

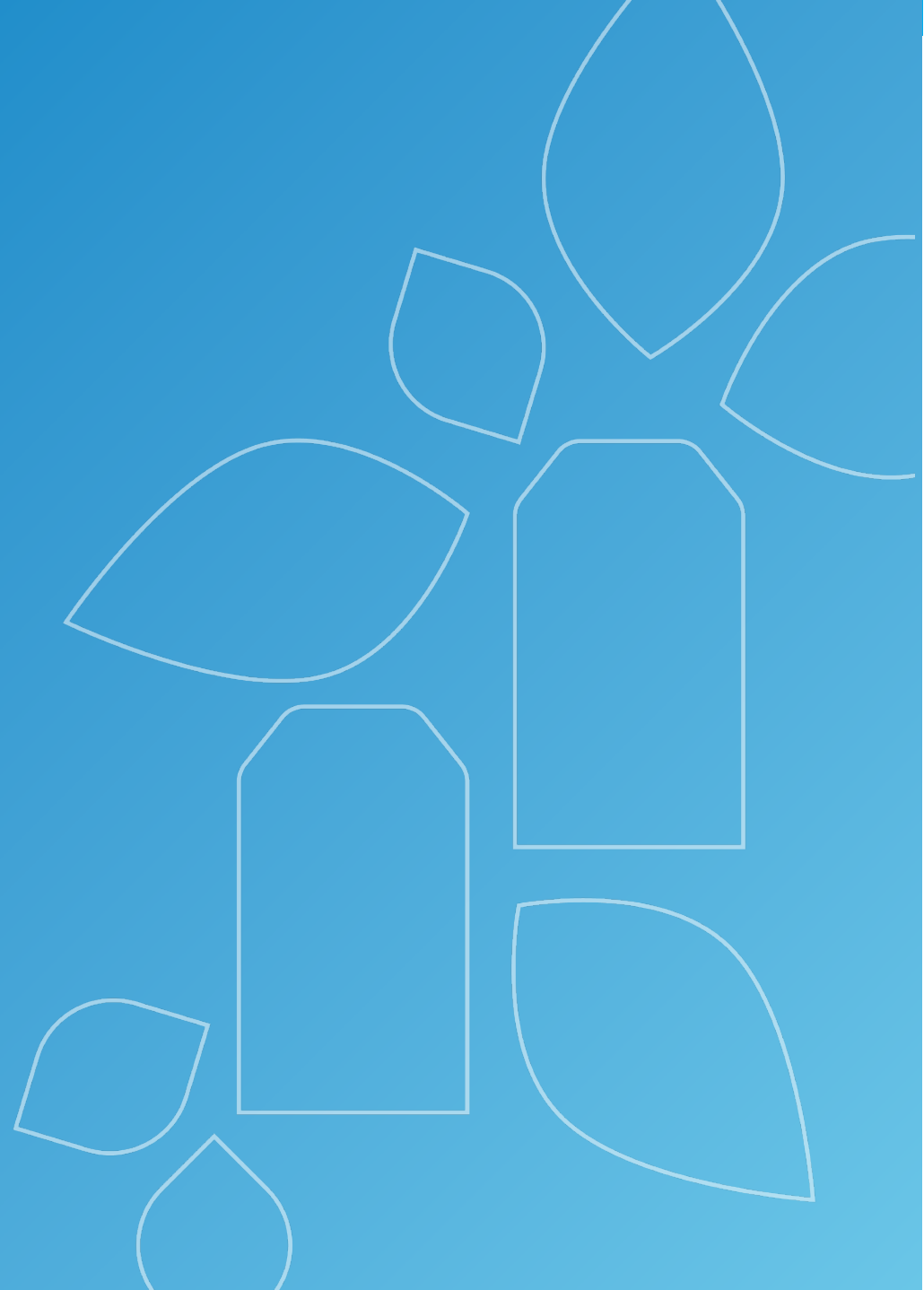


Southeastern Multidisciplinary Approaches to Cancer Symposium

Personalizing Radiation Treatment in Breast Cancer Patients

Lily Shakibnia, MD, MSc

Chief of Radiation Oncology
City of Hope



Disclosures

I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.



Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *Recognition of racial/ethnic disparities in breast cancer outcomes and access to care.*
- *Awareness of language, health literacy, and socioeconomic barriers.*



Outline

Shorter Fractionation schemes

Smaller radiation volumes (partial breast)

Genomic Assays

Omission of SLN biopsy, impact on RT decisions

Updates in post mastectomy radiation therapy PMRT/ regional nodal radiation RNI

Radiation after Neoadjuvant CT

Metastatic breast cancer



Hypofractionation

Moderate hypofractionation has been the standard of care since early 2000s

Table 1
Key studies of hypofractionation versus conventional fractionation after lumpectomy

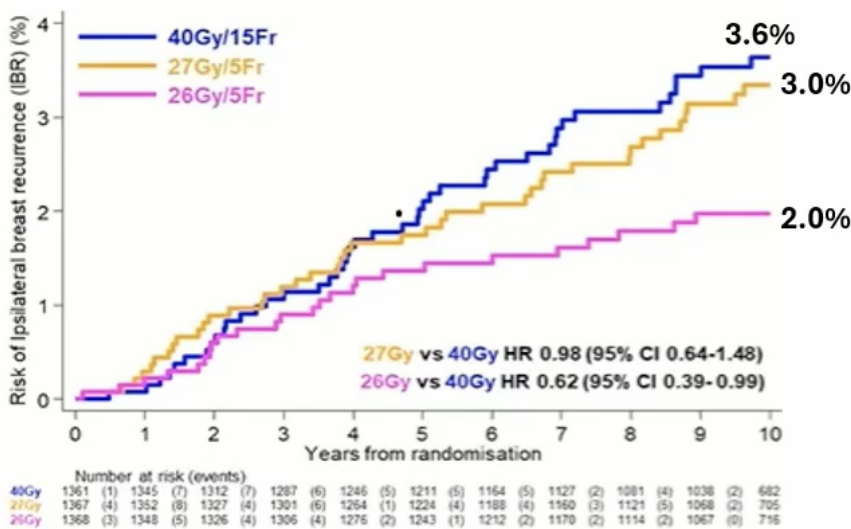
Trial	Duration of Study	No. of Patients	Follow-up (y)	Radiation Dose	Local Recurrence (%)	Toxicity
Whelan (OCOG) ¹¹	1993–1996	1234	12	50 Gy/25 F 42.56 Gy/16 F	6.7 6.2	No significant difference in cosmetic outcomes
RMH/GOC ^{6,7}	1986–1998	1410	9.7	50 Gy/25 F 42.9 Gy/13 F 39 Gy/13 F	7.9 7.1 9.1	28.8% 25.6% 42% (10 y good to excellent cosmesis)
START-A ⁹	1999–2002	2236	9.3	50 Gy/25 F 41.6 Gy/13 F 39 Gy/13 F (all over 5 wk)	6.7 5.6 8.1	No difference 50 Gy, 41.6 Gy with moderate or marked normal tissue effects; reduced induration/telangiectasia, edema with 39 Gy vs 50 Gy
START-B ⁸	1999–2001	2215	10	50 Gy/25 F 40 Gy/15 F	5.2 3.8 (10 y)	Breast shrinkage, telangiectasia, and edema significantly lower with 40 Gy
HYPO ¹¹²	2009–2014	1854	9	50 Gy/25 F 40 Gy/15 F	3.3 3.0	11.8% 9.0% Induration



