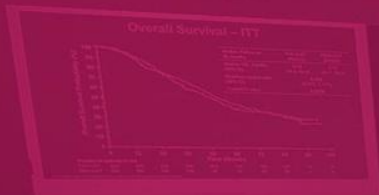
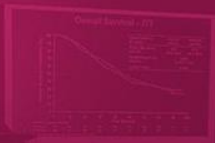


OFFICIAL  
best of SABCS



CONFERÊNCIA BRASILEIRA DE  
**CÂNCER DE MAMA**

LACOG - GBECAM 2024



CONFERÊNCIA BRASILEIRA DE  
**CÂNCER DE MAMA**  
LACOG - GBECAM 2024

REALIZAÇÃO



# Descalonamento da radioterapia adjuvante: *para quem?*

Arthur Accioly Rosa

Titular de Radioterapia | *Oncoclínicas Salvador – HSI*

Lider de Especialidade Radioterapia | *Oncoclínicas&CO*

Diretor de Defesa Profissional | *Sociedade Brasileira de Radioterapia*

De acordo com as normas do Conselho Federal de Medicina (número 1595/2000) e de Vigilância Sanitária RDC 102/2000

Últimos 12 meses

Advisory Board: *Novartis*

Speaker fee: *Roche, Astellas, SBM e Instituto Oncoclínicas*



# O que é Descalonamento?

MICHAELIS Português Inglês Espanhol Alemão Italiano Francês

Dicionário Brasileiro da Língua Portuguesa

Sobre o dicionário · Como consultar · Noções gramaticais · Créditos


Português Brasileiro ·

O verbete não foi encontrado.

Merriam-Webster SINCE 1828 GAMES & QUIZZES THESAURUS WORD OF THE DAY

[Dictionary](#) [Thesaurus](#)

## de-escalate verb

 Save Word

de-es-ca-late | \ ( )dē-'e-skā-lāt ( ), nonstandard -'e-skyə- \

**de-escalated; de-escalating; de-escalates**

### Definition of *de-escalate*

*transitive verb*

: LIMIT sense 2b

// *de-escalate* production

// tried to *de-escalate* the tension

*intransitive verb*

: to decrease in extent, volume, or scope

// violence began to *de-escalate*

Reduzir extensão, volume ou escopo

# Cirurgia CONSERVADORA

## Impacto da Radioterapia

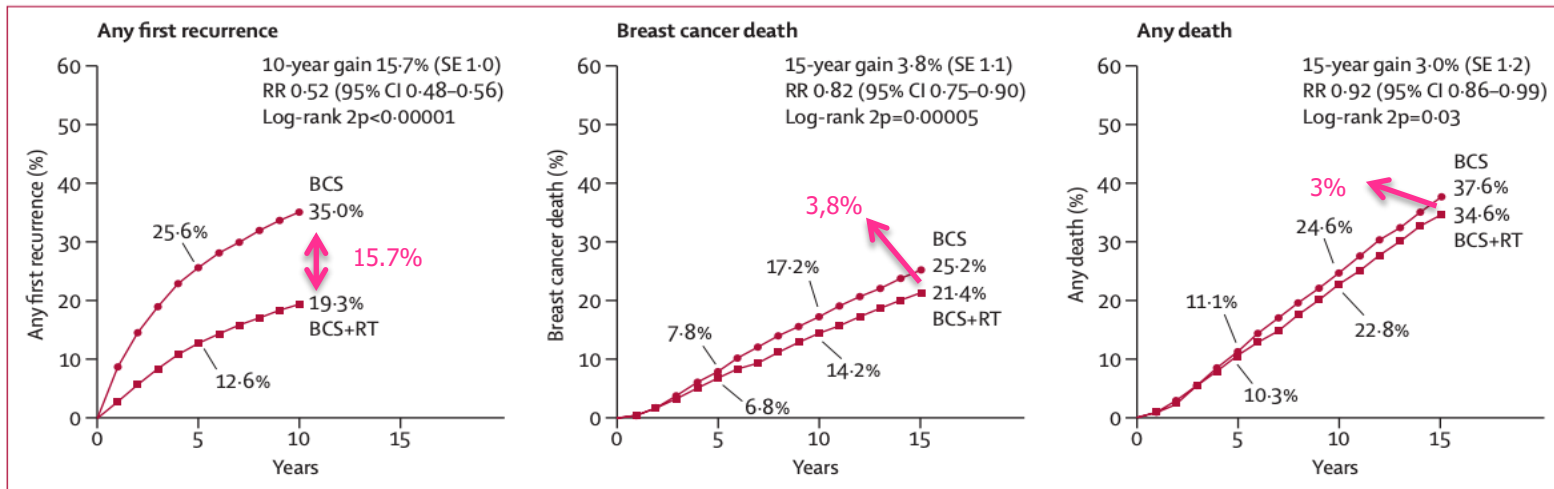
Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials



Early Breast Cancer Trialists' Collaborative Group (EBCTCG)\*

10.801 pacientes (67% com N0)

17 estudos randomizados



“Cerca de 1/5 das recidivas locais evoluem a uma morte por câncer de mama”

# Breast cancer survival by molecular subtype: *a population-based analysis of cancer registry data*

## Different Diseases

### Ontario Cancer Registry

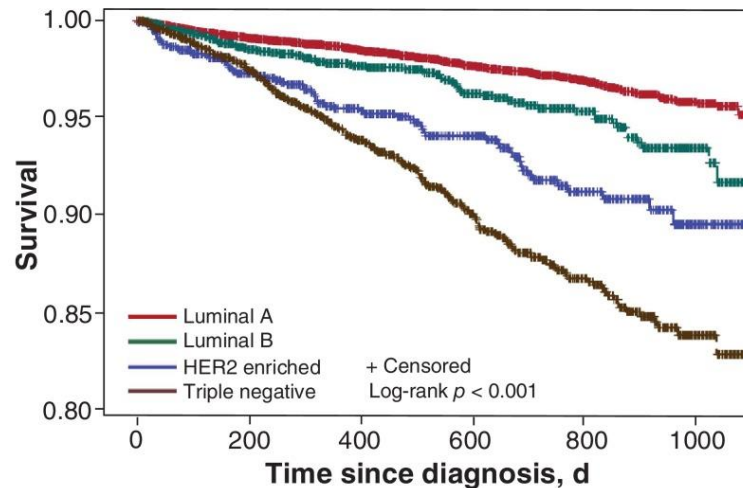
29 833 breast cancer cases  
diagnosed between 2010 and 2012

Cancers were categorized into 4 molecular subtypes:

- 1) **Luminal A** (*estrogen-receptor-positive and/or progesterone-receptor-positive [ER+ and/or PR+] and negative for human epidermal growth factor receptor 2 [HER2-]*)
- 2) **Luminal B** (*ER+ and/or PR+/HER2+*)
- 3) **HER2-enriched** (*ER- and PR-/HER2+*)
- 4) **Triple-negative** (*ER- and PR-/HER2-*).

We estimated associations with predictor variables (age, stage at diagnosis, histologic type, comorbidity and place of residence [urban or rural]) using a multivariate Cox proportional hazards model. Likelihood ratio testing was used to evaluate differences in risk of death.

Kaplan-Meier plot of **overall breast cancer survival** by molecular subtype



Fallahpour et al CMAJ Open. 2017 Jul-Sep; 5(3): E734–E739

## SPECIAL ARTICLE

# De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017

2017

G. Curigliano<sup>1\*,†</sup>, H. J. Burstein<sup>2†</sup>, E. P. Winer<sup>2</sup>, M. Gnant<sup>3</sup>, P. Dubsy<sup>3,4</sup>, S. Loibl<sup>5</sup>, M. Colleoni<sup>1</sup>, M. M. Regan<sup>6</sup>, M. Piccart-Gebhart<sup>7</sup>, H.-J. Senn<sup>8</sup> & B. Thürlimann<sup>9</sup>, on behalf of the Panel Members of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2017

# Consenso

## Painel de especialistas

**Table 2. Treatment recommendations for loco-regional therapy**

Local therapy	Theme	De-escalation	Escalation
Radiotherapy	Hypofractionation	Strong recommendation for ages $\geq 50$ and node negative	Consider standard radiotherapy regimens for all others
	Partial breast irradiation	Consider for ASTRO/ESTRO low risk group, especially when receiving adjuvant endocrine therapy	Consider whole breast irradiation for all others
	Boost	Omit boost in patients $\geq 60$ years, low grade, or favorable biological profile	Consider boost in other patients
	Post-mastectomy radiation therapy (PMRT)	Consider omitting radiotherapy in women with pT1–pT2, pN1 (1–3), and favorable biological profile	PMRT in patients with pT3 or four or more positive lymph nodes
	Regional nodal irradiation (RNI)	Consider omitting RNI in N1 (1–3 positive lymph nodes) in the absence of adverse clinical factors	RNI in N1 cancers and adverse clinical features ( $\leq 40$ years, low or negative estrogen receptor (ER), G3, extensive lympho-vascular invasion) or $> 3$ positive nodes



# De-escalating

Omission of radiotherapy  
in low risk patients



# CALGB9343

RT DE-ESCALATION TRIAL

## Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes, Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirincione, Donald A. Berry, Beryl McCormick, Hyman B. Muss, Barbara L. Smith, Clifford A. Hudis, Eric P. Winer, and William C. Wood

- 636 pts (>70 yo)
- 1994 to 1999
- Stage T1N0M0 (ER+)
- RT+TMX vs TMX**
- Primary endpoints

- ✓ Time to local recurrence
- ✓ Time to regional recurrence
- ✓ Mastectomy frequency
- ✓ Cancer specific survival
- ✓ Time to metastasis
- ✓ Overall survival

Hughes KS. al. JCO 2013; 31(19):2382-7

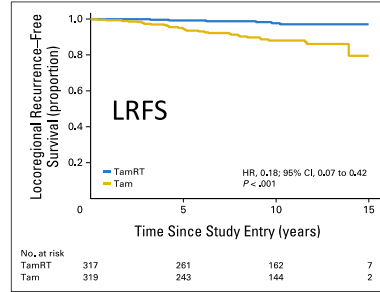


Fig 2. Time to local or regional recurrence. HR, hazard ratio; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

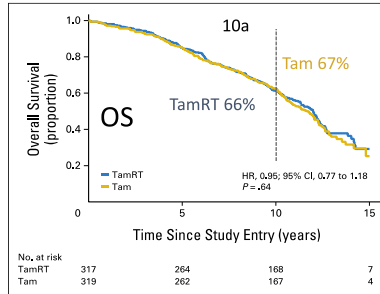


Fig 5. Overall survival. HR, hazard ratio; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

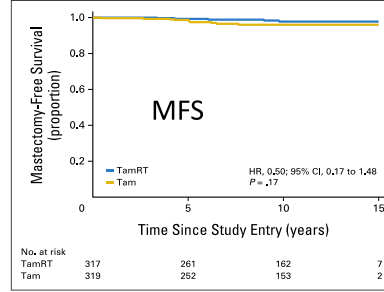


Fig 3. Time to subsequent mastectomy. HR, hazard ratio; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

