



Associazione Italiana
Radioterapia e Oncologia clinica

HIGHLIGHTS in RADIOTERAPIA

*Gli studi del 2019 che modificano la
pratica clinica in radioterapia esclusiva
ed associazione farmacologica*

ROMA,

23 gennaio 2020

Centro Studi dell'Area Radiologica
"Il Cardello"

NEOPLASIE MAMMARIE

Antonella Ciabattoni

UOC Radioterapia Ospedale S. Filippo Neri
ASL Roma 1, Roma

Thanks to Francesca Salerno MD
and Karen Llange MD



No conflict of interests





2019

Edition: ENGLISH DEUTSCH ESPAÑOL FRANÇAIS PORTUGUÊS

Medscape Saturday, January 18, 2020

NEWS & PERSPECTIVE DRUGS & DISEASES CME & EDUCATION ACADEMY CONSULT VIDEO

From Medscape Oncology

Update on Radiation Therapy for Breast Cancer

Authors: Pauline T. Truong, MD, FRCPC [Faculty and Disclosures](#)

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Contemporary Issues in Breast Cancer Radiotherapy



Lior Z. Braunstein, MD^a, Jennifer R. Bellon, MD^{b,*}

2020

Hematol Oncol Clin N Am 34 (2020) 1–12
<https://doi.org/10.1016/j.hoc.2019.08.014>
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KEYWORDS

- Breast cancer • Radiotherapy • Breast conservation • Lumpectomy
- Adjuvant therapy • Postmastectomy radiation • Regional nodal irradiation

KEY POINTS

- Regional nodal irradiation has the potential to improve disease-free survival among patients with limited axillary disease.
- Accelerated partial breast irradiation is a convenient and effective adjuvant radiotherapy (RT) approach for appropriately selected patients.
- RT omission: certain subgroups of patients are of sufficiently low risk to forego adjuvant radiotherapy. Studies in this domain are ongoing.

- REGIONAL NODAL IRRADIATION,
- RT POST-NACT
- ACCELERATED PARTIAL BREAST IRRADIATION
- OMISSION OF ADJUVANT RADIOOTHERAPY FOLLOWING BCS



ACTA ONCOLOGICA
2019, VOL. 58, NO. 1, 9-20
<https://doi.org/10.1080/0284186X.2018.1554259>



Check for updates

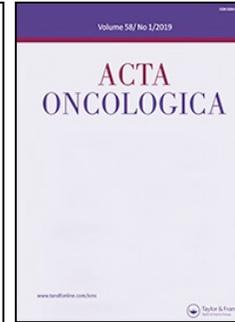
INVITED ARTICLE

Rationale for combination of radiation therapy and immune checkpoint blockers to improve cancer treatment

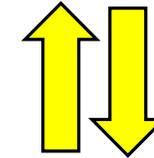
Olav Dahl^{a,b}, Jon Espen Dale^b and Marianne Brydøy^b

2019

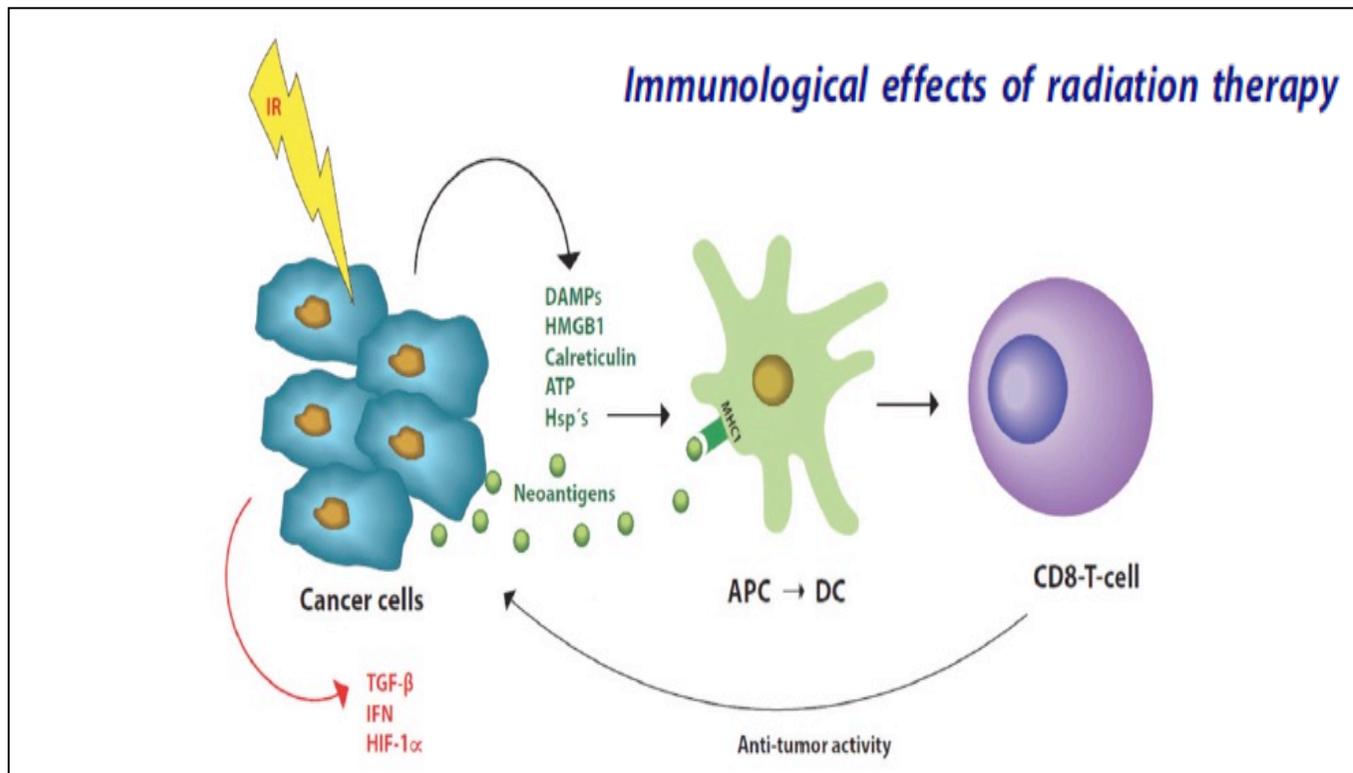
^aDepartment of Clinical Science, Faculty of Medicine, University of Bergen, Bergen, Norway; ^bDepartment of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway



RT and immunosuppression



Microenvironment



Radiation therapy is generally considered to be a local treatment.....and immunosuppressive one.....

However, occasionally response in tumor deposits outside the treated volume has been reported, thus suggesting a systemic effect.....

*This phenomenon has been described as an **abscopal** (out of field) effect*



Associazione Italiana
Radioterapia e Oncologia clinica

2019
Best Clinical Practice
nella Radioterapia della Mammella

Gruppo di Lavoro per la Patologia Mammaria

Best Clinical Practice nella Radioterapia dei Tumori della Mammella 2019



50 QUESITI:

Terapia Sistemica: 2

Carcinoma invasivo: 10

Carcinoma non invasivo e microinvasivo: 5

Situazioni particolari: 10

Recidive loco-regionali e malattia metastatica: 3

Radioterapia dopo chirurgia conservativa: 4

Radioterapia dopo mastectomia : 5

Radioterapia delle stazioni linfonodali: 7

Irradiazione parziale: 2

Appendice di Contornamento: 2

Strategia Generale: 0

Follow up e tox: 0

Appendice boost: 0

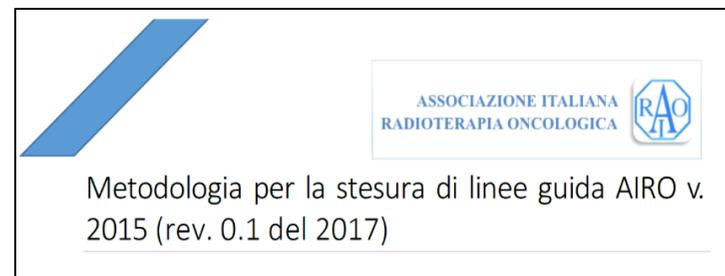
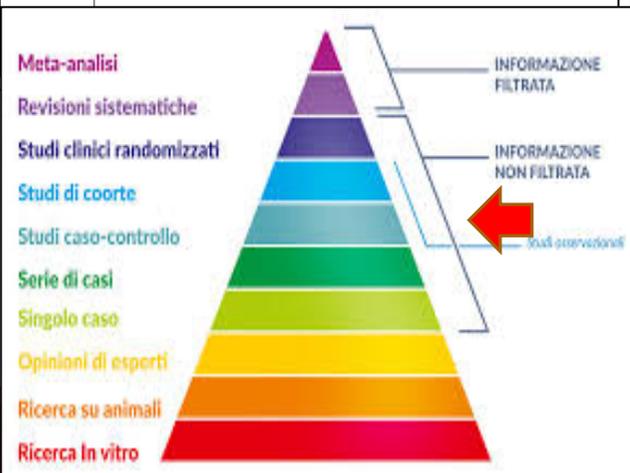


TABELLA I – Livelli di evidenza e descrittori

1 _≥	Revisioni sistematiche e meta-analisi di RCT o singoli RCT
1++	Rischio di bias molto basso
1+	Rischio di bias basso
1-	Rischio di bias elevato ≥ i risultati dello studio non sono
2 _≥	Revisioni sistematiche e meta-analisi di studi caso/controlli o di coorte
2++	Rischio di bias molto basso, probabilità molto bassa di relazione causale tra intervento ed effetto
2+	Rischio di bias basso, bassa probabilità di confondimento, moderata probabilità di relazione causale ed effetto
2-	Rischio di bias elevato ≥ i risultati dello studio non sono elevati rischio che la relazione intervento/effetto non
3 _≥	Disegni di studio non analitici come report di casi e serie

TABELLA II – Grado delle evidenze

A. Almeno una meta-analisi di RCT o di studi caso/controlli o di coorte. Il corpo delle evidenze può essere direttamente applicato al paziente. Le evidenze dovrebbero essere considerate valide per il trattamento.
B. Il corpo delle evidenze è direttamente applicabile alla popolazione per dimensione dell'effetto. Evidenze estrapolate.
C. Il corpo delle evidenze è direttamente applicabile alla popolazione per dimensione dell'effetto. Evidenze estrapolate.
D. Evidenze di livello 3 o 4. Evidenze estrapolate.



Forza della raccomandazione	Descrizione	Esempio esplicativo
Positiva forte	La maggior parte dei pazienti con le caratteristiche descritte devono essere invitati a considerare l'intervento in oggetto; il bilancio tra beneficio e danno è nettamente a favore del beneficio	Nei pazienti X con le caratteristiche Y, il trattamento Z <u>deve</u> essere somministrato
Positiva debole	pazienti con le caratteristiche descritte devono essere informati sull'esistenza di un trattamento che potrebbe avere degli effetti positivi, tuttavia il bilancio tra beneficio e danno del trattamento è carico di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z <u>dovrebbe</u> essere somministrato
Negativa debole	A fronte di una piccola probabilità di beneficio dovuto al trattamento, il bilancio beneficio/ danno tende a dimostrare più eventi dannosi e le evidenze sono cariche di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z <u>non dovrebbe</u> essere somministrato
Negativa forte	I pazienti non devono essere sottoposti all'intervento in oggetto perché il bilancio beneficio/ danno è a favore del danno con un buon margine di certezza	Nei pazienti X con le caratteristiche Y, il trattamento Z <u>non deve</u> essere somministrato



Contemporary Issues in Breast Cancer Radiotherapy



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REGIONAL NODAL IRRADIATION

RT POST-NACT

ACCELERATED PARTIAL BREAST IRRADIATION

OMISSION OF ADJUVANT RADIOOTHERAPY FOLLOWING BREAST CONSERVING SURGERY

RT lfn**QUESITO CLINICO**

Nelle pazienti con carcinoma mammario invasivo sottoposte a chirurgia conservativa in presenza di 1-3 linfonodi ascellari positivi, può essere considerato un trattamento radiante a livello delle stazioni linfonodali loco-regionali non trattate chirurgicamente?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con carcinoma mammario invasivo sottoposte a chirurgia conservativa in presenza di 1-3 linfonodi ascellari positivi, PUÒ ESSERE CONSIDERATO un trattamento radiante a livello delle stazioni linfonodali loco-regionali non trattate chirurgicamente	Positiva debole

Almeno 2 o più caratteristiche biologiche sfavorevoli (età ≤ 40-45 anni, dimensioni tumorali ≥ 3,5-4 cm, negatività recettoriale, presenza di invasione linfovaskolare, estensione extracapsulare della metastasi linfonodale, grading elevato, rapporto tra numero di linfonodi positivi e numero di linfonodi escissi > 20-25%).

In queste situazioni si ritiene indispensabile la discussione multidisciplinare e una scelta condivisa con la paziente, dopo un'attenta valutazione dei rischi-benefici.

(Qualità globale dell'evidenza: MODERATA)



Abstract GS4-02: Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials

D Dodwell, C Taylor, P McGale, C Coles, F Duane, R Gray, T Kühn, C Hennequin, S Oliveros, Y Wang, J Overgaard, P Poortmans, and T Whelan

DOI: 10.1158/1538-7445.SABCS18-GS4-02 Published February 2019 [Check for updates](#)



13,132 women in 14 comparisons of nodal RT versus not.

