Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

Irradiazione dei volumi linfonodali nel carcinoma mammario: quando e quali?

Cynthia Aristei

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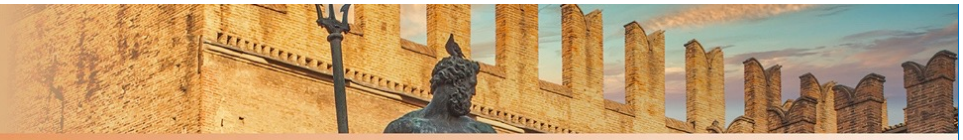
UNIVERSITÀ DEGLI STUDI DI PERUGIA

Associazione Italiana Radioterapia e Oncologia clinica
Società Italiana di Radiobiologia



DICHIARAZIONE

Relatore: Cynthia Aristei

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Altro

INTRODUZIONE

Le indicazioni al trattamento radiante dei linfonodi regionali sono state ampiamente studiate e dibattute

La RT su livelli III e IV e sulle altre porzioni dell'ascella non trattate chirurgicamente rappresenta il trattamento standard dopo:

- BCS in pazienti con ≥ 4 linfonodi ascellari positivi
- Mastectomia nella malattia T1-2 con ≥ 4 linfonodi ascellari positivi, T3 N+, T4 indipendentemente dall'N

A tutt'oggi, rimangono aree grigie che, spesso, richiedono una discussione all'interno del team multidisciplinare

AGENDA

RT in pazienti con:

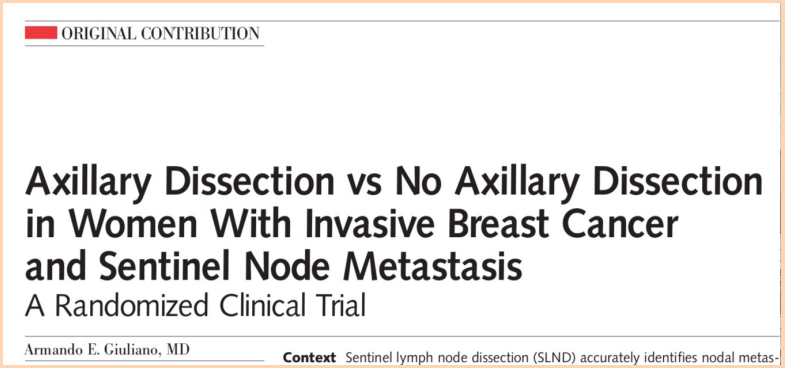
- **1-2 LNs positivo/i, non sottoposte a ALND**
- 1-3 linfonodi positivi dopo ALND

RT su linfonodi mammari interni

RT dopo terapia sistemica neoadiuvante e chirurgia

Frazionamento della dose

RT in pazienti con malattia T1-2 e1-2 LNs macroscopicamente positivo/i, non sottoposte a ALND, il trattamento standard fino alla pubblicazione dei risultati di studi randomizzati di fase III di non inferiorità



ORIGINAL CONTRIBUTION

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis
A Randomized Clinical Trial

Armando E. Giuliano, MD

Context Sentinel lymph node dissection (SLND) accurately identifies nodal metas-

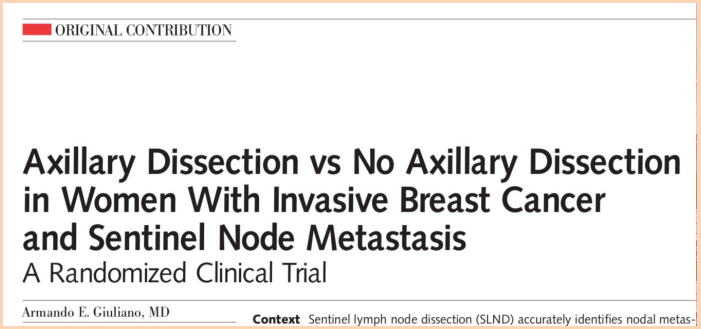
Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

Mila Donker, Geertjan van Tienhoven, Marieke E Straver, Philip Meijnen, Cornelis J H van de Velde, Robert E Mansel, Luigi Cataliotti, A Helen Westenberg, Jean H G Klinkenbijl, Lorenzo Orzalesi, Willem H Bouma, Huub C J van der Mijle, Grard A P Nieuwenhuijzen, Sanne C Veltkamp, Leen Slaets, Nicole J Duez, Peter W de Graaf, Thijs van Dalen, Andreas Marinelli, Herman Rijna, Marko Snoj, Nigel J Bundred, Jos W S Merkus, Yazid Belkacemi, Patrick Petignat, Dominic A X Schinagl, Corneel Coens, Carlo G M Messina, Jan Bogaerts, Emiel J T Rutgers

Summary

Background If treatment of the axilla is indicated in patients with breast cancer who have a positive sentinel node,

Lancet Oncol 2014; 15: 1303-10



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Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

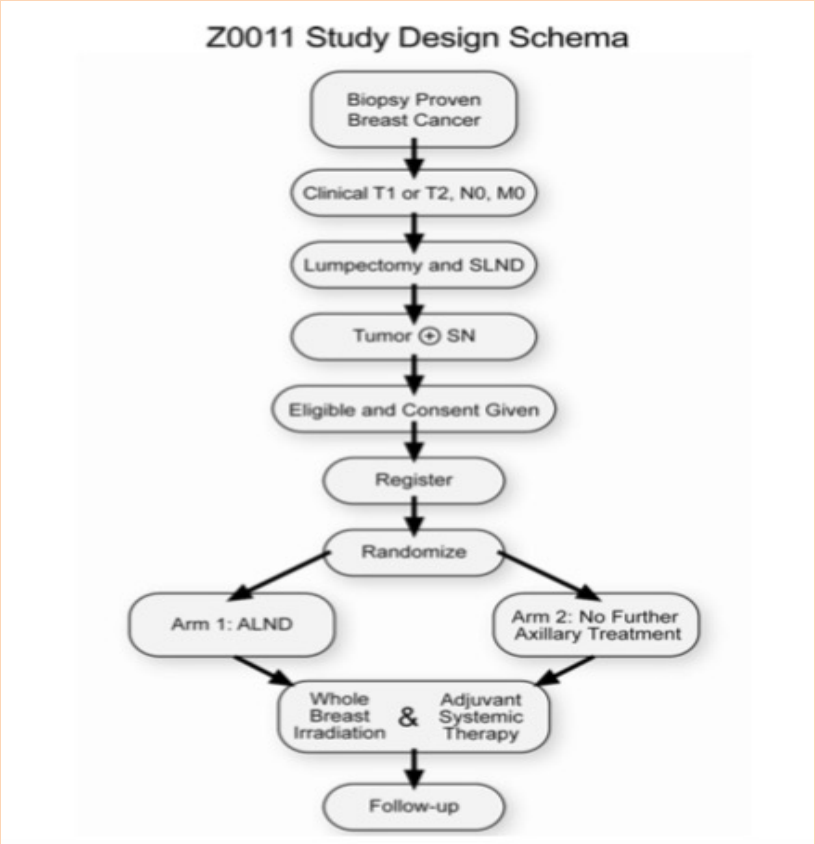
Armando E. Giuliano, MD

Context Sentinel lymph node dissection (SLND) accurately identifies nodal metas-

Accrual: 1999-2004: 856 pazienti

Lo studio avrebbe dovuto arruolare 1.900 pazienti con analisi finale dopo 500 morti

Interrotto prima per ridotta accrual e mortalità rispetto all'atteso



ETÀ	cT1	ER+	G1-2	MET LNs	Terapie sistemiche
≥54	≥68%	83%	± 70%	Micro (44.8% in SLND group *vs* 37.5%)	96%

Trial sottopotenziato per non aver arruolato il campione calcolato
Pazienti perse al follow-up
Micrometastasi in circa la metà dei casi

RECIDIVE ASCELLARI

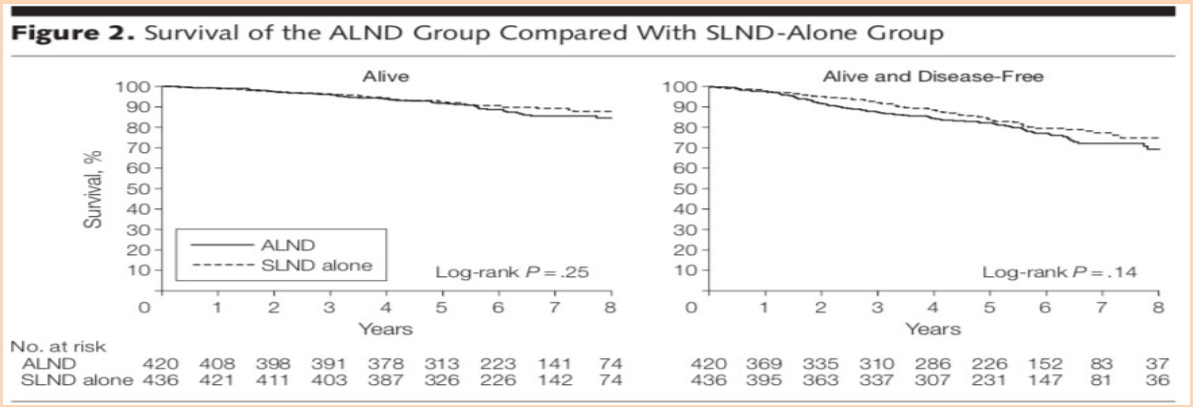
LNs	Dissezione Ascellare
4 (0.9%)	2 (0.5%)

Ad un FU mediano di 6.3 anni non è stata osservata una differenza significativa tra i due gruppi nelle recidive locali (p = 0.11) e linfonodali (p = 0.45)

Giuliano, Ann Surg 2010

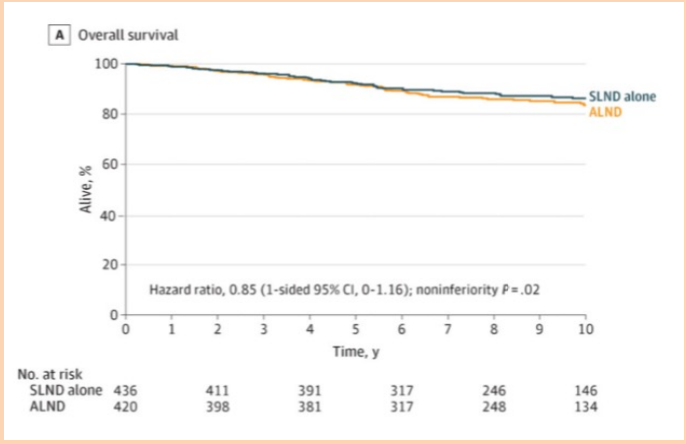
5 anni dopo è stata osservata 1 sola recidiva linfonodale nel gruppo SLN

