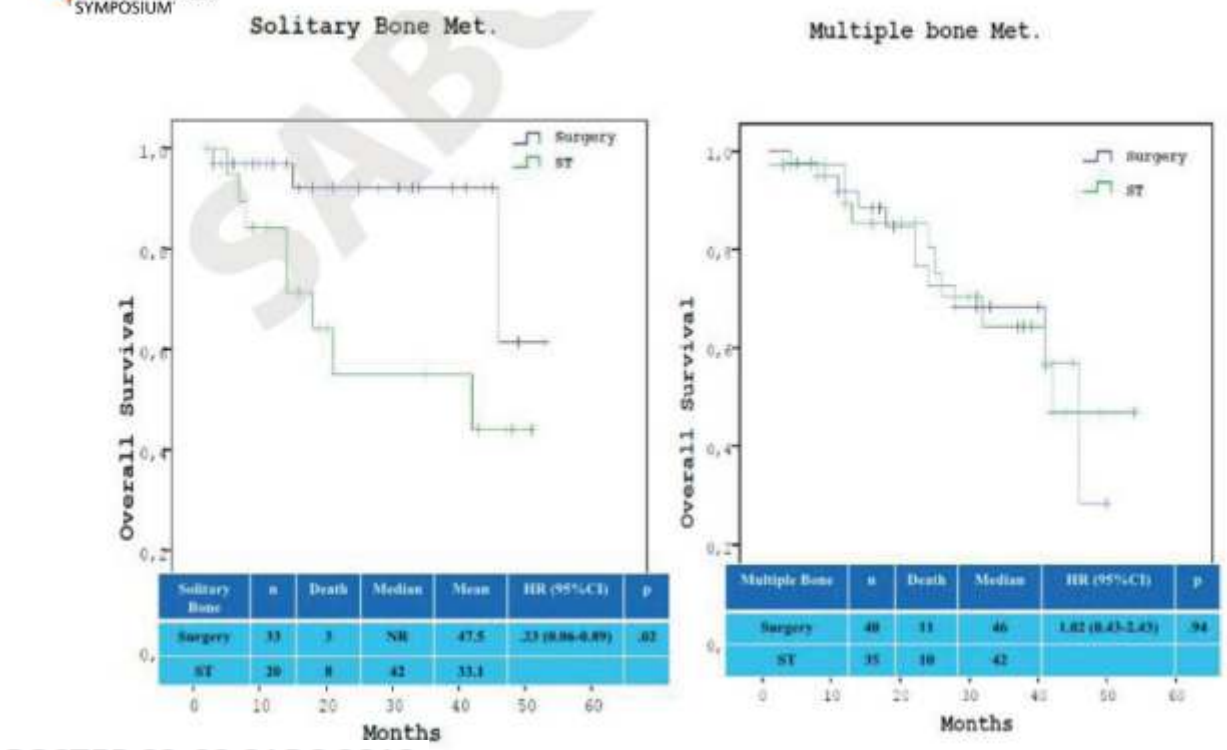
At 54 months OVERALL SURVIVAL was 35% in the surgery group and 31 % in the no surgery group (p=0.24)

	N	Death	Median (months)	HR (95%CI)	p
Surgery	140	38	46	.76 (0.49-1.16)	.20
ST	138	48	42		

Median Follow-up 18 months

POSTER S2-03 SABC 2013

Possible advantage of surgery in women with solitary bone metastases



POSTER S2-03 SABC 2013

Chirurgia elettiva del tumore primario

- C’è necessità di una raccomandazione del Gruppo di Studio sul Carcinoma della mammella?