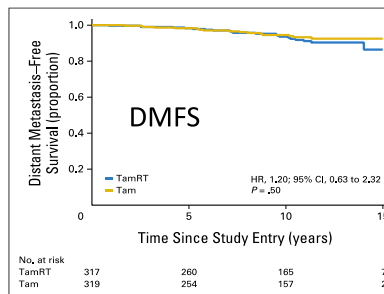


Fig 4. Time to distant metastasis. HR, hazard ratio; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

Freedom from Relapse in 10yrs

RT+TAM	TAM
98%	90%

8% difference

No difference in OS

# CALGB9343

## RT DE-ESCALATION TRIAL

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

### Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes, Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirincione, Donald A. Berry,  
Beryl McCormick, Hyman B. Muss, Barbara L. Smith, Clifford A. Hudis, Eric P. Winer, and William C. Wood

## CONCLUSIONS

- RT improves local control
- No benefit in overall survival
- Adjuvant only TMX approach is an option for older women with ER+

## CRITICS

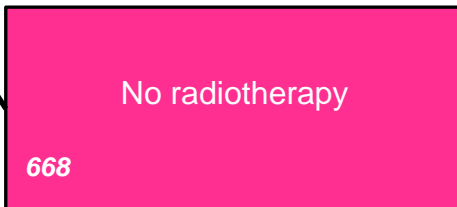
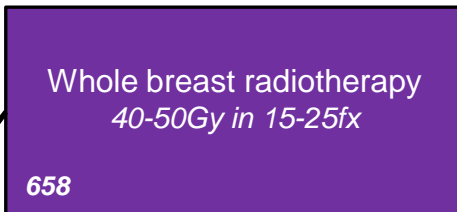
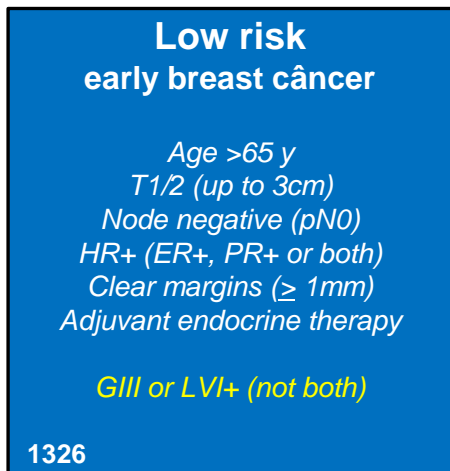
- *No subgroup analysis conducted*
- *EBCCTG shows that GIII is a risk factor for recurrence with or without TMX*
- *Other factors such as LVI+, ki67 and Her2*
- *Did not address factors such as KPS and clinical comorbidities*
- *Very low risk group and an observation group should be used*

# PRIME II

RT DE-ESCALATION TRIAL

Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial

Ian H Kunkler, Linda J Williams, Wilma J L Jack, David A Cameron, J Michael Dixon, on behalf of the PRIME II investigators



**Primary endpoint:**  
ipsilateral breast cancer recurrence

**Secondary endpoints:**  
regional recurrence  
ontralateral breast cancer  
distant metástases  
disease-free survival  
overall survival

## Multicenter phase III

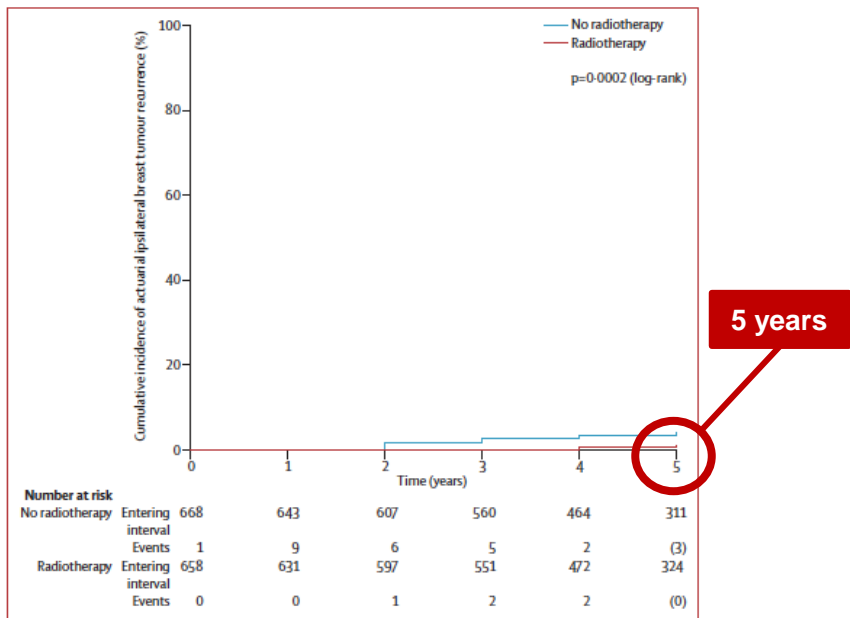
76 centers (UK, Greece, Australia, and Serbia)

Kunkler IH, et al. Lancet Oncol. 2015;(3):266-73.

# PRIME II

RT DE-ESCALATION TRIAL

## Local Recurrence



## Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial

Ian H Kunkler, Linda J Williams, Wilma J L Jack, David A Cameron, J Michael Dixon, on behalf of the PRIME II investigators

LR: 1,3% versus 4,1%

	No radiotherapy (n=668)	Radiotherapy (n=658)
Regional recurrence	1.5% (0.5-2.4) (8)	0.5% (0-1.0) (3)
Distant recurrence	1.0% (0.1-1.7) (4)	0.5% (0-1.0) (5)
Contralateral breast cancer	0.7% (0.01-1.2) (4)	1.5% (0.4-2.5) (7)
New (non-breast) cancer	4.3% (2.6-5.7) (29)	3.7% (2.1-5.0) (26)

Data are Kaplan-Meier estimates of survival (95% CI) (number of events).

**Table 4: Other recurrences (as first event) or new cancers after 5 years**

Kunkler IH, et al. Lancet Oncol. 2015;(3):266-73.

# PRIME II

## RT DE-ESCALATION TRIAL

	No radiotherapy (n=668)	Radiotherapy (n=658)	p value
Local recurrence	26 (4%)	5 (<1%)	
Tumour size (mm)			
0-10	10/258 (4%)	3/265 (1%)	0.04
10.1-20	10/326 (3%)	1/319 (<1%)	0.008
20.1-30	6/84 (7%)	1/74 (1%)	0.08
Margins			
<1 mm	1/10 (10%)	0/9 (0%)	0.32
1-5 mm	10/315 (3%)	4/296 (1%)	0.15
>5 mm	9/227 (4%)	1/239 (<1%)	0.01
Re-excision	6/112 (5%)	0/110 (0%)	0.01
Grade			
1	8/271 (3%)	2/292 (<1%)	0.04
2	15/368 (4%)	3/352 (<1%)	0.006
3	3/23 (13%)	0/13 (0%)	0.21
Age (years)			
65-69	8/308 (3%)	2/331 (<1%)	0.05
≥70	18/360 (5%)	3/327 (1%)	0.002
Lymphovascular involvement			
No	24/631 (4%)	5/628 (<1%)	0.0004
Yes	2/32 (6%)	0/27 (0%)	0.29
Oestrogen receptor status			
Rich	20/593 (3%)	5/601 (<1%)	0.002
Poor	6/65 (9%)	0/55 (0%)	0.03

## Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial

Ian H Kunkler, Linda J Williams, Wilma J L Jack, David A Cameron, J Michael Dixon, on behalf of the PRIME II investigators

# No RT

Up to 9-13%

local recurrence

GIII and ER- status

< 5% of patients were GIII or LVSI+

12% were T2

Kunkler IH, et al. Lancet Oncol. 2015;(3):266-73.

# PRIME II

RT DE-ESCALATION TRIAL

## Treatment received after local recurrence

	No radiotherapy (n=26)	Radiotherapy (n=5)
Patients with data available	23	4
Total undergoing mastectomy	12	2
Mastectomy	5	0
Mastectomy and endocrine treatment	4	2
Mastectomy, radiotherapy, and endocrine treatment	3	0
Total undergoing wide local excision	11	2
Wide local excision	0	1
Wide local excision and endocrine treatment	2	1
Wide local excision and radiotherapy	3	0
Wide local excision, radiotherapy, and endocrine treatment	6	0

Data are number of patients.

**Table 3: Treatment received after local recurrence**

## Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial

Ian H Kunkler, Linda J Williams, Wilma J L Jack, David A Cameron, J Michael Dixon, on behalf of the PRIME II investigators

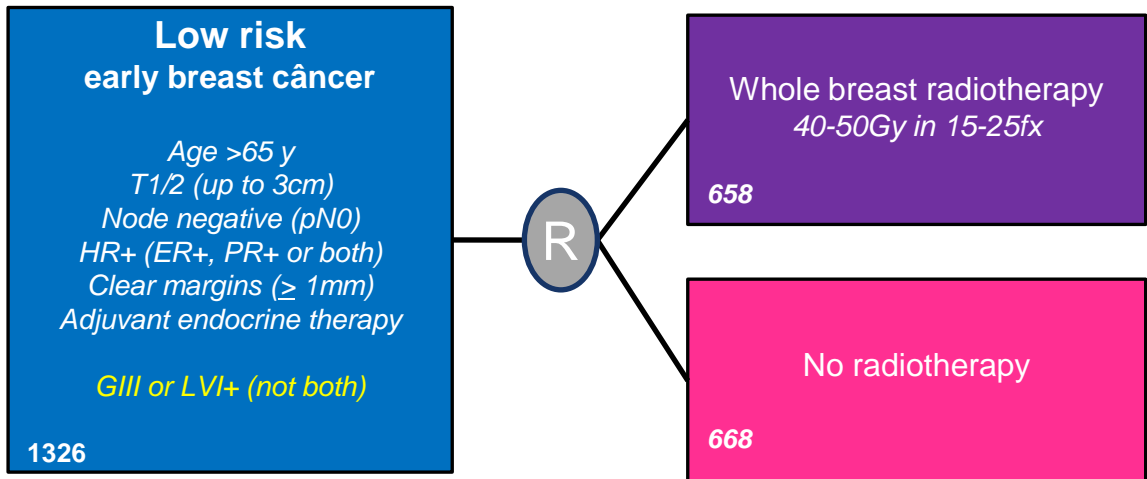
Half of the relapses on the **NO RT** arm underwent mastectomy

Kunkler IH, et al. Lancet Oncol. 2015;(3):266-73.

# PRIME II

RT DE-ESCALATION TRIAL

9.1 yrs  
medium  
follow up



## Multicenter phase III

76 centers (UK, Greece, Australia, and Serbia)

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 16, 2023

VOL. 388 NO. 7

Breast-Conserving Surgery with or without Irradiation  
in Early Breast Cancer

Ian H. Kunkler, M.B., B.Chir., Linda J. Williams, Ph.D., Wilma J.L. Jack, M.B., Ch.B., David A. Cameron, M.D.,  
and J. Michael Dixon, M.D.