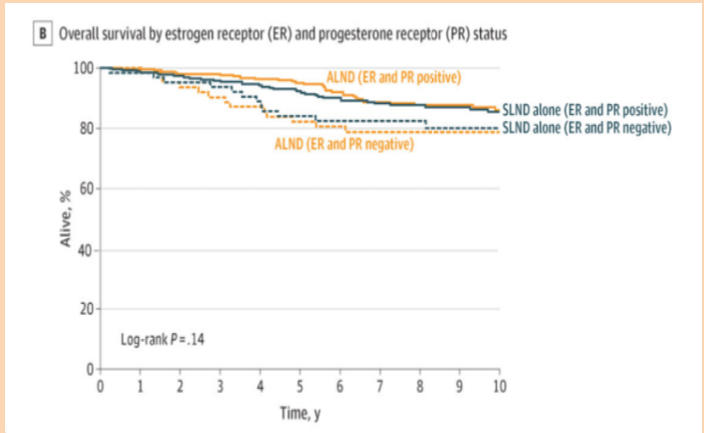
Giuliano, JAMA 2017

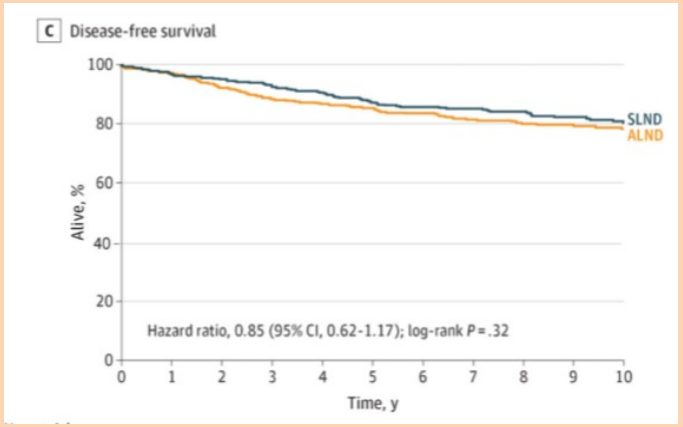


FU MEDIANO 6.3 anni
Giuliano, JAMA 2011

FU MEDIANO 9.3 anni
Giuliano, JAMA 2017





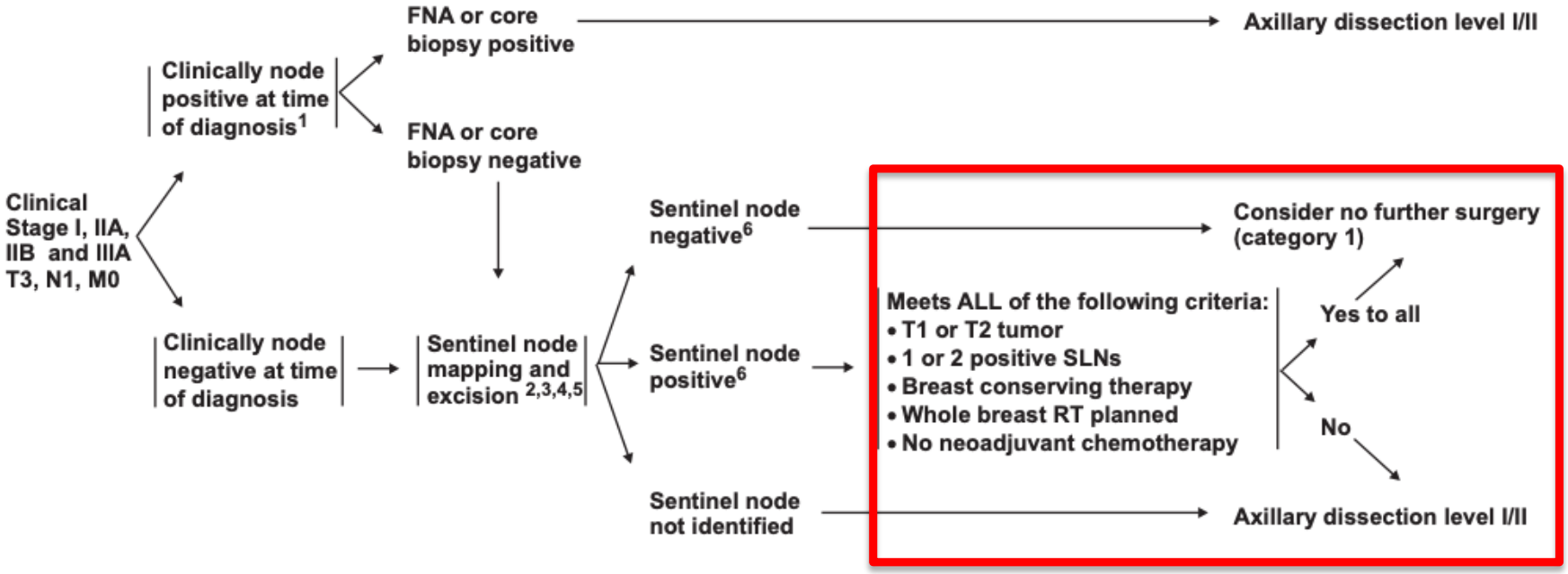


National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2012

NCCN Guidelines Index
Breast Cancer Table of Contents
Staging, Discussion

SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0



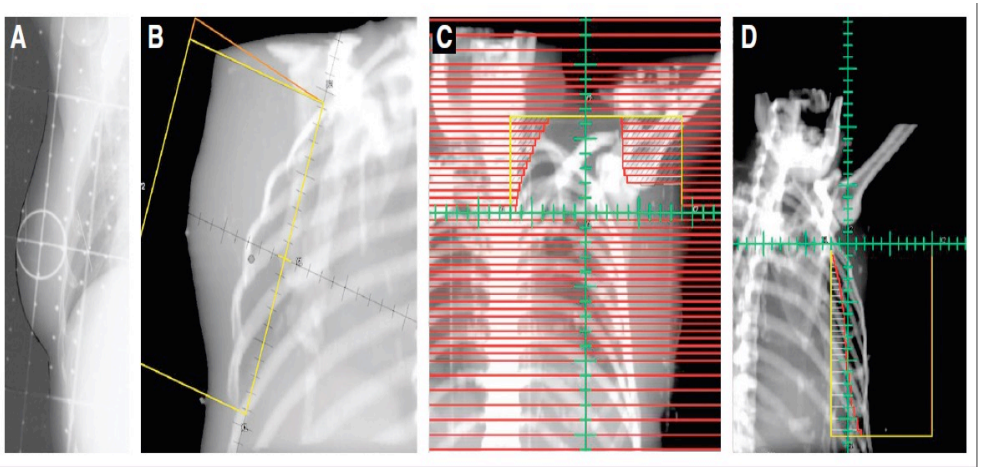
Dissezione ascellare può essere omessa in pazienti cN0, con 1-2 LNs macrometastatici, sottoposte a BCS e trattate con RT postoperatoria

Ipotizzando che l'irradiazione incidentale dei linfonodi ascellari con i campi di irradiazione utilizzati per il trattamento della ghiandola mammaria potesse controllare eventuale malattia linfonodale

VOLUME 32 · NUMBER 32 · NOVEMBER 10 2014
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Radiation Field Design in the ACOSOG Z0011 (Alliance) Trial

Reshma Jagsi, Manjeet Chadha, Janaki Moni, Karla Ballman, Fran Laurie, Thomas A. Buchholz, Armando Giuliano, and Bruce G. Haffty



group after 5 years and none in the ALND group. In an unplanned analysis of the subset of the 228 patients with detailed radiation records available, those treated with nodal-field irradiation experienced no difference in disease-free survival, overall survival, or locoregional recurrence compared with those who did not receive irradiation.

Giuliano, JAMA 2017

Ann Surg Oncol (2022) 29:5732–5744
https://doi.org/10.1245/s10434-022-11866-w

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

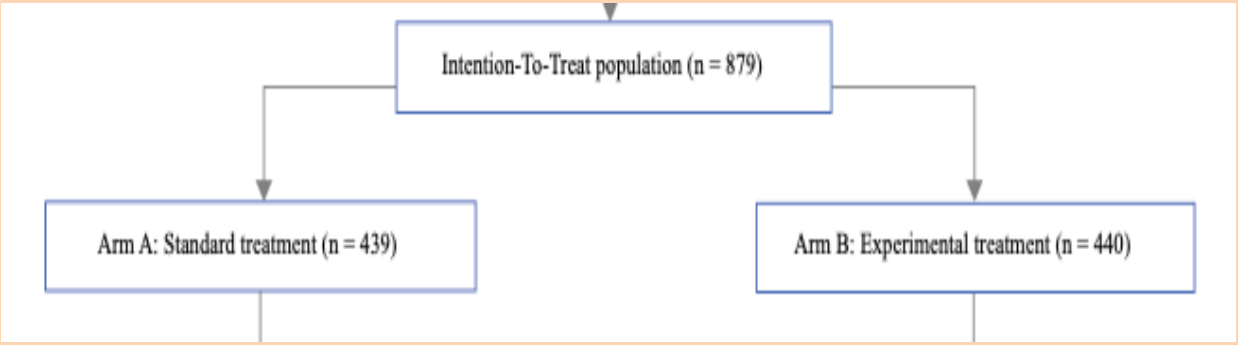
ORIGINAL ARTICLE – BREAST ONCOLOGY

Preservation of Axillary Lymph Nodes Compared with Complete Dissection in T1–2 Breast Cancer Patients Presenting One or Two Metastatic Sentinel Lymph Nodes: The SINODAR-ONE Multicenter Randomized Clinical Trial

Corrado Tinterri, MD[1,2], Damiano Gentile, MD[1], Wolfgang Gatzemeier, MD[1], Andrea Sagona, MD[1], Erika Barbieri, MD[1], Alberto Testori, MD[1], Valentina Errico, MD[3], Alberto Bottini, MD[1], Emilia Marrazzo, MD[3], Carla Dani, MD[4], Beatrice Dozin, MD[4], Luca Boni, MD[4], Paolo Bruzzi, MD, MPH, PhD[4], Bethania Fernandes, MD[5], Davide Franceschini, MD[6], Ruggero Spoto, MD[6], Rosalba Torrisi, MD[7], Marta Scorsetti, MD, PhD[2,6], Armando Santoro, MD[2,7], Giuseppe Canavese, MD[1] the SINODAR-ONE Collaborative Group

Eligibility

Age ≥ 40 and ≤ 75 years
Invasive BC (cytology/core biopsy assessment)
Unilateral lesion
Tumor size ≤ 5 cm (cT1–2) (ultrasound/mammography assessment)
Clinically negative axillary nodes (N0) (ultrasound assessment)
No more than two SLNs proven metastatic (histological assessment)
Involved SLNs with macrometastasis (≥ 2 mm)
No distant metastasis (M0)
No neoadjuvant therapy
No previous invasive BC
Signed and dated written informed consent



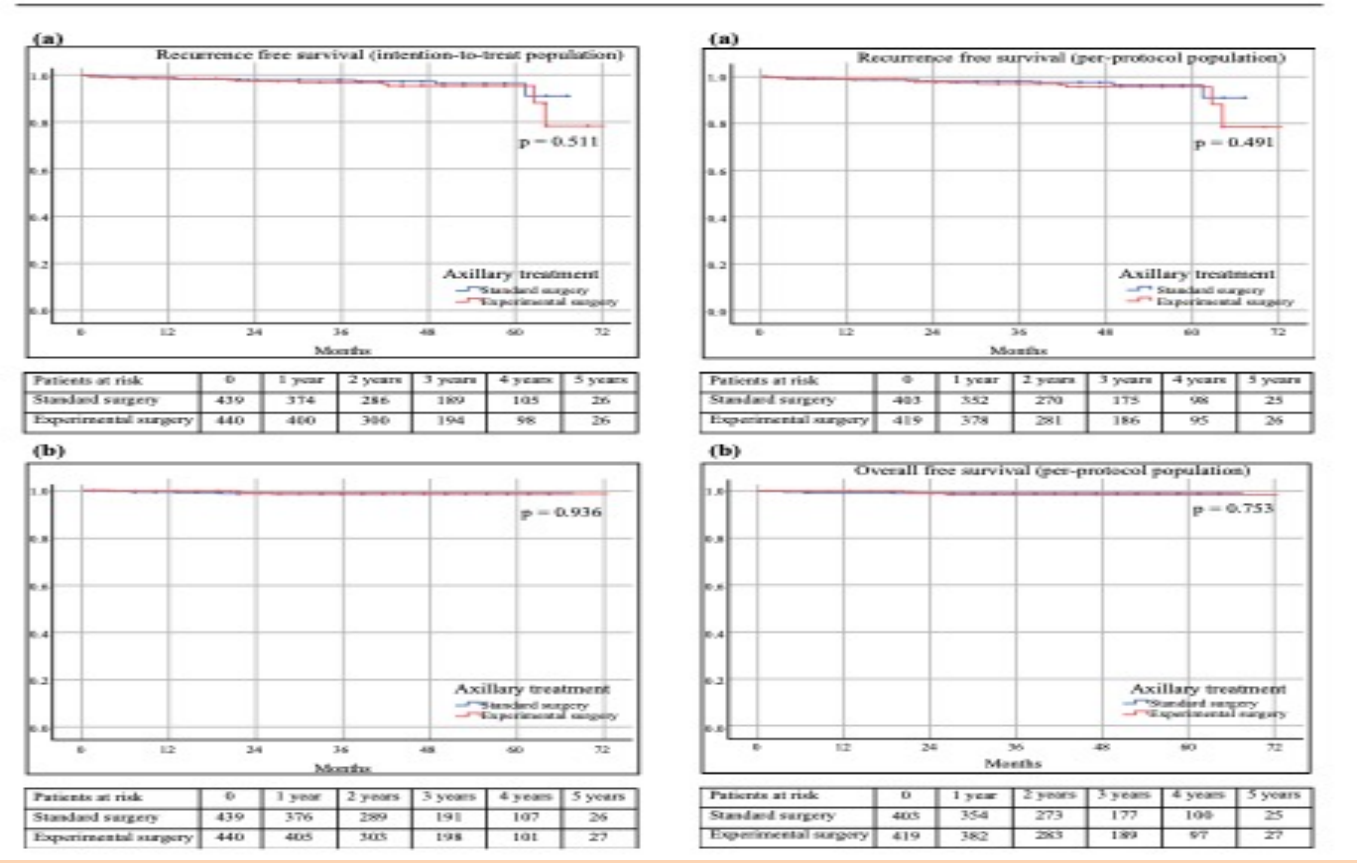
Accrual: 2015-2020, 889 pz.
Follow-up mediano: 34 mesi

Lo studio avrebbe dovuto arruolare 2.000 pazienti o avere 535 eventi

Interrotto prima per ridotta accrual e pochi eventi rispetto all'atteso

«Only one axillary lymph node recurrence was observed in each group of treatment»

Cautela deve essere posta nell'accettare il risultato di non inferiorità per pazienti mastectomizzate, che rappresentano solo il 25% circa delle arruolate



Patients at risk	0	1 year	2 years	3 years	4 years	5 years
Standard surgery	439	374	286	189	105	26
Experimental surgery	440	400	300	194	98	26

Patients at risk	0	1 year	2 years	3 years	4 years	5 years
Standard surgery	403	352	270	175	98	25
Experimental surgery	419	378	281	186	95	26

Patients at risk	0	1 year	2 years	3 years	4 years	5 years
Standard surgery	439	376	289	191	107	26
Experimental surgery	440	405	305	198	101	27

Patients at risk	0	1 year	2 years	3 years	4 years	5 years
Standard surgery	405	354	273	177	100	25
Experimental surgery	419	382	283	189	97	27

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

Mila Donker, Geertjan van Tienhoven, Marieke E Straver, Philip Meijnen, Cornelis J H van de Velde, Robert E Mansel, Luigi Cataliotti, A Helen Westenberg, Jean H G Klinkenbijl, Lorenzo Orzalesi, Willem H Bouma, Huub C J van der Mijle, Grard A P Nieuwenhuijzen, Sanne C Veltkamp, Leen Slaets, Nicole J Duez, Peter W de Graaf, Thijs van Dalen, Andreas Marinelli, Herman Rijna, Marko Snoj, Nigel J Bundred, Jos W S Merkus, Yazid Belkacemi, Patrick Petignat, Dominic A X Schinagl, Corneel Coens, Carlo G M Messina, Jan Bogaerts, Emiel J T Rutgers

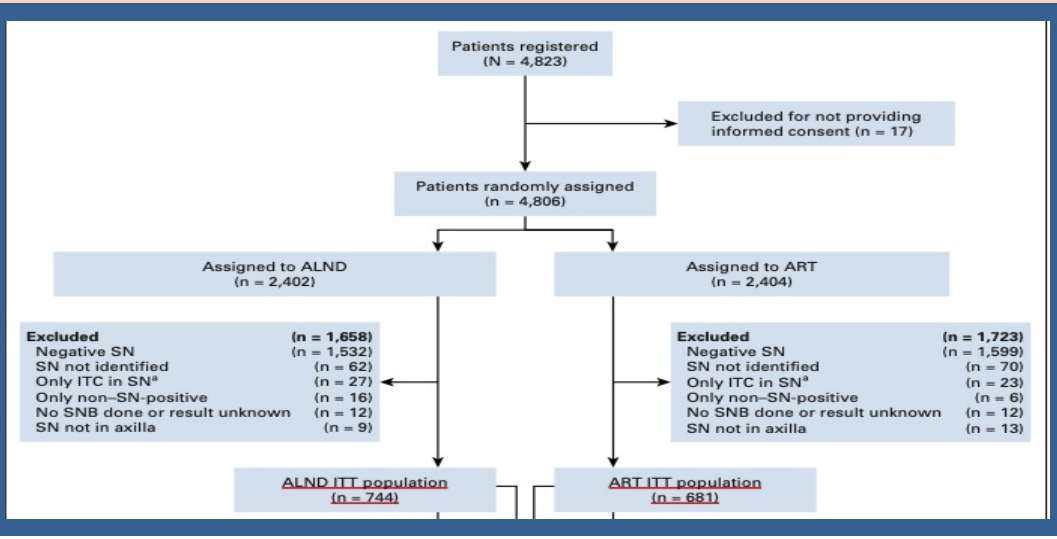
Summary

Background If treatment of the axilla is indicated in patients with breast cancer who have a positive sentinel node,

Lancet Oncol 2014; 15: 1303-10

Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node in Breast Cancer: 10-Year Results of the Randomized Controlled EORTC 10981-22023 AMAROS Trial

