

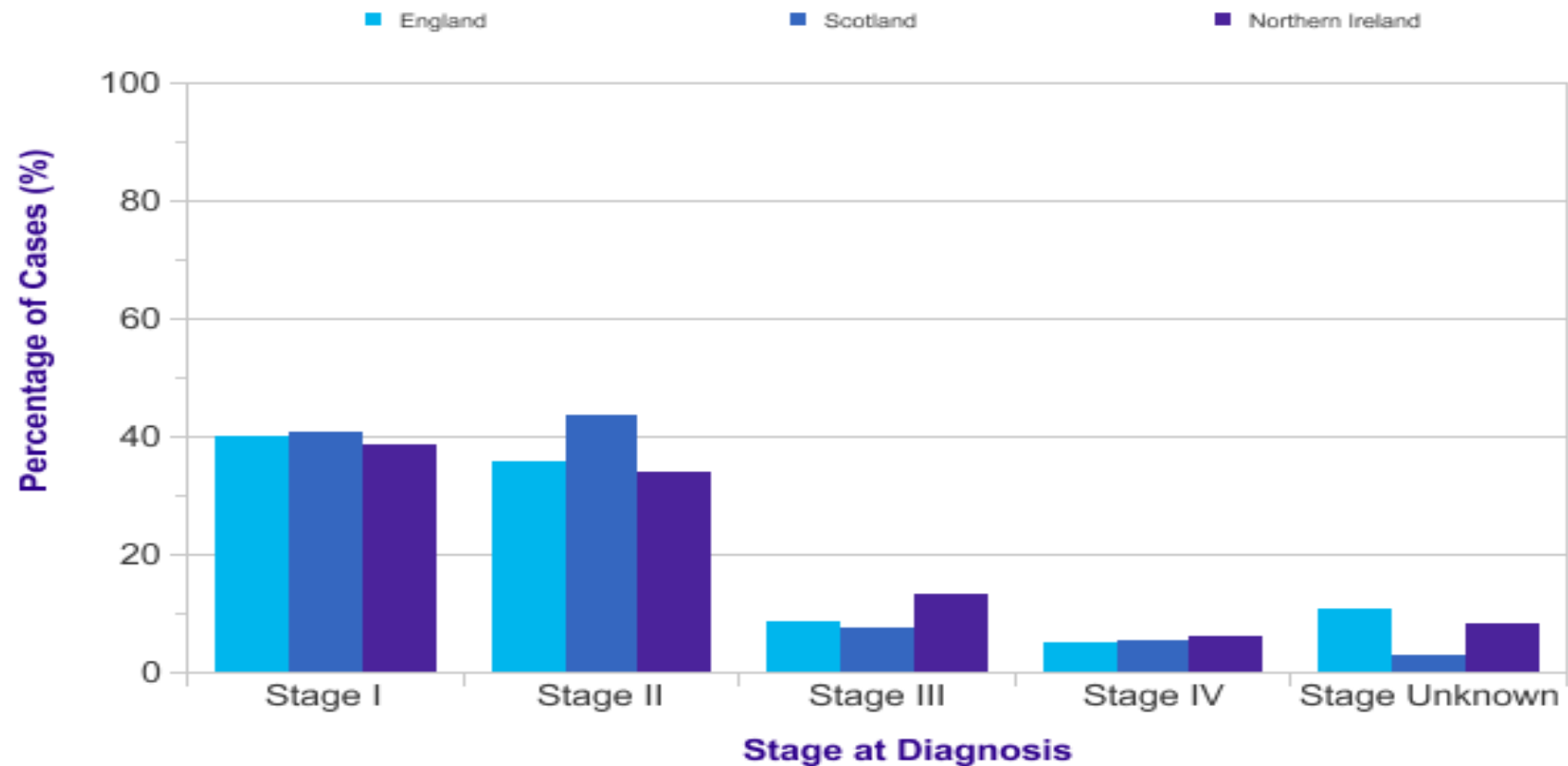
When is local surgery indicated in metastatic breast cancer?