- Early Breast Cancer Trialists' Collaborative Group (EBCTCG)
- Over 13,000 patients in 14 trials

Node RT versus not

No. trials

No. patients

Axilla and SC

IMC

Axilla, SC and IMC

All Trials

8 trials starting 1/19

6 trials starting 1/18

Overall outcome:

- | | | | | |
|-------------------------------------|-----------|----|-------------|--------------------|
| | No Reg RT | vs | Regional RT | |
| • Any recurrence at 15 years: | 34.6% | vs | 31.7% | (RR=0.89, p=0.002) |
| • Breast cancer mortality at 15 yr: | 29.1% | vs | 25.1% | (RR=0.88, p=0.003) |

Newer trials:

- | | | | | |
|--|-------|----|-------|--------------------|
| • pN0 | | | | |
| • Breast cancer mortality at 10 yr: | 8.9% | vs | 7.6% | (RR=0.80, p=0.10) |
| • pN1-3 | | | | |
| • Breast cancer mortality at 10 yr: | 16.2% | vs | 14.8% | (RR=0.88, p=0.08) |
| • pN4+ | | | | |
| • Breast cancer mortality at 10 yr: | 42.3% | vs | 34.4% | (RR=0.77, p=0.001) |
| • No excess of non-breast cancer mortality | | | | |

2019



Abstract GS4-02: Regional lymph node irradiation in early stage breast cancer: An EBCTCG meta-analysis of 13,000 women in 14 trials

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DOI: 10.1158/1538-7445.SABCS18-GS4-02 Published February 2019 [Check for updates](#)



pN0:

Thoracic wall: T3 (with additional risk factors) and T4
Nodes: no nodal irradiation

N1-3 positive nodes - medial tumors:

Thoracic wall: according to additional risk factors
Nodes: consider IMC irradiation

N1-3 positive nodes - lateral tumors:

Thoracic wall: according to additional risk factors
Nodes: regional irradiation for high risk patients

N4+ positive nodes:

Thoracic wall: yes
Nodes: regional irradiation

Conclusions RT to regional lymph nodes in older (1961–78) studies increased the overall risk of death, probably explained by radiation exposure of the lungs and heart. Nodal RT in more recent (1989–2003) studies reduced breast cancer recurrence, breast cancer mortality and overall mortality without increasing non–breast cancer mortality. The proportional benefits from today's RT may be larger. Absolute benefits for individual women will depend on their absolute recurrence and breast cancer mortality risks.



QUESITO CLINICO

Nelle pazienti con carcinoma mammario invasivo pT1-2 pN+ (1-3 linfonodi ascellari positivi) o pT3 pN0 sottoposte a mastectomia totale, è indicata l'irradiazione della parete toracica e delle stazioni linfonodali loco-regionali non trattate chirurgicamente?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
A	<p>Nelle pazienti con carcinoma mammario invasivo pT1-2 pN+ (1-3 linfonodi ascellari positivi) con almeno due fattori di rischio sottoposte a mastectomia totale, PUÒ ESSERE CONSIDERATA l'irradiazione della parete toracica e delle stazioni linfonodali loco-regionali non trattate chirurgicamente.</p> <p>Nelle pazienti pT3 pN0 con almeno due fattori di rischio sottoposte a mastectomia totale può essere considerata l'irradiazione della sola parete toracica</p>	Positiva debole

Almeno 2 o più caratteristiche biologiche sfavorevoli (età ≤ 40-45 anni, dimensioni tumorali ≥ 3,5-4 cm, negatività recettoriale, presenza di invasione linfovaskolare, estensione extracapsulare della metastasi linfonodale, grading elevato, rapporto tra numero di linfonodi positivi e numero di linfonodi escissi > 20-25%).

In queste situazioni si ritiene indispensabile la discussione multidisciplinare e una scelta condivisa con la paziente, dopo un'attenta valutazione dei rischi-benefici.

(Qualità globale dell'evidenza: MODERATA)



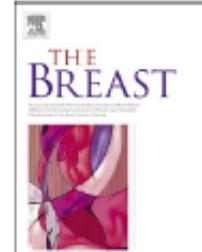
Review

The Breast 48 (2019) 73–81

Postmastectomy radiotherapy in T1-2 patients with one to three positive lymph nodes – Past, present and future

Filip Kaššák, Christine Rossier, Cristina Picardi, Jacques Bernier*

Radiation Oncology Department, Swiss Oncology Network, Genolier Clinic and Oncological Center of Eaux-Vives, Switzerland



25 STUDIES

5. Risk factors to guide indication

2019

Age

Number of dissected LFN and ratio (20%) 15 TOT!!

Absolute number of positive LFN and size: 1 and N1mi better

Primary tumor size and stage

Grade, lymphovascular invasion and receptor status

Extracapsular

Cdis component

Close margins

Future: A prospective randomized controlled trial SUPREMO will release its final results in 2023 and shed light onto the subject. Genomic tumor cell profiling will likely provide further guidelines in terms of risk stratification. SUPREMO translational sub-study will also offer material for genomic analyses. A

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Radiation Therapy or Standard Therapy in Treating Women With Stage II Breast Cancer Who Have Undergone Mastectomy

Experimental: Arm I **RT**

Beginning 12 weeks after mastectomy or 6 weeks after adjuvant chemotherapy, patients undergo radiotherapy 5 days a week for 3-5 weeks in the absence of disease progression or unacceptable toxicity.

Active Comparator: Arm II **no RT**

Patients receive standard of care and observation only.

No > 3 LFN pathologically involved

**RT Ifn****QUESITO CLINICO**

Nelle pazienti con pN1 mic/mac dopo BLS, in presenza di fattori prognostici sfavorevoli, l'irradiazione linfonodale può sostituire/compensare l'astensione dalla ALND?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con pN1 mic/mac dopo BLS, in presenza di fattori prognostici sfavorevoli, l'irradiazione linfonodale PUO' sostituire/compensare l'astensione dalla ALND	Positiva debole

STUDI IN CORSO

Tecnicamente il I° e il II° livello andrebbero sempre contornati, in modo da verificare la reale copertura con i campi tangenti, che potrebbero eventualmente essere modificati per includere questi livelli all'interno di dosi adeguate e con un rischio minimo di aumento di tossicità

(Qualità globale dell'evidenza: MODERATA)

Table 2

Ongoing or recently closed European trials on management of the axilla in patients with operable invasive breast cancer.

Study	Country of origin	Design	Target patient accrual	Start-End dates
SOUND (Sentinel node vs. Observation after axillary Ultrasound) [28]	Italy	cT1 cN0, for BCS + WBRT <u>randomized to</u> <i>No axillary surgery vs. SLNB</i>	1,560	Mar 2012–Jun 2017
POSNOG (Positive Sentinel Node: adjuvant therapy alone versus adjuvant therapy plus Clearance or axillary radiotherapy) [29]	UK	cT1-2 cN0 with 1–2 (+)SLNs (macrometastasis ^a only), for BCS or Mastectomy <u>randomized to</u> <i>No ALND vs. ALND or ax-RT</i>	1,900	Jan 2014–Dec 2023
INSEMA (Intergroup Sentinel Mamma) [30,31]	Germany	cT1-2 cN0, for BCS + WBRT <u>randomized to</u> <i>No axillary surgery vs. SLNB (1:4 allocation) cases with 1–3 (+)SLNs (macrometastasis^a only)</i> <u>2nd randomization to</u> <i>No ALND vs. ALND (1:1 ratio)</i>	7,095	Sep 2015–Sep 2024
BOOG 2013-07 (The value of completion axillary treatment in sentinel node positive breast cancer patients undergoing a mastectomy) [32]	Netherlands	cT1-2 cN0 with 1–3 (+)SLNs (micro ^b or macrometastasis ^a), for Mastectomy <u>randomized to</u> <i>No ALND vs. ALND or ax-RT</i>	878	Jun 2014–Jun 2027
SINODAR ONE (Randomized Clinical Trial to Assess the Role of Axillary Surgery in Breast Cancer Patients with One or Two Macrometastatic Sentinel Nodes) [33]	Italy	cT1-2 cN0 with 1–2 (+)SLNs (macrometastasis ^a only), for BCS or Mastectomy <u>randomized to</u> <i>No ALND vs. ALND</i>	2,000	Apr 2015–Mar 2018
SENOMAC (Omission of Axillary Clearance in Breast Cancer Patients with Sentinel Node Macrometastases) [34,35]	Sweden	cT1-3 cN0 with 1–2 (+)SLNs (macrometastasis ^a only), including also patients prior to neoadjuvant chemo, for BCS or Mastectomy <u>randomized to</u> <i>No ALND vs. ALND</i>	3,500	Jan 2015–Jan 2022
TAXIS (Tailored axillary surgery with or without axillary lymph node dissection followed by radiotherapy in patients with clinically node-positive breast cancer) [36]	Switzerland	Any cT cN1-2(f), +/- neoadjuvant chemo, also isolated rcT, for BCS + WBRT or Mastectomy + chest wall RT <u>randomized to</u> <i>TAS + ALND + RN-RT vs. TAS + RNax-RT</i>	1,500	Aug 2018–Mar 2029



Original Article

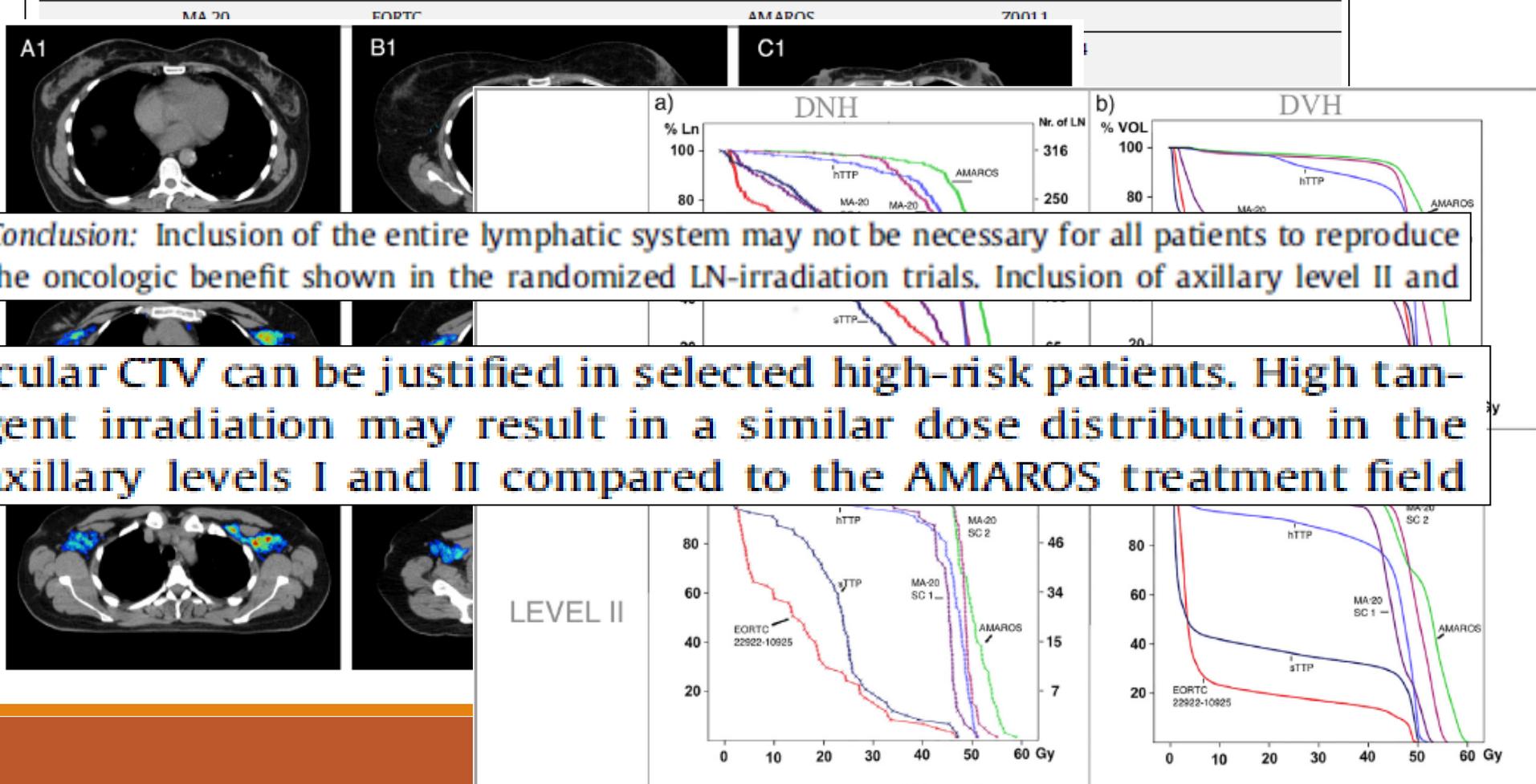
Irradiation of regional lymph node areas in breast cancer – Dose evaluation according to the Z0011, AMAROS, EORTC 10981-22023 and MA-20 field design

Kai Joachim Borm^a, Markus Oechsner^a, Mathias Düsberg^a, Gabriel Buschner^b, Wolfgang Weber^b, Stephanie Elisabeth Combs^{a,c,d}, Marciana-Nona Duma^{a,e,*}

2019

Table 1

Overview randomized lymph node treatment and irradiation trials. ALND = axillary lymph node dissection, SLND = sentinel lymph node dissection, OS = overall survival.





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OMISSION OF ADJUVANT RADIOOTHERAPY FOLLOWING BREAST CONSERVING SURGERY

RT post NACT



QUESITO CLINICO

Nelle pazienti con carcinoma mammario invasivo cT1-cT2 cN1 sottoposte a terapia medica neoadiuvante e chirurgia conservativa, è indicato completare il trattamento con la radioterapia che comprenda tutta la mammella?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
A	Nelle pazienti con carcinoma mammario invasivo cT1-cT2 cN1 sottoposte a terapia medica neoadiuvante e chirurgia conservativa, SI DOVREBBE completare il trattamento con la radioterapia che comprenda tutta la mammella residua.	Positiva forte

L'irradiazione delle stazioni linfonodali dovrebbe essere valutata considerando la risposta alla NACT, riscontrata con la biopsia del linfonodo sentinella post-NACT cui segue o meno la dissezione ascellare

(Qualità globale dell'evidenza: ALTA)

RT post NACT

QUESITO CLINICO

Nelle pazienti con carcinoma mammario invasivo cT1-cT2 cN1 sottoposte a terapia medica neoadiuvante e mastectomia, è possibile omettere l'irradiazione loco-regionale?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con carcinoma mammario invasivo cT1-cT2 cN1 sottoposte a terapia medica neoadiuvante e mastectomia, con risposta patologica completa sia su T che su N, in caso di basso rischio di recidiva loco-regionale PUÒ ESSERE presa in considerazione l'omissione dell'irradiazione della parete toracica.	Positiva debole

L'irradiazione della parete toracica e delle stazioni linfonodali dovrebbe essere considerata anche in pazienti con ypCR/ypN0 in presenza di fattori di rischio (giovane età, ER/PR negativi, invasione linfovaskolare) . In caso di persistenza di malattia nelle stazioni linfonodali, queste dovrebbero essere irradiate, indipendentemente dai fattori di rischio

(Qualità globale dell'evidenza: MODERATA)



RT post NACT

QUESITO CLINICO

Nelle pazienti con carcinoma mammario invasivo cT3 cN0 sottoposte a terapia medica neoadiuvante e mastectomia, è indicata l'irradiazione della parete toracica +/- stazioni linfonodali locoregionali?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con carcinoma mammario invasivo cT3 cN0 sottoposte a terapia medica neoadiuvante e mastectomia, PUÒ ESSERE presa in considerazione l'irradiazione della parete toracica.	Positiva debole

In caso di malattia di grandi dimensioni, anche in presenza di remissione completa, l'indicazione alla RT sulla parete toracica dovrebbe essere tenuta in considerazione, soprattutto in presenza dei già citati fattori di rischio.