### Primary endpoint:

ipsilateral breast cancer recurrence

### Secondary endpoints:

regional recurrence  
contralateral breast cancer  
distant metastases  
disease-free survival  
overall survival

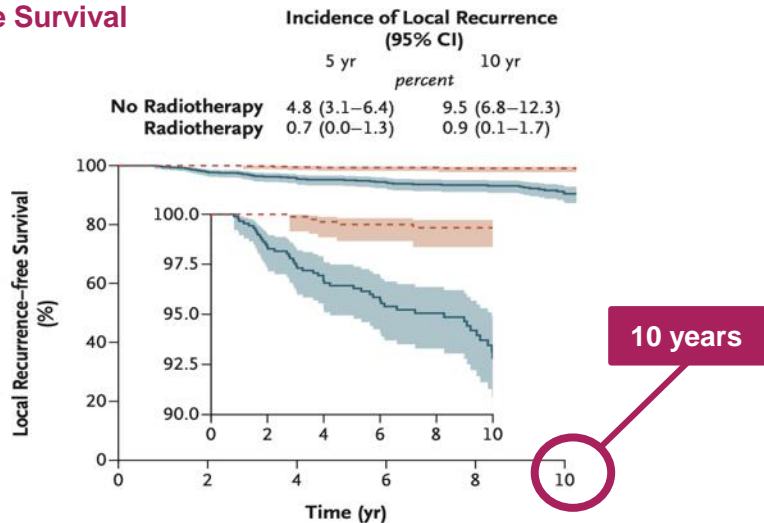
Kunkler IH, et al. NEJM. 2023; 388(7) :585-94



# PRIME II

RT DE-ESCALATION TRIAL

Local Recurrence  
Free Survival



**No. at Risk**

No radiotherapy	668	628	569	463	369	209
Radiotherapy	658	625	585	478	383	207

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 16, 2023

VOL. 388 NO. 7

Breast-Conserving Surgery with or without Irradiation  
in Early Breast Cancer

LR: 0,9% versus 9,5%

Kunkler IH, et al. NEJM. 2023; 388(7) :585-94.

CONFERÊNCIA BRASILEIRA DE

**CÂNCER DE MAMA**

LACOG - GBECAM 2024

REALIZAÇÃO



APOIO



# PRIME II

RT DE-ESCALATION TRIAL

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 16, 2023

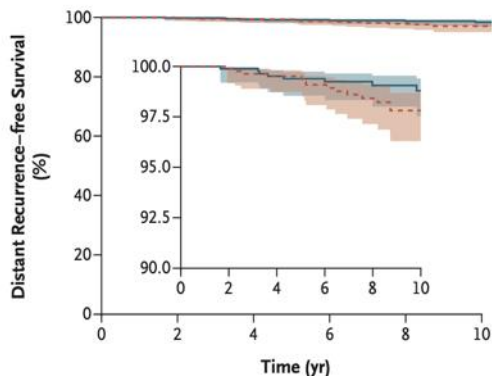
VOL. 388 NO. 7

Breast-Conserving Surgery with or without Irradiation  
in Early Breast Cancer

## Distance Recurrence Free

Incidence of Distant Recurrence  
as First Event (95% CI)

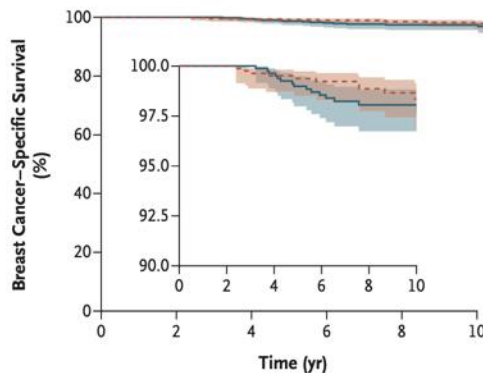
	5 yr percent	10 yr
No Radiotherapy	0.8 (0.1–1.5)	1.6 (0.4–2.8)
Radiotherapy	0.6 (0.0–1.3)	3.0 (1.4–4.5)



## Breast Cancer Specific Survival

Breast Cancer–Specific Survival  
(95% CI)

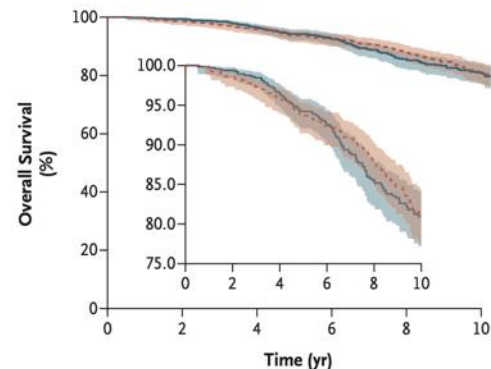
	5 yr percent	10 yr
No Radiotherapy	98.6 (97.7–99.6)	97.4 (96.0–98.8)
Radiotherapy	99.2 (98.4–99.9)	97.9 (96.5–99.2)



## Overall Survival

Overall Survival  
(95% CI)

	5 yr percent	10 yr
No Radiotherapy	94.2 (92.3–96.0)	80.8 (77.2–84.3)
Radiotherapy	93.7 (91.7–95.6)	80.7 (76.9–84.3)



No difference (~80%)

Kunkler IH, et al. NEJM. 2023; 388(7) :585-94.

CONFERÊNCIA BRASILEIRA DE

CÂNCER DE MAMA

LACOG - GBECAM 2024

REALIZAÇÃO



GRUPO BRASILEIRO  
DE ESTUDOS EM CÂNCER  
DE MAMA



OFFICIAL



AN INITIATIVE OF  
ENCORE  
MEDICAL EDUCATION



APOIO



Instituto Projeto

cura.

# PRIME II

RT DE-ESCALATION TRIAL

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

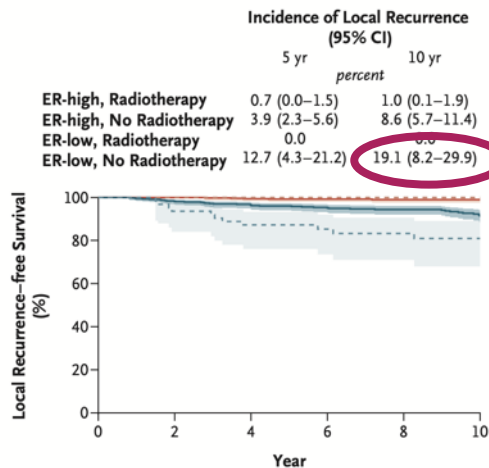
FEBRUARY 16, 2023

VOL. 388 NO. 7

Breast-Conserving Surgery with or without Irradiation  
in Early Breast Cancer

## Local recurrence ER status

— ER-high, radiotherapy — ER-high, no radiotherapy  
- - - ER-low, radiotherapy - - - ER-low, no radiotherapy



19.1%

ER low with  
almost 20% LR  
in 10yrs

Kunkler IH, et al. NEJM. 2023; 388(7) :585-94.

CONFERÊNCIA BRASILEIRA DE

CÂNCER DE MAMA

LACOG - GBECAM 2024

REALIZAÇÃO

LACOG  
LATIN AMERICAN COOPERATIVE  
ONCOLOGY GROUP

GBECAM  
GRUPO BRASILEIRO  
DE ESTUDOS EM CÂNCER  
DE MAMA

OFFICIAL

AN INITIATIVE OF  
ENCORE  
MEDICAL EDUCATION

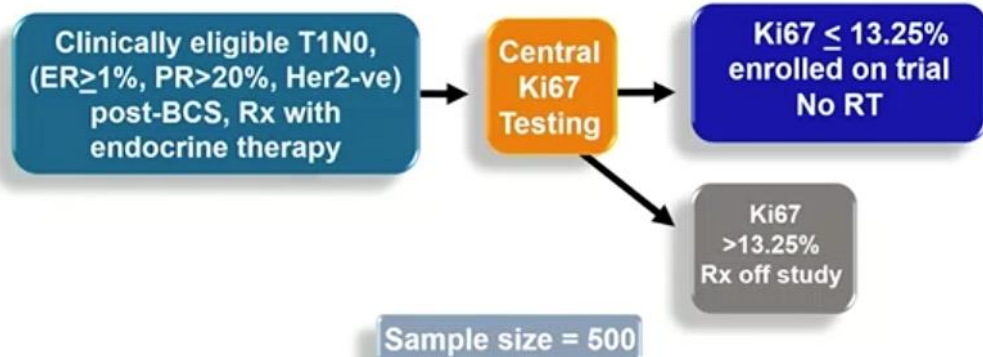
SAN ANTONIO  
BREAST CANCER  
SYMPOSIUM

APOIO

Instituto Projeto  
cura.

# LUMINA Trial

## RT DE-ESCALATION TRIAL



### Multicentric protective cohort

26 centers across Canada  
2013 to 2017  
5 Years follow up

Whelan TJ, et al. NEJM. 2023; 389(7) :612-19.

## Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer

T.J. Whelan, S. Smith, S. Parpia, A.W. Fyles, A. Bane, F.-F. Liu, E. Rakovitch, L. Chang, C. Stevens, J. Bowen, S. Provencher, V. Théberge, A.M. Mulligan, Z. Kos, M.A. Akra, K.D. Voduc, T. Hijal, I.S. Dayes, G. Pond, J.R. Wright, T.O. Nielsen, and M.N. Levine, for the LUMINA Study Investigators\*

**Primary endpoint:**  
Local recurrence  
(any invasive or non-invasive)

**Secondary endpoints:**  
Contralateral breast cancer  
Any recurrence  
Disease free survival  
Overall survival

# LUMINA Trial

## RT DE-ESCALATION TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer

T.J. Whelan, S. Smith, S. Parpia, A.W. Fyles, A. Bane, F.-F. Liu, E. Rakovitch, L. Chang, C. Stevens, J. Bowen, S. Provencher, V. Théberge, A.M. Mulligan, Z. Kos, M.A. Akra, K.D. Voduc, T. Hijal, I.S. Dayes, G. Pond, J.R. Wright, T.O. Nielsen, and M.N. Levine, for the LUMINA Study Investigators\*

Characteristic	All Patients (N = 500)
<b>Mean age, yr</b>	67
55 to <65, n (%)	200 (40)
65 to <75, n (%)	242 (48)
≥75, n (%)	58 (12)
<b>Mean tumor size, cm</b>	1.1
<0.5, n (%)	40 (8)
0.51-1.0, n (%)	216 (43)
1.1-2.0, n (%)	244 (49)
<b>Tumor grade, n (%)</b>	
1	330 (66)
2	170 (34)
<b>Endocrine therapy, n (%)</b>	
Tamoxifen	200 (41)
Aromatase inhibitor	292 (59)

#### Inclusion Criteria

Age >55 years

T1N0 ( $t > 2.0$ cm and N0)

G1 and GII Luminal A subtype

Ki67  $\leq 13.25\%$

Receive endocrine RT

**No Radiotherapy**

#### Exclusion criteria

Multifocal or multicentric

Extensive intraductal component (>25%)

Lymphatic vascular invasion

Whelan TJ, et al. NEJM. 2023; 389(7) :612-19.