Sanne A.L. Bartels, MD, PhD, MSc[1,2]; Mila Donker, MD, PhD[2,3]; Coralie Poncet, MSc[1]; Nicolas Sauvé, MSc[1]; Marieke E. Straver, MD, PhD[4]; Cornelis J.H. van de Velde, MD, PhD[5]; Robert E. Mansel, MD, MS[6]; Charlotte Blanken, MD, PhD[7]; Lorenzo Orzalesi, MD, PhD[8]; Jean H.G. Klinkenbijl, MD, PhD[9]; Huub C.J. van der Mijle, MD, PhD[10]; Grard A.P. Nieuwenhuijzen, MD, PhD[11]; Sanne C. Veltkamp, MD, PhD[12]; Thijs van Dalen, MD, PhD[13]; Andreas Marinelli, MD, PhD[4]; Herman Rijna, MD, PhD[14]; Marko Snoj, MD, PhD[15]; Nigel J. Bundred, MD, PhD[16]; Jos W.S. Merkus, MD, PhD[17]; Yazid Belkacemi, MD, PhD[18,19]; Patrick Petignat, MD[20]; Dominic A.X. Schinagl, MD, PhD[21]; Corneel Coens, MSc[1]; Geertjan van Tienhoven, MD, PhD[22]; Frederieke van Duijnhoven, MD, PhD[2]; and Emiel J.T. Rutgers, MD, PhD[2]

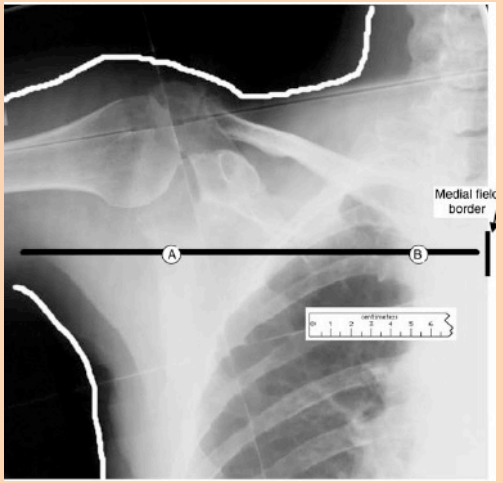


ELSEVIER
Radiotherapy and Oncology 68 (2003) 233–240
RADIOTHERAPY & ONCOLOGY
www.elsevier.com/locate/radonline

Quality assurance of axillary radiotherapy in the EORTC AMAROS trial 10981/22023: the dummy run

Coen W. Hurkmans[a,*], Jacques H. Borger[b], Emiel J. Th. Rutgers[c], Geertjan van Tienhoven[d],

On behalf of the EORTC Breast Cancer Cooperative Group and the Radiotherapy Cooperative Group



	Axillary lymph node dissection (n=744)	Axillary radiotherapy (n=681)
(Continued from previous page)		
Adjuvant radiotherapy		
Breast	597 (80%)	546 (80%)
Chest wall	34 (5%)	51 (7%)
Internal mammary chain	72 (10%)	65 (10%)

RT su livelli I, II, III, IV
2 Gy x 25 frazioni

RECIDIVE ASCELLARI

	Dissezione Ascellare (744 pz)		RT (681 pz)		HR
	FU 6.1 aa	FU 10.0 aa	FU 6.1 aa	FU 10.0 aa	
Incidenza	4 (0.5%)	7 (0.9%)	7 (1%)	11 (1.6%)	
Incidenza cumulativa	0.43%	0.93%	1.19%	1.82%	1.71; 95% CI: 0.67-4.39

Death due to breast cancer:
ALND 65 (8.7%)
RT 70 (10.3%)

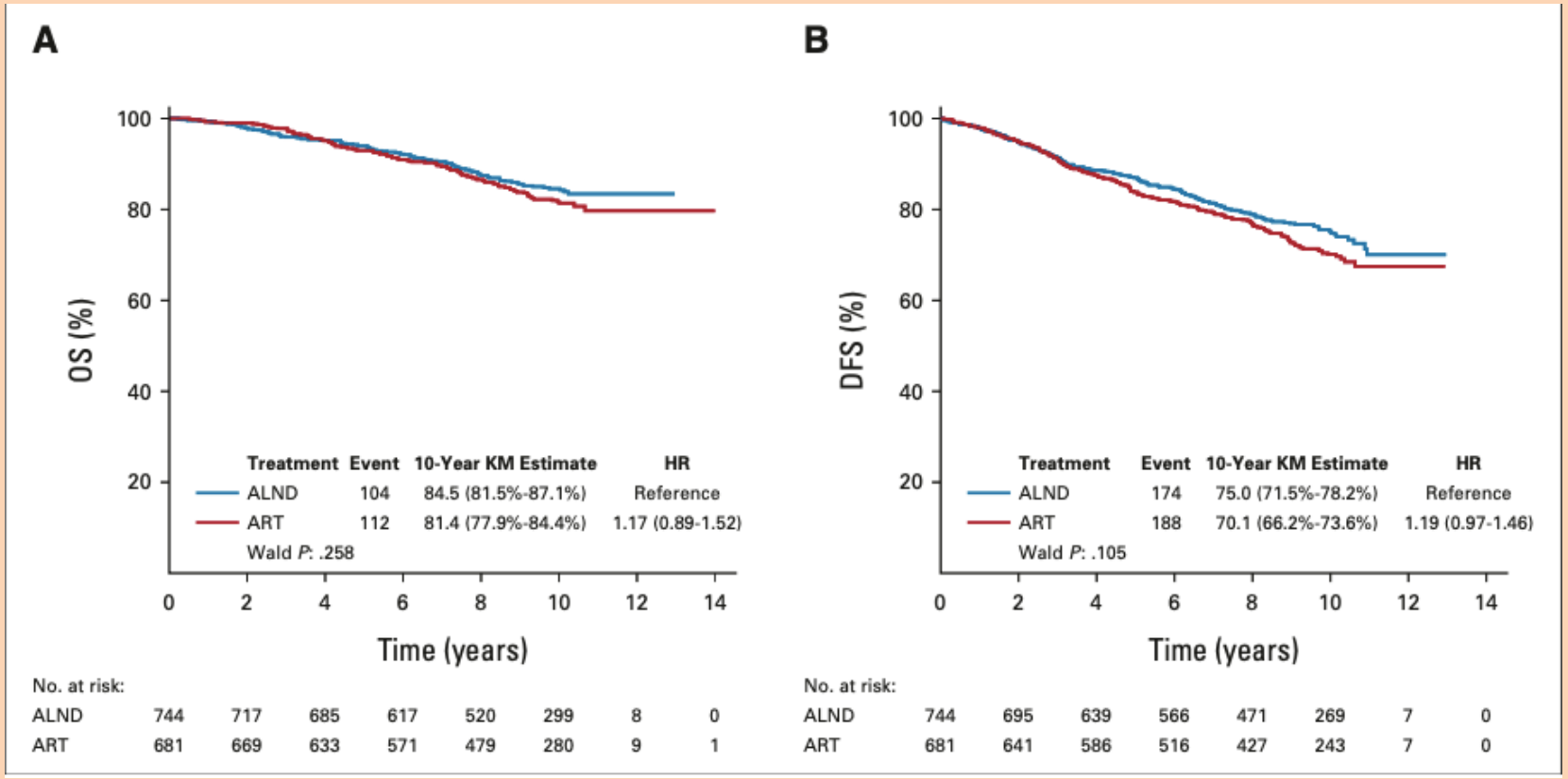


Table S1. Lymphedema in ipsilateral arm

	ALND N (%)	ART N (%)	
Number of forms received			**Compliance (% of expected)**
Baseline	655	586	98
1 year	411	410	65
3 years	394	364	62
5 years	412	377	67
Clinical sign of lymphedema			**P-value**
Baseline	3 (0.5)	0 (0)	0.252
1 year	114 (27.8)	62 (15.1)	<0.001
3 years	93 (23.6)	53 (14.6)	0.002
5 years	101 (24.5)	45 (11.9)	<0.001
During any point in follow-up	**257 (44.2)**	**159 (28.6)**	**<0.001**
Treatment for lymphedema in last year			
Baseline	6 (0.9)	3 (0.5)	0.512
1 year	129 (31.4)	66 (16.1)	<0.001
3 years	86 (21.8)	40 (11.0)	<0.001
5 years	75 (18.2)	25 (6.6)	<0.001
During any point in follow-up	**209 (36.0)**	**112 (20.2)**	**<0.001**
Arm circumference increase ≥ 10%†			
Baseline	33 (5.0)	24 (4.1)	0.497
1 year	32 (7.8)	24 (5.9)	0.333
3 years	41 (10.4)	23 (6.3)	0.050
5 years	52 (12.6)	20 (5.3)	<0.001
During any point in follow-up	**123 (21.2)**	**89 (16.0)**	**0.027**

Figure S4. Cumulative incidence plot of second primary cancers

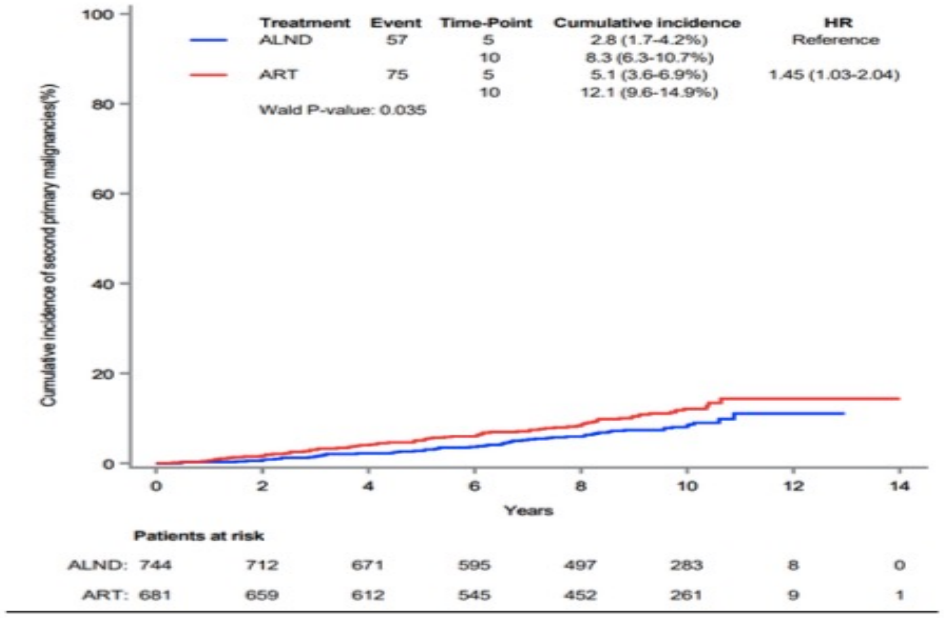


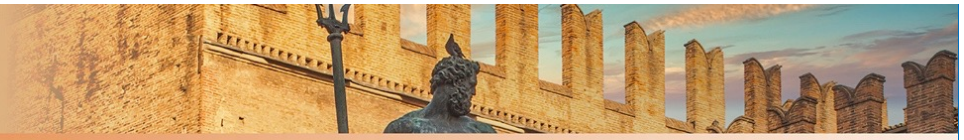
Table S2. Causes of death due to second primary cancer

	ALND (N=744)	ART (N=681)
Lung cancer	5	7
Colorectal cancer	2	5
Stomach/ biliary/ pancreatic cancer	2	4
Endometrium/ ovarian cancer	-	3
Skin/ soft tissue cancer	2	-
Contralateral breast cancer	2	-
Hematological (MDS, AML)	1	1
Other (omental, oesophageal, bladder, unknown)	2	2
Total	**16**	**22**

however, most patients in both treatment arms also had breast- or chest wall radiotherapy and we are not sure if this relatively small difference in RT fields could cause the higher number of second primary cancers after ART.

Bias dello studio AMAROS

Sottodimensionato per basso numero di eventi



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the Journal of Cancer Surgery

EJSO 43 (2017) 672–679

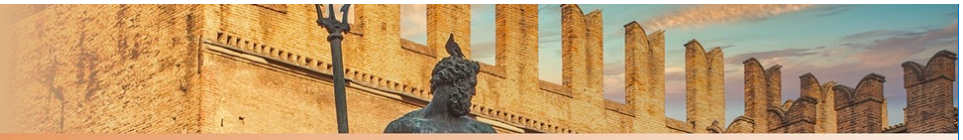
www.ejso.com

CrossMark

Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla – Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer: A randomized, single centre, phase III, non-inferiority trial

Á. Sávolt [a,*], G. Péley [b,†], C. Polgár [c], N. Udvarhelyi [d], G. Rubovszky [d], E. Kovács [e], B. Győrffy [f], M. Kásler [a], Z. Mátrai [a]

Conclusions: The long term follow-up results of this prospective-randomized trial suggest that RNI without cALND does not increase the risk of axillary failure in selected patients with early-stage invasive breast cancer (cT ≤ 3 cm, cN0) and pN1(sn). Axillary radiotherapy should be an alternative treatment for selected patients with sentinel lymph node metastases.



ARTICLE IN PRESS

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

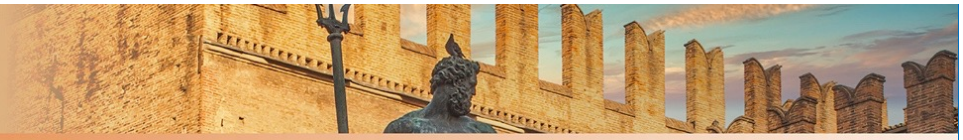
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Customizing local and systemic therapies for women with early breast cancer: the St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021

H. J. Burstein[1*†], G. Curigliano[2*†], B. Thürlimann[3], W. P. Weber[4], P. Poortmans[5], M. M. Regan[1], H. J. Senn[6], E. P. Winer[1] & M. Gnant[7], Panelists of the St Gallen Consensus Conference[i]

require no further axillary surgery. Women with T1-T2, clinically node-negative cancers with positive sentinel nodes who meet the criteria of the ACOSOG Z0011 trial[16] (breast-conserving surgery, with one or two positive sentinel lymph nodes) or the EORTC 10981-22023 AMAROS trial[17] [breast-conserving surgery or mastectomy, with positive sentinel node(s)], with planned breast radiation after breast-conserving surgery or axillary radiation after mastectomy, do not need additional axillary surgery in most cases. A complete axillary dissection remains standard for women with more than two positive sentinel lymph nodes, when radiation therapy is to be omitted, or in the clinical situations when knowing the extent of axillary involvement would affect systemic or radiation recommendations.