NICOLA ROCHE

THE ROYAL MARS DEN HOSPITAL

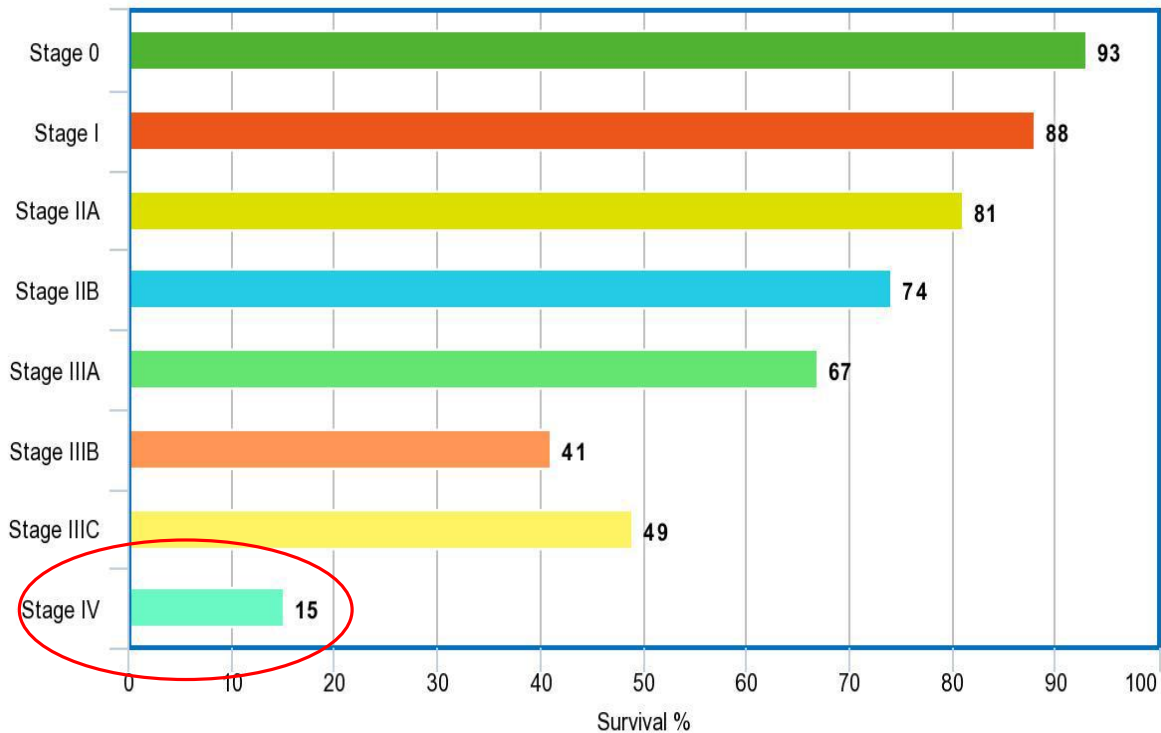
IBCS 2018

Stage at diagnosis 2014



Survival with Stage IV breast cancer

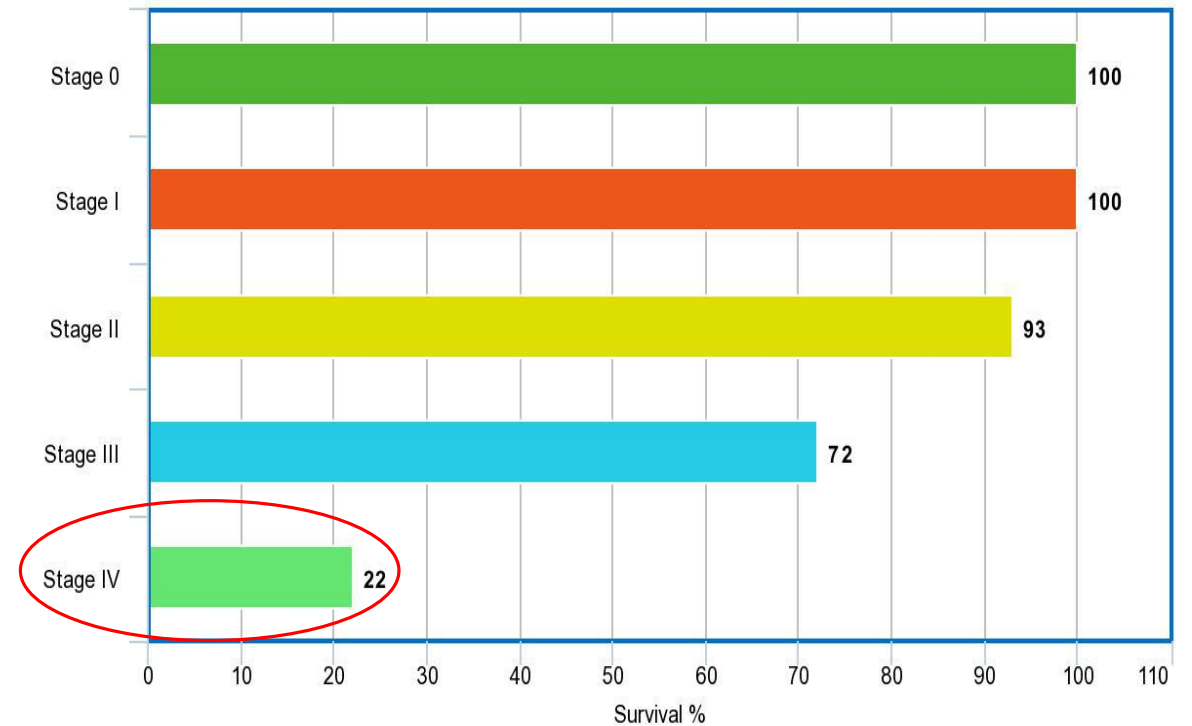
5 Year % Survival Rate for Breast Cancer by Stage
SEERS data (2001 - 2002)