(Qualità globale dell'evidenza: MODERATA)

RT post NACT

QUESITO CLINICO

Nelle pazienti con carcinoma mammario invasivo localmente avanzato, cT3 cN1; qualunque cT cN2: cT4 qualunque cN, sottoposte a terapia medica neoadiuvante e mastectomia, è indicata l'irradiazione della parete toracica e delle stazioni linfonodali loco-regionali non trattate chirurgicamente?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
A	Nelle pazienti con carcinoma mammario invasivo localmente avanzato, cT3 cN1; qualunque cT cN2: cT4 qualunque cN, sottoposte a terapia medica neoadiuvante e mastectomia SI DOVREBBE eseguire la RT adiuvante, estesa alla parete toracica e ai drenaggi linfonodali	Positiva forte

Si tratta di una situazione clinica ad alto rischio di ripresa di malattia sia a livello loco-regionale che a distanza.

(Qualità globale dell'evidenza: ALTA)



St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment

Radiotherapy

Review Article

Breast Care 2019;14:103–110
DOI: 10.1159/000499931

With regard to post-mastectomy radiotherapy (PMRT; chest wall and RNI), the panel was divided concerning pT3 pN0 situations (yes 56%, no 44%) and N+ 1–3 ER+ or HER2+ (yes 43%, no 43%), but clear on N+ 1–3 with adverse features such as TNBC (yes 85%, no 8%) and pT2 pN0 with bad features (yes 28%, no 64%). For patients with 1–2 positive nodes but no axillary dissection, the panel recommended PMRT + RNI (yes 66%, no 17%).

2019

**NEOADJUVANT CHEMOTHERAPY COMPLICATES CLINICAL DECISION-
MAKING REGARDING USE OF PMRT**



Ann Surg Oncol
<https://doi.org/10.1245/s10434-019-07635-x>

Annals of
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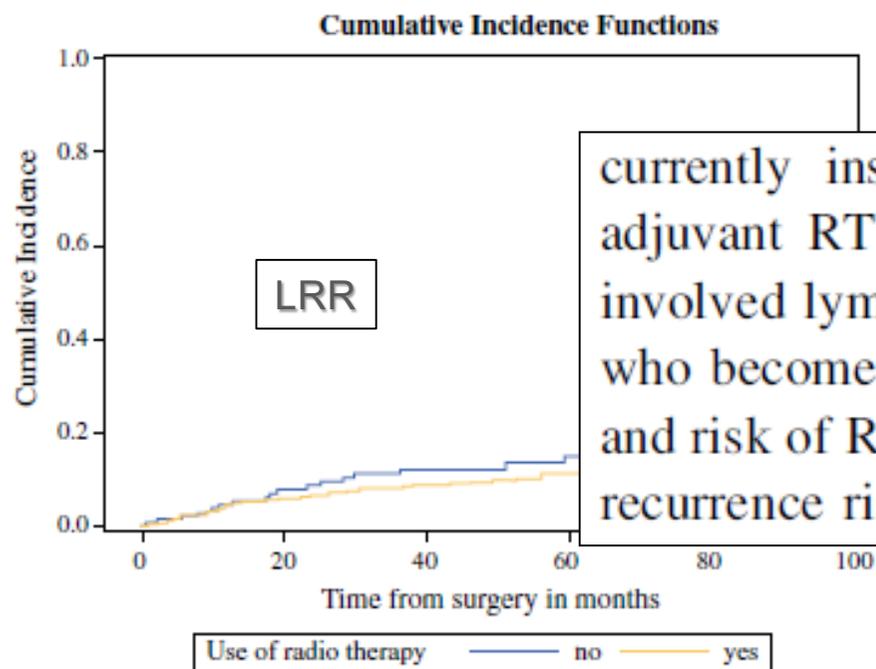
ORIGINAL ARTICLE – BREAST ONCOLOGY

**Post-Mastectomy Radiotherapy After Neoadjuvant
 Chemotherapy in Breast Cancer: A Pooled Retrospective Analysis
 of Three Prospective Randomized Trials**

trials (GeparTrio, GeparQuattro, and GeparQuinto) have been published elsewhere.^{13–19}

A total of 6139 patients were treated in these trials from

2019



currently insufficient evidence for routine omission of adjuvant RT in patients with cT3/4 tumors or clinically involved lymph nodes.^{11,27,35} In patients with cT1–2 cN+ who become ypN0 or have pCR after NACT, the benefit and risk of RT should be discussed based on the individual recurrence risk for each patient.



Original Article

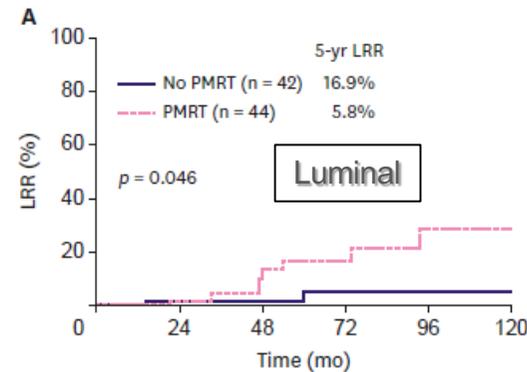
Check for updates

J Breast Cancer. 2019 Jun;22(2):285-296
https://doi.org/10.4048/jbc.2019.22.e25
pISSN 1738-6756·eISSN 2092-9900

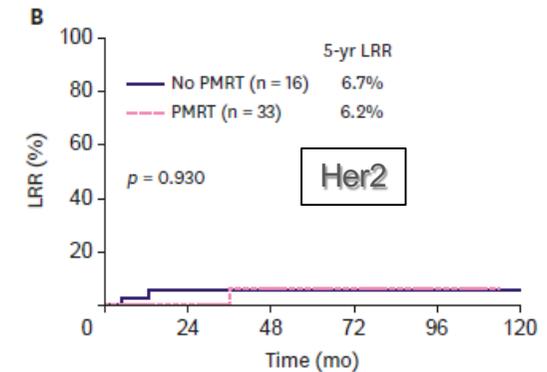
The Benefit of Post-Mastectomy Radiotherapy in ypN0 Patients after Neoadjuvant Chemotherapy According to Molecular Subtypes

following NAC. From 1
and 2011, a total of 189

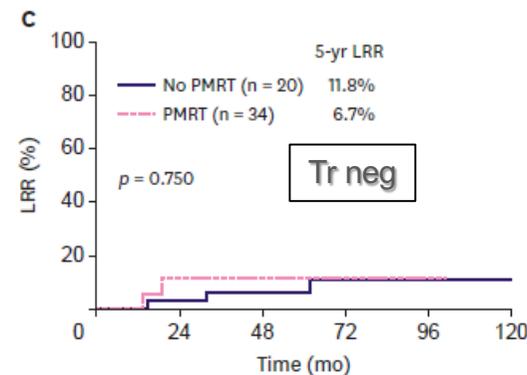
2019



No. at risk						
No PMRT	42	40	30	22	11	2
PMRT	44	39	34	24	10	6



No. at risk						
No PMRT	16	16	15	12	2	1
PMRT	33	27	23	21	10	6



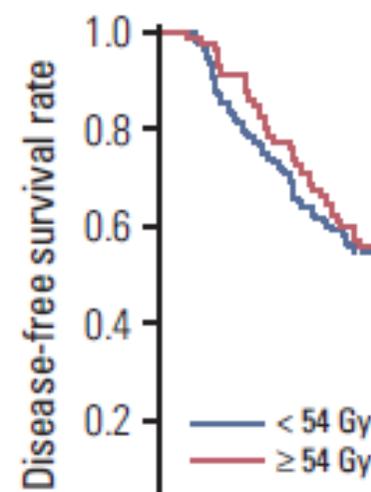
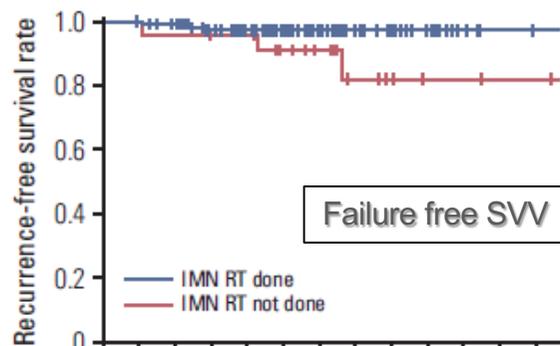
Conclusion: In patients who achieve ypN0 following NAC and mastectomy, PMRT shows no additional survival benefits for any molecular subtype.

Impact of Regional Nodal Irradiation for Breast Cancer Patients with Supraclavicular and/or Internal Mammary Lymph Node Involvement: A Multicenter, Retrospective Study (KROG 16-14)

Materials and Methods

A total of 353 patients from 11 institutions were included. One hundred and thirty-six patients had SCL involvement, 148 had IMN involvement, and 69 had both. All patients received neoadjuvant systemic therapy followed by breast-conserving surgery and postoperative RT to whole breast/chest wall. As supraclavicular RT was given to 344 patients, and IMN RT to 236 patients.

2019



Conclusion

Neoadjuvant chemotherapy followed by surgery and postoperative RT achieved an acceptable in-field regional control rate in patients with SCL and/or IMN involvement. However, a higher RT dose to SCL or IMN RT was not associated with the improved DFS in these patients.

RT post NACT: LFN

QUESITO CLINICO

Nelle pazienti con carcinoma mammario avviate a terapia medica neoadiuvante e chirurgia con dissezione linfonodale ascellare è indicata l'irradiazione delle stazioni linfonodali rispetto alla non irradiazione per ridurre la recidiva locoregionale?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione
A	Nelle pazienti con carcinoma mammario avviate a terapia medica neoadiuvante e chirurgia con dissezione linfonodale ascellare l'irradiazione delle stazioni linfonodali DOVREBBE ESSERE proposta IN PRESENZA DI LINFONODI PATOLOGICI dopo terapia medica neoadiuvante per ridurre il rischio di recidiva locoregionale	Positiva forte

Si precisa che nelle pazienti con carcinoma mammario avviate a terapia medica neoadiuvante e dissezione linfonodale ascellare **non vi è parere unanime sulla radioterapia delle stazioni linfonodali in caso di risposta patologica completa dopo dissezione**. In questo caso infatti la qualità delle evidenze è molto bassa (Livello SIGN 2-, Qualità B) e la stima dell'effetto è inaffidabile per esprimere raccomandazioni congruenti



(Qualità globale dell'evidenza: ALTA)



RT post NACT: LFN

QUESITO CLINICO

Nelle pazienti con carcinoma mammario avviate a terapia medica neoadiuvante e sola biopsia del linfonodo sentinella dopo terapia medica neoadiuvante è indicata l'irradiazione delle stazioni linfonodali ascellari rispetto alla non irradiazione per ridurre la recidiva locoregionale?

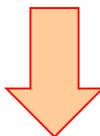
Qualità dell'evidenza SIGN	Raccomandazione clinica		Forza della raccomandazione
B	Nelle mam all'es asce med biops nega DOV risch bass	Qualità dell'evidenza SIGN	Forza della raccomandazione
	B	Nelle pazienti con carcinoma mammario cl clinicamente positivo all'esordio per interessamento ascellare di malattia, avviate a terapia medica neoadiuvante con risposta clinico-radiologica e successiva biopsia del linfonodo sentinella risultata negativa , la radioterapia delle stazioni linfonodali NON DOVREBBE essere eseguita.	Negativa debole

(Qualità globale dell'evidenza: BASSA)

(Qualità globale dell'evidenza: BASSA)