ASCO special articles

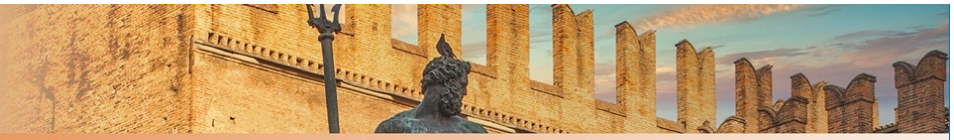
Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer Care Ontario) and ASCO Guideline

Muriel Brackstone, MD, PhD[1]; Fulvia G. Baldassarre, MSc[2]; Francisco E. Perera, MD[1]; Tulin Cil, MD, MEd[3]; Mariana Chavez Mac Gregor, MD, MSc[4]; Ian S. Dayes, MD[5]; Jay Engel, MBBCh[6]; Janet K. Horton, MD[7]; Tari A. King, MD[8]; Anat Kornecki, MD[9]; Ralph George, MD[10]; Sandip K. SenGupta, MD[11]; Patricia A. Spears, BS[12]; and Andrea F. Eisen, MD[13]

Recommendation 3

(A) No further axillary surgery beyond SLNB compared with ALND

Clinicians should not recommend ALND for women with early-stage breast cancer who have one or two sentinel lymph node metastases and will receive breast-conserving surgery with conventionally fractionated whole-breast radiotherapy (endorsed from ASCO 2017 guideline,[9,10] Recommendation 2.1) (Type: evidence based; benefits outweigh harms; Evidence quality: high for patients who received breast-conserving surgery; Strength of recommendation: strong for those who had breast-conserving surgery. For patients who had mastectomy and for those excluded from the trials, the strength of the body of the evidence is insufficient and the recommendation is weak).



Qualità globale delle evidenze	Raccomandazione clinica	Forza della raccomandazione
MODERATA	Nelle pazienti con carcinoma mammario invasivo cT1-2, cN0 con macrometastasi in 1-2 linfonodi sentinella, sottoposte a chirurgia conservativa, trattate con radioterapia sulla mammella e terapia sistemica, l'omissione della dissezione ascellare può essere presa in considerazione[99].	**Condizionata a favore**
COI: nessun conflitto di interesse		
Condizionata a favore	"Nei pazienti con (criteri di selezione) l'intervento xxx **può** essere preso in considerazione come opzione terapeutica di prima intenzione, in alternativa a yyy"	L'intervento in esame può essere considerato come opzione di prima intenzione, consapevoli dell'esistenza di alternative ugualmente proponibili (incertezza riguardo alla prevalenza dei benefici sui danni)


NO RT?
SI RT?

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2022
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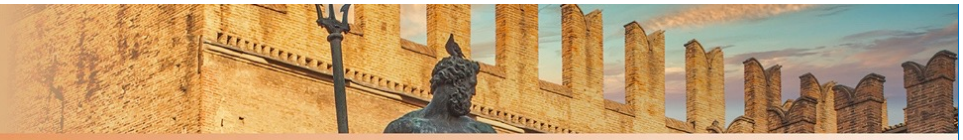
LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a]
BREAST-CONSERVING SURGERY (BCS) FOLLOWED BY RT

RT AFTER COMPLETION OF BCS AND AXILLARY STAGING

BCS with surgical axillary staging (category 1)[i,j,k,l]

- Negative axillary nodes → WBRT ± boost[n] to tumor bed, and consider comprehensive regional nodal irradiation (RNI) in patients with central/medial tumors, pT3 tumors, or pT2 tumors with <10 axillary nodes removed and one of the following high-risk features: grade 3, extensive lymphovascular invasion [LVI], or ER-negative.
  or
  Consideration of APBI in selected low-risk patients.[n,o]
  or
  Consider omitting breast irradiation in patients ≥70 y of age with ER-positive, cN0, pT1 tumors who receive adjuv[illegible]
- 1–3 positive axillary nodes → Meets ALL of the following criteria:
  • cT1–T2, cN0
  • No preoperative chemotherapy
  • 1–2 positive sentinel lymph node (SLNs)
  • WBRT planned
  - Yes to all → WBRT ± boost (use of comprehensive RNI with or without intentional inclusion of axilla is at the discretion of the radiation oncologist) (category 1)
  - No → WBRT with inclusion of any portion of the undissected axilla at risk ± boost[n] to tumor bed (category 1). Strongly consider comprehensive RNI.
- ≥4 positive[m] axillary nodes → WBRT ± boost[n] to tumor bed (category 1) + comprehensive RNI with inclusion of any portion of the undissected axilla at risk (category 1)

See BINV-4



ASCO special articles

Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer Care Ontario) and ASCO Guideline

Muriel Brackstone, MD, PhD[1]; Fulvia G. Baldassarre, MSc[2]; Francisco E. Perera, MD[1]; Tulin Cil, MD, MEd[3]; Mariana Chavez Mac Gregor, MD, MSc[4]; Ian S. Dayes, MD[5]; Jay Engel, MBBCh[6]; Janet K. Horton, MD[7]; Tari A. King, MD[8]; Anat Kornecki, MD[9]; Ralph George, MD[10]; Sandip K. SenGupta, MD[11]; Patricia A. Spears, BS[12]; and Andrea F. Eisen, MD[13]

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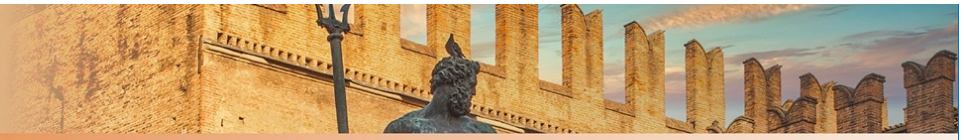
(C) Radiotherapy to the axilla compared with further surgery (ALND)

We recommend radiotherapy of the axilla in lieu of ALND in patients who are clinically node-negative and pathologically sentinel lymph node–positive with tumors of up to 5 cm and unifocal or multifocal disease restricted to one quadrant. In patients who receive breast-conserving surgery, we recommend no ALND if one or two sentinel lymph nodes are positive. LRNI is a reasonable option, especially when there are high-risk features as in (B). ALND and LRNI to the axilla are recommended if ≥ 3 sentinel lymph nodes are positive. In patients who receive mastectomy and have one to two positive nodes, postmastectomy radiation (PMRT) to the axilla is recommended and ALND can be safely omitted. In patients declining PMRT (ie, patients with immediate reconstruction), either radiation to the axilla without the chest wall or completion ALND can be considered. In patients who receive mastectomy and have ≥ 3 positive nodes, ALND followed by LRNI can be considered (Type: informal consensus; benefits outweigh harms in the short term; Evidence quality: low; Strength of recommendation: weak).



JAMA Network Insights
February 2018

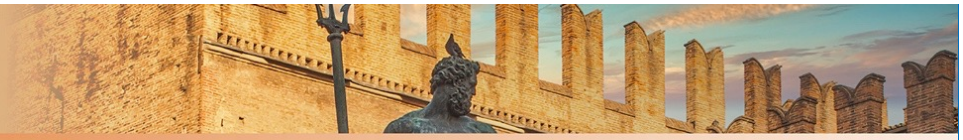
Management of the Node-Positive Axilla in Breast Cancer in 2017

Selecting the Right Option

Monica Morrow, MD[1,2]
≫ Author Affiliations

JAMA Oncol. 2018;4(2):250-251. doi:10.1001/jamaoncol.2017.3625

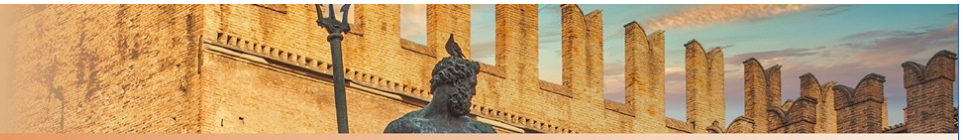
argue against this approach. At present, features predictive of heavier nodal tumor burden such as extent of nodal involvement, microscopic extracapsular tumor extension in the sentinel nodes, larger primary tumor size, and lymphovascular invasion are used to select higher-risk patients for nodal irradiation after SLNB. In contrast to the options available for



Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node in Breast Cancer: 10-Year Results of the Randomized Controlled EORTC 10981-22023 AMAROS Trial

Sanne A.L. Bartels, MD, PhD, MSc[1,2]; Mila Donker, MD, PhD[2,3]; Coralie Poncet, MSc[1]; Nicolas Sauvé, MSc[1]; Marieke E. Straver, MD, PhD[4]; Cornelis J.H. van de Velde, MD, PhD[5]; Robert E. Mansel, MD, MS[6]; Charlotte Blanken, MD, PhD[7]; Lorenzo Orzalesi, MD, PhD[8]; Jean H.G. Klinkenbijl, MD, PhD[9]; Huub C.J. van der Mijle, MD, PhD[10]; Grard A.P. Nieuwenhuijzen, MD, PhD[11]; Sanne C. Veltkamp, MD, PhD[12]; Thijs van Dalen, MD, PhD[13]; Andreas Marinelli, MD, PhD[4]; Herman Rijna, MD, PhD[14]; Marko Snoj, MD, PhD[15]; Nigel J. Bundred, MD, PhD[16]; Jos W.S. Merkus, MD, PhD[17]; Yazid Belkacemi, MD, PhD[18,19]; Patrick Petignat, MD[20]; Dominic A.X. Schinagl, MD, PhD[21]; Corneel Coens, MSc[1]; Geertjan van Tienhoven, MD, PhD[22]; Frederieke van Duijnhoven, MD, PhD[2]; and Emiel J.T. Rutgers, MD, PhD[2]

SNB the radiotherapy field can be defined based on risk factors for locoregional recurrence (grade, LVI, size, age, triple negative tumours and systemic treatment given). In patients with a very low risk ART could be omitted altogether, and in patients with an intermediate risk



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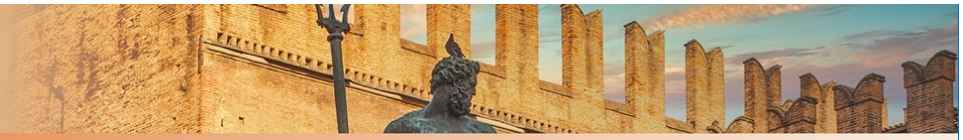
AIRO Breast Cancer Group
Best Clinical Practice 2022 Update

Antonella Ciabattoni[1], Fabiana Gregucci[2],

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione
B	Nelle pazienti con pN1mac dopo BLS, in presenza di fattori prognostici sfavorevoli, l'irradiazione linfonodale può sostituire/ compensare l'astensione dalla ALND	Positiva debole

QUALITÀ GLOBALE DELL'EVIDENZA: **Moderata**



POSNOC

***PO*sitive *S*entinel *NO*de: adjuvant therapy alone versus adjuvant therapy plus *C*learance or axillary radiotherapy**

A randomised controlled trial of axillary treatment in women with early stage breast cancer who have metastases in one or two sentinel nodes

Arm 1: ***adjuvant systemic therapy*** and if indicated ***breast/chest wall irradiation therapy*** (no further axillary treatment).

Arm 2: Level I-III ***Axillary lymph node dissection (ALND) or Axillary radiotherapy (ART), adjuvant systemic therapy*** and if indicated, ***breast/chest wall irradiation therapy***.

8.2.6 Adjuvant Breast or Chest wall Radiotherapy (Arm 1 & 2)

Patients will undergo adjuvant breast or chest wall irradiation therapy if needed as per pre-defined local institutional guidelines. The irradiation therapy to be done on this protocol specifically excludes axillary irradiation in Arm 1 because that would confound the issue being addressed by the study.

Potranno i risultati di questi studi aumentare la richiesta di dissezioni ascellari?

ORIGINAL ARTICLE

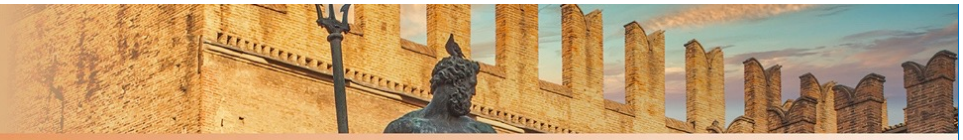
21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky, W.E. Barlow, J.R. Gralow, F. Meric-Bernstam, K.S. Albain, D.F. Hayes, N.U. Lin, E.A. Perez, L.J. Goldstein, S.K.L. Chia, S. Dhesy-Thind, P. Rastogi, E. Alba, S. Delaloge, M. Martin, C.M. Kelly, M. Ruiz-Borrego, M. Gil-Gil, C.H. Arce-Salinas, E.G.C. Brain, E.-S. Lee, J.-Y. Pierga, B. Bermejo, M. Ramos-Vazquez, K.-H. Jung, J.-M. Ferrero, A.F. Schott, S. Shak, P. Sharma, D.L. Lew, J. Miao, D. Tripathy, L. Pusztai, and G.N. Hortobagyi

rapid communications

Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2−, Node-Positive, High-Risk, Early Breast Cancer (monarchE)

Stephen R. D. Johnston, MD, PhD[1]; Nadia Harbeck, MD, PhD[2]; Roberto Hegg, MD, PhD[3]; Masakazu Toi, MD, PhD[4]; Miguel Martin, MD, PhD[5]; Zhi Min Shao, MD[6]; Qing Yuan Zhang, MD, PhD[7]; Jorge Luis Martinez Rodriguez, MD[8]; Mario Campone, MD, PhD[9]; Erika Hamilton, MD[10]; Joohyuk Sohn, MD, PhD[11]; Valentina Guarneri, MD, PhD[12]; Morihito Okada, MD, PhD[13]; Frances Boyle, MD, MBBS, PhD[14]; Patrick Neven, MD, PhD[15]; Javier Cortés, MD, PhD[16]; Jens Huober, MD[17]; Andrew Wardley, MD, MBChB[18]; Sara M. Tolaney, MD, MPH[19]; Irfan Cicin, MD[20]; Ian C. Smith, MD[21,22]; Martin Frenzel, PhD[22]; Desirée Headley, MSc[22]; Ran Wei, PhD[22]; Belen San Antonio, PhD[22]; Maarten Hulstijn, PhD[22]; Joanne Cox, MD[22]; Joyce O'Shaughnessy, MD[23]; and Priya Rastogi, MD[24]; on behalf of the monarchE Committee Members and Investigators



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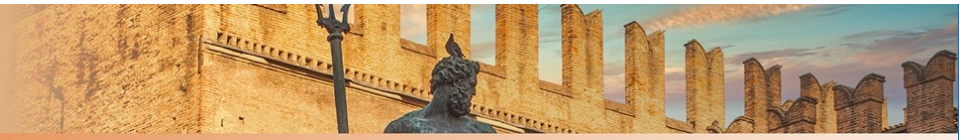
METHODS

In a prospective trial, we randomly assigned women with hormone-receptor–positive, HER2-negative breast cancer, one to three positive axillary lymph nodes, and a recurrence score of 25 or lower (scores range from 0 to 100, with higher scores indicating a worse prognosis) to endocrine therapy only or to chemotherapy plus endocrine (chemoendocrine) therapy. The primary objective was to determine the effect of chemotherapy on invasive disease–free survival and whether the effect was influenced by the recurrence score. Secondary end points included distant relapse–free survival.