Ultrahypofractionation

Fast Forward (Brunt et al. Lancet 2026 10 year update):
4096 patients
pT1-3 pN0-1, age >=18

40 Gy in 15 fractions
27 Gy in 5 fractions
26 Gy in 5 fractions



Moderate/Marked normal tissue effects breast:
40 Gy: 26.8%
27 Gy: 35.1% (HR 1.4, 1.2-1.6)
26 Gy: 28.5% (HR 1.1, 0.9-1.3)

Event (moderate/marked)	Absolute Difference 26 Gy vs. 40 Gy	Risk Ratio 26 Gy vs. 40 Gy
Any breast/CW AE	+1.9%	1.19 (0.9-1.53)
Breast distortion	+2.1%	1.59 (1.03-2.44)
Breast shrinkage	+1.3%	1.25 (0.87-1.78)
Breast induration	+2.0%	19.1 (2.57-141.9)
Telangiectasia	+0.2%	1.17 (0.58-2.37)
Breast/CW edema	+1.0%	2.35 (0.98-5.64)
Breast/CW discomfort	0.0%	0.99 (0.63-1.56)

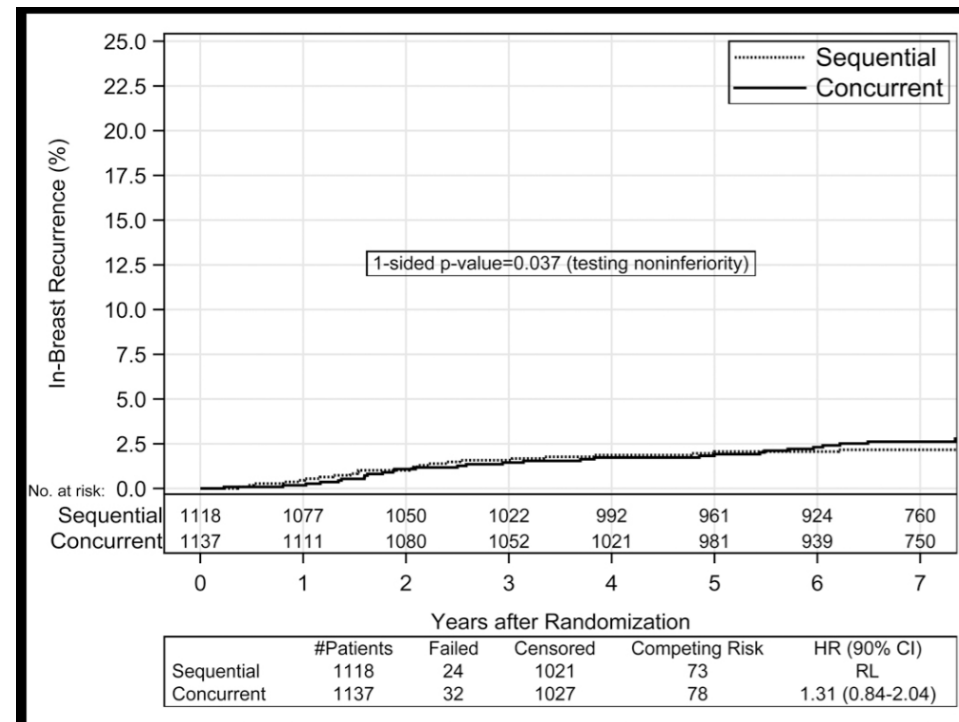


Concomitant Boost

RTOG 1005, Vicini et. Al, JCO 2026.

40 Gy with sequential boost vs 48 Gy concomitant boost

HF with SIB can be considered a standard of care for adjuvant radiotherapy after BCS



Ultra hypofractionated concomitant boost?

Tata Memorial, Wadasadawala et al. 2025:

26 Gy in 5 fractions with SIB to 32 Gy

cosmetic deterioration at 1 year was 17%, doubled to 34% at 2 years.

Mayo, Laughlin et al, 2024:

25 Gy in 5 fractions with SIB to 30 Gy (n=23)

Excellent/good ~96%

Ongoing UK Fast Forward boost trial: 26 Gy in 5 with SIB to 30 Gy

Partial breast Irradiation : 27.5 - 30 Gy in 5 fractions

	Median Age	InvasiveN0	T1	Grade 1-2	ER/PR +
U. Florence, median F/U=10.7 y (IMRT 30Gy/5 F QOD) ¹	62	86.2 %	93 %	89 %	96%
NIO Budapest, median F/U=10.2 y (MCT 34 Gy/10 F BID) ²	62	94 %	100 %	100 %	89 %
GEC-ESTRO, median F/U=6.6 y (MCT 34 Gy/10 F BID) ³	62	95 %	89 %	90 %	95 %
OCOG Rapid, median F/U=8.6 y (3DCRT 38.5 Gy/10 F BID) ⁴	61	99%	90 %	83 %	90 %
SHARE, median F/U=5.8 y (3DCRT 38.5Gy-40 Gy/10 F BID) ⁵	62	100%	100%	-	~ 95%
NSABP B39/RTOG 0413, median F/U=10 y (38.5 Gy/10 F BID)	54	84%	86%	64%	81%