# LUMINA Trial

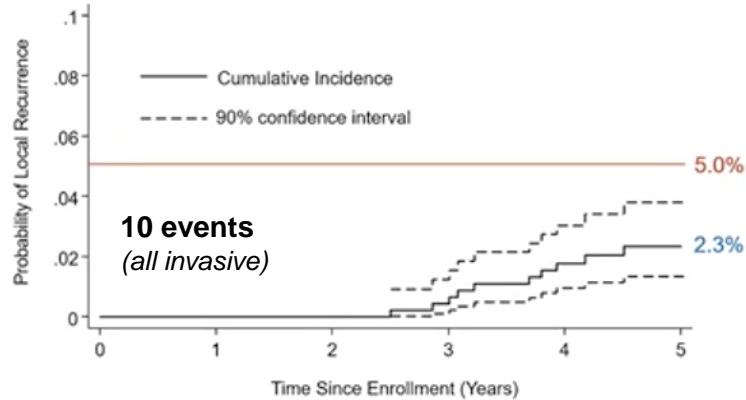
## RT DE-ESCALATION TRIAL

ORIGINAL ARTICLE

### Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer

T.J. Whelan, S. Smith, S. Parpia, A.W. Fyles, A. Bane, F.-F. Liu, E. Rakovitch, L. Chang, C. Stevens, J. Bowen, S. Provencher, V. Théberge, A.M. Mulligan, Z. Kos, M.A. Akra, K.D. Voduc, T. Hijal, I.S. Dayes, G. Pond, J.R. Wright, T.O. Nielsen, and M.N. Levine, for the LUMINA Study Investigators\*

## Local Recurrence



Very few local recurrences

PRIME II 5yrs fu with 1,3% LR

Outcome	Total Events at 5 Yr	5-Yr Rate (90% CI)
Local recurrence	10	2.3 (1.3-3.8)
Contralateral breast cancer	8	1.9 (1.1-3.2)
Any recurrence	12	2.7 (1.6-4.1)
DFS	47*	89.9 (87.5-92.2)
OS	13 <sup>†</sup>	97.2 (95.9-98.4)

\*23 second primary nonbreast cancer.

<sup>†</sup>1 death from breast cancer.

Whelan TJ, et al. NEJM. 2023; 389(7) :612-19.

# IDEA Trial

RT DE-ESCALATION TRIAL

Patients 50-59 years old  
*unifocal stage I  
Invasive breast cancer*

Lumpectomy

Margins > 2mm  
ER+, PR+, Her2 -ve  
Node negative  
(i+ with no cluster >0.2mm allowed)  
*Oncotype DX RS ≤18*

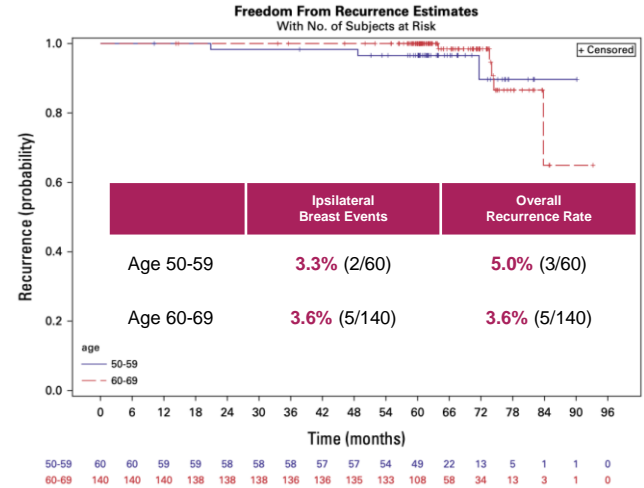
June 2015 to October 2018  
**200 pts enrolled**  
fu at least 56 months  
Mean age 62 yo  
Mean Oncotype RS of 11.2

5 Years of endocrine therapy  
and surveillance study

## Omission of Radiotherapy After Breast-Conserving Surgery for Women With Breast Cancer With Low Clinical and Genomic Risk: 5-Year Outcomes of IDEA

Reshma Jaggi, MD, DPhil<sup>1,2</sup>; Kent A. Griffith, MS<sup>2</sup>; Eleanor E. Harris, MD<sup>3</sup>; Jean L. Wright, MD<sup>4</sup>; Abram Recht, MD<sup>5</sup>; Alphonse G. Taghian, MD, PhD<sup>6</sup>; Lucille Lee, MD<sup>7</sup>; Meena S. Moran, MD<sup>8</sup>; William Small Jr, MD<sup>9</sup>; Candice Johnstone, MD<sup>10</sup>; Asal Rahimi, MD<sup>11</sup>; Gary Freedman, MD<sup>12</sup>; Mahvish Muzaffar, MD<sup>13</sup>; Bruce Haffty, MD<sup>14</sup>; Kathleen Horst, MD<sup>15</sup>; Simon N. Powell, MD, PhD<sup>16</sup>; Jody Sharp, BS<sup>1</sup>; Michael Sabel, MD<sup>1</sup>; Anne Schott, MD<sup>1</sup>; and Mahmoud El-Tamer, MD<sup>16</sup>

DOI <https://doi.org/10.1200/JCO.23.02270>



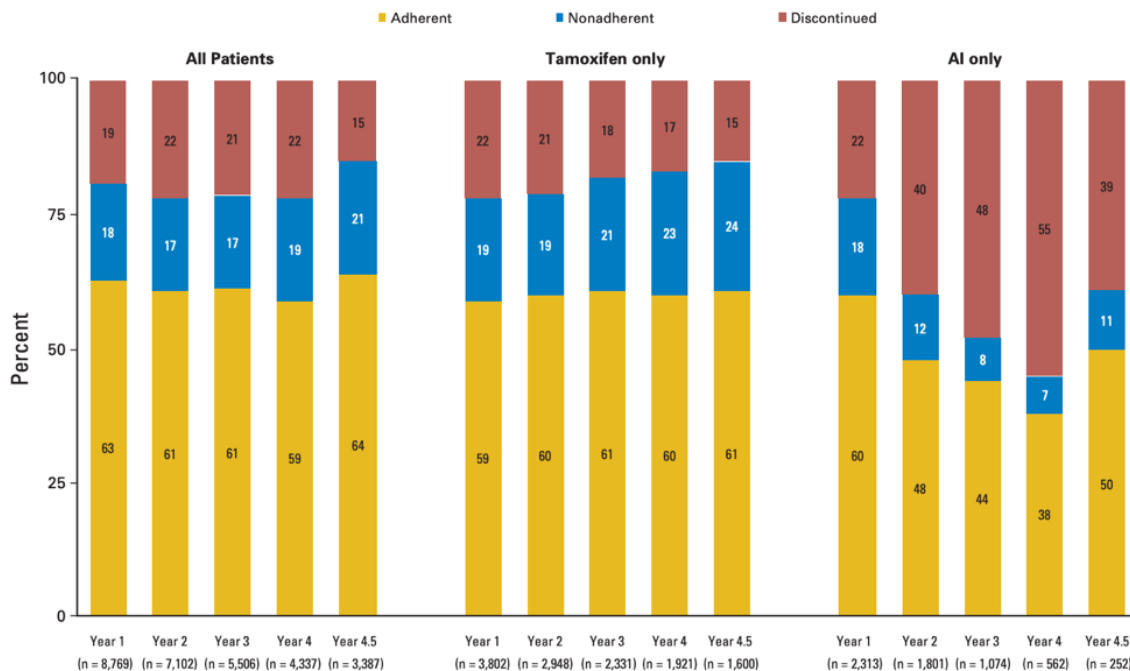
Jaggi R, et al. JCO. 2024; 42(4) :390-98.

	IDEA	LUMINA	PRECISION	PRIMETIME	EXPERT	Natural	EUROPA	DEBRA
Design	Single arm	Single arm	Single arm	Single arm	Randomized	Randomized	Randomized	Randomized
Years	2015-2018	2013-2017	2016-present	2017-2022	2017-present	2018-present	2021-present	2021-present
Accrual Goal	200	501	672	2400	1167	926	926	1670
Age	≥ 50 ≤ 69	≥ 55	≥ 50 ≤ 75	≥ 60	≥ 50	≥ 60	≥ 70	≥ 50 ≤ 70
T Stage	pT1	pT1	pT1	pT1	pT1	pT1	pT1	pT1
N Stage	pN0, pN0(IHC+)	pN0	pN0, pN0(IHC+)	pN0	pN0, pN0(IHC+)	pN0	cN0, pN0, pN0(IHC+)	pN0
Grade	Any	1-2	1-2	1-2	1-2	1-2	Any if ≤1 cm 1-2 if >1 cm	Any
Biologic criteria	<b>Oncotype</b> Score ≤18 <b>IHC</b> ER/PR+ HER2-	<b>IHC</b> ER≥ 1% PR>20% HER2- Ki67≤13.25%	<b>PAM-50</b> Low risk <b>IHC</b> ER/PR≥10% HER2-	<b>IHC</b> ER/PR+ HER2- <b>IHC4+C</b> Very low	<b>PAM-50</b> Luminal A ROR ≤60	<b>IHC</b> ER≥10% HER2-	<b>IHC</b> ER/PR≥10% HER2- Ki67≤20%	<b>Oncotype</b> Score ≤18 <b>IHC</b> ER/PR≥1% HER2-
Trial Arms	ET	ET	ET	ET	ET vs. ET + RT	ET vs. ET + APBI	ET vs. APBI	ET vs. ET + RT

Endocrine therapy is the studied alternative to omission of RT



# Endocrine Therapy Adherence



Average adherence of  
**60%**  
 up to the 5th year

Hershman DL et al J Clin Oncol 2010; 28(27): 4120-8

## Adherence to Endocrine Therapy in Breast Cancer Adjuvant and Prevention Settings

Rowan T. Chlebowski<sup>1,2</sup>, Jisang Kim<sup>2</sup>, and Reina Haque<sup>3</sup>

# Half of patients on endocrine therapy do not complete the 5 years of treatment

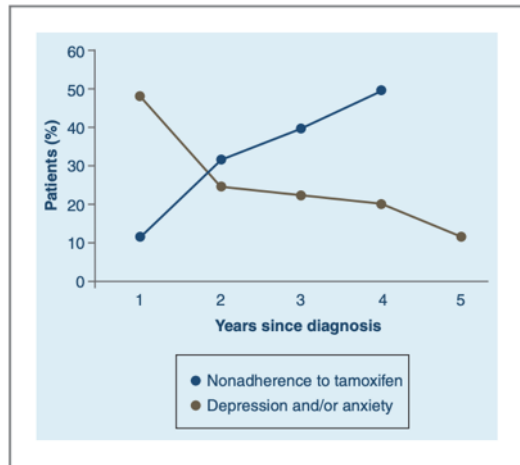


Figure 1. Nonadherence rates for adjuvant tamoxifen therapy in clinical practice and incidence of depression and/or anxiety in breast cancer patients with early stage disease.