Neo-nod 2: Study Design

Chemioterapia Neoadiuvante : cT1-2-3 cN+

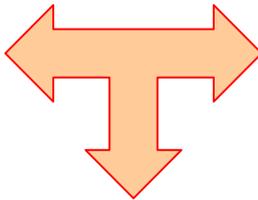


cN0

Chirurgia:
Quadrantectomia o
Mastectomia

2019

BLS pN0
No DA



BLS pN \geq 1
DA

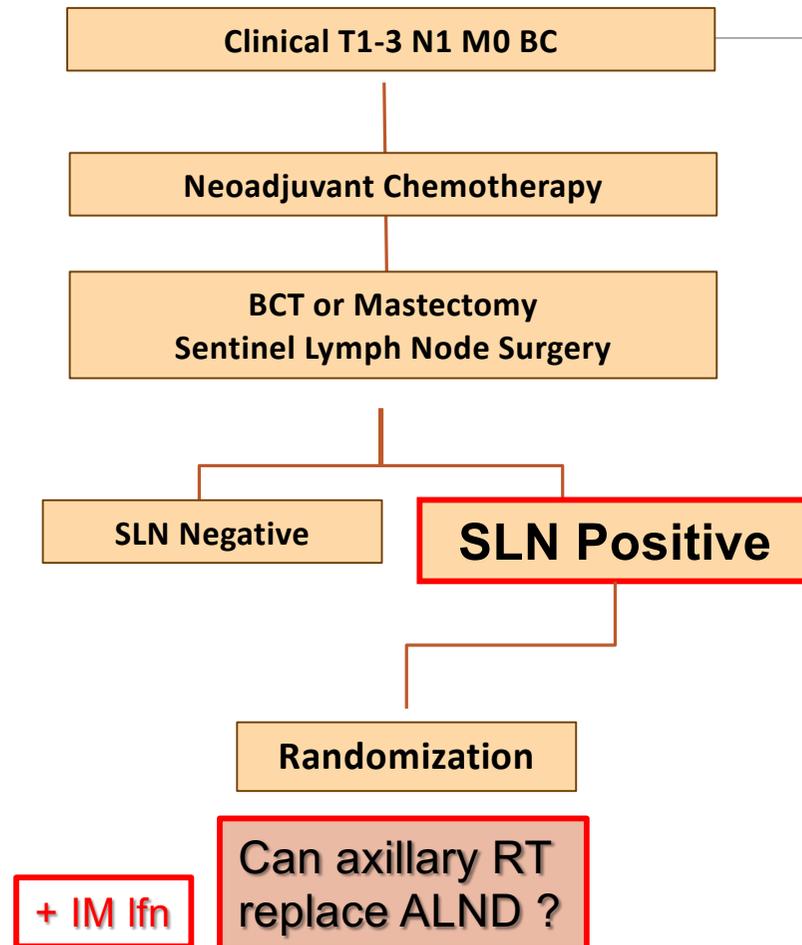
BLS pN1mi
No DA
No RT



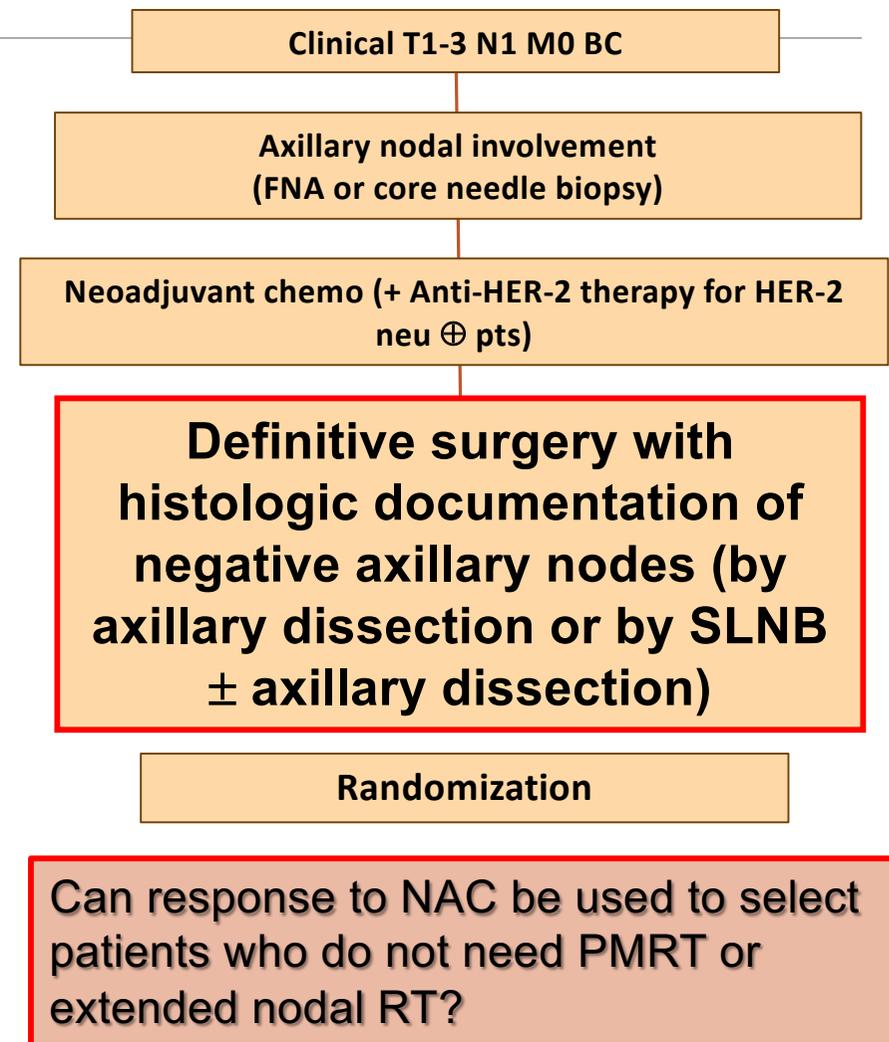


Post NACT Trials of Axillary Management

ALLIANCE A11202 Schema

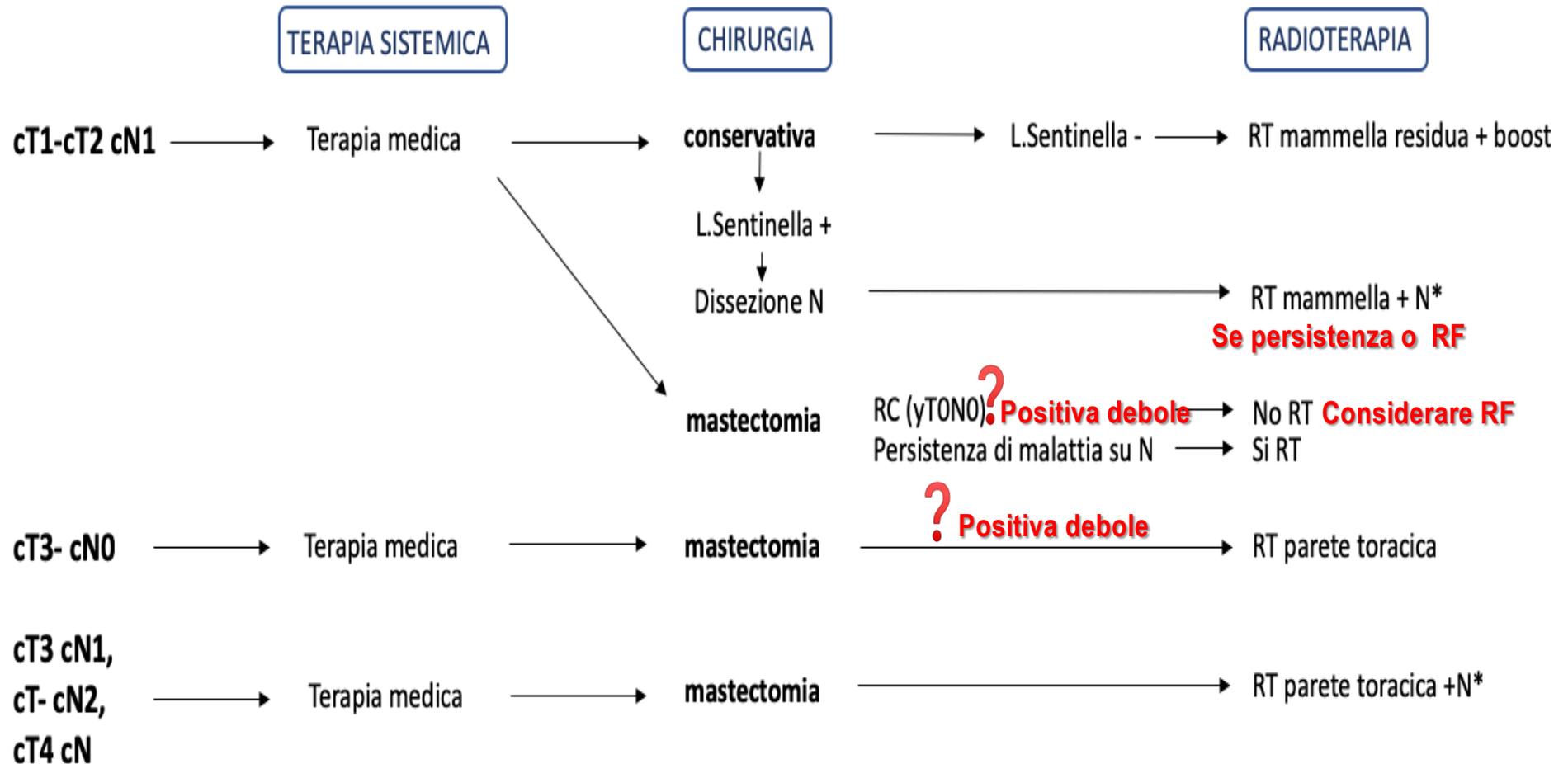


NSABP B-51/RTOG 1304 (NRG 9353) Schema



Linee Guida Neoplasia della Mammella V. 2019

Radioterapia Dopo Chemioterapia Neoadiuvante



*Vedi capitolo 4.2.3 Radioterapia delle stazioni linfonodali



Contemporary Issues in Breast Cancer Radiotherapy



Lior Z. Braunstein, MD^a, Jennifer R. Bellon, MD^{b,*}

2020

Hematol Oncol Clin N Am 34 (2020) 1–12
<https://doi.org/10.1016/j.hoc.2019.08.014>
0889-8588/20/© 2019 Elsevier Inc. All rights reserved.

KEYWORDS

- Breast cancer • Radiotherapy • Breast conservation • Lumpectomy
- Adjuvant therapy • Postmastectomy radiation • Regional nodal irradiation

KEY POINTS

- Regional nodal irradiation has the potential to improve disease-free survival among patients with limited axillary disease.
- Accelerated partial breast irradiation is a convenient and effective adjuvant radiotherapy (RT) approach for appropriately selected patients.
- RT omission: certain subgroups of patients are of sufficiently low risk to forego adjuvant radiotherapy. Studies in this domain are ongoing.

REGIONAL NODAL IRRADIATION

RT POST-NACT

ACCELERATED PARTIAL BREAST IRRADIATION

OMISSION OF ADJUVANT RADIO THERAPY FOLLOWING BREAST CONSERVING SURGERY

APBI

QUESITO CLINICO

Nelle pazienti affette da carcinoma infiltrante a basso rischio, è indicata la PBI rispetto alla WBI, per ridurre il rischio di la recidiva locale?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
A	Pazienti con età ≥ 50 anni, affette da carcinoma mammario invasivo in stadio iniziale (≤ 3 cm , pN0), grado nucleare 1-2, ER+, HER2 negativo, sottoposte a chirurgia conservativa con almeno 2 millimetri come margini chirurgici, DOVREBBERO essere considerate per PBI	Positiva forte

ASTRO, GEC-ESTRO, IMPORT-LOW

(Qualità globale dell'evidenza: ALTA)

Nelle pazienti affette da carcinoma in situ, è indicata la PBI rispetto alla WBI, per ridurre il rischio di recidiva locale?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti affette da carcinoma duttale in situ la PBI NON DOVREBBE essere impiegata al di fuori di studi clinici.	Negativa debole

(Qualità globale dell'evidenza: BASSA)



St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment

Review Article

Breast Care 2019;14:103–110
DOI: 10.1159/000499931

HF Radiotherapy

The panel indicated that hypofractionated breast irradiation can be used for most patients as a care standard (52% for all patients, 19% following breast conservation only, and 21% abstention). With respect to radiotherapy on the breast and on regional lymph nodes (LNs), hypofractionated radiotherapy did not find a clear consensus (36% for most patients, age >50 years 30%, and 30% abstention).

2019

APBI

The panel endorsed (accelerated) partial breast irradiation for patients with low-risk features according to ASTRO/GEC-ESTRO guidelines by a small majority (44%), with some indicating that this may also be done for intermediate/cautionary risk features (18%), but 21% felt that (accelerated) partial breast irradiation should not be the standard because of worse cosmetic outcomes and/or higher recurrence risks.



Cancer Research

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General Session Abstracts

Abstract GS4-04: Primary results of NSABP B-39/RTOG 0413 (NRG Oncology): A randomized phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) for women with stage 0, I, or II breast cancer

FA Vicini, RS Cecchini, JR White, TB Julian, DW Arthur, RA Rabinovitch, RR Kuske, DS Parda, PA Ganz, MF Scheier, KA Winter, S Paik, HM Kuerer, LA Vallow, LJ Pierce, EP Mamounas, JP Costantino, HD Bear, I Germaine, G Gustafson, L Grossheim, IA Petersen, RS Hudes, WJ Curran Jr., and N Wolmark

DOI: 10.1158/1538-7445.SABCS18-GS4-04 Published February 2019 [Check for updates](#)



February 2019
Volume 79, Issue 4
Supplement
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2019

Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial



THE LANCET

www.thelancet.com Published online December 5, 2019 [https://doi.org/10.1016/S0140-6736\(19\)32514-0](https://doi.org/10.1016/S0140-6736(19)32514-0)

Frank A Vicini, Reena S Cecchini, Julia R White, Douglas W Arthur, Thomas B Julian, Rachel A Rabinovitch, Robert R Kuske, Patricia A Ganz, David S Parda, Michael F Scheier, Kathryn A Winter, Soonmyung Paik, Henry M Kuerer, Laura A Vallow, Lori J Pierce, Eleftherios P Mamounas, Beryl McCormick, Joseph P Costantino, Harry D Bear, Isabelle Germain, Gregory Gustafson, Linda Grossheim, Ivy A Petersen, Richard S Hudes, Walter J Curran Jr, John L Bryant*, Norman Wolmark

BREAST CANCER—LOCAL/REGIONAL/ADJUVANT

Patient-reported outcomes (PROs) in NRG oncology/NSABP B-39/RTOG 0413: A randomized phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) in stage 0, I, or II breast cancer.

Patricia A. Ganz, Reena S. Cecchini, Julia R. White, Frank Vicini, Thomas B. Julian, Douglas Arthur, ...