¹ Livi et al. Eur J Ca 2015

² Polgar et al. Rad & Onc, 2013

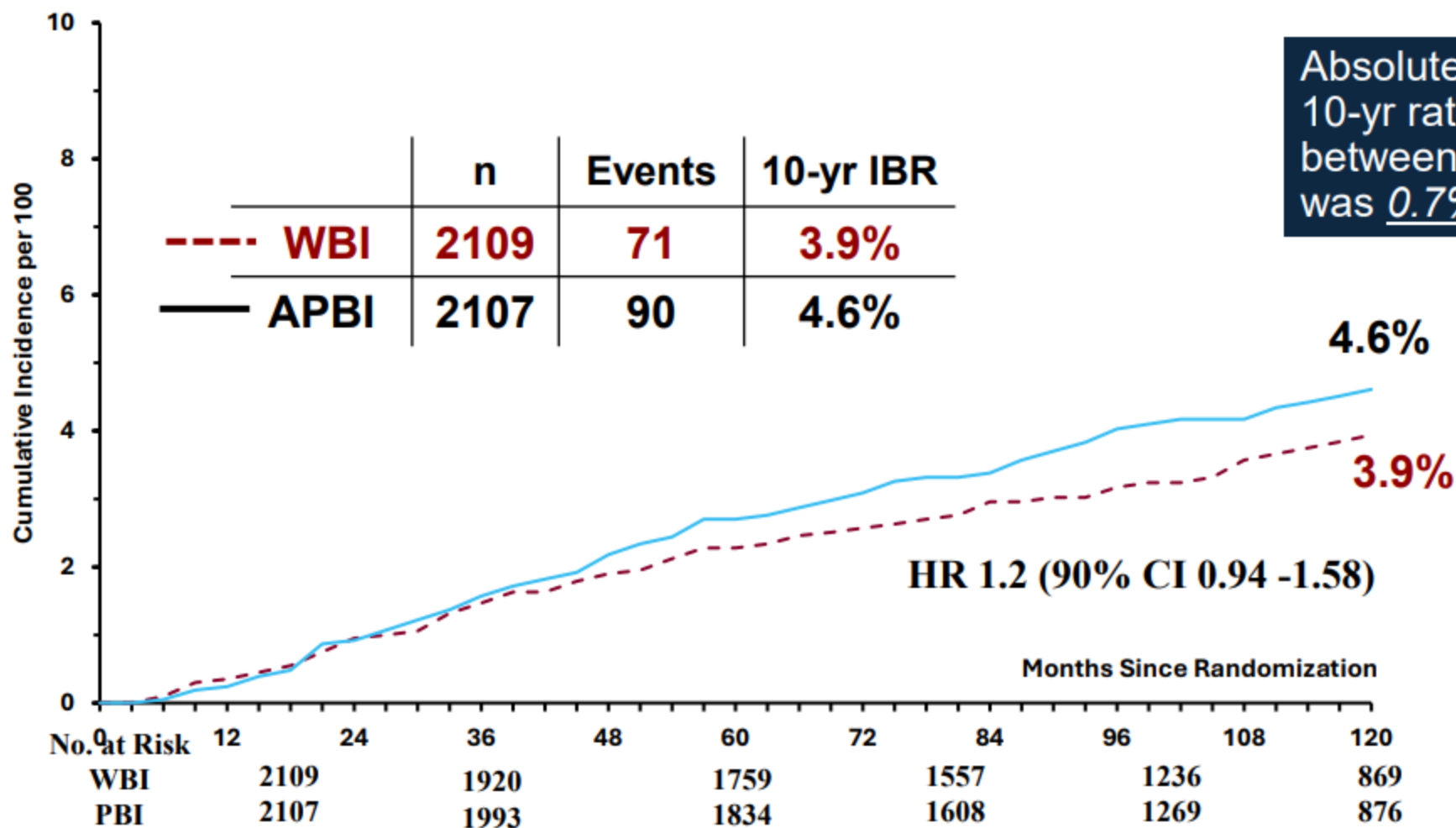
³ Strnad et al. Lancet Oncol 2016

⁴ Whelan, et al., Lancet, 2019

⁵ Belkacemi et al, ASCO 2025

⁶ Vicini et al. Lancet Oncol 2019

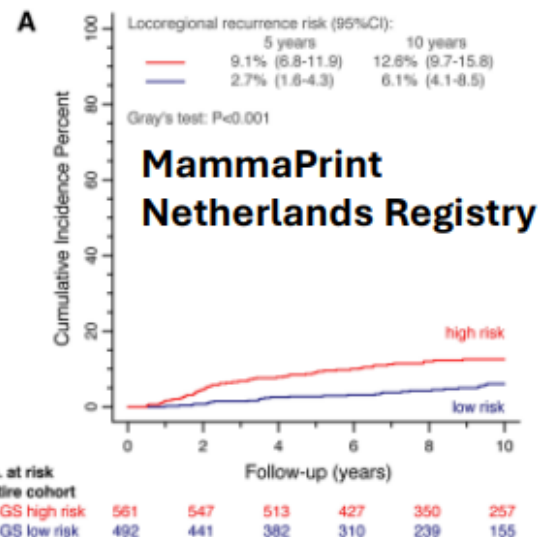
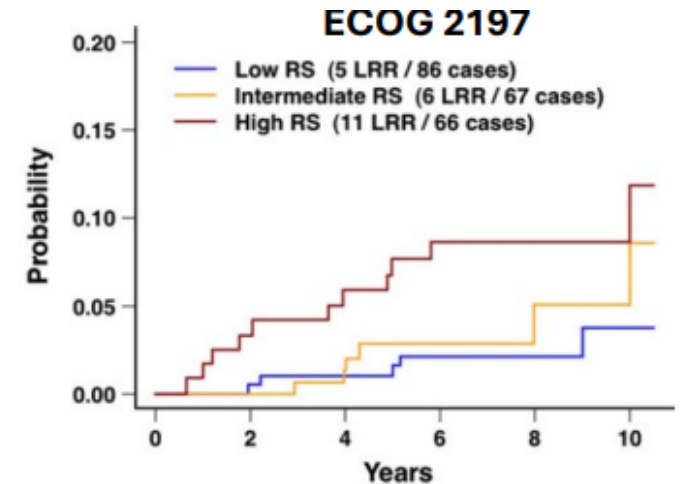
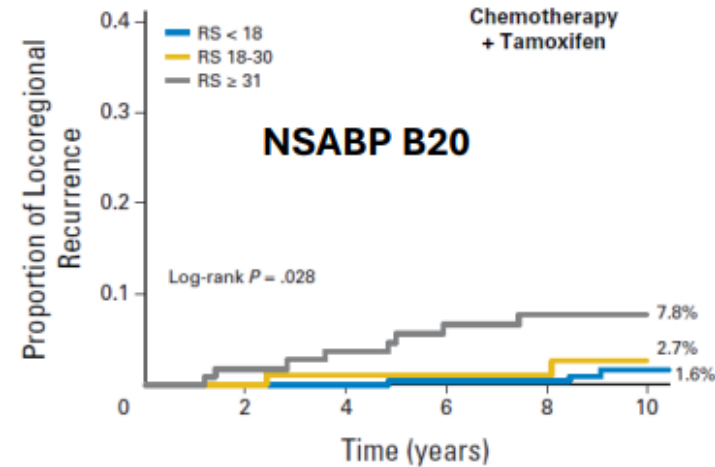
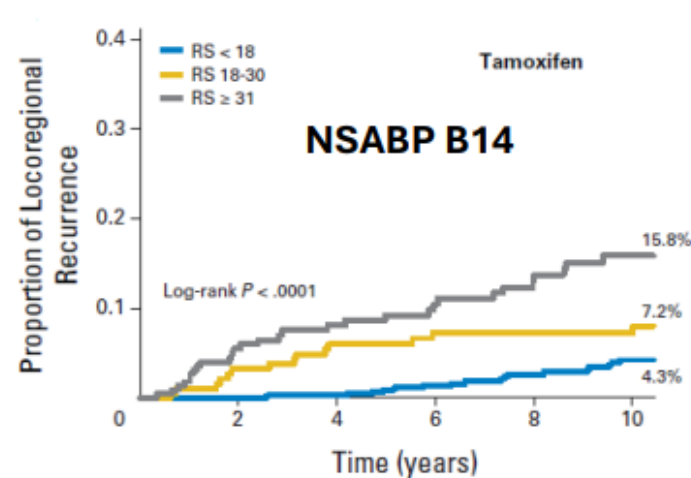
B39/0413