Figures for % Survival by Stage

meta-chart.com

5 Year % Relative Survival Rate for Breast Cancer by Stage
SEERS data (2012)



Figures for % Survival by Stage

meta-chart.com

Hypothesis

Surgical removal of the primary tumour will improve survival in a patient with de novo metastatic breast cancer

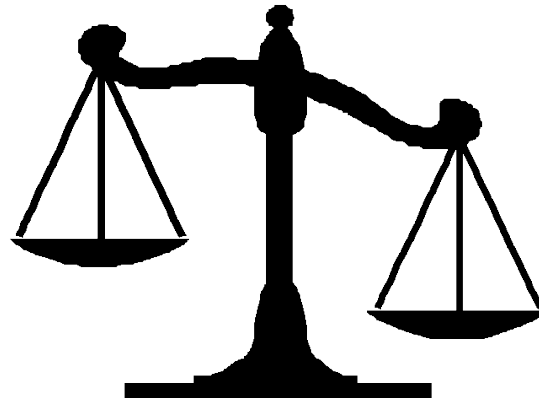
Evidence

For surgery

- ↓ Tumour burden
- ↓ Genetic diversity / remove clonal resistant cell lines
- ↓ Seeding
- Benefit in other tumour types
- Retrospective series

Against

- Anti-angiogenic tumour factors
- Wound response
- Metastases metastasize
- Retrospective studies: selection bias
- RCT and prospective data are not consistent