**Table 4.** Correlates associated with discontinuing endocrine therapy or nonadherence

Reason	Study
Side effects	Demissie et al. (55), Kahn et al. (56), Lash et al. (57), Cluze et al. (65)
Higher comorbidity	Hershman et al. (23), Hadji (26), Sedjo and Devine (62)
Financial considerations or low socioeconomic status	Kimmeck et al. (85), Riley et al. (60), Neugut et al. (61), Liu et al. (66)
Very young or older age	Hershman et al. (23), Land et al. (50), Owusu et al. (58)
Lack of physician recommendation	Davidson et al. (41)
Perception of low risk of recurrence	Fink et al. (54)
Lack of social support	Cluze et al. (86), Land et al. (50)
Follow-up care with general practitioner vs. oncologist	Murphy et al. (21)
African American race/ethnicity	Hershman et al. (23)
Cigarette smoking	Land et al. (50)
Presence of anxiety/depression linked to better adherence	Kyvernitakis et al. (71), Hadji (26)
Alcohol use	Land et al. (50)

Chlebowski RT, et al. Cancer Prev Res 2014; 7(4): 378-87

# *De-escalating RT schedule* **HYPOFRACTIONATION**



# HYPOFRACTIONATION

## OUTCOMES

No difference for shorter courses

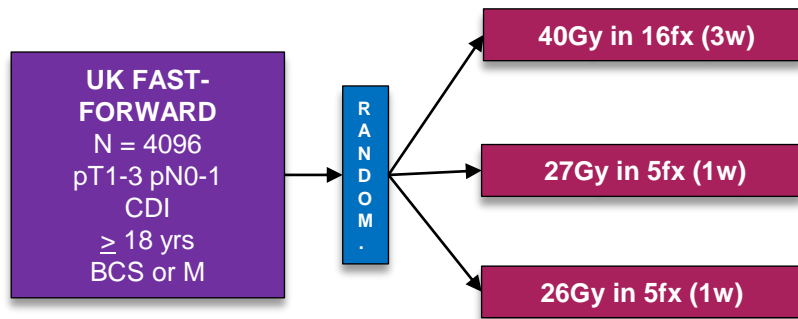
Study	Local recurrence			Distant recurrence			Any cause mortality		
	Arm	Result	p	Arm	Result	p	Arm	Result	p
CANADIAN	50 Gy	7.5%	NS		Não Reportado		50 Gy	15.6%	NS
	42.5 Gy	7.4%					42.5 Gy	15.4%	
RMH / GOC	50 Gy	12.1%	0.027		Não Reportado		Não Reportado		
	42.9 Gy	9.6%							
	39 Gy	14.8%							
START A	50 Gy	6.7%	NS	50 Gy	14.7%	NS	50 Gy	19.8%	NS
	41.6 Gy	5.6%		41.6 Gy	16.8%		41.6 Gy	18.4%	
	39 Gy	8.1%		39 Gy	18.0%		39 Gy	20.3%	
START B	50 Gy	5.2%	NS	50 Gy	16.0%	0.014	50 Gy	19.2%	0.042
	40 Gy	3.8%		40 Gy	12.3%		40 Gy	15.9%	
UK FAST TRIAL	30 Gy	7.5%	NS	30 Gy	4.9%	NS	30 Gy	10.7%	NS
	28.5 Gy	7.4%		28.5 Gy	4.9%		28.5 Gy	10.8%	
FAST FORWARD	40 Gy	2.1%	NS	40 Gy	5.4%	Non-inf	40 Gy	5.4%	NS
	27 Gy	1.7%		27 Gy	6.9%		27 Gy	6.9%	
	26 Gy	1.4%		26 Gy	5.6%		26 Gy	5.6%	

# HYPOFRACTIONATION

FAST FORWARD TRIAL

5 fractions

Multicentric UK (97 hospitals)  
From 2011 to 2014



## Primary Endpoint :

*Ipsilateral relapse*

- ✓ 15% < 50 yo
- ✓ 38% high risk factors
- ✓ 18% positive nodes
- ✓ 90% HR+

## Secondary Endpoint:

*Skin toxicity*

	40 Gy in 15 fractions (n=1361)	27 Gy in five fractions (n=1367)	26 Gy in five fractions (n=1368)
Age, years			
Median (IQR)	60 (53-66)	61 (53-67)	61 (52-66)
Range	29-89	25-90	25-89
<40	12 (0.9%)	16 (1.2%)	28 (2.0%)
40-49	186 (13.7%)	173 (12.7%)	189 (13.8%)
50-59	440 (32.3%)	423 (30.9%)	414 (30.3%)
60-69	506 (37.2%)	511 (37.4%)	524 (38.3%)
70-79	175 (12.9%)	197 (14.4%)	172 (12.6%)
≥80	42 (3.1%)	47 (3.4%)	41 (3.0%)
Sex			
Female	1355 (99.6%)	1365 (99.9%)	1362 (99.6%)
Male	6 (0.4%)	2 (0.1%)	4 (0.3%)
Unknown	0	0	2 (0.1%)
Tumour grade			
1	315 (23.1%)	315 (23.0%)	300 (21.9%)
2	660 (48.5%)	663 (48.5%)	690 (50.4%)
3	386 (28.4%)	389 (28.5%)	378 (27.6%)
Risk group			
Low (age ≥50 and grade 1 or 2)	843 (61.9%)	854 (62.5%)	854 (62.4%)
High (age <50 or grade 3, or both)	518 (38.1%)	513 (37.5%)	514 (37.6%)

Brunt AM Lancet 2020; 395:1613-26

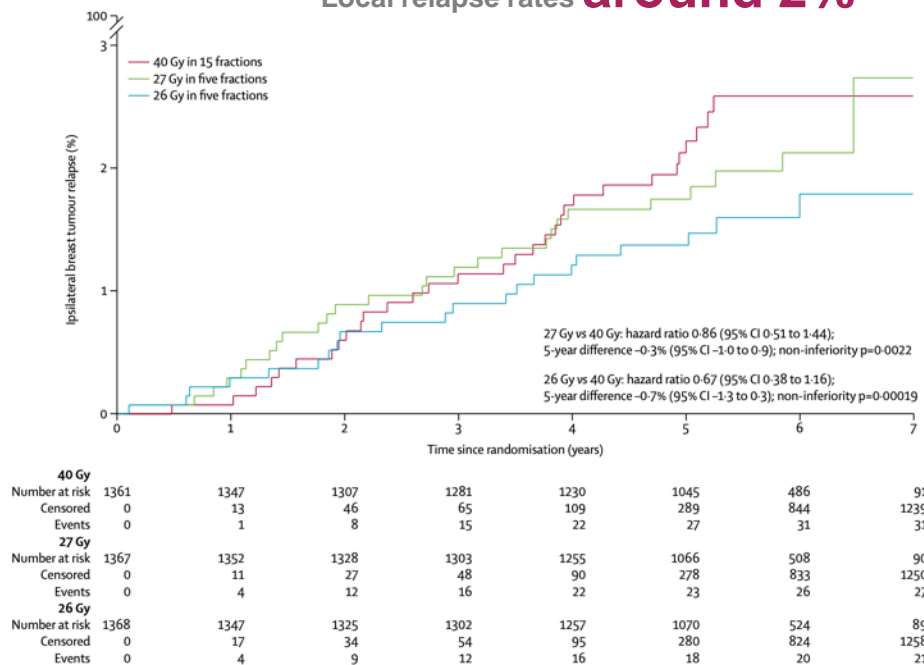
# HYPOFRACTIONATION FAST FORWARD TRIAL

	40 Gy in 15 fractions (n=1361)	27 Gy in five fractions (n=1367)	26 Gy in five fractions (n=1368)
Local tumour control event (primary endpoint)*	31 (2.3%)	27 (2.0%)	21 (1.5%)
Local relapse	23 (1.7%)	22 (1.6%)	17 (1.2%)
Ipsilateral breast, new primary	6 (0.4%)	3 (0.2%)	4 (0.3%)
Cannot differentiate	2 (0.1%)	2 (0.1%)	0
Regional relapse	13 (1.0%)	11 (0.8%)	10 (0.7%)
Distant relapse	59 (4.3%)	69 (5.0%)	76 (5.5%)
Contralateral breast, second primary	23 (1.7%)	20 (1.5%)	23 (1.7%)
Invasive	18 (1.3%)	17 (1.2%)	20 (1.5%)
Ductal carcinoma in situ	5 (0.4%)	3 (0.2%)	2 (0.1%)
Unknown	0	0	1 (0.1%)
Non-breast, second primary	42 (3.1%)	37 (2.7%)	44 (3.2%)
Death	92 (6.8%)	105 (7.7%)	90 (6.6%)
Breast cancer†	47 (3.5%)	51 (3.7%)	53 (3.9%)
Second cancer	12 (0.9%)	16 (1.2%)	10 (0.7%)
Cardiac	10 (0.7%)	9 (0.7%)	8 (0.6%)
Other cause	17 (1.7%)	27 (2.0%)	16 (1.2%)
Unknown	6 (1.2%)	2 (0.1%)	3 (0.2%)

Data are n (%). Patients reporting events of more than one type are included in each relevant row. \*Includes angiosarcoma in ipsilateral breast (one in the 40 Gy group and two in the 26 Gy group) and six patients with ductal carcinoma in situ (three in the 40 Gy group, two in the 27 Gy group, and one in the 26 Gy group). †Includes 13 patients with distant relapse before death from other causes (four in the 40 Gy group, four in the 27 Gy group, and five in the 26 Gy group).