ALND: 62.6%
SLNB: 37.4%
Extent of nodal disease:
1 positive node in 65.3%,
2 in 25.2%,
3 in 9.2%

CONCLUSIONS

Among premenopausal women with one to three positive lymph nodes and a recurrence score of 25 or lower, those who received chemoendocrine therapy had longer invasive disease–free survival and distant relapse–free survival than those who received endocrine-only therapy, whereas postmenopausal women with similar characteristics did not benefit from adjuvant chemotherapy. (Funded by the National Cancer Institute and others; RxPONDER ClinicalTrials.gov number, NCT01272037.)



rapid communications

Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2−, Node-Positive, High-Risk, Early Breast Cancer (monarchE)

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METHODS This open-label, phase III study included patients with HR+, HER2−, high-risk EBC, who had surgery and, as indicated, radiotherapy and/or adjuvant/neoadjuvant chemotherapy. Patients with four or more positive nodes, or one to three nodes and either tumor size ≥ 5 cm, histologic grade 3, or central Ki-67 ≥ 20%, were eligible and randomly assigned (1:1) to standard-of-care adjuvant endocrine therapy (ET) with or without

CONCLUSION Abemaciclib when combined with ET is the first CDK4/6 inhibitor to demonstrate a significant improvement in IDFS in patients with HR+, HER2− node-positive EBC at high risk of early recurrence.

AGENDA

RT in pazienti con:

- 1-2 LNs positivo/i, non sottoposte a ALND
- **1-3 linfonodi positivi dopo ALND**

RT su linfonodi mammari interni

RT dopo terapia sistemica neoadiuvante e chirurgia

Frazionamento della dose

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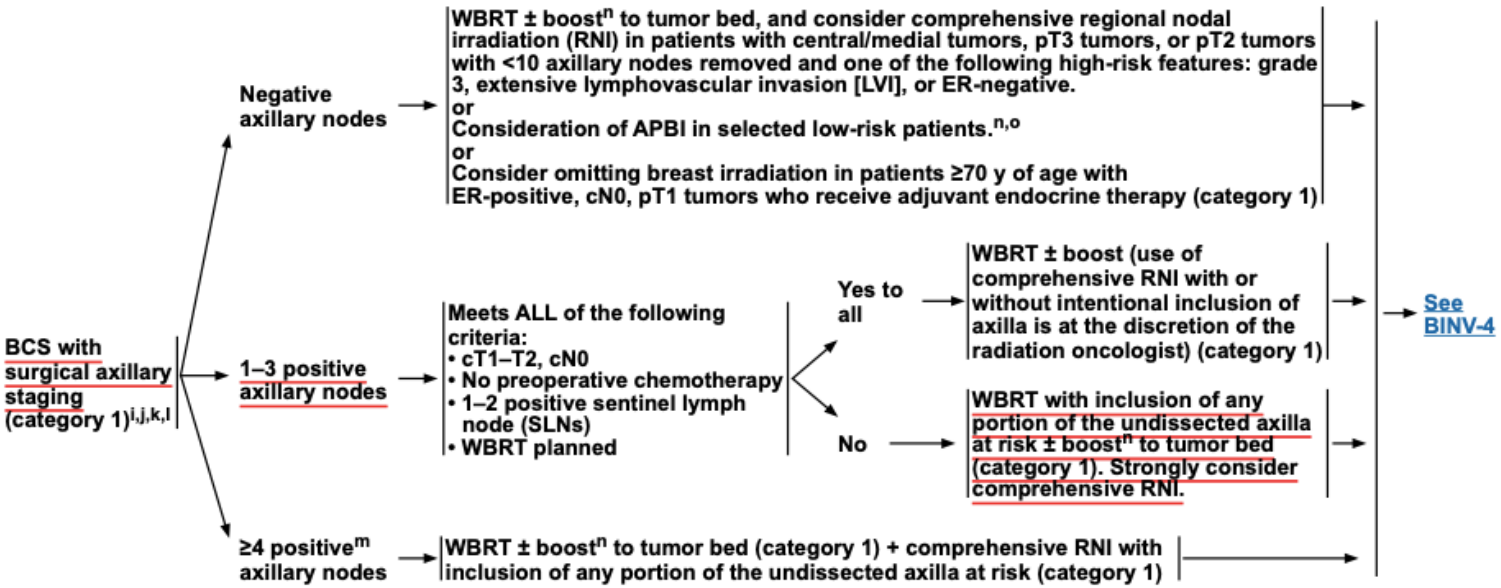

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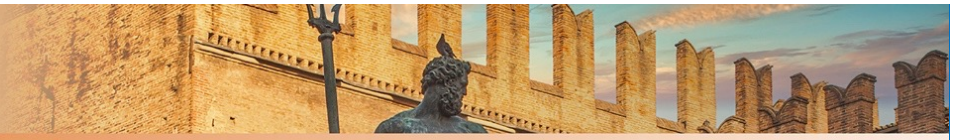
LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a,q]
MASTECTOMY FOLLOWED BY RT

RT AFTER COMPLETION OF MASTECTOMY AND AXILLARY STAGING

Total mastectomy with surgical axillary staging[i,j,k] (category 1) ± reconstruction[p]

- **Negative axillary nodes and tumor ≤5 cm and margins ≥1 mm** → **No RT[s]**
- **Negative axillary nodes and tumor ≤5 cm and negative margins but <1 mm** → **Consider RT[n] to chest wall. For patients with additional high-risk features,[s] consider addition of comprehensive RNI (including any portion of the undissected axilla at risk).**
- **Negative axillary nodes and tumor >5 cm** → **Consider RT[n] to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).**
- **1–3 positive axillary nodes[r]** → **Strongly consider RT[n] to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk).**
- **≥4 positive axillary nodes[m]** → **RT[n] to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk) (category 1)**
- **Margins positive** → **Re-excision to negative margins is preferred. If not feasible, then strongly consider RT[n] to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).**

See BINV-4



Practical Radiation Oncology (2016) 6, e219–e234

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ASCO Special Articles

Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update

Abram Recht [a], Elizabeth A. Comen [b], Richard E. Fine [c], Gini F. Fleming [d], Patricia H. Hardenbergh [e], Alice Y. Ho [b], Clifford A. Hudis [b], E. Shelley Hwang [f], Jeffrey J. Kirshner [g], Monica Morrow [b], Kilian E. Salerno [h], George W. Sledge Jr [i], Lawrence J. Solin [j], Patricia A. Spears [k], Timothy J. Whelan [l], Mark R. Somerfield [m,*], Stephen B. Edge [h]

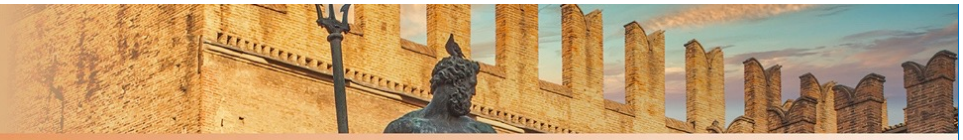
Clinical Question 1

Is PMRT indicated in patients with T1-2 tumors with one to three positive axillary lymph nodes who undergo ALND?

Recommendations

Recommendation 1a.

The panel unanimously agreed that the available evidence shows that PMRT reduces the risks of locoregional failure (LRF), any recurrence, and breast cancer mortality for patients with T1-2 breast cancer and one to three positive lymph nodes. However, some subsets of these patients are likely to have such a low risk of LRF that the absolute benefit of PMRT is outweighed by its potential toxicities. In addition, the acceptable ratio of benefit to toxicity varies among patients and physicians. Thus, the decision to recommend PMRT or not requires a great deal of clinical judgment. The panel agreed clinicians making such recommendations for individual patients should consider factors that may decrease the risk of LRF, attenuate the benefit of reduced breast cancer–specific mortality, and/or increase the risk of complications resulting from PMRT. These factors include: patient characteristics (age > 40 to 45 years, limited life expectancy because of older age or comorbidities, or coexisting conditions that might increase the risk of complications), pathologic findings associated with a lower tumor burden (eg, T1 tumor size, absence of lymphovascular invasion, presence of only a single positive node and/or small size of nodal metastases, or substantial response to NAST), and biologic characteristics of the cancer associated with better outcomes and survival and/or greater effectiveness of systemic therapy (eg, low tumor grade or strong hormonal sensitivity; type: informal consensus; evidence quality: intermediate; strength of recommendation: moderate).



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Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update

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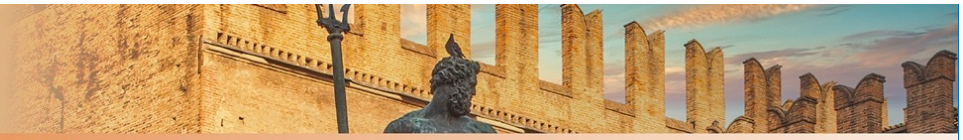
Recommendation 1b.

The decision to use PMRT should be made in a multidisciplinary fashion through discussion among providers from all treating disciplines early in a patient's treatment course (soon after surgery or before or soon after the initiation of systemic therapy), either in the context of a formal tumor board or by referral (type: informal consensus; evidence quality: insufficient; strength of recommendation: strong).

Recommendation 1c.

Decision making must fully involve the patient, whose values as to what constitutes sufficient benefit and how to weigh the risk of complications against this in light of the best information the treating physicians can provide regarding PMRT in her situation must be respected and incorporated into the final treatment choice (type: informal consensus; evidence quality: insufficient; strength of recommendation: strong).



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AIRO Breast Cancer Group
Best Clinical Practice 2022 Update

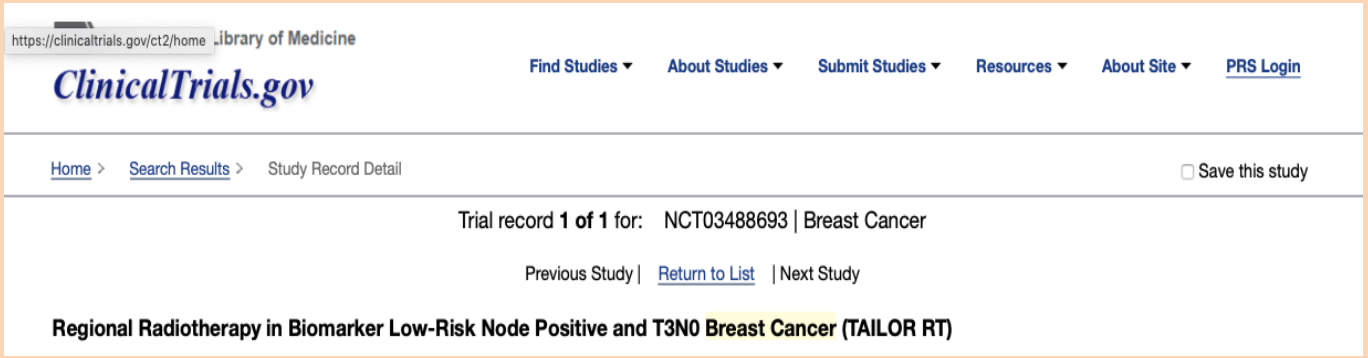
Antonella Ciabattoni[1], Fabiana Gregucci[2],

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, in presenza di fattori di rischio può essere considerato un trattamento radiante a livello delle stazioni linfonodali loco-regionali non trattate chirurgicamente	Positiva debole

QUALITÀ GLOBALE DELL'EVIDENZA: **Moderata**

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

QUALITÀ GLOBALE DELL'EVIDENZA: **Moderata**



The ongoing TAILOR-RT - NCIC MA.39 trial was designed to assess whether RT was needed after mastectomy in patients with pT1-2N1a who are ER-positive, HER2-negative and at low biological risk (21-gene RS < 18)

AGENDA

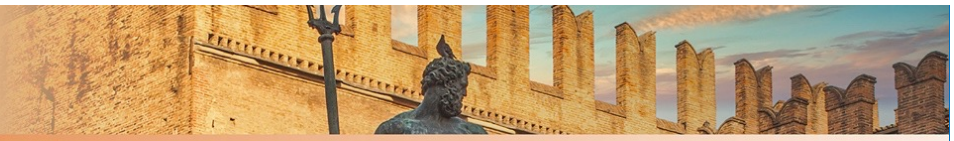
RT in pazienti con:

- 1-2 LNs positivo/i, non sottoposte a ALND
- 1-3 linfonodi positivi dopo ALND

RT su linfonodi mammari interni

RT dopo terapia sistemica neoadiuvante e chirurgia

Frazionamento della dose



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Regional Nodal Irradiation in Early-Stage Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Ivo A. Olivotto, M.D., Wendy R. Parulekar, M.D., Ida Ackerman, M.D., Boon H. Chua, M.B., B.S., Ph.D., Abdenour Nabid, M.D., Katherine A. Vallis, M.B., B.S., Ph.D., Julia R. White, M.D., Pierre Rousseau, M.D., Andre Fortin, M.D., Lori J. Pierce, M.D., Lee Manchul, M.D., Susan Chafe, M.D., Maureen C. Nolan, M.D., Peter Craighead, M.D., Julie Bowen, M.D., David R. McCready, M.D., Kathleen I. Pritchard, M.D., Karen Gelmon, M.D., Yvonne Murray, B.Sc., Judy-Anne W. Chapman, Ph.D., Bingshu E. Chen, Ph.D., and Mark N. Levine, M.D., for the MA.20 Study Investigators*