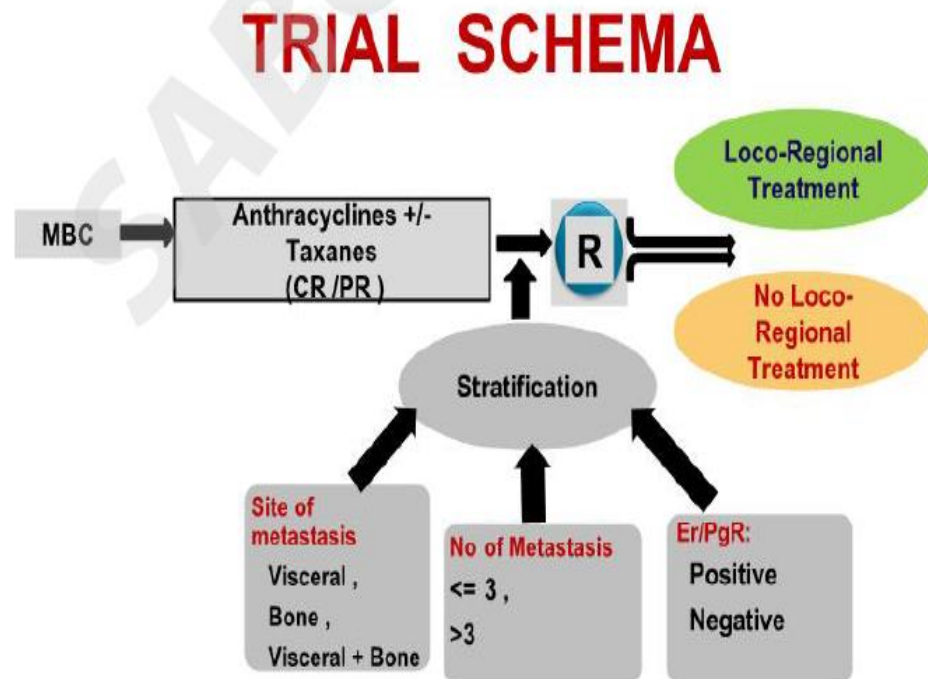


Retrospective studies

- Numerous
- Majority showing advantage of surgery
- Matched pair analysis Cady et al 2008 Ann Surg Oncol
- Meta-analysis
 - Petrelli Med Oncol 2012
 - Harris et al Ann Surg Oncol 2013

RCTs

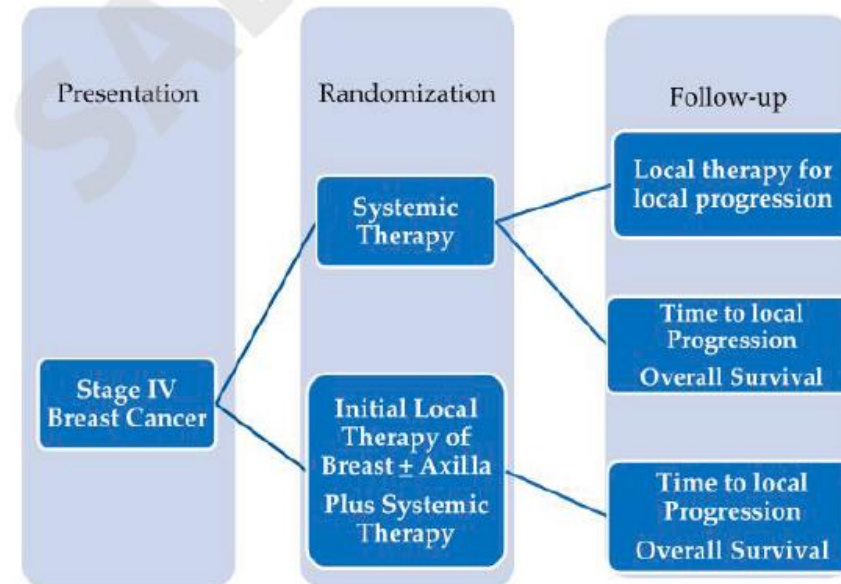
Badwe et al Lancet Oncol 2015



Soran et al SABC 2013

San Antonio Breast Cancer Symposium - Cancer Therapy and Research Center at UT Health Science Center - December 10-14, 2013

Design MF07-01



This presentation is the intellectual property of the Turkish Federation of Societies for Breast Diseases. Contact asoran@upmc.edu

Patient Demographics Indian Study

	Locoregional treatment group (n=173)	No locoregional treatment group (n=177)
Age (years)		
Median	48	48
Site of metastasis		
Bone	50 (29%)	50 (28%)
Visceral	75 (43%)	77 (44%)
Bone and visceral	48 (28%)	50 (28%)
Number of metastases		
≤3	44 (25%)	45 (26%)
>3	129 (75%)	132 (74%)
Oestrogen receptor or progesterone receptor		
Negative	71 (41%)	71 (40%)
Positive	102 (59%)	106 (60%)
Menopausal status†		
Pre and peri	74 (43%)	88 (50%)
Post	99 (57%)	89 (50%)
HER2 status		
Negative (including 1+)	124 (72%)	108 (61%)
Positive (3+)	45 (26%)	62 (35%)
Not known or equivocal (2+)	4 (2%)	7 (4%)

Data are n (%) unless stated otherwise. †Perimenopausal: history of no menstruation up to one preceding year; postmenopausal: cessation of menstrual cycles for more than 1 year.