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

THE LANCET

www.thelancet.com Published online December 5, 2019 [https://doi.org/10.1016/S0140-6736\(19\)32514-0](https://doi.org/10.1016/S0140-6736(19)32514-0)

External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial



Timothy J Whelan, Jim A Julian, Tanya S Berrang, Do-Hoon Kim, Isabelle Germain, Alan M Nichol, Mohamed Akra, Sophie Lavertu, Francois Germain, Anthony Fyles, Theresa Trotter, Francisco E Perera, Susan Balkwill, Susan Chafe, Thomas McGowan, Thierry Muanza, Wayne A Beckham, Boon H Chua, Chu Shu Gu, Mark N Levine, Ivo A Olivetto, for the RAPID Trial Investigators*



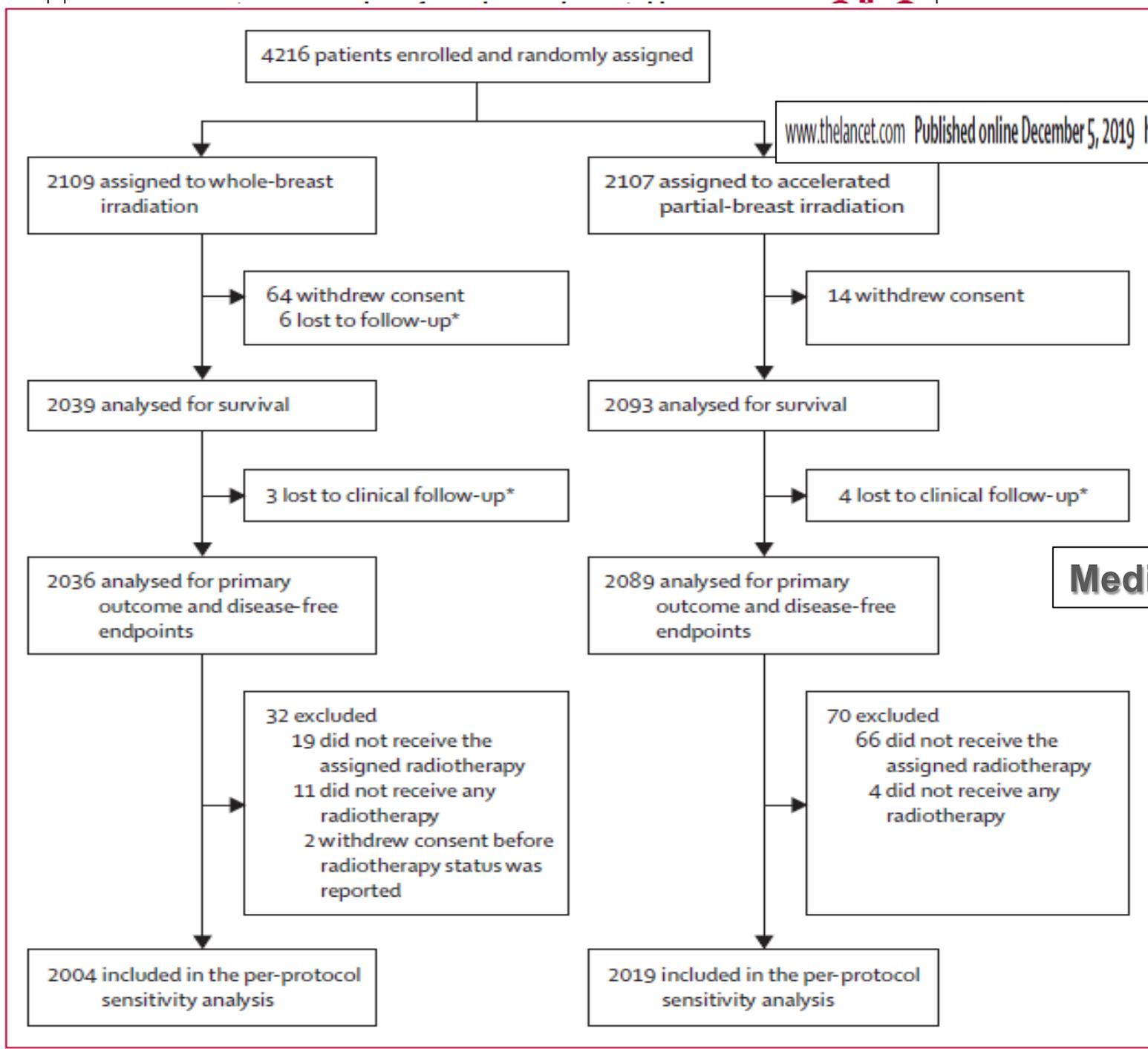
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www.thelancet.com Published online December 5, 2019 [https://doi.org/10.1016/S0140-6736\(19\)32514-0](https://doi.org/10.1016/S0140-6736(19)32514-0)

2005-2013:
154 centres
4216 pts,
2109 WBI
2107 APBI

Median FUP: 10,2 ys

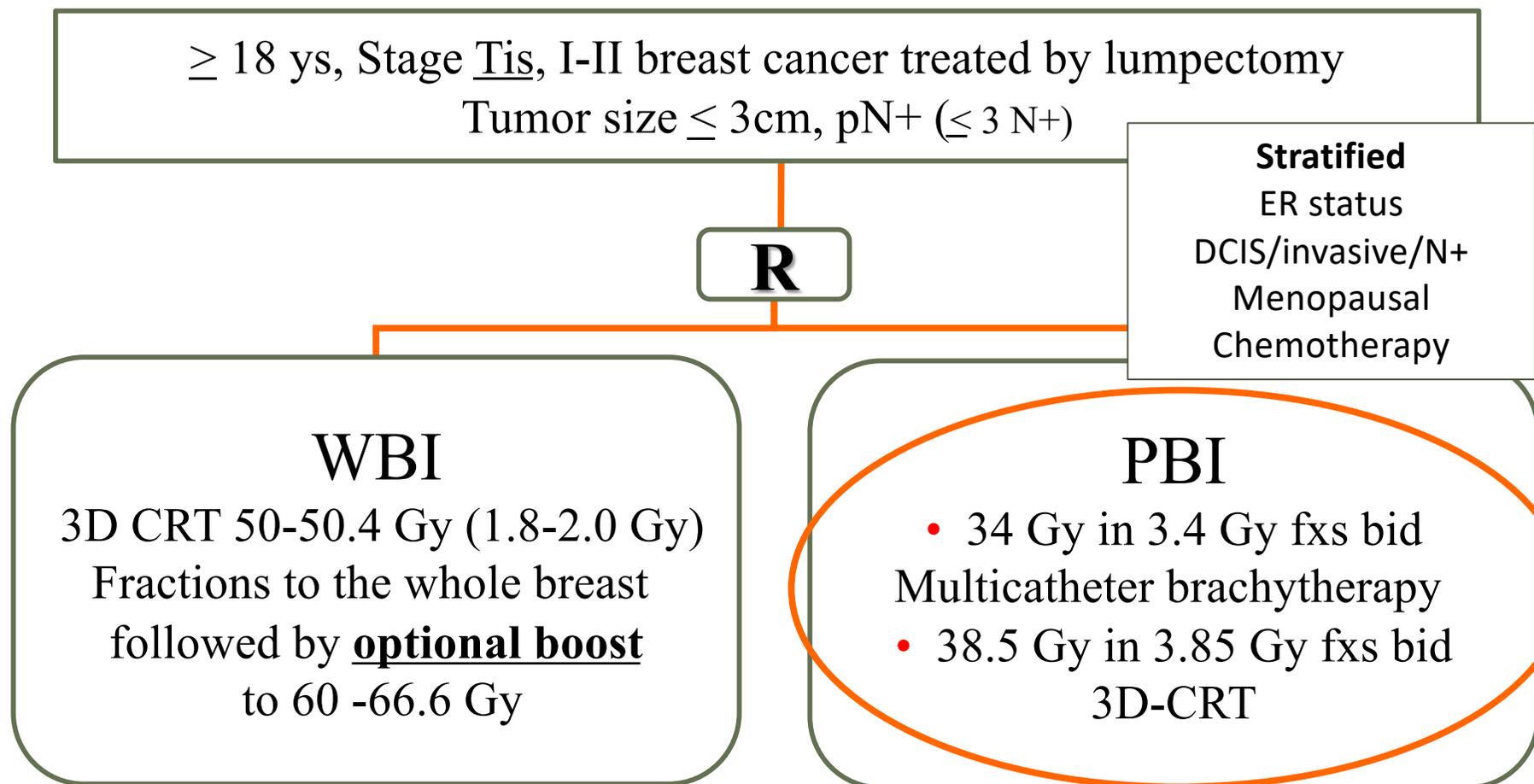
ights in Radioterapia 2020





NSABP-B39 / RTOG 0413

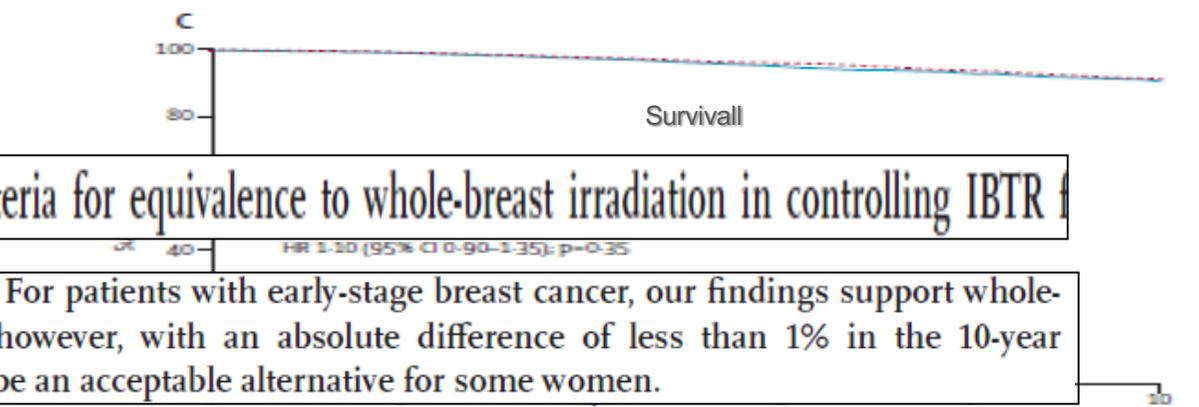
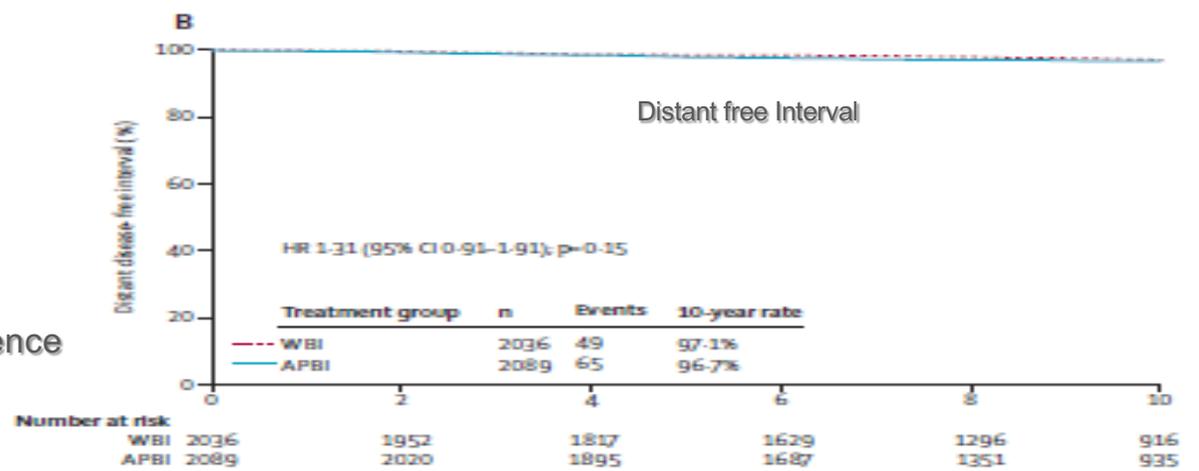
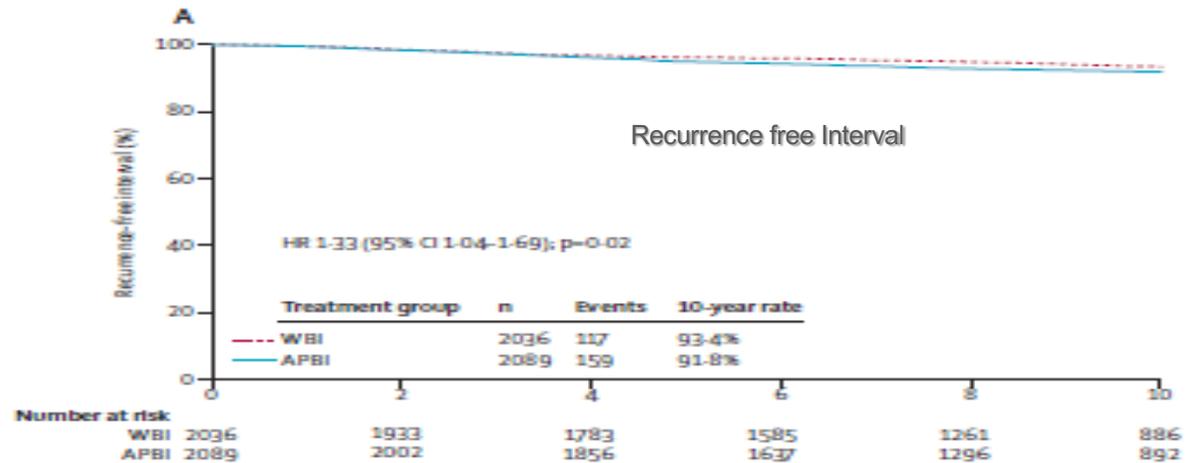
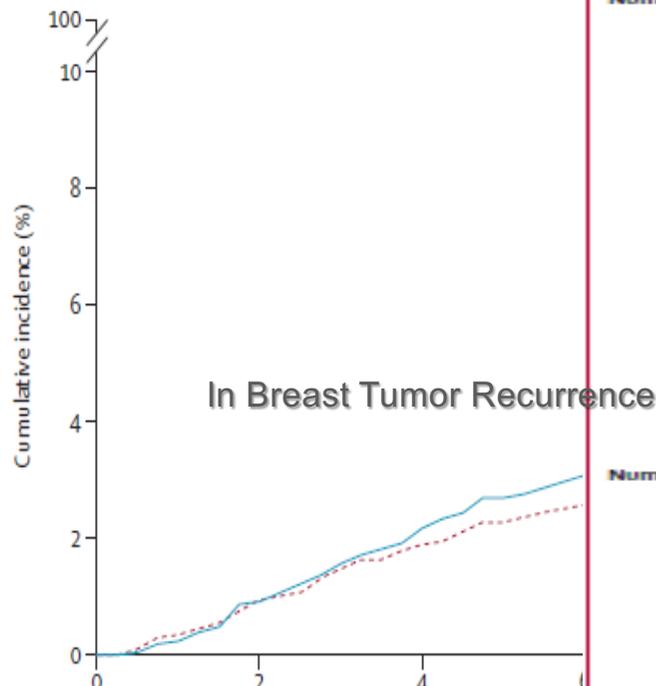
Frank Vicini, MD (NSABP) / Julia White, MD (RTOG)





Long-term primary results of accelerated irradiation after breast-conserving surgery for breast cancer: a randomised, phase 3, ec

Frank A Vicini, Reena S Cecchini, Julia R White, Douglas W Arthur, Thomas B Julian, Rachel A Ra David S Parda, Michael F Scheier, Kathryn A Winter, Soonmyung Paik, Henry M Kuerer, Laura A Beryl McCormick, Joseph P Costantino, Harry D Bear, Isabelle Germain, Gregory Gustafson, Linc Walter J Curran Jr, John L Bryant*, Norman Wolmark



Interpretation APBI did not meet the criteria for equivalence to whole-breast irradiation in controlling IBTR

For patients with early-stage breast cancer, our findings support whole-breast irradiation following lumpectomy; however, with an absolute difference of less than 1% in the 10-year cumulative incidence of IBTR, APBI might be an acceptable alternative for some women.