N+ (85% N+1-3) and high risk N- breast cancer treated with BCS

Breast RT

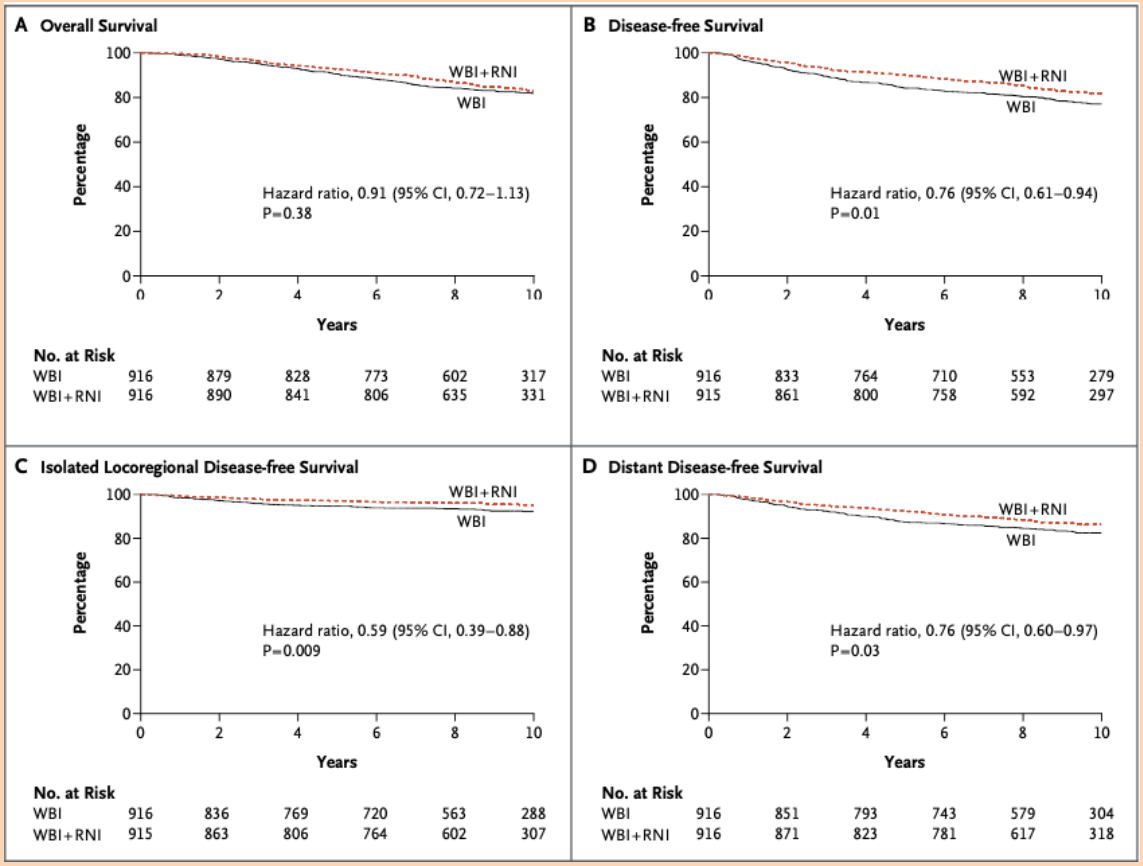
Breast + RN RT

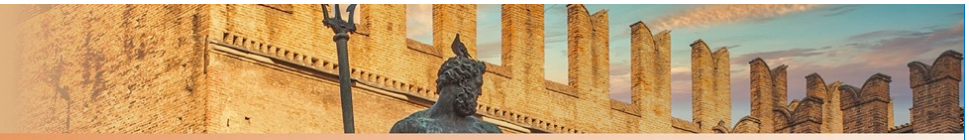
fined as a primary tumor measuring 5 cm or more or 2 cm or more with fewer than 10 axillary nodes removed and at least one of the following: grade 3 histologic categorization, estrogen-receptor (ER) negativity, or lymphovascular invasion.

CONCLUSIONS

Among women with node-positive or high-risk node-negative breast cancer, the addition of regional nodal irradiation to whole-breast irradiation did not improve overall survival but reduced the rate of breast-cancer recurrence. (Funded by the Canadian Cancer Society Research Institute and others; MA.20 ClinicalTrials.gov number, NCT00005957.)

diation), there were significant increases in the rates of lymphedema, telangiectasia of the skin, and subcutaneous fibrosis in the nodal-irradia-


A Overall Survival
Percentage
Years
WBI+RNI
WBI
Hazard ratio, 0.91 (95% CI, 0.72–1.13)
P=0.38
No. at Risk
WBI 916 879 828 773 602 317
WBI+RNI 916 890 841 806 635 331
B Disease-free Survival
Percentage
Years
WBI+RNI
WBI
Hazard ratio, 0.76 (95% CI, 0.61–0.94)
P=0.01
No. at Risk
WBI 916 833 764 710 553 279
WBI+RNI 915 861 800 758 592 297
C Isolated Locoregional Disease-free Survival
Percentage
Years
WBI+RNI
WBI
Hazard ratio, 0.59 (95% CI, 0.39–0.88)
P=0.009
No. at Risk
WBI 916 836 769 720 563 288
WBI+RNI 915 863 806 764 602 307
D Distant Disease-free Survival
Percentage
Years
WBI+RNI
WBI
Hazard ratio, 0.76 (95% CI, 0.60–0.97)
P=0.03
No. at Risk
WBI 916 851 793 743 579 304
WBI+RNI 916 871 823 781 617 318



Internal mammary and medial supraclavicular lymph node chain irradiation in stage I–III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial

Philip M Poortmans, Caroline Weltens, Catherine Fortpied, Carine Kirkove, Karine Peignaux-Casasnovas, Volker Budach, Femke van der Leij, Ernest Vonk, Nicola Weidner, Sofia Rivera, Geertjan van Tienhoven, Alain Fourquet, Georges Noel, Mariacarla Valli, Matthias Guckenberger, Eveline Kaiter, Severine Racadot, Roxolyana Abdah-Bortnyak, Frik F Van Limbergen, Antoine Engelen, Peter De Brouwer, Henk Struikmans, Harry Bartelink, for the European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups

Summary
Background 10-year results from several studies showed improved disease-free survival and distant metastasis-free

Lancet Oncol 2020

4004 patients with Stage I-III breast cancer treated with mastectomy or breast conserving surgery N+ (43% N+1-3) o N0 if in the inner or central breast

R

→ **BREAST / CHEST WALL RT**

→ **BREAST / CHEST WALL RT**
+
SUPRACLAVICULAR, INTERNAL MAMMARY NODES and UNDESSECTED PART OF THE AXILLA

Interpretation The 15-year results show a significant reduction of breast cancer mortality and any breast cancer recurrence by IM-MS irradiation in stage I–III breast cancer. However, this is not converted to improved overall survival.

	IM-MS irradiation group (n=2002)	Control group (n=2002)
Death (any cause)	554 (27·7%)	569 (28·4%)
Breast cancer recurrence*	468 (23·4%)	525 (26·2%)
Local recurrence	133 (6·6%)	128 (6·4%)
Regional recurrence†	65 (3·2%)	100 (5·0%)
Axillary	35 (1·7%)	48 (2·4%)
Medial supraclavicular	33 (1·6%)	51 (2·5%)
Internal mammary	5 (0·2%)	16 (0·8%)

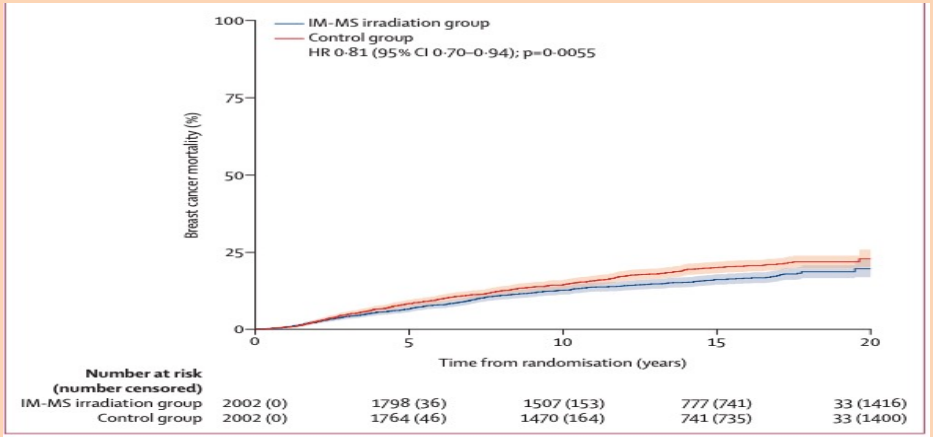
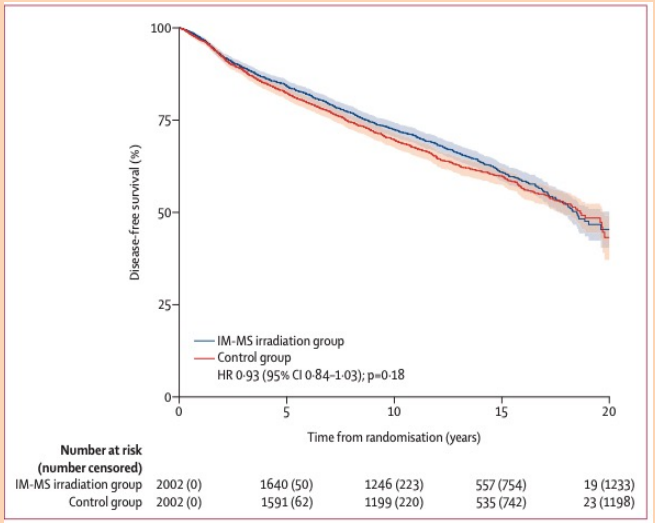
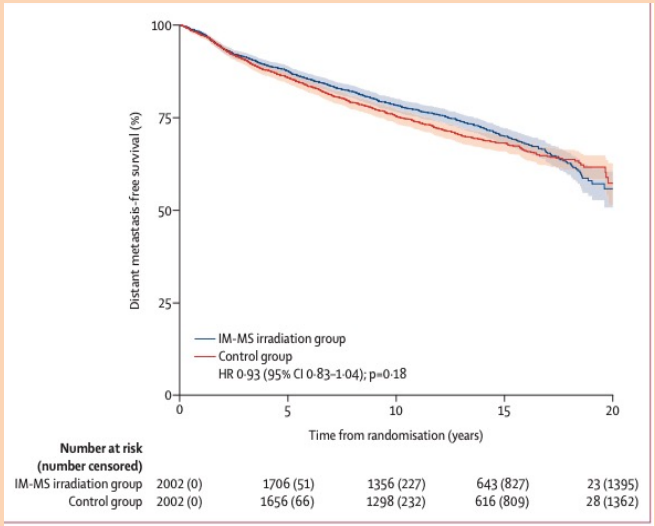


Figure 4: **Cumulative incidence of breast cancer mortality at 15 years of follow-up in the intention-to-treat population**



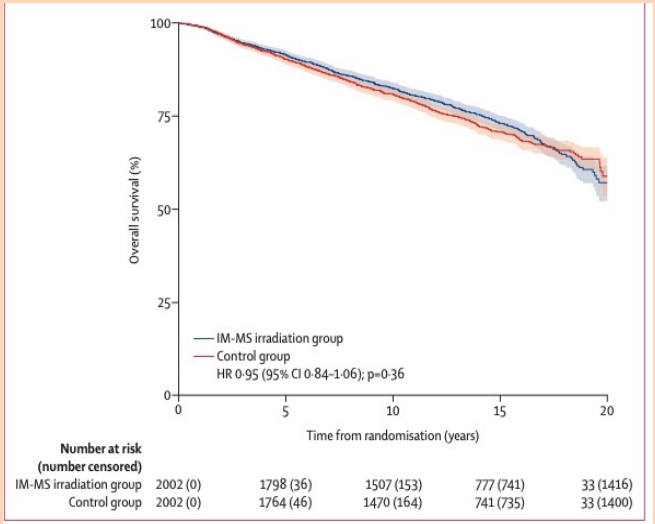
Number at risk (number censored)					
IM-MS irradiation group	2002 (0)	1640 (50)	1246 (223)	557 (754)	19 (1233)
Control group	2002 (0)	1591 (62)	1199 (220)	535 (742)	23 (1198)

Figure 2: **Disease-free survival at 15 years of follow-up in the intention-to-treat population**
The shaded areas show the 95% CI. HR=hazard ratio.



Number at risk (number censored)					
IM-MS irradiation group	2002 (0)	1706 (51)	1356 (227)	643 (827)	23 (1395)
Control group	2002 (0)	1656 (66)	1298 (232)	616 (809)	28 (1362)

Figure 3: **Distant metastasis-free survival at 15 years of follow-up in the intention-to-treat population**
The shaded areas show the 95% CI. HR=hazard ratio.



Number at risk (number censored)					
IM-MS irradiation group	2002 (0)	1798 (36)	1507 (153)	777 (741)	33 (1416)
Control group	2002 (0)	1764 (46)	1470 (164)	741 (735)	33 (1400)

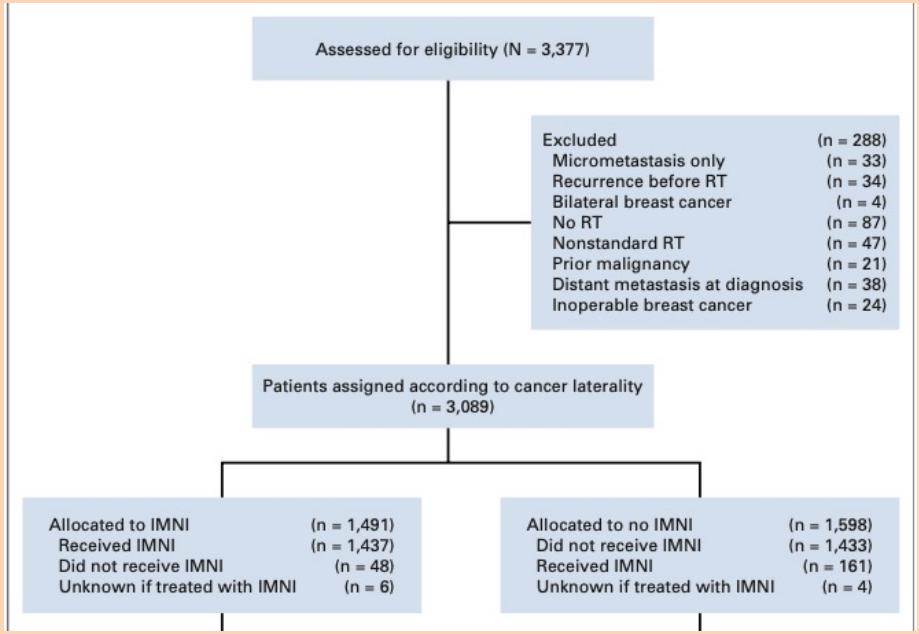
Figure 1: **Overall survival at 15 years of follow-up in the intention-to-treat population**
The shaded areas show the 95% CI. HR=hazard ratio.

follow-up, any grade of pulmonary fibrosis was recorded in 98 (5·1%) patients in the IM-MS irradiation group versus 44 (2·3%) patients in the control group, cardiac fibrosis in 38 (2·0%) patients versus 22 (1·1%) patients, and any cardiac disease in 165 (8·6%) patients versus 139 (7·2%) patients. Table 3 shows the reported cardiac