Absolute difference in 10-yr rate of In-BTR between PBI and WBI was 0.7%



New Era of De-Escalation : Combining Breast Cancer Subtype with Genomic Assays



New Era of De-Escalation : Combining Breast Cancer Subtype with Genomic Assays

Ongoing NRG BR007

>50 yo , pT1N0M0, ER Positive HER2- neg

Oncotype-DX RS ≤ 18

Must have had SLN biopsy

➤ Randomized to RT + ET vs ET alone

Omission of SLN biopsy

- Patients that meet criteria for omission of SLNB are those that are candidates for APBI
 - Age>50 & postmenopausal
 - cT1N0 (node negative by axillary US)
 - HR+/HER2-, grade 1-2 AGREEABLE TO WHOLE BREAST RT & endocrine therapy
 - Caution in those with lobular histology
- Risk of macrometastases in these patients is ~8-10%

Our approach:

≤pT1c; grade 1-2; no LVSI; low risk by genomic assay

- If meet all criteria: APBI may still be an option
- If any of the criteria not met, discuss if SLNB needed or proceed with whole breast RT

DCIS : individualizing risk : Genomic Assays

Oncotype DCIS score
DCISionRT

Ongoing trials:

OCOG Elisa trial	NRG CC 2416:
DCIS < 2.5 cm in size Age > 45 yo S/p lumpectomy margins > 2 mm Any Grade, Any ER/PR Oncotype DCIS Score IBR risk < 10% by 10 years Observation without RT : prospective cohort study	DCIS non palpable Age >18 yo S/p lumpectomy margins > 2 mm Any Grade, Any ER/PR DCISion RT low risk score <=2.8 Randomized to RT vs no RT



PMRT and RNI

2014: EBCTCG Meta analysis PMRT

2015: NCIC MA.20 Phase III Clinical Trial 10 yr

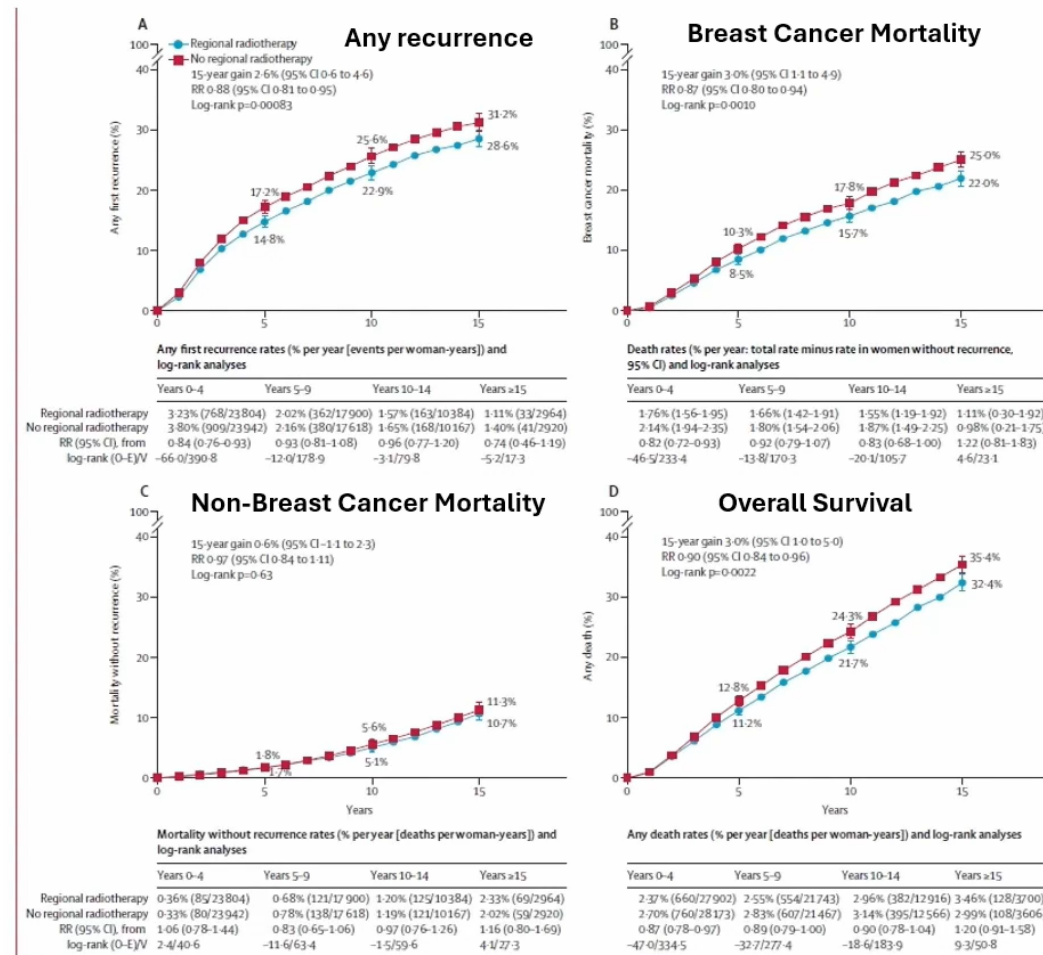
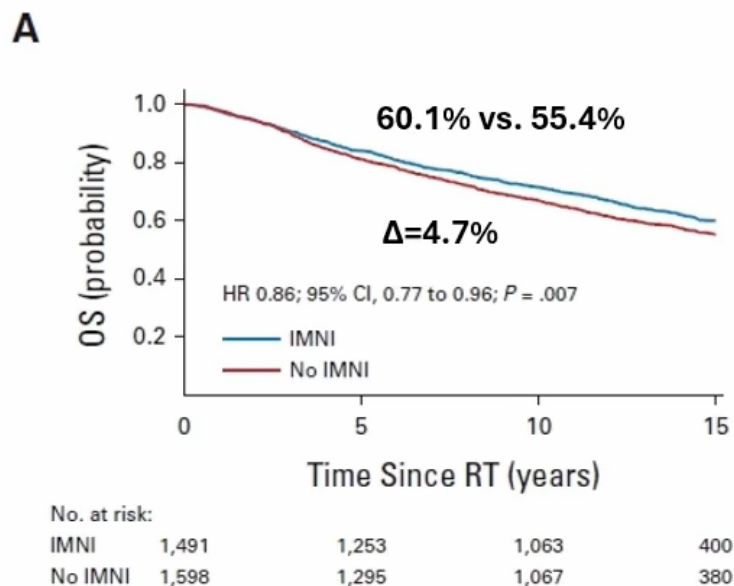
2015: EORTC 22922/10925 Phase III Clinical Trial 10yr