**Table 3: Relapses, second primary cancers, and deaths by fractionation schedule (n=4096)**

## Local relapse rates around 2%



Brunt AM Lancet 2020; 395:1613-26

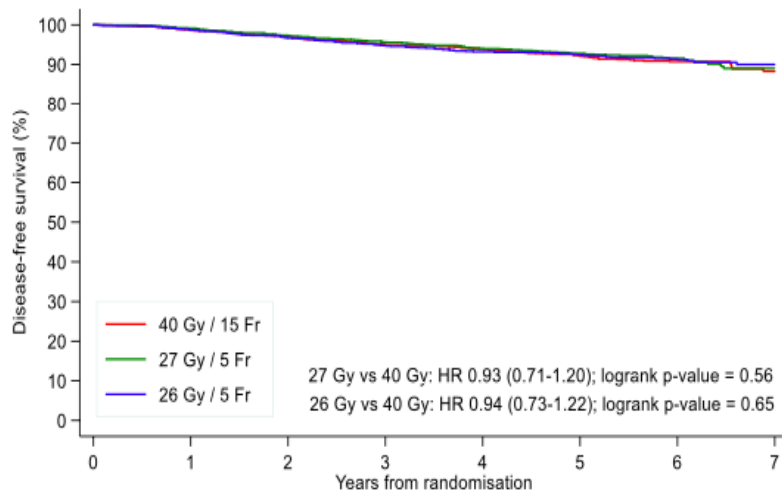
# HYPOFRACTIONATION

FAST FORWARD TRIAL

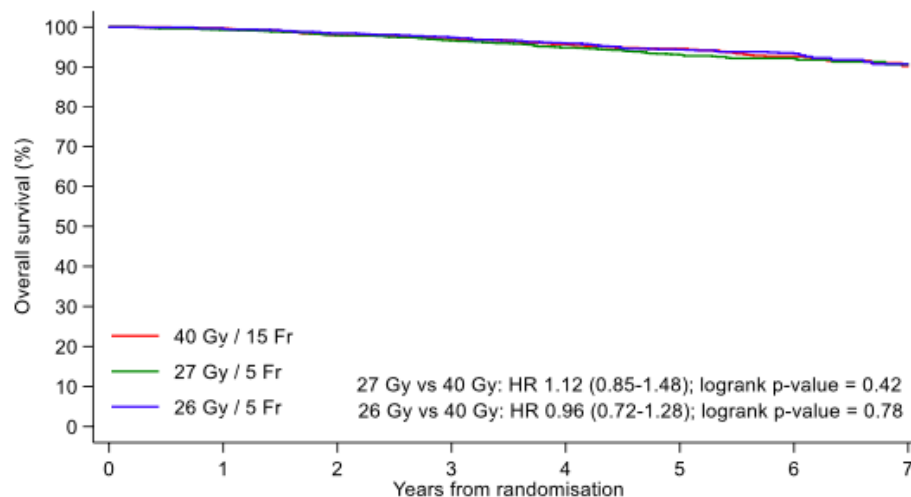
## Low late toxicity

- Breast induration: 1.6%
- Teleangectasias: 1.6%
- Breast oedema: 2.4%

## Disease-Free Survival



## Overall Survival



Brunt AM Lancet 2020; 395:1613-26

CONFERÊNCIA BRASILEIRA DE

**CÂNCER DE MAMA**

LACOG - GBECAM 2024

REALIZAÇÃO

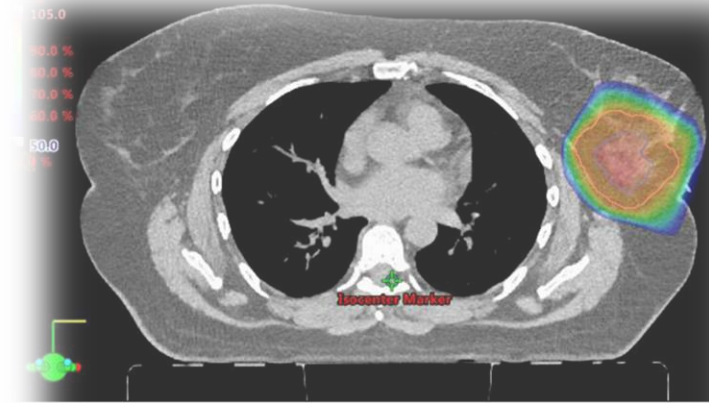


APOIO



# De-escalating RT volume

**A**ccelerated **P**artial **B**reast **I**rradiation





# APBI

FLORENCE Trial

## Single center phase III trial

University of Florence - Italy

Mar 2005 to Jun 2013

### Invasive Breast Cancer

Tumor up to 2,5cm

Age >40 yo

Suitable for BCS

Clips placement

R

### WBRT

50Gy in 25fx  
Boost of 10Gy in 5 fx

260

### IMRT APBI

Circunferencial margin  
of 10mm around clips  
30Gy in 5fx

246

### Exclusion Criteria:

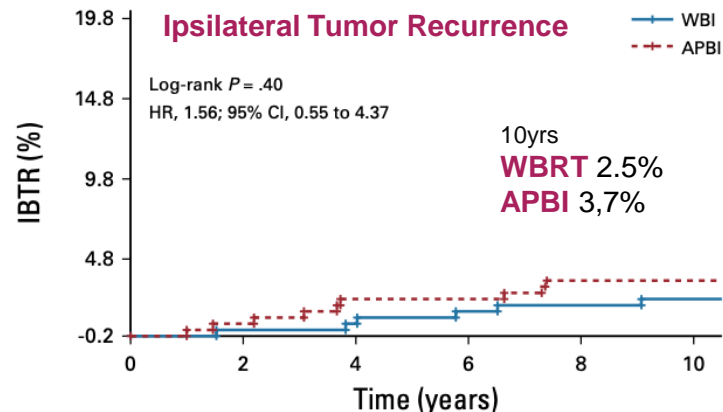
Final margins < 5mm

Multiple foci

Extensive intraductal carcinoma

## Accelerated Partial-Breast Irradiation Compared With Whole-Breast Irradiation for Early Breast Cancer: Long-Term Results of the Randomized Phase III APBI-IMRT-Florence Trial

Icro Meattini, MD<sup>1,2</sup>; Livia Marrazzo, MS<sup>3</sup>; Calogero Saieva, MD<sup>4</sup>; Isacco Desideri, MD<sup>1,2</sup>; Vieri Scotti, MD<sup>2</sup>; Gabriele Simontacchi, MD<sup>2</sup>; Pierluigi Bonomo, MD<sup>2</sup>; Daniela Greto, MD<sup>2</sup>; Monica Mangoni, MD, PhD<sup>1,2</sup>; Silvia Scoccianti, MD<sup>2</sup>; Sara Lucidi, MD<sup>1</sup>; Lisa Paoletti, MD<sup>1</sup>; Massimiliano Fambrini, MD<sup>1,2</sup>; Marco Bernini, MD, PhD<sup>2</sup>; Luis Sanchez, MD<sup>2</sup>; Lorenzo Orzalesi, MD<sup>1,2</sup>; Jacopo Nori, MD<sup>2</sup>; Simonetta Bianchi, MD<sup>1,2</sup>; Stefania Pallotta, MS<sup>1,2</sup>; and Lorenzo Livi, MD<sup>1,2</sup>



No. at risk (No. of events):

APBI	260 (0)	257 (2)	251 (6)	249 (7)	189 (9)	141 (9)
WBI	260 (0)	257 (1)	253 (2)	246 (4)	220 (5)	168 (6)

Meattini I, et al. JCO. 2020; 38(35) :4175-83

CONFERÊNCIA BRASILEIRA DE

# CÂNCER DE MAMA

LACOG - GBECAM 2024

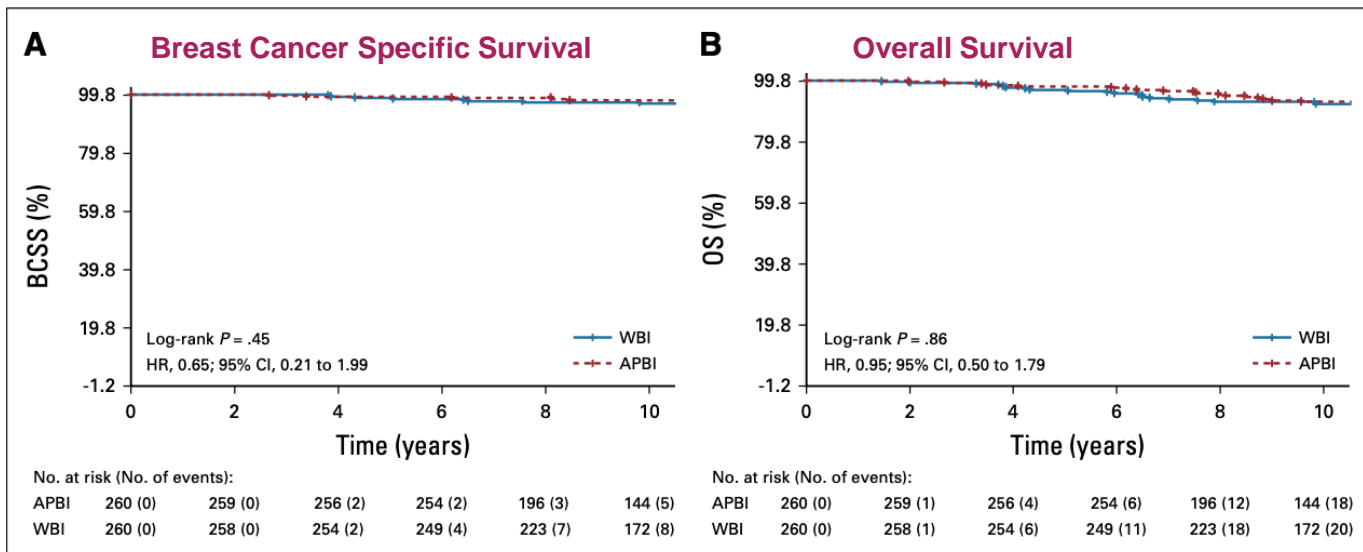
REALIZAÇÃO



APOIO



Icro Meattini, MD<sup>1,2</sup>; Livia Marrazzo, MS<sup>3</sup>; Calogero Saleva, MD<sup>4</sup>; Isacco Desideri, MD<sup>1,2</sup>; Vieri Scotti, MD<sup>2</sup>; Gabriele Simontacchi, MD<sup>2</sup>; Pierluigi Bonomo, MD<sup>5</sup>; Daniela Greto, MD<sup>6</sup>; Monica Mangoni, MD, PhD<sup>1,2</sup>; Silvia Scoccianti, MD<sup>7</sup>; Sara Lucidi, MD<sup>1</sup>; Lisa Paoletti, MD<sup>8</sup>; Massimiliano Fambrini, MD<sup>1,2</sup>; Marco Bernini, MD, PhD<sup>9</sup>; Luis Sanchez, MD<sup>10</sup>; Lorenzo Orzalesi, MD<sup>1,2</sup>; Jacopo Nori, MD<sup>11</sup>



Meattini I, et al. JCO. 2020; 38(35) :4175-83

### Acute Toxicity

Assessment	APBI (n = 246)	WBI (n = 260)	P
Acute period adverse events <sup>a</sup>			
None	194 (78.9)	87 (33.5)	.0001
Yes, any grade	52 (21.1)	173 (66.5)	
Grade 1	47 (19.1)	75 (28.8)	.0001
Grade 2	5 (2.0)	81 (31.2)	
Grade 3	—	17 (6.5)	
Grade 4	—	—	
Grade 0-1	241 (98.0)	162 (62.3)	.0001
Grade ≥ 2	5 (2.0)	98 (37.7)	.0001

**Grade ≥ 2**  
2% vs 37,7%

### Late Toxicity

Assessment	APBI (n = 246)	WBI (n = 260)	P
Late period adverse events <sup>a</sup>			
None	235 (95.5)	182 (70.0)	.0001
Yes, any grade	11 (4.5)	78 (30.0)	.0001
Grade 1	11 (4.5)	71 (27.3)	.0001
Grade 2	—	7 (2.7)	
Grade 3	—	—	
Grade 4	—	—	
Grade 0-1	246 (100)	253 (97.3)	.015
Grade ≥ 2	0	7 (2.7)	

**Grade ≥ 2**  
0% vs 2,7%

### Cosmesis

Assessment	APBI (n = 246)	WBI (n = 260)	P
Physician-rated cosmesis <sup>b</sup>			
Excellent	233 (94.7)	189 (72.7)	.0001
Good	13 (5.3)	66 (25.4)	
Fair	—	5 (1.9)	
Poor	—	—	
Patient-rated cosmesis <sup>b</sup>			
Excellent	44 (17.9)	13 (5.1)	.0001
Good	200 (81.3)	209 (80.3)	
Fair	2 (0.8)	38 (14.6)	
Poor	—	—	