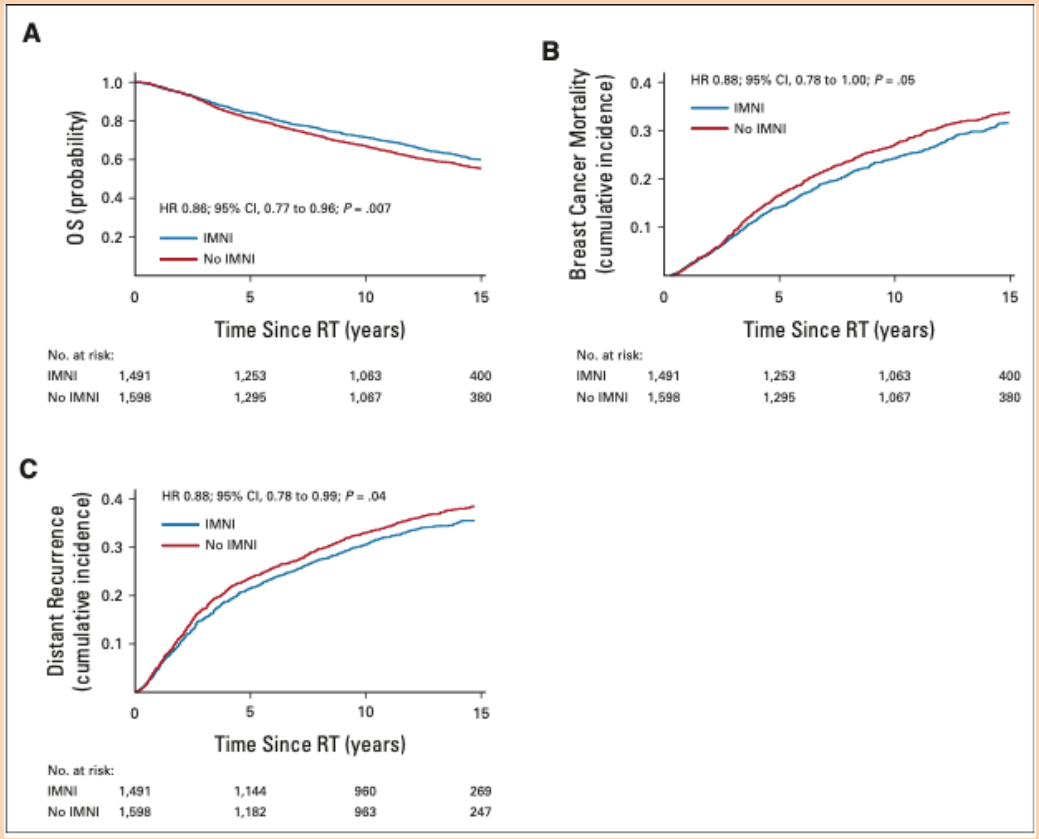
original reports

Internal Mammary Node Irradiation in Patients With Node-Positive Early Breast Cancer: Fifteen-Year Results From the Danish Breast Cancer Group Internal Mammary Node Study

Lise B.J. Thorsen, MD, PhD[1,2]; Jens Overgaard, MD, DMSc[1]; Louise W. Matthiessen, MD, PhD[3]; Martin Berg, MSc[4]; Lars Stenbygaard, MD[5]; Anders N. Pedersen, MD, PhD[6]; Mette H. Nielsen, MD, PhD[7]; Marie Overgaard, MD[2]; and Birgitte Vrou Offersen, MD, PhD[1,2] on behalf of the DBCG Radiotherapy Committee



CONCLUSION In patients with node-positive early breast cancer treated with IMNI or without IMNI depending on breast cancer laterality, IMNI reduced the risk of distant recurrence and death from breast cancer, thereby improving long-term survival.



OS advantage was significant in patients with 4-9 positive nodes

Subgroup	IMNI Patients	IMNI Events	No IMNI Patients	No IMNI Events	HR (95% CI)	15-Year Survival Rate (%) IMNI	No IMNI
No. of positive nodes							
1-3	864	267	946	319	0.90 (0.76 to 1.06)	68.6	65.3
4-9	398	172	415	213	0.80 (0.65 to 0.97)	56.0	48.7
≥ 10	217	146	229	165	0.87 (0.70 to 1.09)	33.5	27.4
Test for heterogeneity, P = .67							

AGENDA

RT in pazienti con:

- 1-2 LNs positivo/i, non sottoposte a ALND
- 1-3 linfonodi positivi dopo ALND

RT su linfonodi mammari interni

RT dopo terapia sistemica neoadiuvante e chirurgia

Frazionamento della dose

L' assenza di studi prospettici randomizzati rende difficile dare precise indicazione al trattamento radiante post-operatorio e sui volumi di irradiazione dopo terapia sistemica neoadiuvante

- cN0 ypN0 → NO RT
- cN+ ypN0 → Argomento di discussione
- ypN1
- cIII

→ SI RT

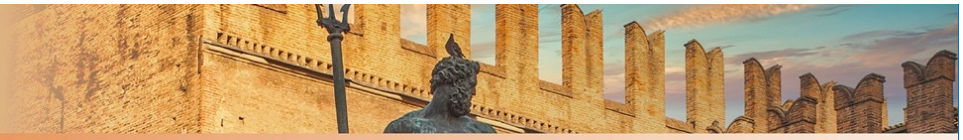
National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2022
Invasive Breast Cancer

NCCN Guidelines Index
Table of Contents
Discussion

OPERABLE DISEASE:
SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT[uu]

	SURGICAL TREATMENT	ADJUVANT THERAPY
BCS possible	BCS with surgical axillary staging[j] (see BINV-D)	Adjuvant systemic therapy[pp,vv] (see BINV-16) + post-lumpectomy adjuvant RT[n] • cN+ and ypN0: Adjuvant RT to the whole breast ± boost to the tumor bed;[n,ww] and strongly consider comprehensive RNI with inclusion of any portion of the undissected axilla at risk. • Any ypN+: Adjuvant RT to the whole breast ± boost to the tumor bed;[n,ww] and comprehensive RNI with inclusion of any portion of the undissected axilla at risk. • Any cN0, ypN0: Adjuvant RT to whole breast ± boost to tumor bed
BCS not possible	Mastectomy and surgical axillary staging[j] (see BINV-D) + reconstruction (optional)[p]	Adjuvant systemic therapy[pp,vv] (see BINV-16) + post-mastectomy adjuvant RT[n] • cN+ and ypN0: Strongly consider RT to the chest wall and comprehensive RNI with inclusion of any portion of the undissected axilla at risk. • Any ypN+: RT is indicated to the chest wall + comprehensive RNI with inclusion of any portion of the undissected axilla at risk. or Adjuvant systemic therapy[pp,vv] (see BINV-16) without adjuvant RT for any cN0,ypN0 if axilla was assessed by SLNB or axillary node dissection[j]



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY
driving innovation in oncology

SPECIAL ARTICLE

Customizing local and systemic therapies for women with early breast cancer: the St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021

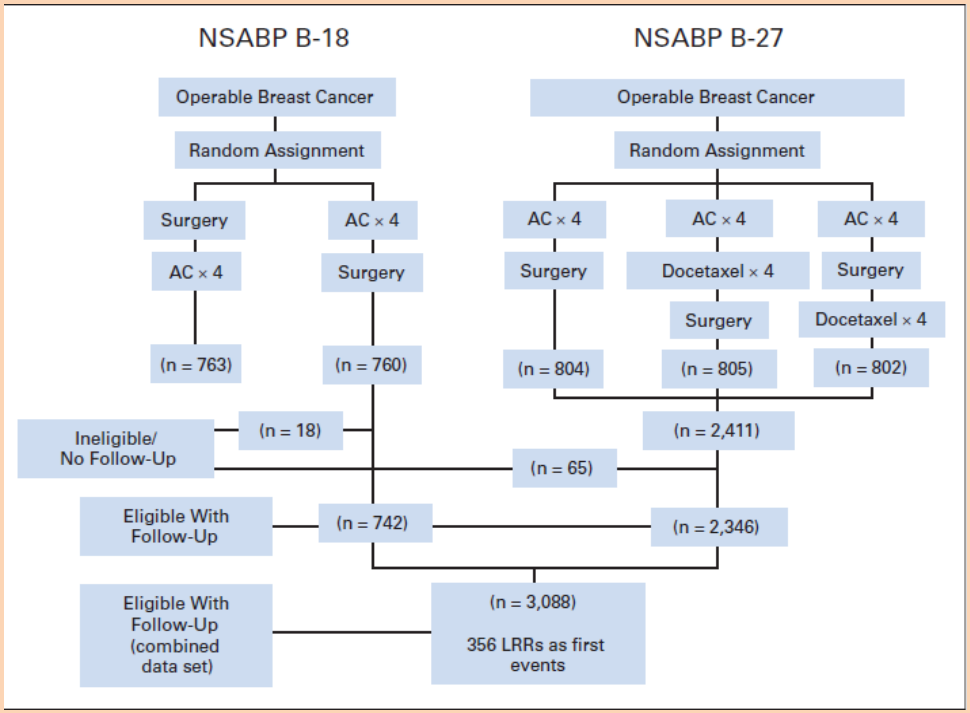
H. J. Burstein[1*†], G. Curigliano[2*†], B. Thürlimann[3], W. P. Weber[4], P. Poortmans[5], M. M. Regan[1], H. J. Senn[6], E. P. Winer[1] & M. Gnant[7], Panelists of the St Gallen Consensus Conference[‡]

Panel strongly favored RNI for patients who initially presented with a clinically positive axillary node(s), even when such patients achieve a pCR with neoadjuvant therapy.

VOLUME 30 · NUMBER 32 · NOVEMBER 10 2012
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Predictors of Locoregional Recurrence After Neoadjuvant Chemotherapy: Results From Combined Analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27

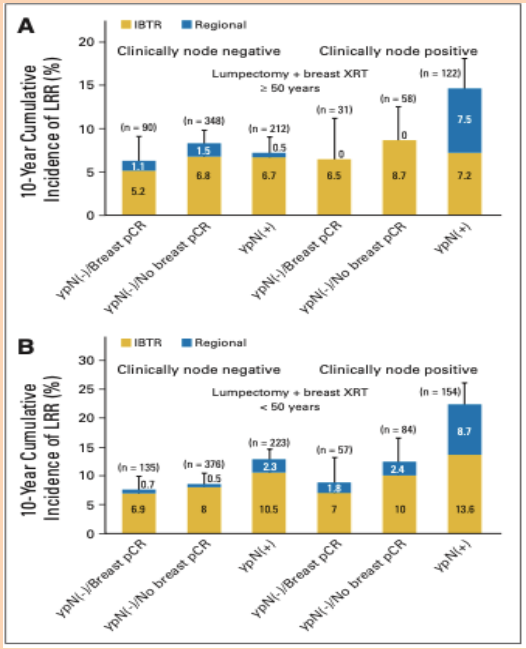
Eleftherios P. Mamounas, Stewart J. Anderson, James J. Dignam, Harry D. Bear, Thomas B. Julian, Charles E. Geyer Jr, Alphonse Taghian, D. Lawrence Wickerham, and Norman Wolmark

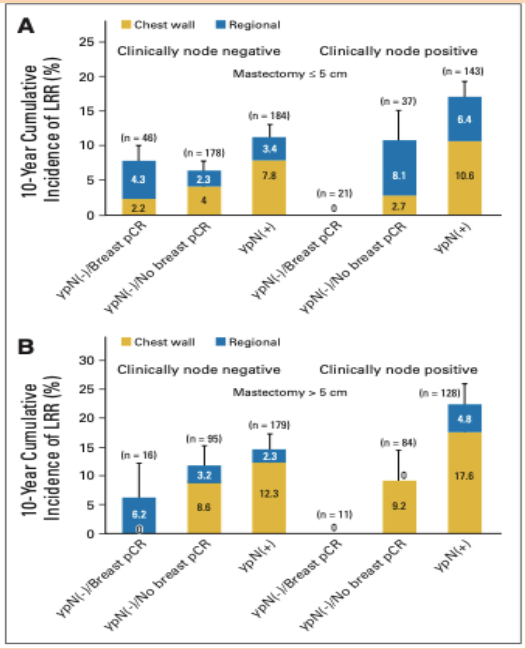


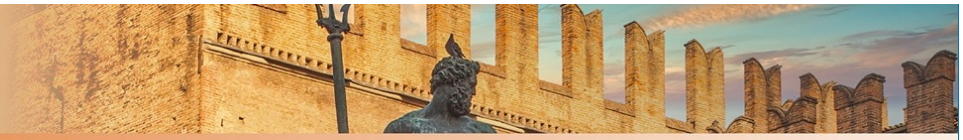
STADIO CLINICO: T1-3/N0-1
(solo 30% cN1)
BIAS

- Poche pazienti in pCR su T e N
- Non conferma istologica stato linfonodale pre-CT
- Assenza di informazioni su caratterizzazione biopatologica e su presenza o meno di invasione linfovascolare

the risk of locoregional recurrence. Pathologic response in the breast and nodes (residual disease in the breast and nodes negative *v* complete pathologic response: hazard ratio [HR], 2.21; residual positive nodes *v* complete pathologic response: HR, 4.48) was a more powerful predictor of locoregional recurrence than initial nodal status (clinically node positive *v* clinically node negative: HR, 1.53) or tumor size (< 5 *v* > 5 cm: HR, 1.58). Notably, all patients with residual nodal involvement by cancer had a $> 10\%$ risk of locoregional recurrence.