2016: DBCG IMN Prospective Trial

2021: EORTC 22922/10925 Phase III Clinical Trial 15yr

2023: EBCTCG Meta analysis RNI →

2025: DBCG IMN 2 Prospective Trial ↓



Hypofractionated Regional Nodal Irradiation

Chestwall and/or breast and regional nodal irradiation has historically used conventional fractionation 48-50 Gy / 2 Gy per treatment for 5-6 weeks

Multiple Randomized trials have established that hypofractionated RNI has equivalent LRR, and toxicity to standard fractions, including reconstruction complications

	Beijing, China	FABREC	RT CHARM
No. of Patients	820	400	825
Study years	2008-2016	2018-2021	2018-2021
Stage eligibility	pN2; T3-T4	Stage 0-III (T4 excl)	N1/N2, T3N0 (T4 excl)
Median f/u (years)	4.9	3.4	3.3
Treatment arms	CF: 50 Gy/25 F HF: 43.5 Gy/15 F	CF: 50 Gy/25 F HF: 42.56 Gy/16 F	CF: 50 Gy/25 F HF: 42.56 Gy/16 F
Chemotherapy (%)	100%	68%	88%
RNI	100% (0% IMNs)	CF: 87% HF: 90%	100% (100% IMNs)
Reconstruction	0%	100% (implant)	100% (implant or AR)
LRR	CF: 8.1% HF: 8.3%	CF: 1 LRR HF: 1 LRR	CF: 1.9% HF: 1.5%
Acute Grade 3+ tox.	CF: 8% HF: 3%	Grade 3 CW Toxicity CF: 9.7% HF: 10.5%	CF 5.5% HF: 5.0%
Late Toxicity	CF: 1% HF: 1%		CF: 5.5% HF: 6.1%
Reconstruction Comp.	N/A	HR for HF: 1.02 (0.52-2.0)	CF: 12.2% HF: 14.2%



What about ultrahypofractionated PMRT/WBI with RNI?

UK Nodal fast forward study, Murray Brunt et al. 2026 :

Axillary radiotherapy (levels 1–4), no IMN coverage

Not powered for efficacy, excluded IMN coverage, and lacks long-term follow-up

Efficacy data for this schedule in the axillary nodal radiotherapy setting are reassuring; however, sample size limits precision of estimation for this subgroup on its own.

Deescalation of PMRT/RNI

Can we identify patients with 1-3 positive nodes with low risk by approaching RNI-PMRT by breast cancer subtype?

Ongoing MA 39 Tailor RT Phase III trial:

>40 yo

1-3 + axillary metastases (or pT3N0 or N1mic)