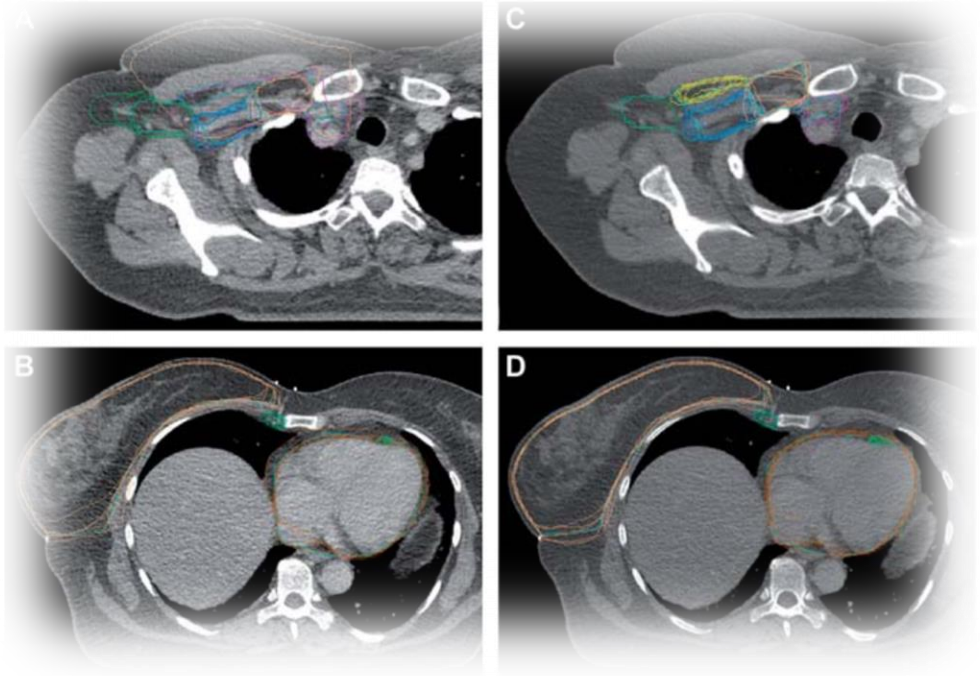
**Good and Excellent**  
99,2% vs 85,4%

**Excelente tolerância e resultado cosmético**

Meatinni I, et al. JCO. 2020; 38(35) :4175-83

# De-escalating RT volume

**R**egional **N**odal **I**rradiation

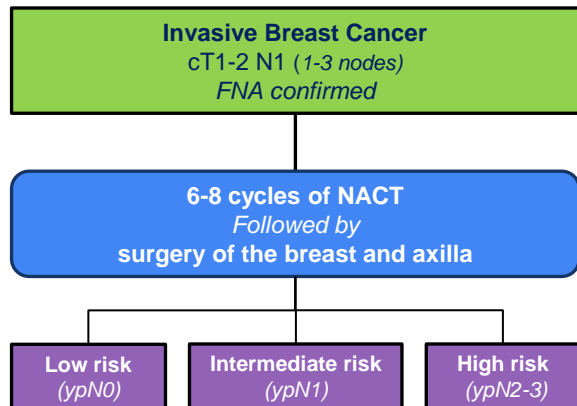


# RAPCHEM; BOOG 2010-03

RT DE-ESCALATION TRIAL

## Dutch prospective registry study

- Jan/11 to jan/15
- 838 patients
- 5yr follow up
- IMRT forward of inverse planning



## De-escalation of radiotherapy after primary chemotherapy in cT1–2N1 breast cancer (RAPCHEM; BOOG 2010–03): 5-year follow-up results of a Dutch, prospective, registry study

Sabine R de Wild, Linda de Munck, Janine M Simons, Janneke Verloop, Thijs van Dalen, Paula H M Elkhuizen, Ruud M A Houben, A Elise van Leeuwen, Sabine C Linn, Ruud M Pijnappel, Philip M P Poortmans, Luc J A Strobbe, Jelle Wesseling, Adri C Voogd, Liesbeth J Boersma

	RT after BCS	RT after Mastectomy
<b>Low risk group (291)</b>		
ypN0 (ALND)	WBRT	-
If SLNB before NACT and no ALND: cN1mi (SLNB), no risk factor*; or if SLNB after NACT and no ALND: ypN0 (SLNB)	WBRT	-
<b>Intermediate risk group (370)</b>		
ypN01(ALND)	WBRT	Chestwall RT
If SLNB before primary chemotherapy and no ALND <sup>†</sup> : cN1mi (SLNB), ≥1 risk factor*, or cN1 (SLNB), ≤2 macrometastases, no risk factor*; or if SLNB after primary chemotherapy and no ALND <sup>†</sup> : ypN1mi (SLNB), no risk factor*	WBRT + Axilla level I-II †	Chestwall RT + Axilla level I-II †
<b>High risk group (177)</b>		
ypN2-3 (ALND)	WBRT + Axilla level III-IV	Chestwall RT + Axilla level III-IV
If SLNB before primary chemotherapy and no ALND <sup>†</sup> : cN1 (SLNB), with ≤2 macrometastases and ≥1 risk factor*, or ≥3 macrometastases; or if SLNB after primary chemotherapy and no ALND <sup>†</sup> : ypN1mi (SLNB), ≥1 risk factor*, or ypN1 (SLNB)	WBRT + Axilla Level III-IV in addition to level I – II †	Chestwall RT + Axilla Level III-IV in addition to level I – II †

ALND=axillary lymph node dissection. SLNB=sentinel lymph node biopsy. \*Risk factor: grade 3, lymphovascular invasion, tumour size more than 3 cm. †If ALND was omitted in the intermediate-risk or high-risk group, radiotherapy of the axilla (level I and II) was recommended. Radiotherapy of the axilla (level I and II) after ALND, and radiotherapy of the internal mammary chain were optional

De Wild SR et al Lancet Oncol 2022, 23:1201-10

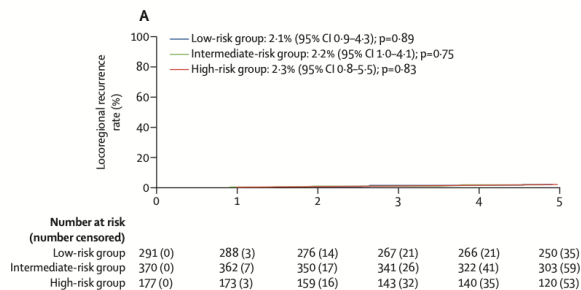
# RAPCHEM; BOOG 2010-03

RT DE-ESCALATION TRIAL

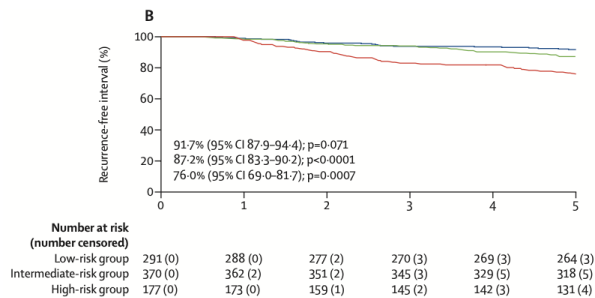
## De-escalation of radiotherapy after primary chemotherapy in cT1–2N1 breast cancer (RAPCHEM; BOOG 2010–03): 5-year follow-up results of a Dutch, prospective, registry study

Sabine R de Wild, Linda de Munck, Janine M Simons, Janneke Verloop, Thijs van Dalen, Paula H M Elkhuizen, Ruud M A Houben, A Elise van Leeuwen, Sabine C Linn, Ruud M Pijnappel, Philip M P Poortmans, Luc J A Strobbe, Jelle Wesseling, Adri C Voogd, Liesbeth J Boersma

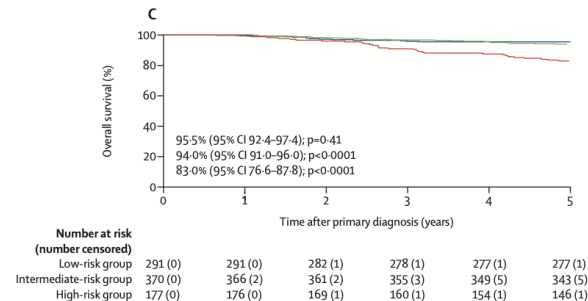
### Locoregional Recurrence



### Recurrence Free Interval



### Overall Survival



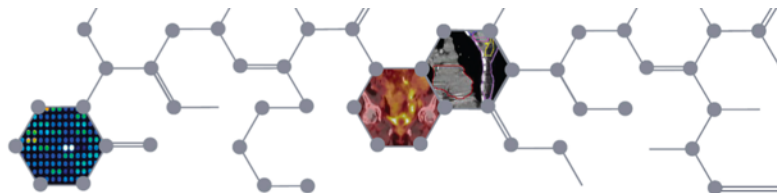
	All patients	Low risk	Intermediate risk	High risk
<b>5yr Locoregional recurrence</b>	2.2%	2.1%	2.2%	2.3%

## Low rates of locoregional recurrences

De Wild SR et al Lancet Oncol 2022, 23:1201-10

**NRG**  
ONCOLOGY

Advancing Research. Improving Lives.™



 DEC 5-9, 2023  
SAN ANTONIO  
BREAST CANCER  
SYMPOSIUM

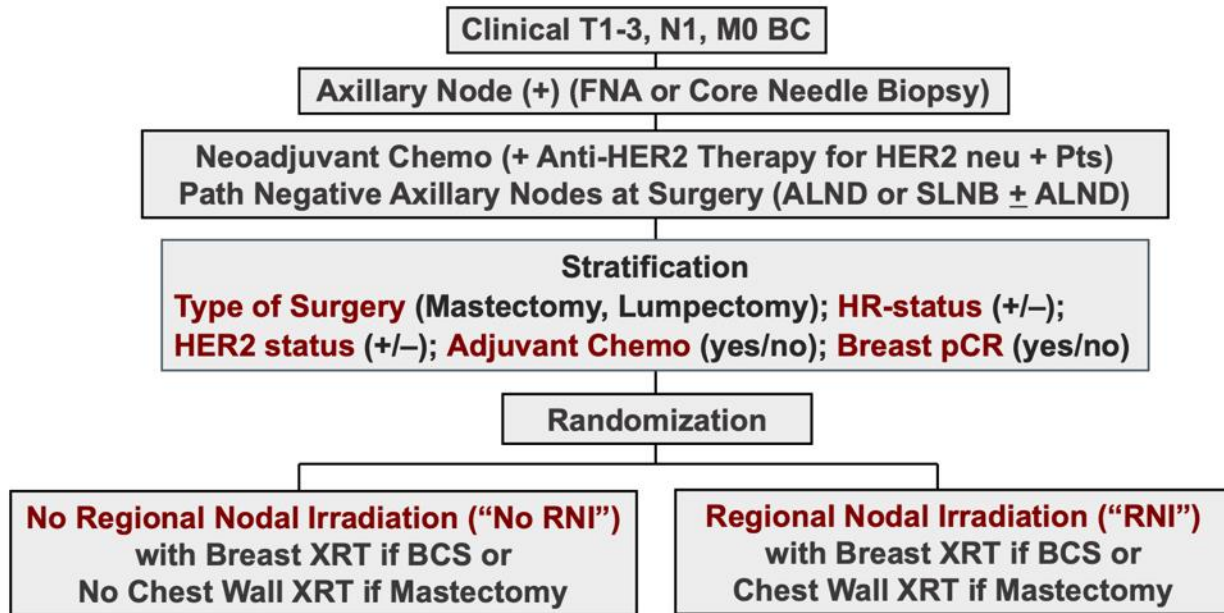
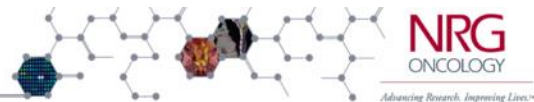
# Loco-regional Irradiation in Patients with Biopsy-proven Axillary Node Involvement at Presentation