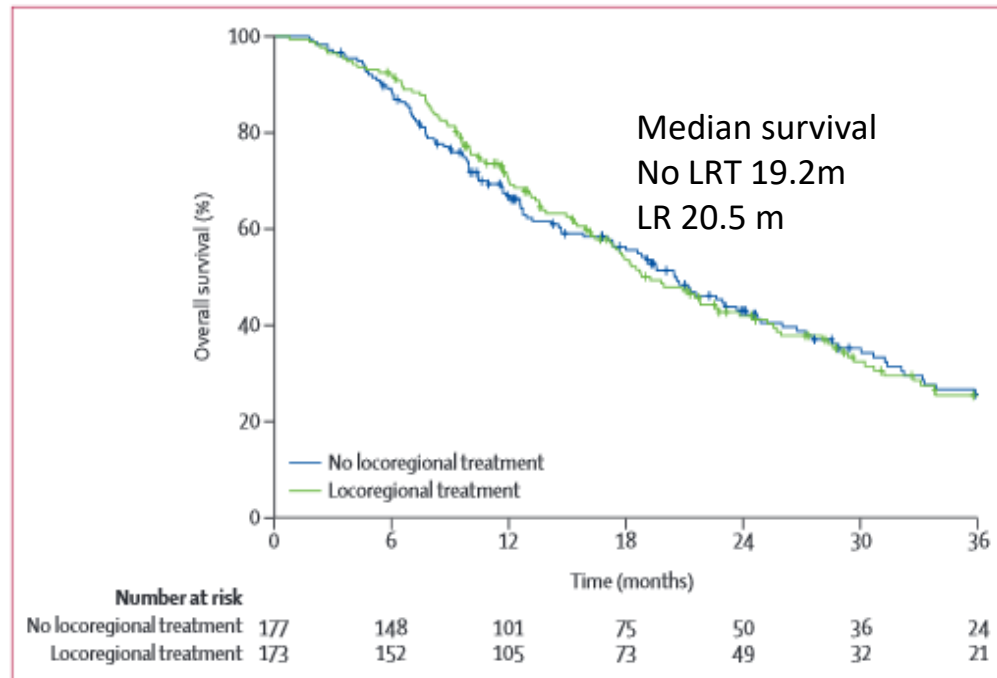
Table 1: Baseline characteristics of the intention-to-treat population

Patient Demographics Turkish Study

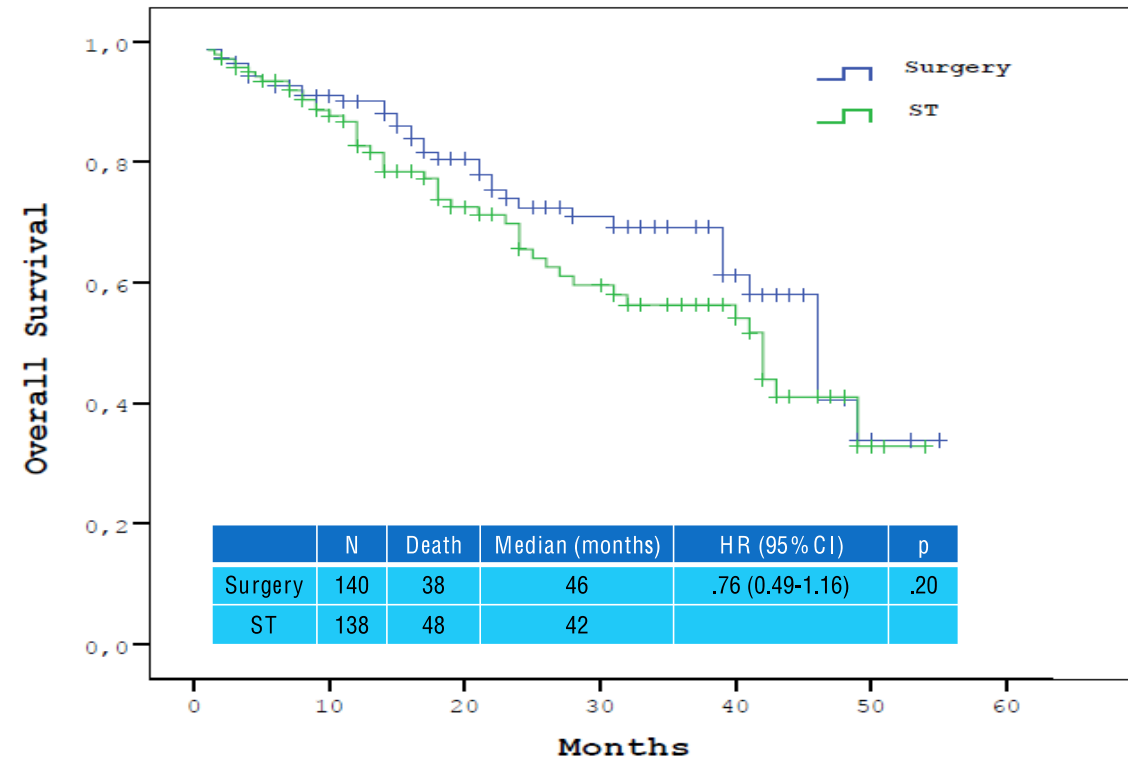
	Initial Surgery n= 140 N (%)	Systemic Therapy n=138 N (%)
Median age	51.8	51.5
Bone only	73 (52)	55 (40)
Other	34 (24)	46 (33)
Bone and other	33 (24)	37 (27)
1 organ	106 (76)	89 (65)
>1 organ	34 (24)	49 (35)
T1	12 (8.6)	11 (8)
T2	73 (52.1)	59 (42.8)
T3	31 (22.1)	30 (21.7)
T4	24 (17.1)	38 (27.5)
Grade 1	6 (4.3)	10 (9.5)
Grade 2	56 (40)	34 (32.4)
Grade 3	78 (55.7)	61 (58.1)
ER +ve	121 (86.4)	99 (72.3)
Her 2 +ve	30.7 (42)	42 (30.4)
TNT	10 (7.1)	24 (17.6)