Number at risk	0	2	4	6	8	10
WBI	2039	1977	1861	1682	1368	1010
APBI	2093	2040	1945	1762	1438	1027

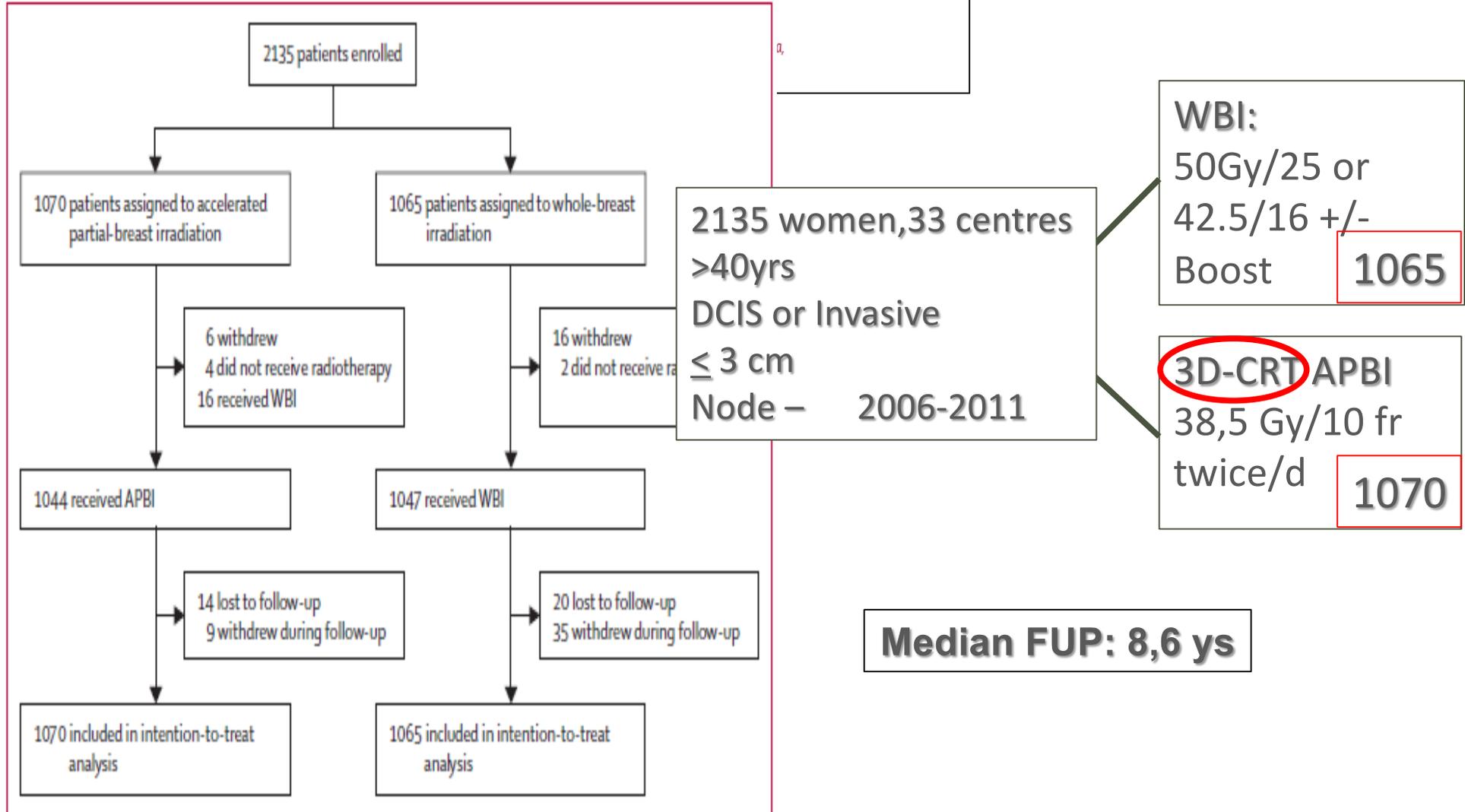


External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial



THE LANCET

www.thelancet.com Published online December 5, 2019 [https://doi.org/10.1016/S0140-6736\(19\)32514-0](https://doi.org/10.1016/S0140-6736(19)32514-0)





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IBTR

	APBI (n=1070)			WBI (n=1065)		
	Grade 2	Grade 3	Total	Grade 2	Grade 3	Total
Acute period						
Radiation dermatitis	101 (9.4%)	1 (<0.5%)	102 (9.5%)	322 (30.2%)	6 (0.6%)	328 (30.8%)
Fatigue	130 (12.1%)	9 (0.8%)	139 (13.0%)	146 (13.7%)	5 (0.5%)	151 (14.0%)
Breast swelling	63 (5.9%)	1 (<0.5%)	64 (6.0%)	90 (8.5%)	1 (<0.5%)	91 (8.5%)
Breast pain	69 (6.4%)	2 (<0.5%)	71 (6.6%)	78 (7.3%)	4 (<0.5%)	82 (7.7%)
Pneumonitis	2 (<0.5%)	0	2 (<0.5%)	7 (0.7%)	1 (<0.5%)	8 (0.8%)
Any acute toxicity	281 (26.3%)	19 (1.8%)	300 (28.0%)	466 (43.8%)	18 (1.7%)	484 (45.4%)
Late period						
Induration or fibrosis	214 (20.0%)	31 (2.9%)	245 (22.9%)	48 (4.5%)	1 (<0.5%)	49 (4.6%)
Telangiectasia	86 (8.0%)	13 (1.2%)	99 (9.3%)	39 (3.7%)	0	39 (3.7%)
Breast pain	48 (4.5%)	3 (<0.5%)	51 (4.8%)	19 (1.8%)	1 (<0.5%)	20 (1.9%)
Chest wall	26 (2.4%)	1 (<0.5%)	27 (2.5%)	2 (<0.5%)	0	2 (<0.5%)

Interpretation External beam APBI was non-inferior to whole breast irradiation in preventing IBTR. Although less acute toxicity was observed, the regimen used was associated with an increase in moderate late toxicity and adverse cosmesis, which might be related to the twice per day treatment. Other approaches, such as treatment once per day, might not adversely affect cosmesis and should be studied.



Accelerated partial breast irradiation: more questions than answers?

*Charlotte E Coles, Judith M Bliss, Philip M Poortmans



2019

Results of the RAPID⁴ and NSABP B-39/RTOG 0413⁵ randomised trials have been eagerly awaited, as they report outcomes in more than 6000 patients followed up for 8–10 years. So do these studies provide sufficient answers to the hypotheses on APBI?

NSABP B-39/RTOG 0413: Equivalence Trial.

RAPID: Non non-inferiority Trial

NSABP B-39/RTOG0413 defined a smaller tolerated increase in relative risk than RAPID....

DOSE: 38,5 Gy/10 twice-daily was equivalent to 62 Gy/ 2 Gy fr

TARGET VOLUME: excessively large or missing an important part of the target (Oncoplastic)

TECHNIQUE: Differences between Surgical Bed and Primary Tumour Bed (safety margins on the basis of histology)

....*The recurrence of IBTR incidence is reassuringly low in both trials....*

Meattini et al, SABCS 2019: *disease control is related to the adequate selection of patients. The safety profile and cosmetic outcome is more strongly associated with the technique.*

520 pts, 30 Gy/5 fr APBI vs 50 Gy/25 fr WBI + boost 1,5% LR in both, better toxicity, same SV



Frazionamento

QUESITO CLINICO

Nelle pazienti affette da carcinoma duttale infiltrante (DCI) in stadio precoce trattate con chirurgia conservativa e radioterapia, è indicato uno schema di trattamento ipofrazionato?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
A	Nelle pazienti affette da carcinoma duttale infiltrante (DCI) in stadio precoce trattate con chirurgia conservativa e radioterapia, è indicato uno schema di trattamento ipofrazionato	Positiva forte



NCCN Clinica

B

NCCN Guida

Whole Breast Radiation

- Target definition is the breast tissue in entirety.
- RT dosing:
 - ▶ The whole breast should receive a dose of 45–50.4 Gy in 25–28 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred).
 - ▶ A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical boost doses are 10–16 Gy in 4–8 fractions.
- All dose schedules are given 5 days per week.

Table 1
Characteristics of included studies.

Study	Start A ^{(1) (2)}	Start B ^{(2) (3)}	RMH/GOC ^{(4) (5)}	Canadian ^{(6) (7)}	FAST 2011 ⁽⁸⁾	Taher 2004 ⁽⁹⁾
Population	Women with invasive operable primary breast cancer (T1-3, N0-1, M0)	Women with invasive operable primary breast cancer (T1-3, N0-1, M0)	Women with invasive operable primary breast cancer (T1-3, N0-1, M0)	Women with invasive operable primary breast cancer (T1-3, N0-1, M0)	Women > 50 years with invasive carcinoma, (T1-2, N0, M0)	Women > 60 years, T1-2, N0-M0, tumor larger than 1 cm
Number of patients (n)	2236	2215	1410	1234	950	30
Experimental group intervention	41.6 Gy/13 fractions/5 weeks (3.2 Gy/fraction) or 39 Gy/13 fractions/5 weeks (3 Gy/fraction)	40 Gy/15 fractions/3 weeks (2.67 Gy/fraction)	42.9 Gy/13 fractions/5 weeks (3.3 Gy/fraction) or 39 Gy/13 fractions/5 weeks (3 Gy/fraction)	42.5 Gy/16 fractions/4.4 weeks (2.66 Gy/fraction)	28.5 Gy/5 fractions/1 week (5.7 Gy/fraction) or 30 Gy/5 fractions/1 week (6 Gy/fraction)	42.5 Gy/16 fractions/4.4 weeks (2.66 Gy/fraction)
Control group intervention	50 Gy/25 fractions/5 weeks (2 Gy/fraction)	50 Gy/25 fractions/5 weeks (2 Gy/fraction)	50 Gy/25 fractions/5 weeks (2 Gy/fraction)	50 Gy/25 fractions/5 weeks (2 Gy/fraction)	50 Gy/25 fractions/5 weeks (2 Gy/fraction)	50 Gy/25 fractions/5 weeks (2 Gy/fraction)
Maximum follow-up	12.4 years	12.4 years	18.4 years	12 years	37.3 months *	27 months
Outcomes	Locoregional recurrence, effect on normal tissue, patient reported outcomes, disease-free survival, overall survival, secondary cancer due to	Locoregional recurrence, effect on normal tissue, patient reported outcomes, disease-free survival, overall survival, secondary cancer due to	Change in breast appearance, Ipsilateral recurrence, distant recurrence.	Local recurrence, Distant recurrence, outcomes reported by patients, late radiation toxicity, death	Breast appearance, changes in breast induced by radiation, local tumor control	Acute skin reaction due to radiation, late breast cosmetic results

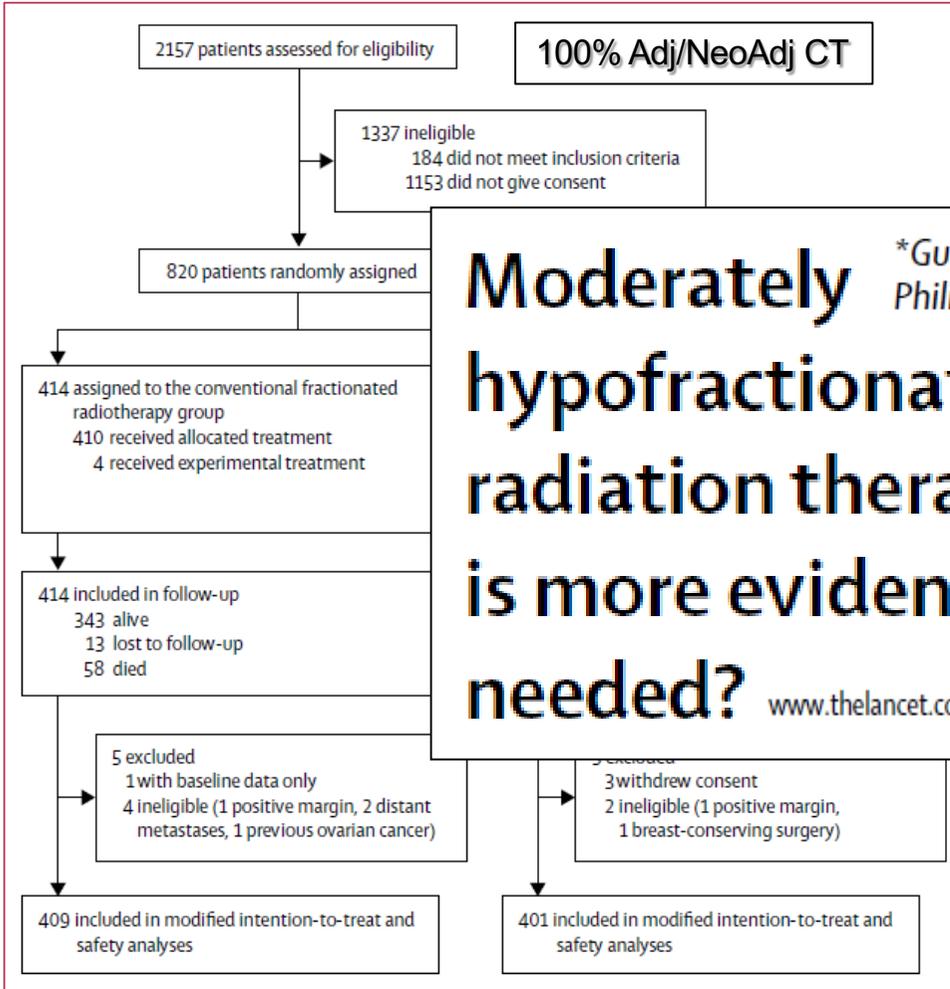
Conclusion: There is no difference between conventional fractionation and hypofractionated in terms of efficacy when we evaluate local recurrence, loco-regional recurrence, distance recurrence, disease-free survival and mortality. There is also no difference concerning safety when we assess the occurrence of fibrosis, ischemia and ribs fractures. Hypofractionated showed better results in relation to breast edema, telangiectasia, and acute skin radiation toxicity.



hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial **Lancet Oncol 2019**

Shu-Lian Wang*, Hui Fang*, Yong-Wen Song, Wei-Hu Wang, Chen Hu, Yue-Ping Liu, Jing Jin, Xin-Fan Liu, Zi-Hao Yu, Hua Ren, Ning Li, Ning-Ning Lu, Yu Tang, Yuan Tang, Shu-Nan Qi, Guang-Yi Sun, Ran Peng, Shuai Li, Bo Chen, Yong Yang, Ye-Xiong Li

Published Online
January 30, 2019



Moderately hypofractionated breast radiation therapy: is more evidence needed?
*Gustavo Nader Marta, Philip Poortmans
www.thelancet.com/oncology Vol 20 May 2019

	Conventional fractionated radiotherapy group (n=409)	Hypofractionated radiotherapy group (n=401)	p value
Acute toxicity			
Skin toxicity	<0.0001
Grade 1-2	357 (87%)	351 (89%)	..
Grade 3	32 (8%)	14 (3%)	..
Pneumonitis	0.278
Grade 1	62 (15%)	61 (15%)	..
Grade 2	7 (2%)	14 (3%)	..
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Contemporary Issues in Breast Cancer Radiotherapy



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2020

Hematol Oncol Clin N Am 34 (2020) 1–12
<https://doi.org/10.1016/j.hoc.2019.08.014>
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KEYWORDS

- Breast cancer • Radiotherapy • Breast conservation • Lumpectomy
- Adjuvant therapy • Postmastectomy radiation • Regional nodal irradiation

KEY POINTS

- Regional nodal irradiation has the potential to improve disease-free survival among patients with limited axillary disease.
- Accelerated partial breast irradiation is a convenient and effective adjuvant radiotherapy (RT) approach for appropriately selected patients.
- RT omission: certain subgroups of patients are of sufficiently low risk to forego adjuvant radiotherapy. Studies in this domain are ongoing.

REGIONAL NODAL IRRADIATION

RT POST-NACT

ACCELERATED PARTIAL BREAST IRRADIATION

OMISSION OF ADJUVANT RADIOOTHERAPY AFTER BCS



Pz anziana

QUESITO CLINICO

Nelle pazienti di età superiore ai 70 anni affette da carcinoma infiltrante della mammella tipo luminal A, in stadio precoce, è indicata la radioterapia dopo chirurgia conservativa, rispetto alla sola chirurgia conservativa e ormonoterapia, per ridurre la recidiva locale?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con età ≥ 70 anni, sottoposte a chirurgia conservativa per un carcinoma mammario invasivo ≤ 2 cm cN0, Luminal A, che ricevono ormonoterapia adiuvante, l'omissione della radioterapia PUÒ ESSERE considerata comunque un'opzione proponibile. Le pazienti devono essere, tuttavia, attentamente selezionate dal team multidisciplinare ed adeguatamente informate.	Positiva debole

(Qualità globale dell'evidenza: MODERATA)

D	Nelle pazienti con età ≥ 70 anni, sottoposte a chirurgia conservativa per un carcinoma mammario invasivo ≤ 2 cm cN0, Luminal A, che non ricevono ormonoterapia adiuvante, la radioterapia PUÒ ESSERE considerata comunque un'opzione proponibile. Le pazienti devono essere, tuttavia, attentamente selezionate dal team multidisciplinare ed adeguatamente informate.	Positiva debole
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(Qualità globale dell'evidenza: MOLTO BASSA)

2019

RESEARCH

Open Access

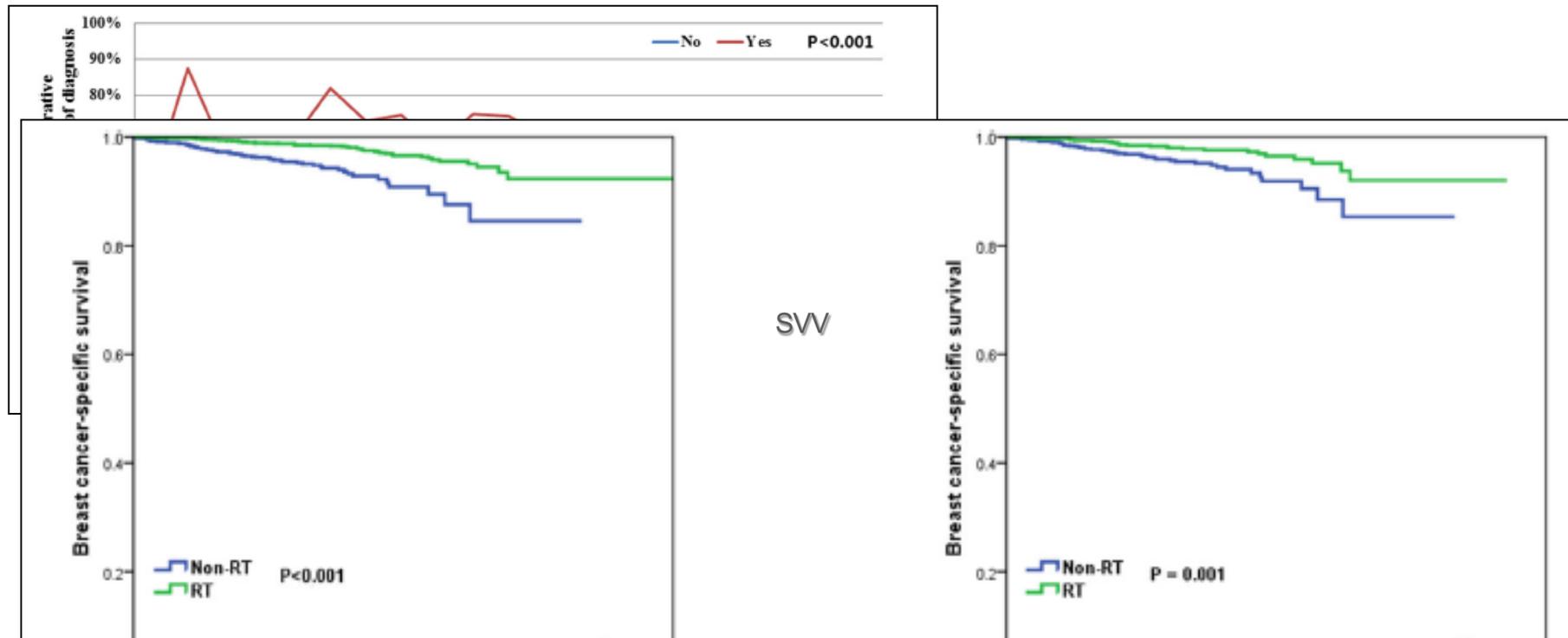
Omission of adjuvant radiotherapy following breast-conserving surgery for elderly women with early-stage pure mucinous breast carcinoma

Wu et al. *Radiation Oncology* (2019) 14:190
<https://doi.org/10.1186/s13014-019-1394-x>



San-Gang Wu^{1†}, Feng-Yan Li^{2†}, Jun Wang¹, Chen-Lu Lian¹, Juan Zhou^{3*} and Zhen-Yu He^{2*}

3416 pts, SEER, 1990-2010
 Median age 75 (66-99)



Conclusions: This study shows a decreasing utilization of postoperative radiotherapy following BCS of elderly PMBC patients over time. However, postoperative radiotherapy following BCS should be administered for elderly women with PMBC owing to independent association with better survival.

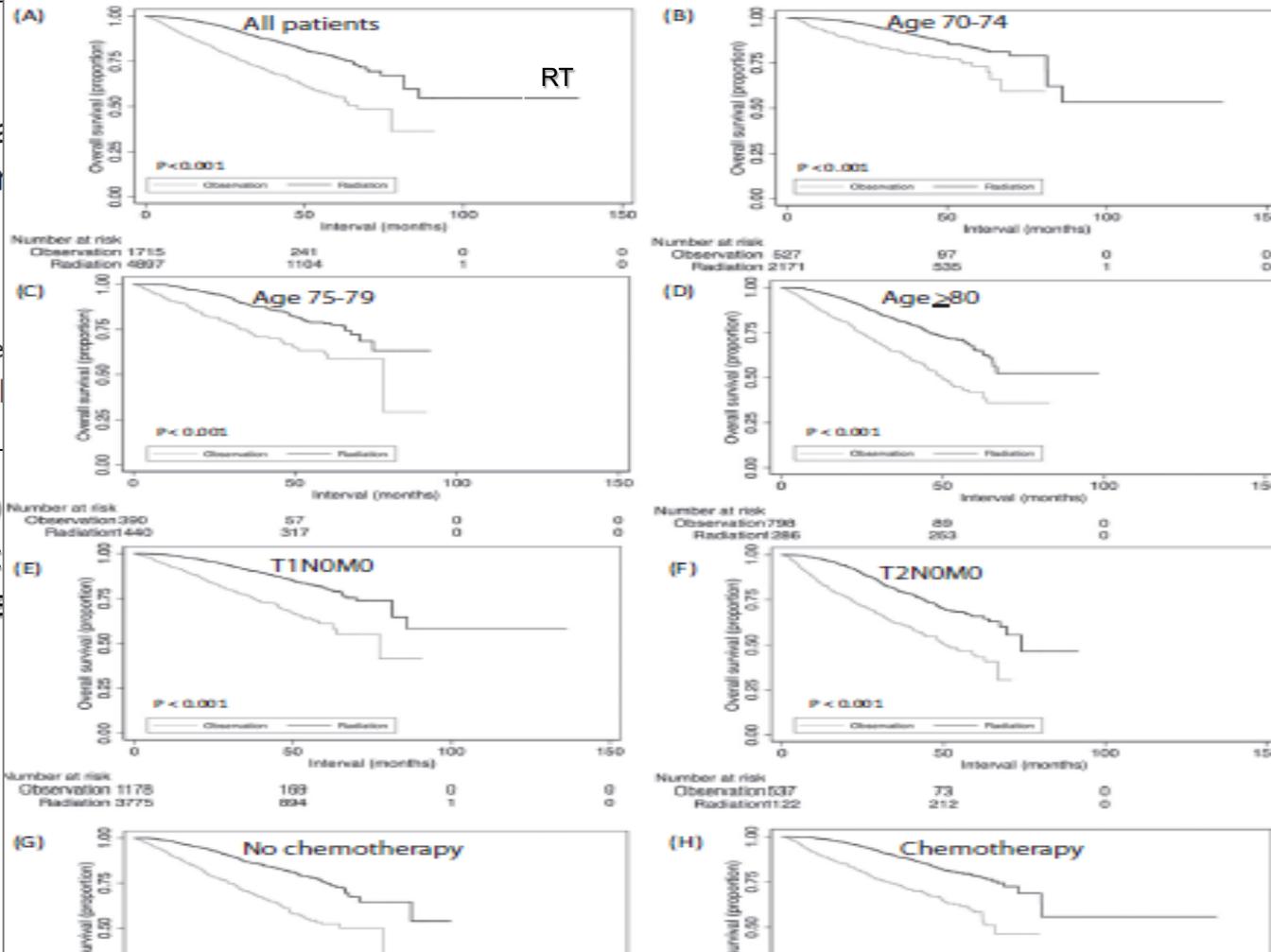


ORIGINAL ARTICLE

Omission of radiation in older (≥ 70 year) cancer

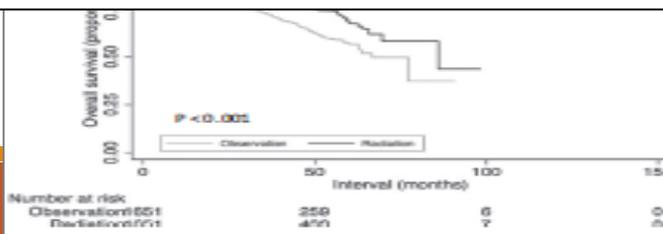
Waqar Haque MD¹ | Candy Arentz MD⁴ | Elizabeth Bonefas MD⁴ | Bin S. Teh MD¹

National Cancer D
T1-2N0M0 TNBC t
8526 pts, 74% re



CONCLUSIONS

caution must be exercised when considering omission of adjuvant RT in node-negative TNBC patients.





Radiotherapy and Immune Therapy

Key points

- Radiotherapy not only exerts direct cytotoxic effects on tumour cells, but also re-programmes the tumour microenvironment to exert a potent antitumour immune response
- Tumour-cell proliferation and cell death due to **T-cell** cytotoxic killing coexist in irradiated tumours, resulting in stable disease that might provide a window of opportunity for immune-modulation
- **Radiotherapy is immunosuppressive, but also enhances antitumour immunity and induces immunosuppressive responses**
- The combination of immunotherapy and radiotherapy presents a multimodal treatment approach that involves stimulating and suppressing various pathways

Local Immune Cancer Effects

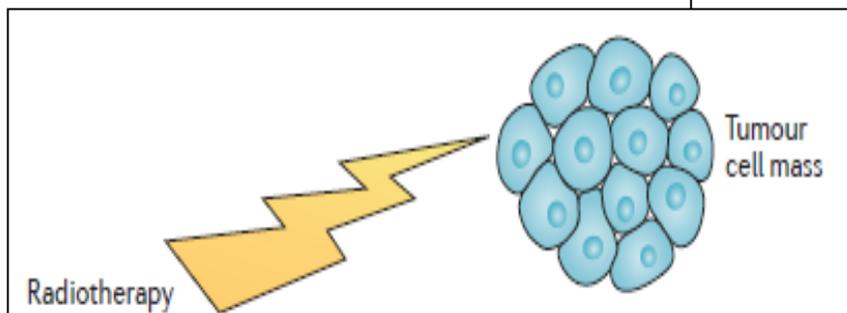
Increased TILs concentration predicted response to NACT in all molecular subtypes and was also associated with a survival benefit in HER2-positive breast cancer and triple-negative breast cancer.