ER+ and/or PR+, HER2-Negative

Oncotype-DX RS $\leq$ 25

➤ Being randomized to ET + Breast RT/RNI or ET + Breast RT alone

Radiation after Neoadjuvant CT

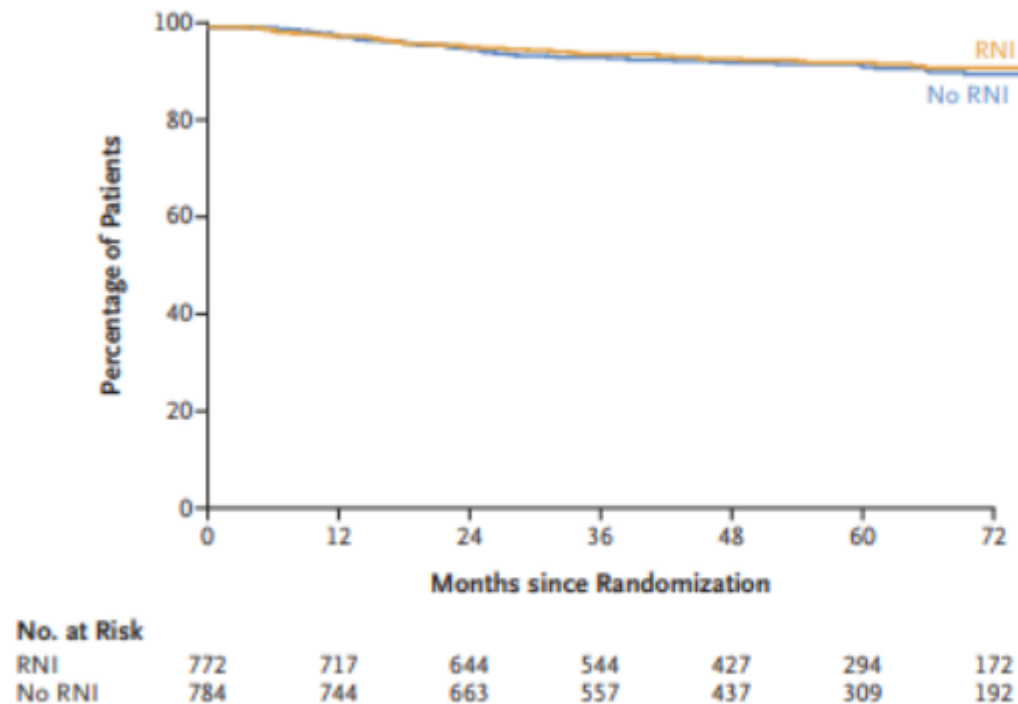
NSABP B51, Mamounas et al. 2025

cT1-3 N1

Neoadj CT (+anti HER2 if HER2+)

Node pCR, ypN0

Randomized to RNI vs no RNI

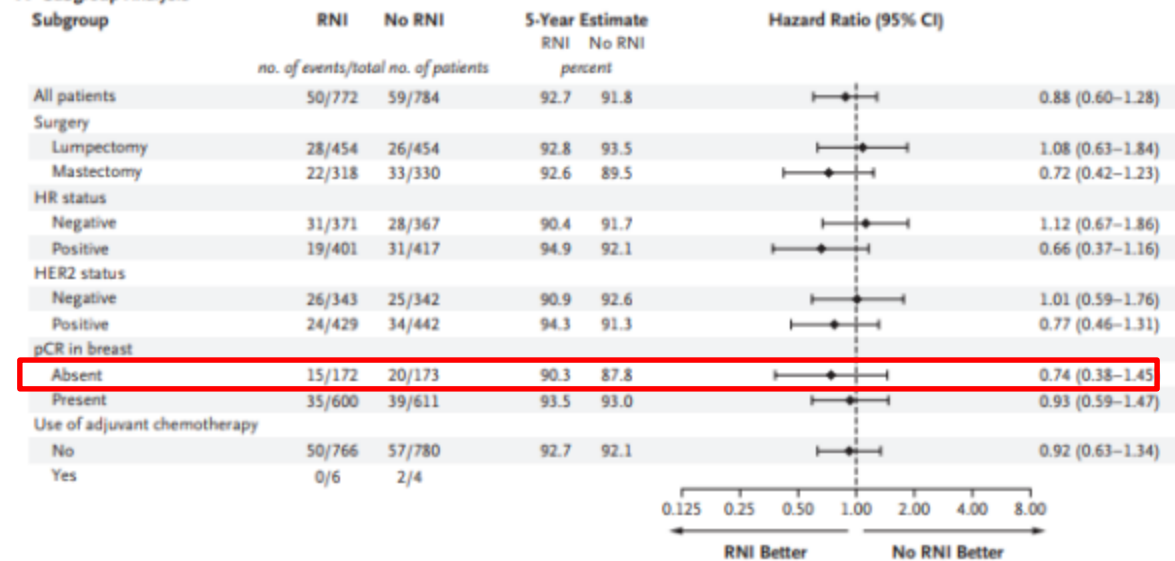


	No. of Events	5-Year Estimate percent
RNI	50	92.7
No RNI	59	91.8

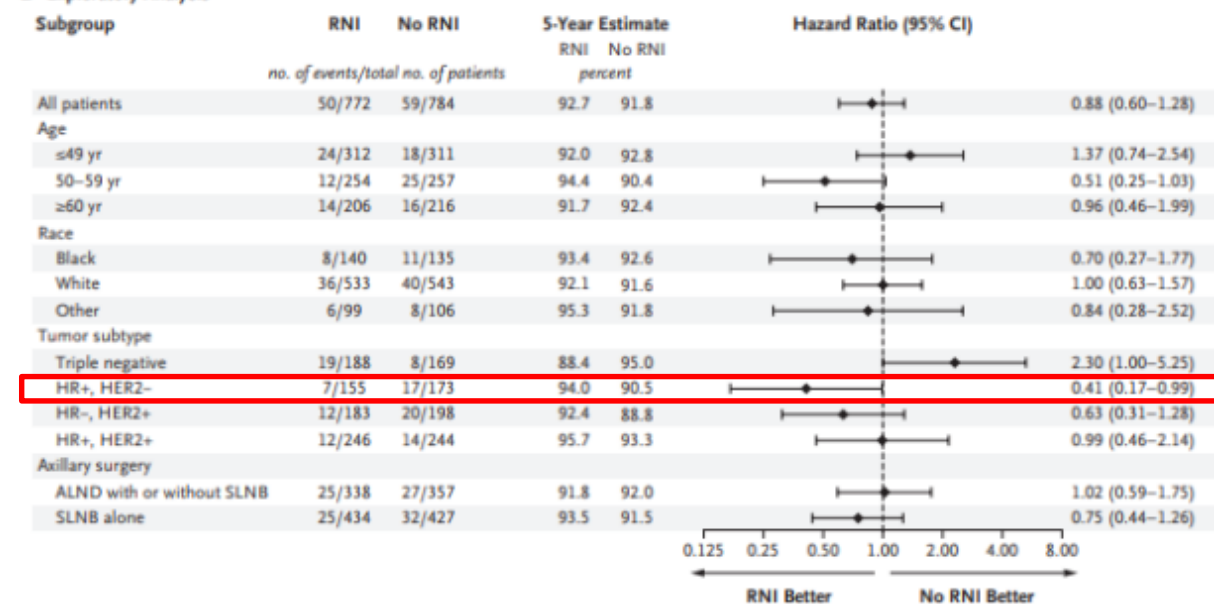
Hazard ratio for invasive
breast cancer recurrence or
death from breast cancer
0.88 (95% CI, 0.60–1.28)
P=0.51