RCTs

Badwe et al Lancet Oncol 2015



Soran et al SABC 2013



MF07-01 ASCO 2016

- OS at 5 years
 - LRT 41.6%
 - No LRT 24.4 %
 - HR 0.66 p = 0.005
- Median Survival 46 m v 37m
- Sub group analysis
 - LRT benefit in ER +ve, Her 2 –ve, younger age, solitary bone mets
 - Multiple visceral mets 31% LRT versus 67% no LRT
- Loco-regional relapse
 - LRT 1%
 - No LRT 11%

TBCRC 013: Prospective Registry

Eligibility

de novo Stage IV breast cancer with an intact primary tumor
metastatic disease identified within 3 months of primary surgery
tissue from primary tumor and metastatic lesion

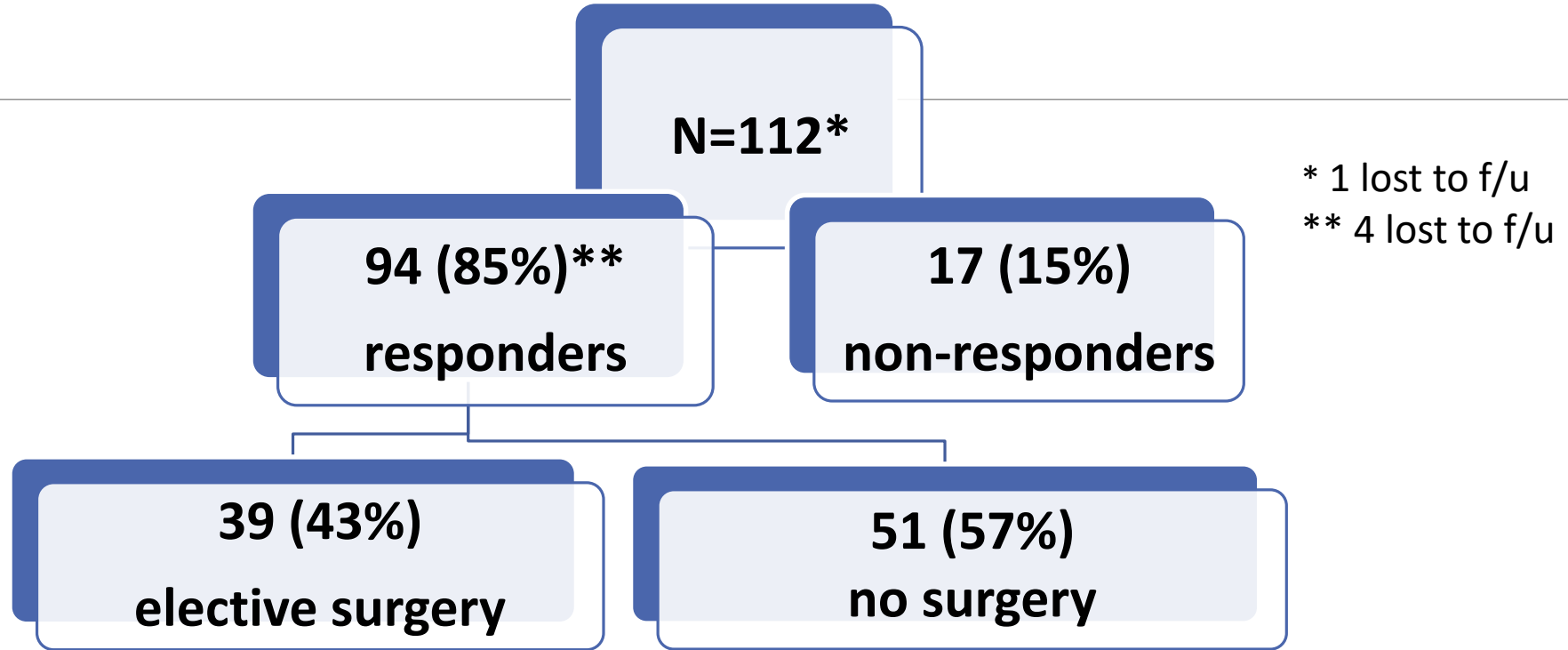
Accrual July 2009 – April 2012

127 eligible patients, 14 institutions, two cohorts

cohort A: intact primary tumor (n=112)

cohort B: metastases within 3 months of primary surgery (n=15)

TBCRC 013: Surgical Uptake



	N	Median Survival	30 m survival (95%CI)
Non-Responders	16	13 m (9-31)	24% (11-58)
Responders, No Surgery	51	65 (50-NR)	76% (66-89)
Responders, Surgery	39	71 (46-NR)	77% (65-91)