By contrast, increased TILs were an adverse prognostic factor for survival in luminal HER2-negative, suggesting a different biology of the immunological infiltrate in this subtype. Our data support the hypothesis that breast cancer is immunogenic and might be targetable by immune-modulating therapies.

Denkert C et al, Lancet Oncol 19, 40-50, 2018

ANTICANCER RESEARCH 38: 2311-2321 (2018)
doi:10.21873/anticanres.12476

Prediction of Treatment Response to Neoadjuvant Chemotherapy in Breast Cancer by Subtype Using Tumor-infiltrating Lymphocytes

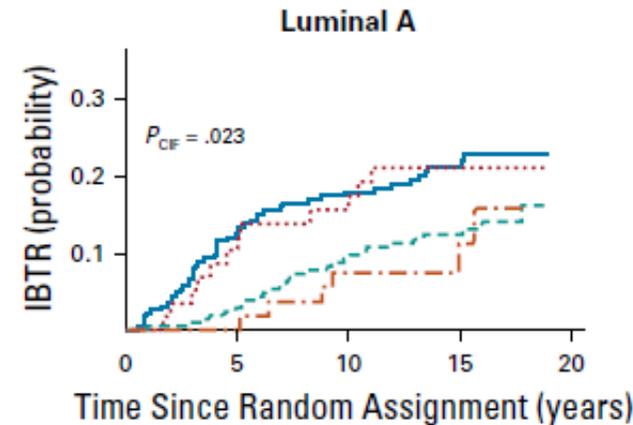
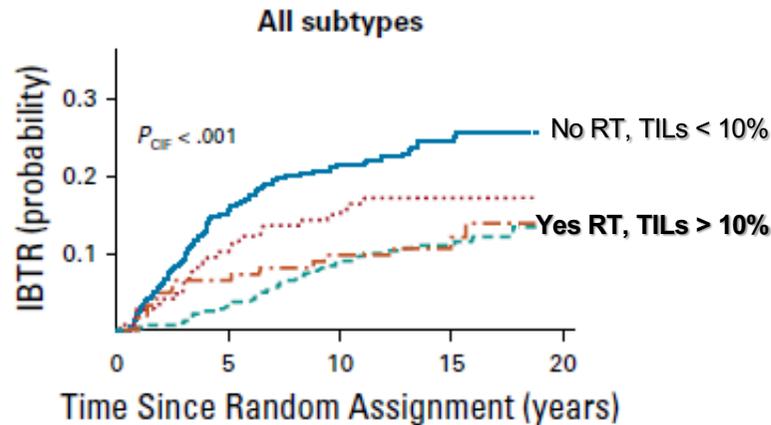




Effect of Radiotherapy After Breast Conserving

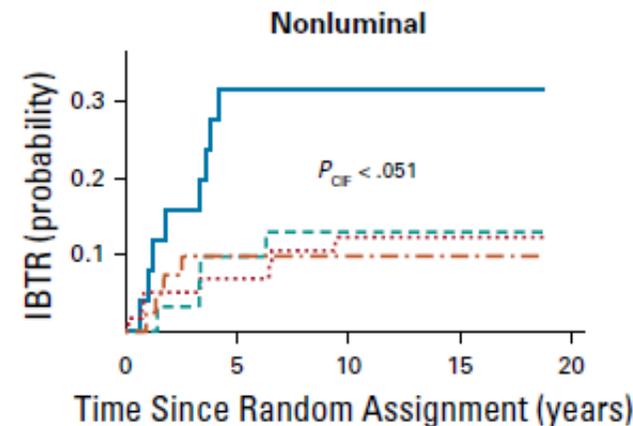
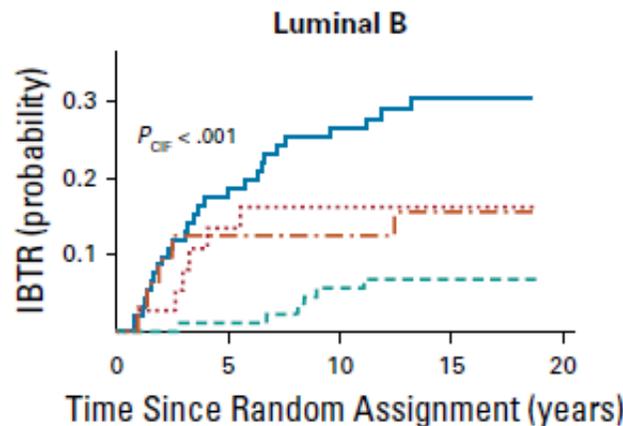
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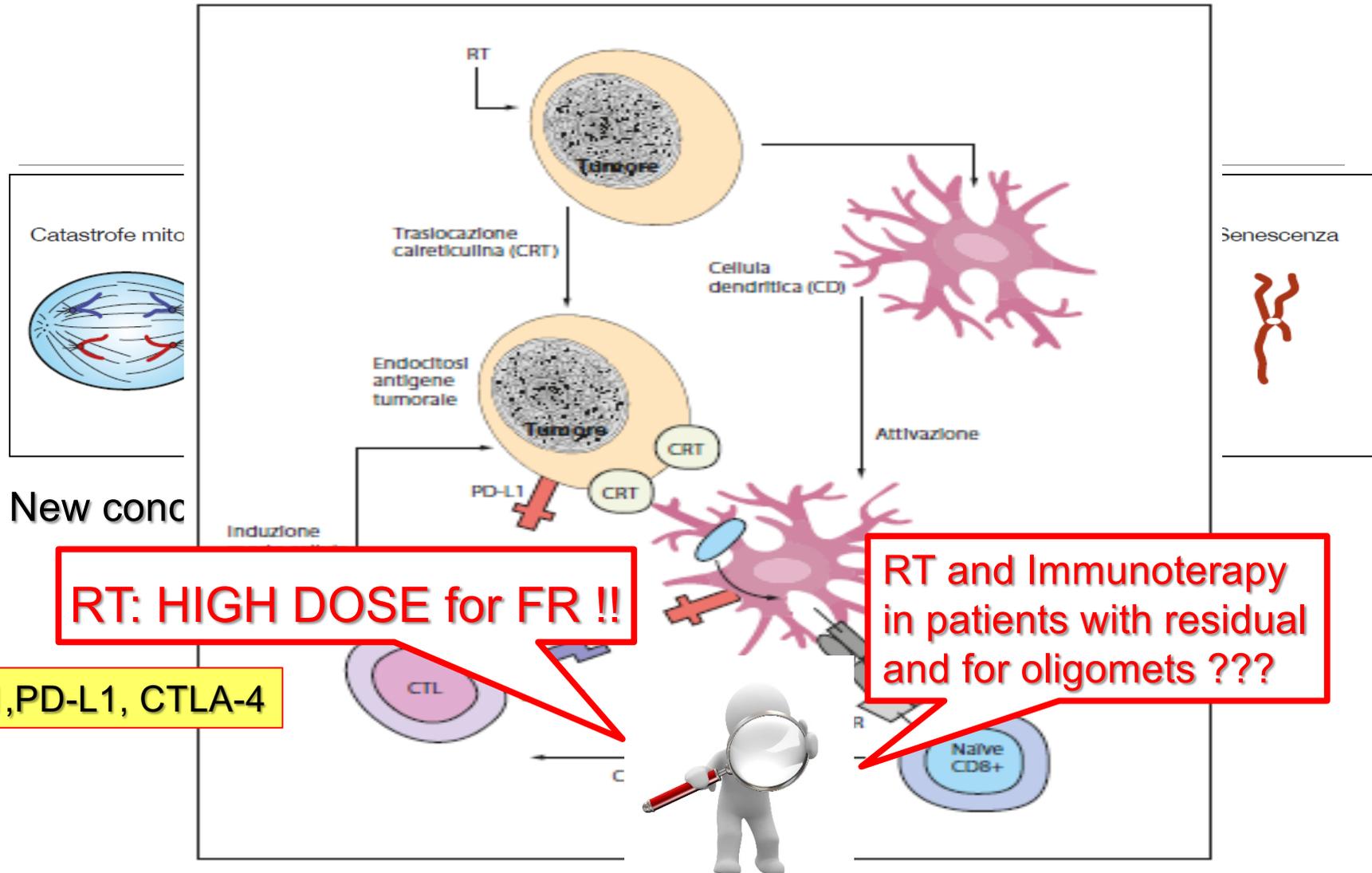
	No. at risk:				HR (95% CI):	
RT-, TILs < 10	340	260	204	98	0	1.00
RT-, TILs ≥ 10	148	113	89	45	0	0.70 (0.44 to 1.13)
RT+, TILs < 10	330	291	236	125	0	0.37 (0.24 to 0.58)
RT+, TILs ≥ 10	124	101	82	39	0	0.44 (0.24 to 0.82)

	No. at risk:				HR (95% CI):	
RT-, TILs < 10	225	182	139	67	0	1.00
RT-, TILs ≥ 10	58	50	40	16	0	0.81 (0.39 to 1.68)
RT+, TILs < 10	212	188	151	89	0	0.49 (0.28 to 0.83)
RT+, TILs ≥ 10	55	51	41	17	0	0.37 (0.13 to 1.02)



CONCLUSION This study shows that high values of TILs in the primary tumor independently seem to reduce the risk for an IBTR. Our findings further suggest that patients with breast cancer with low TILs may derive a larger benefit from RT regarding the risk of IBTR.

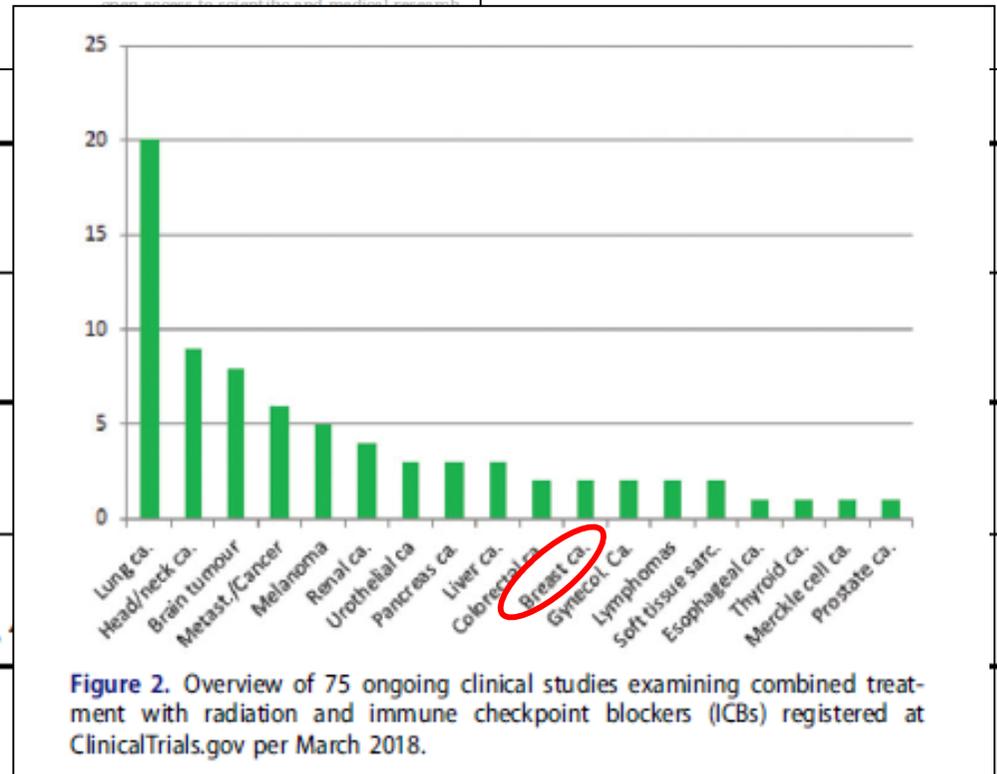
0.98)
1.10)
0.88)



The mechanism improves the recognition and killing of cancer cells by CD8+ cytotoxic T cells (CTLs) by promoting antigen presentation

Table 1 Landmark Clinical Trials

Trial	Checkpoint Inhibitor	Response
KEYNOTE-012 (N=27)	Pembrolizumab	ORR 18.5%
KEYNOTE-028 (N=25)	Pembrolizumab	ORR 12%
KEYNOTE-086 Cohort A (N=170, 61.8% PD-LI+)	Pembrolizumab	ORR 4.7% (4.8% for PD-LI+, 0% for PD-LI-)
KEYNOTE-086 Cohort B (N=84)	Pembrolizumab	ORR 23.1%
Emens et al (N=115)	Atezolizumab	ORR 10% (12% for PD-LI+, 0% for PD-LI-)
JAVELIN (N=168)	Avelumab	ORR 4.8% (2.3% for PD-LI+, 2.4% for PD-LI-)
IMPASSION 130 (N=912)	Atezolizumab + nab-paclitaxel	



Conclusion By customizing immunotherapy to both the disease as well as the individual, breast cancer can become a chronic disease potentially curable as well as preventable.

+))



2019 Breast Cancer : Take Home Message

- Breast cancer biologic subtypes do not predict RT benefit
- Indication to RT after BCS or PM considering risk factors (low level evidence)
- In pts who achieve ypN0 following NACT and mastectomy, PMRT shows no additional survival benefits for any molecular subtype
- Low level evidence for omitting RT after cN+ → pN0, consider risk factors
- APBI can be used in suitable pts, prefer moderate fractionation
- Long term efficacy and safety of moderate hypofractionation are demonstrated
- It's time to use moderate hypofractionation for RNI (studies on)
- Caution in omission of adjuvant RT after BCS
- Synergic action with Immunotherapy, particularly at high dose/fr

2019 Breast Cancer Take Home Message



For low level evidence indications outside trials, RT decision-making has to be individualized and based on clinical, biological, pathological and immunological characteristics
Consider patient preference...



Time to change Practice, but no too much!

THANK YOU