## Who Become Pathologically Node-negative After Neoadjuvant Chemotherapy: Primary Outcomes of NRG Oncology/NSABP B-51/RTOG 1304

Eleftherios P. Mamounas<sup>1\*</sup>, Hanna Bandos<sup>2</sup>, Julia R. White<sup>3\*</sup>, Thomas B. Julian<sup>4</sup>, Atif J. Khan<sup>5</sup>, Simona F. Shaitelman<sup>6</sup>, Mylin A. Torres<sup>7</sup>, Frank A. Vicini<sup>8</sup>, Patricia A. Ganz<sup>9</sup>, Susan A. McCloskey<sup>10</sup>, Peter C. Lucas<sup>11,12</sup>, Nilendu Gupta<sup>3</sup>, X. Allen Li<sup>13</sup>, Beryl McCormick<sup>5</sup>, Saumil Gandhi<sup>6</sup>, Rahul D. Tendulkar<sup>14</sup>, Vivek S. Kavadi,<sup>15</sup> Masahiko Okamoto<sup>16</sup>, Samantha Andrews Seaward<sup>17</sup>, William J. Irvin, Jr.<sup>18</sup>, Jolinta Lin<sup>7</sup>, Robert Mutter<sup>19</sup>, Thierry M. Muanza<sup>20</sup>, Andrew A. Muskovitz<sup>21</sup>, Reshma Jagasi<sup>22</sup>, Anna C. Weiss<sup>23,24</sup>, Walter J. Curran, Jr.<sup>7</sup>, and Norman Wolmark<sup>12</sup>

\*These authors contributed equally.

# Study Schema



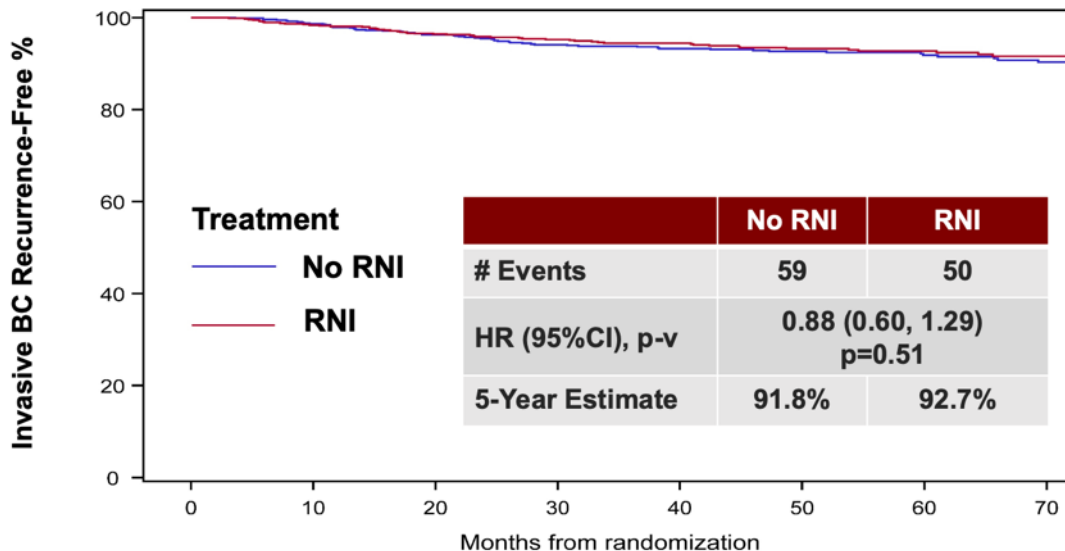
FNA: Fine Needle Aspiration; ALND: Axillary Lymph Node Dissection; SLNB: Sentinel Lymph Node Biopsy; XRT: Radiation

Dec 5-9, 2023  
SAN ANTONIO  
BREAST CANCER  
SYMPOSIUM



# Primary Endpoint

## Invasive Breast Cancer Recurrence-free Interval (IBCRFI)

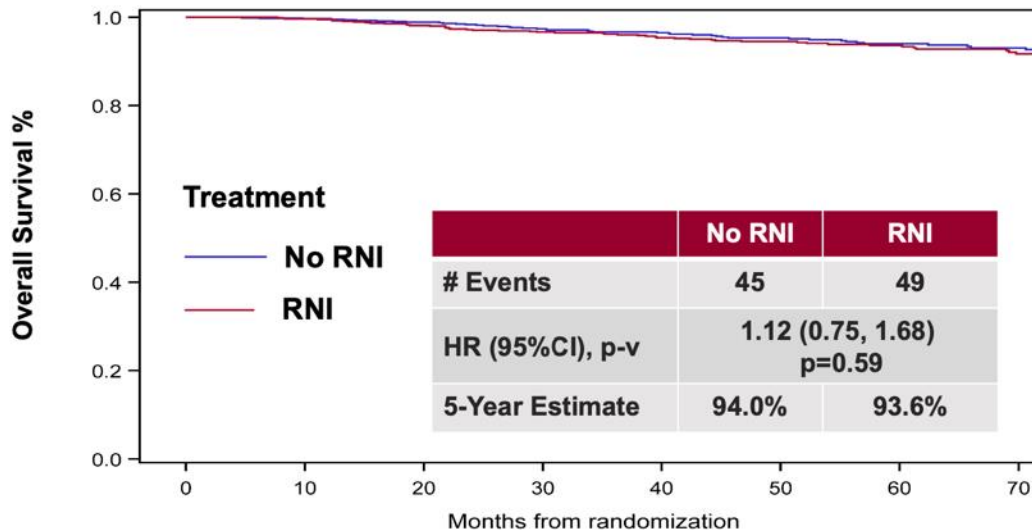


	0	10	20	30	40	50	60	70
<b>No RNI</b>	784	756	700	610	508	386	309	215
<b>RNI</b>	772	724	682	605	498	389	294	200

Dec 5-9, 2023 SAN ANTONIO BREAST CANCER SYMPOSIUM

# Secondary Endpoints (cont.)

## Overall Survival (OS)



	0	10	20	30	40	50	60	70
<b>No RNI</b>	802	779	761	698	591	462	371	263
<b>RNI</b>	800	752	730	676	568	459	360	247

SAN ANTONIO BREAST CANCER SYMPOSIUM  
 Dec 5-9, 2023

# “Real World” Clinical Applications

## Limitations and Applications

### Limitations

1. Longer follow-up needed
2. Unknown # of patients with ITCs

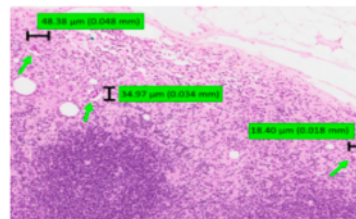
### Applications

Omission of nodal RT for cN1 patients with nodal pCR or cN0 patients with TE in nodes

### Does not apply to:

1. Locally advanced breast cancer
2. ypN+ patients

## Is IHC of SLNs necessary after NAC?

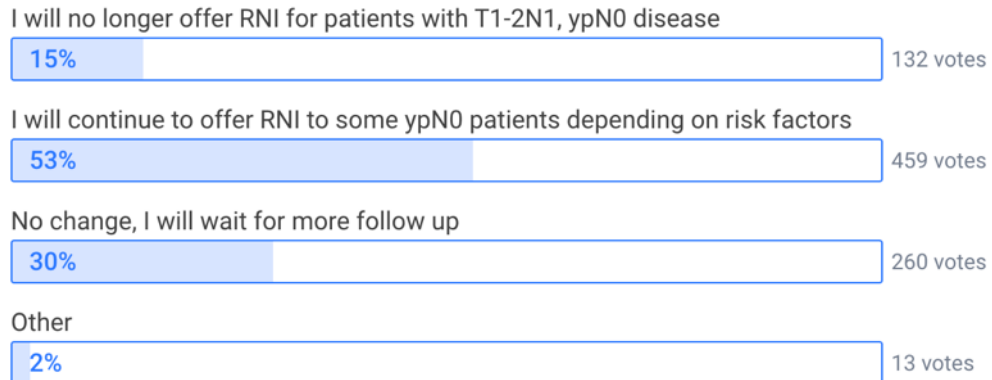


Based on data from B-51/1304 and OPBC/EUBREAST, ITCs post-NAC appear prognostically insignificant and the routine use of IHC on SLNs after NAC should be abandoned

Poll began: 12/11/2023

Show results since: 12/11/2023 ↓

## How have the results of NSABP B51 changed your practice?



<https://www.themednet.org/>

## Only Radoncs

How have the results of NSABP B51 changed your practice?

✓ Selecione uma opção

I will no longer offer RNI for patients with T1-2N1, ypN0 disease 0

I will continue to offer RNI to some ypN0 patients depending on risk factors 32

No change, I will wait for more follow up 3

Other 2

86.4%

8.1%

5.5%

## 2 radoncs, 4 breast surgeons and 4 oncologists

How have the results of NSABP B51 changed your practice?

✓ Selecione uma opção

I will no longer offer RNI for patients with T1-2N1, ypN0 disease 10

I will continue to offer RNI to some ypN0 patients depending on risk factors 0

No change, I will wait for more follow up 0

Other 0

100%

# Descalonamento de radioterapia adjuvante

## Pra quem?

- A omissão de radioterapia em pacientes pos-menopausicas com câncer de mama inicial de baixo risco é uma **alternativa**
- Paciente com  $\geq 65$  anos, T1N0, G1 ou G2, RH+, IAL-, Baixo risco genômico e com potencial aderência a HT
- O custo dessa estratégia tem o **preço** de um risco aumentado de **recorrência local**
- Sem impacto de sobrevida
- Terapia endócrina não é um tratamento fácil e de boa aderência
- O uso da radioterapia ultra-hipofracionada ou APBI traz uma conveniência logística com boa tolerância que pode ser inclusive uma alternativa a terapia endócrina nesses pacientes

# Descalonamento de radioterapia adjuvante

## Pra quem?

- A população de pacientes ypN0 **tem baixo risco de recidiva regional** e a irradiação nodal pode ser omitida nessa população
- A omissão da RT de parede torácica em pacientes N+ **pode ser uma estratégia** segura em uma população de pacientes que ainda precisamos entender melhor com a publicação do B51



[arthur.rosa@gmail.com](mailto:arthur.rosa@gmail.com)

[arthur.rosa@médicos.oncclinicas.com](mailto:arthur.rosa@médicos.oncclinicas.com)

CONFERÊNCIA BRASILEIRA DE  
**CÂNCER DE MAMA**  
LACOG - GBECAM 2024

REALIZAÇÃO



AN INITIATIVE OF  
**ENCORE**  
MEDICAL EDUCATION



APOIO

Instituto Projeto  
**cura.**