TBCRC 013: Overall Survival

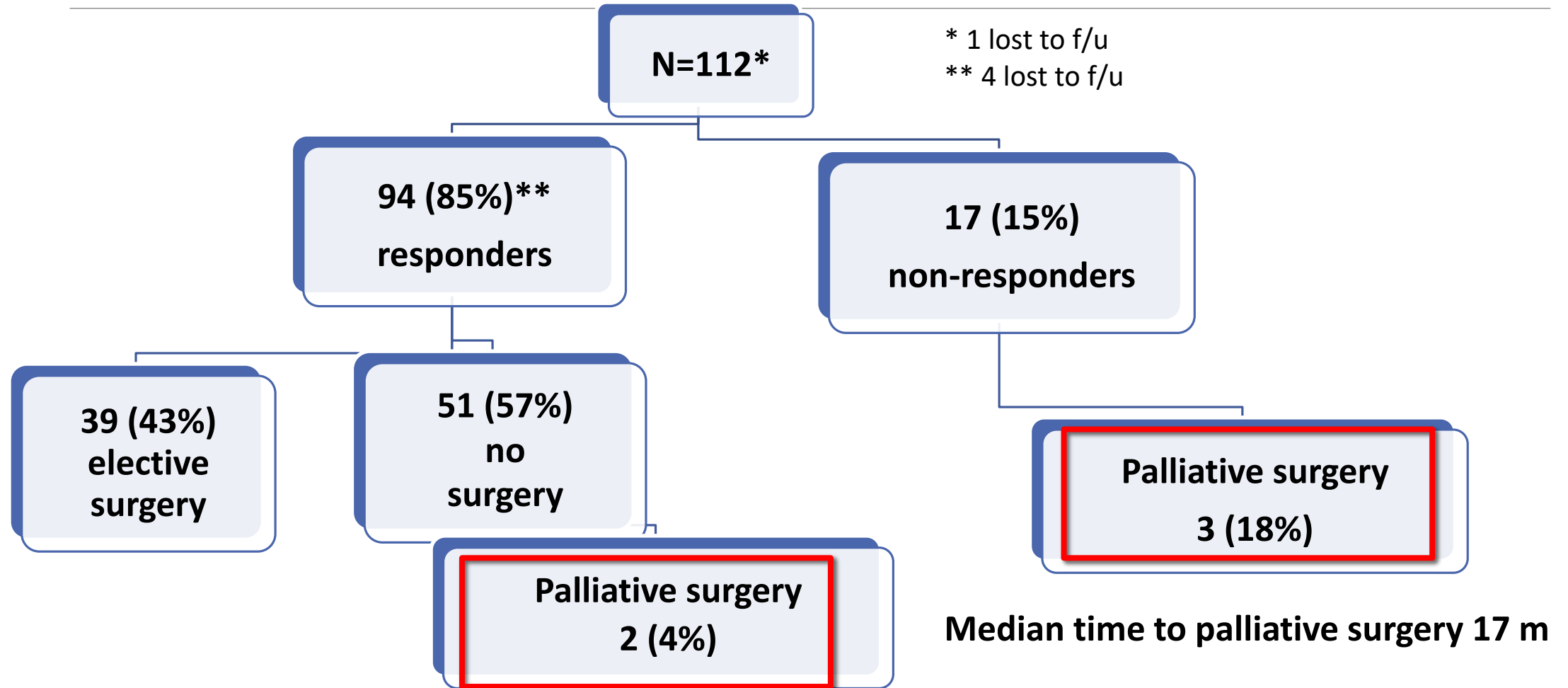
N=112

3yrs OS 70% (95%CI 63-79%)

Median Survival 69 m (51 – NR)

Responders	Surgery	N	Median Survival m	3y OS (95%CI)	p
ER +	N	46	71	78 (67-91)	0.85
	Y	34	77	79 (67-94)	
Her2 +	N	12	NR	83 (65-100)	0.47
	Y	15	77	100 (100-100)	

TBCRC 013: Palliative Surgery



Prospective studies

	Overall Survival LRS v NS	Median Survival LRS v NS	% Requiring palliative surgery in NS
Indian	41.9% v 43% at 2 years	19.2 v 20.5 months	10% at 2 years
Turkish	68% v 51% at 3 years 41.6% v 24.4% at 5 years	46 v 37 months	11% LRP at 5 years
TBCRC 013	77% v 76% at 2.5 years	71 v 65 months	4% at 2.5 years

Current RCT of primary surgery in Stage IV disease

	Number enrolled	Start date	First reporting	Protocol
Austrian NCT01015625	Active not recruiting N = 254E	Oct 2010	2021	Surgery to breast and axilla, clear margins +/- RT
US/Canadian NCT01242800 ECOG2108	Active not recruiting N= 391	Feb 2011	2022	Surgery/clear margins (?axilla) Radiotherapy CTCs / HRQoL
Japanese JCOG1017	Active N= 307	May 2011		Surgery to breast only. No RT
Turkish	Active	Feb 2016		Bone only – bx proven Surgery to breast.

When is local surgery indicated in metastatic breast cancer?

CONCLUSIONS

- Retrospective data biased
- RCT and prospective data remains inconclusive
- Turkish data with longer follow up demonstrates statistical survival advantage for LRT
- Need for palliative surgery low

UN-ANSWERED QUESTIONS

- QoL data
- Extent of LRT
 - Primary only
 - Clear margins
 - Axilla
 - RT
 - Reconstruction
- LRT before or after surgery

ABC guidelines

- Removal of the primary tumor in patients with de novo stage IV breast cancer has not been associated with prolongation of survival, with the possible exception of the subset of patients with bone only disease
- Removal of the primary can be considered in selected patients, particularly to improve quality of life, always taking into account the patient's preferences
- Some studies suggest that surgery is only valuable if performed with the same attention to detail (e.g. complete removal of the disease) as in patients with early stage disease

ABC guidelines

- A subset of patients with ABC, such as those with oligo-metastatic disease or low volume metastatic disease that is highly sensitive to systemic therapy, can achieve complete remission and a long survival.
- A multimodal approach, including local-regional treatments with curative intent, should be considered for these selected patients

When is local surgery indicated in metastatic breast cancer?

- Extent and site of metastases
- Response to treatment
- Patient co-morbidity
- HR / Her2
- Patient's preference

When is local surgery indicated in metastatic breast cancer?

- For symptoms / local control
- Within a prospective data bases / RCT
- In oligometastatic disease or very low volume disease that has had a complete response to systemic therapy but with residual disease in the breast
- Complete imaging response to treatment in breast and distant disease but relapse in breast

Questions?