A Subgroup Analysis



B Exploratory Analysis



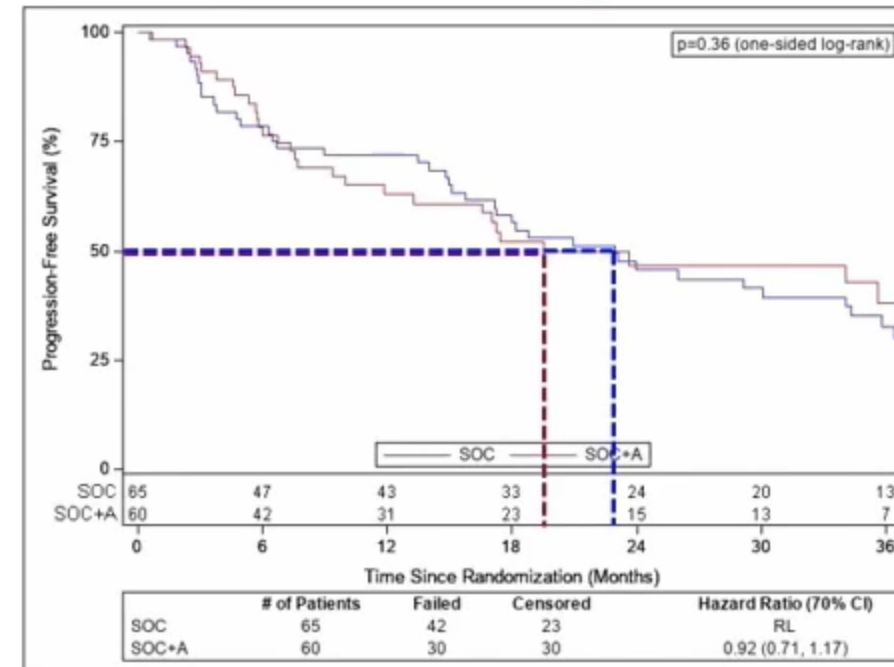
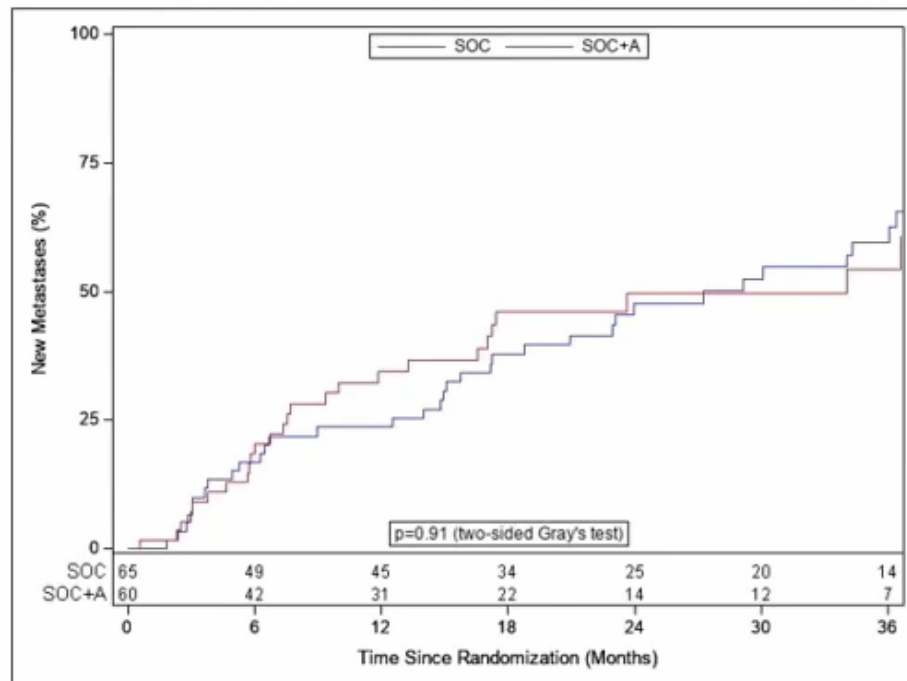
Radiation therapy for Metastatic breast cancer

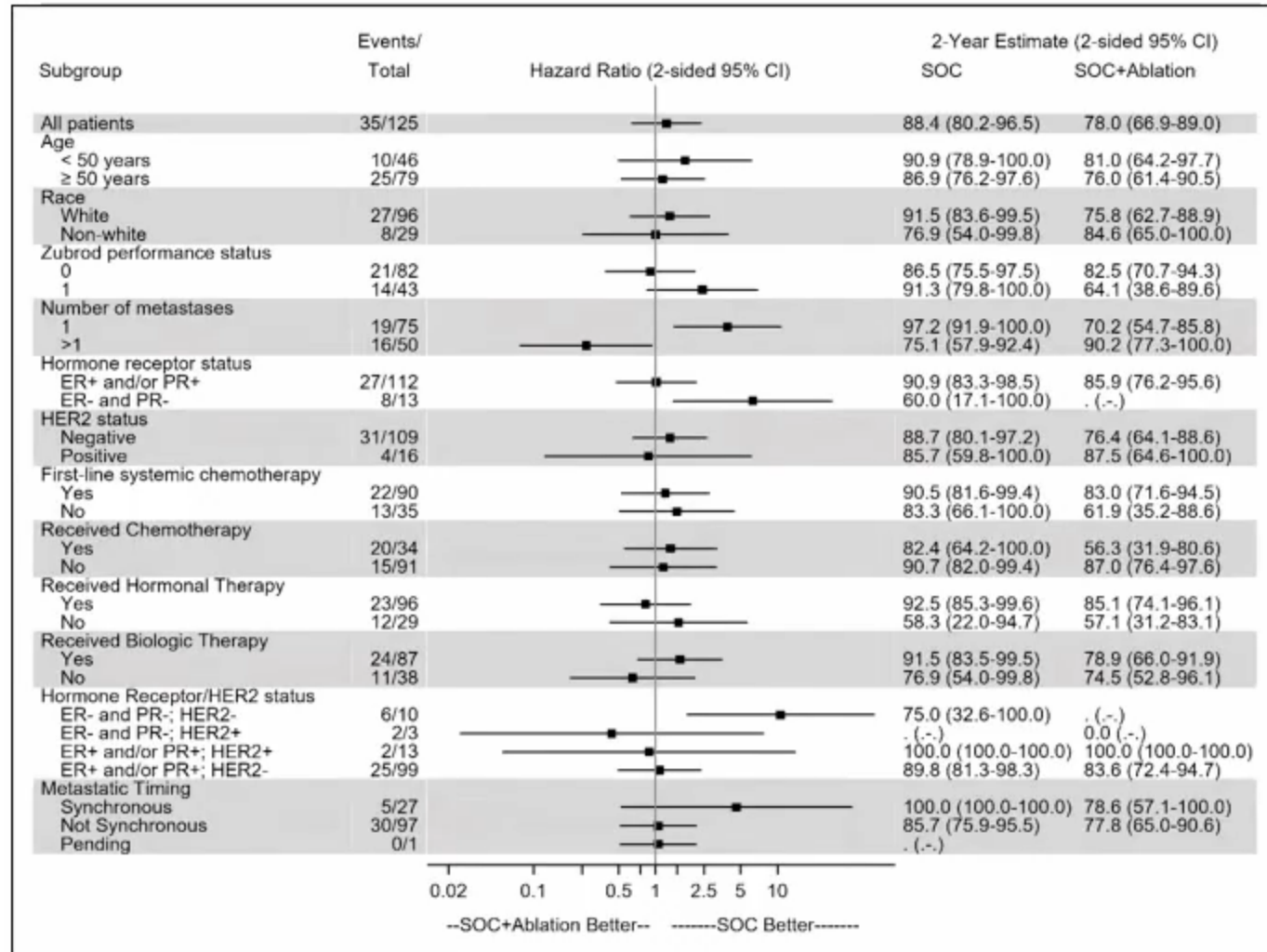
NRG BR002:

Controlled locoregional disease and ≤ 4 Metastases

Randomized to Total ablation of all metastases vs Standard of care

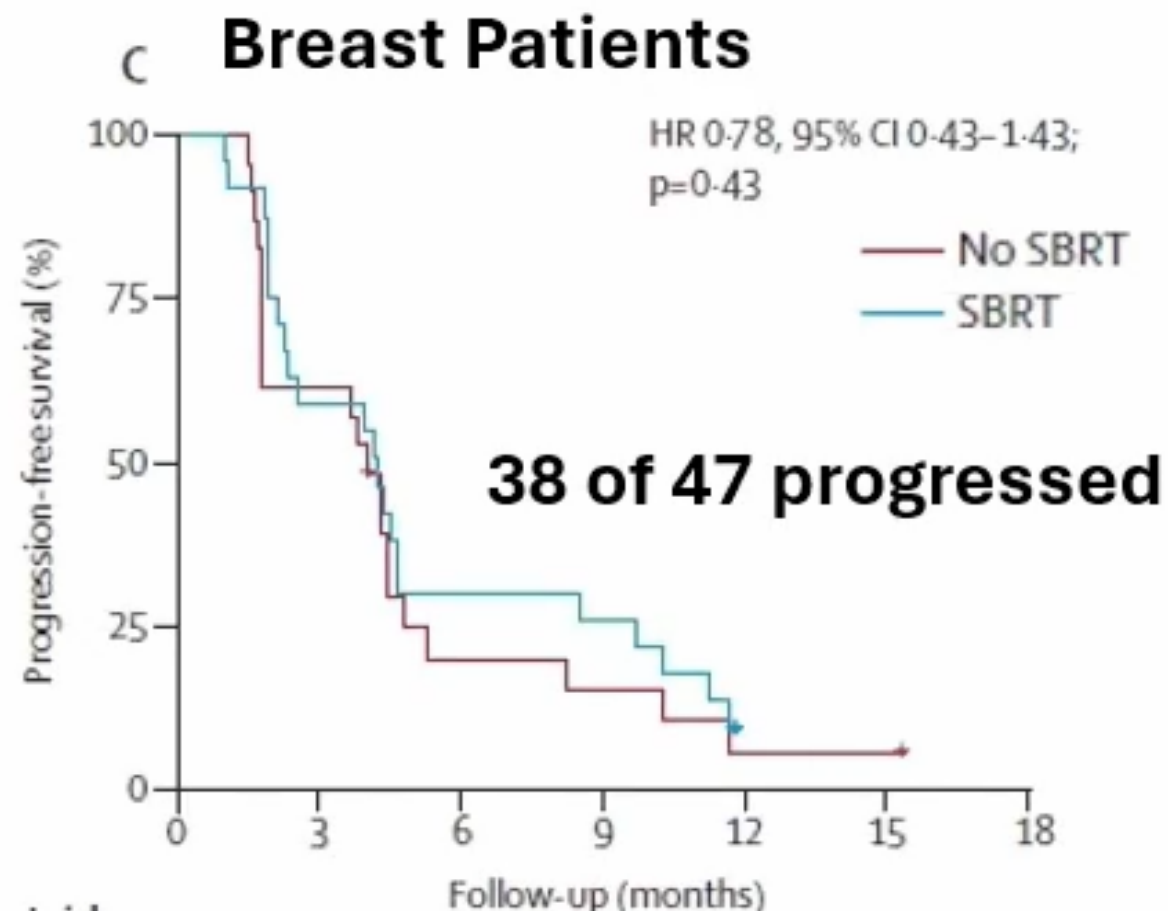
Most patients had 1 metastatic lesion (60%) and were ER/PR positive / HER2 negative (80%)





What about Oligoprogressive disease?

CURB Trial , Tsai et al. 2024



Clinical Question #1

45 year old premenopausal woman post lumpectomy and sentinel node biopsy for a pT2 (2.4 cm) N0 (0/2 sn) M0 grade 3 invasive ductal carcinoma resected with negative margins, ER/PR positive, HER2 negative, oncotype 18.

What would your preferred adjuvant radiation approach be?

- A. 30 Gy in 5 fractions partial breast radiation
- B. 50 Gy in 25 fractions to the whole breast followed by a 10 Gy in 4 fractions boost to the lumpectomy cavity
- C. 40 Gy in 15 fractions to the breast with a simultaneous boost to 48 Gy in 15 fractions to the lumpectomy cavity
- D. 26 Gy in 5 fractions to the breast with simultaneous boost to 30 Gy to the lumpectomy cavity



Clinical Question #2

A 56 year old postmenopausal woman presented with a cT3 N1 M0 left breast, UOQ, invasive ductal carcinoma, grade 3, triple negative. She was treated with neoadjuvant chemotherapy and is now post mastectomy and ALND ypT0 N1 with 1 macrometastasis in 1 of 5 axillary nodes with no extranodal extension. She has an expander in place and is planning on reconstruction

What adjuvant radiation therapy regimen would you favor :

- A. Omit adjuvant radiation therapy
- B. Adjuvant chest wall and regional nodal radiation including IMN to 50 Gy in 25 fractions
- C. Adjuvant chest wall and regional nodal radiation including IMN to 42.56 Gy in 16 fractions
- D. Adjuvant chest wall and regional nodal radiation excluding IMN to 42.56 Gy in 16 fractions



Questions?