TJ Tumori Journal

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2022, Vol. 108(2S) 1–144
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AIRO Breast Cancer Group
Best Clinical Practice 2022 Update

Antonella Ciabattoni[1], Fabiana Gregucci[2],

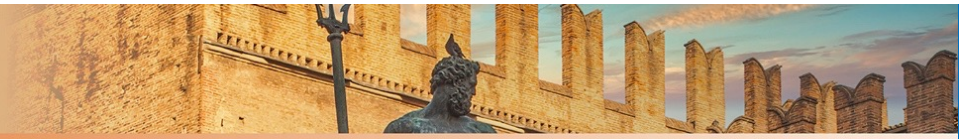
Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
B	Nelle pazienti con carcinoma mammario invasivo cT1-cT2 cN1 sottoposte a terapia medica neoadiuvante e mastectomia, con risposta patologica completa sia su T che su N, in caso di basso rischio di recidiva loco-regionale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

QUALITÀ GLOBALE DELL'EVIDENZA: **Moderata**

Quale approccio in pz cN1 con LNs negativo/i dopo terapia sistemica neoadiuvante

non c'è indicazione a un ulteriore approccio chirurgico

Kim, J Breast Cancer 2015
Barron, JAMA Surg. 2018
Martelli, Ann Surg 2020
Kahler-Ribeiro-Fontana, JSO 2021
Wong, Ann Surg Oncol 2021
Barrio, Jama Oncol 2021



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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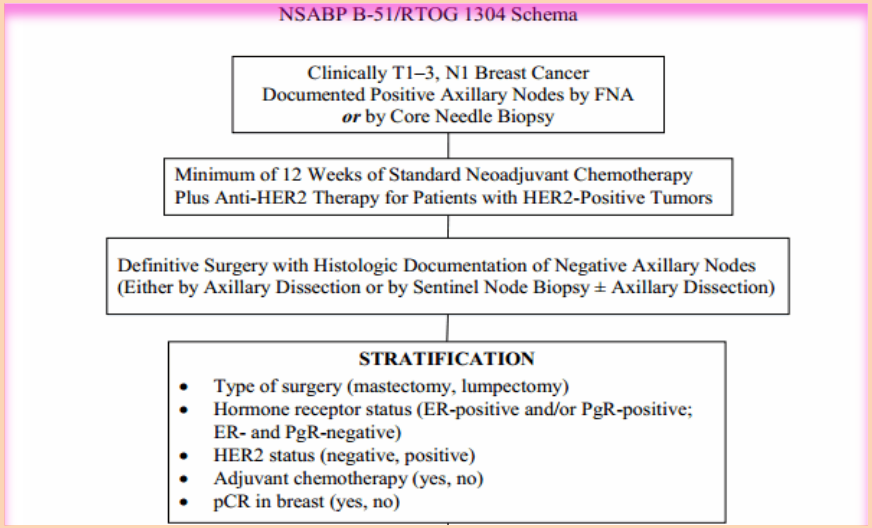
Customizing local and systemic therapies for women with early breast cancer: the St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021

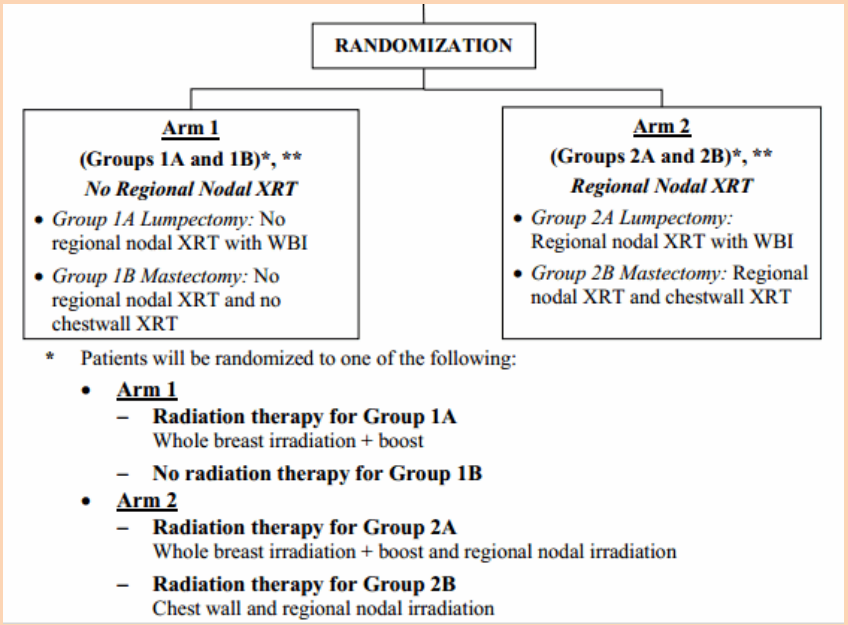
H. J. Burstein[1*†], G. Curigliano[2*†], B. Thürlimann[3], W. P. Weber[4], P. Poortmans[5], M. M. Regan[1], H. J. Senn[6], E. P. Winer[1] & M. Gnant[7], Panelists of the St Gallen Consensus Conference[‡]

patients who present with a clinical N1 axilla, and who convert to a clinically negative axilla (cN0) after neo-adjuvant treatment, are potential candidates for SNB. Those without residual nodal disease, when the initially sampled and clipped or at least three sentinel nodes are identified and resected, do not require axillary dissection.[35-37] How-

C'è indicazione al trattamento radiante su linfonodi regionali?

A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy





RNI to the undissected axilla plus supraclavicular and internal mammary nodes

Radiotherapy and Oncology 162 (2021) 52–59

Contents lists available at ScienceDirect

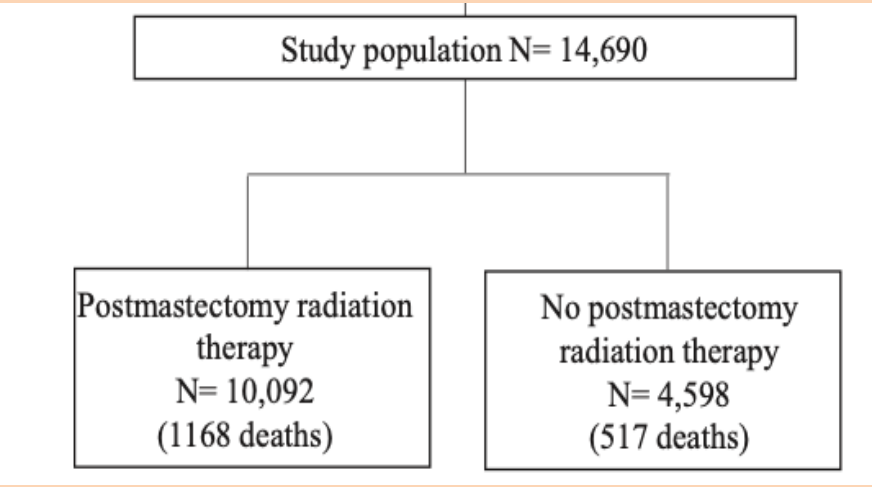
Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Postmastectomy radiation therapy following pathologic complete nodal response to neoadjuvant chemotherapy: A prelude to NSABP B-51? ☆

Waqar Haque [a,*,1], Anukriti Singh [b], Vivek Verma [c], Mary R. Schwartz [d], Neil Chevli [e], Sandra Hatch [e], Monica Desai [f], E. Brian Butler [a], Candy Arentz [g], Andrew Farach [a], Bin S. Teh [a]



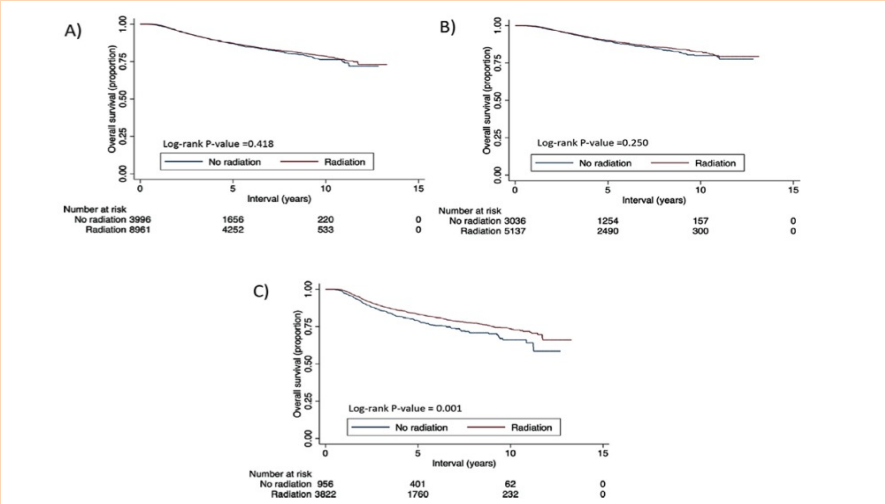


Fig. 2. Kaplan-Meier curves comparing overall survival for (A) all patients, (B) the NSABP B-51 population of cT1–3 cN1 patients, and (C) in all other patients (cT4 and/or cN2-3).

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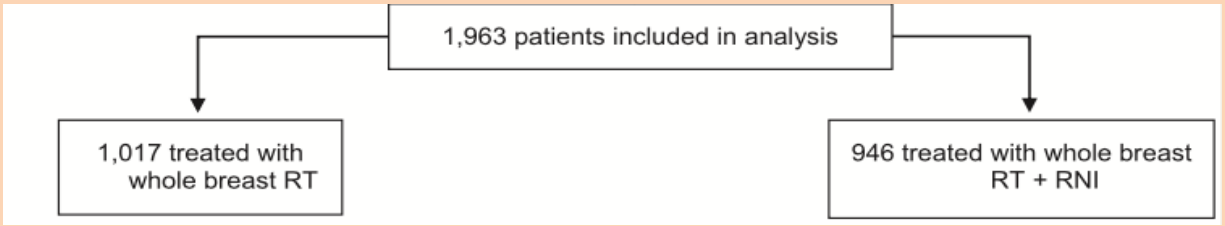
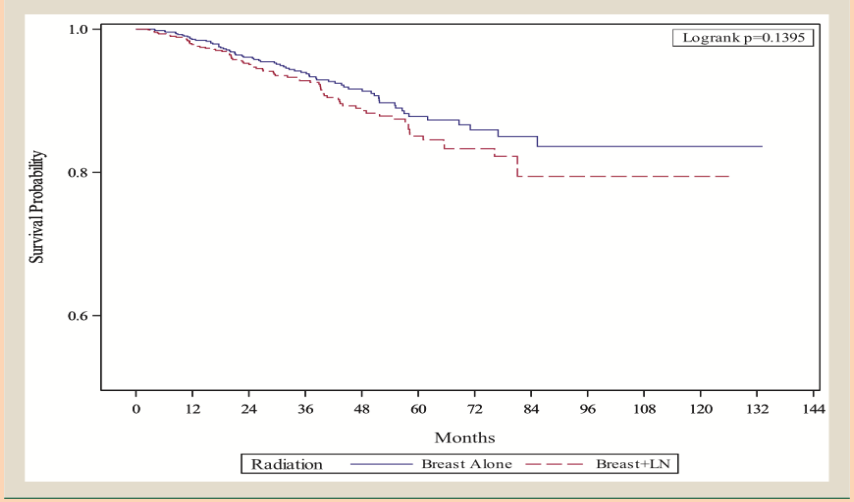
Original article

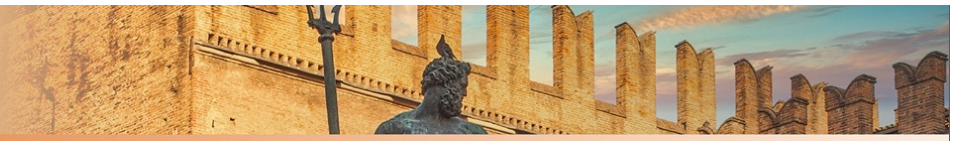
Regional Nodal Irradiation for Clinically Node-Positive Breast Cancer Patients With Pathologic Negative Nodes After Neoadjuvant Chemotherapy

Ashley Schlafstein,[1] Yuan Liu,[2] Subir Goyal,[2] Shannon Kahn,[1] Karen Godette,[1] Jolinta Lin,[1] Mylin A. Torres,[1] Trevor J. Royce,[3] Sagar A. Patel[1]





benefit. To our knowledge, this study is the largest assessment of the impact of RNI in this particular cohort, though limited due to this retrospective design using a population-based registry. We eagerly await the results of the NSABP B-51 phase III randomized clinical trial which will prospectively test this question.



TI Tumori

AIRO Breast Cancer Group
Best Clinical Practice 2022 Update

Antonella Ciabattoni[1], Fabiana Gregucci[2],

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 loco-regionale.	Positiva debole

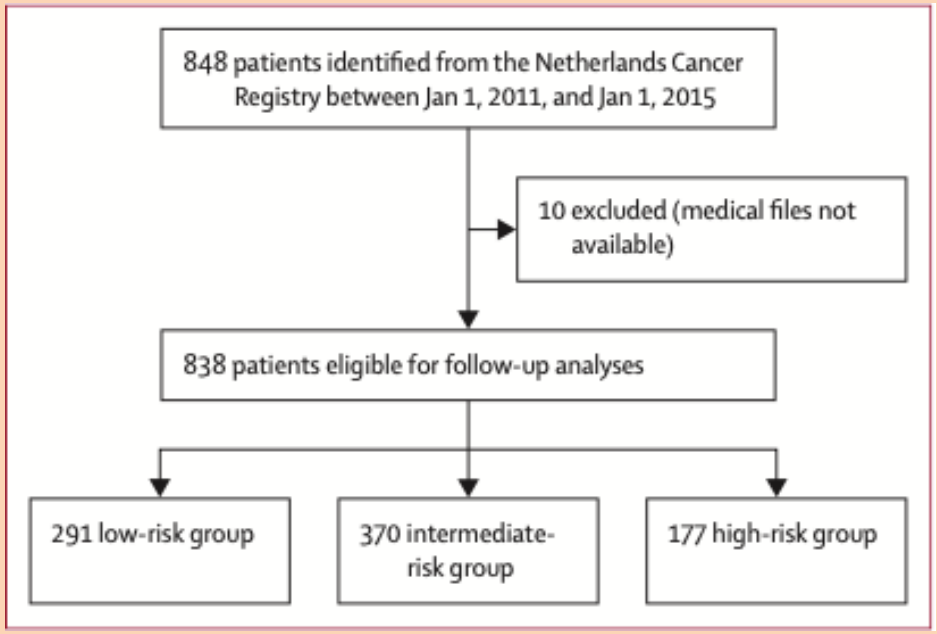
QUALITÀ GLOBALE DELL'EVIDENZA: **Moderata**

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione
B	Nelle pazienti con carcinoma mammario clinicamente positivo all'esordio per interessamento ascellare di malattia (cT1-2 N1con basso rischio di recidiva loco-regionale), 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**

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

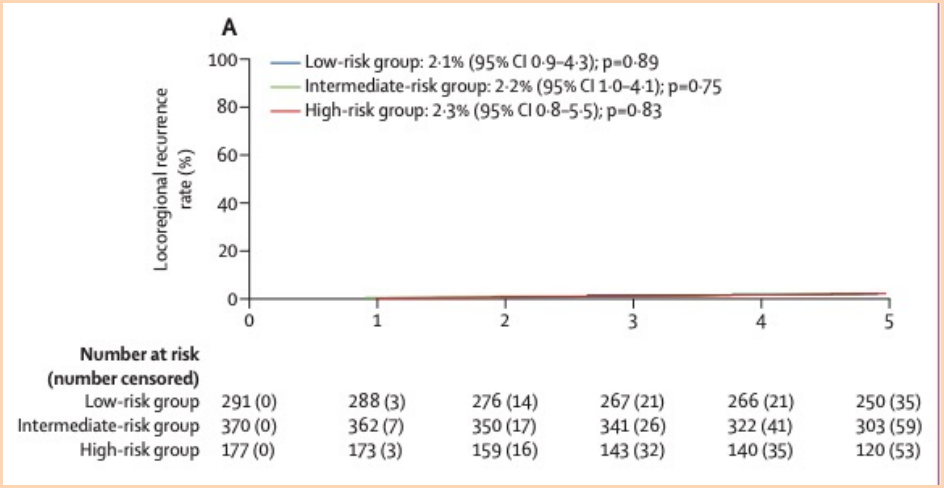
Sabine R de Wild, Linda de Munck, Janine M Simons, Janneke Verloop, Thijs van Dalen, Paula H M Elkhuizen, Ruud M A Houben, A Elise van Leeuwen, Sabine C Linn, Ruud M Pijnappel, Philip M P Poortmans, Luc J A Strobbe, Jelle Wesseling, Adri C Voogd, Liesbeth J Boersma

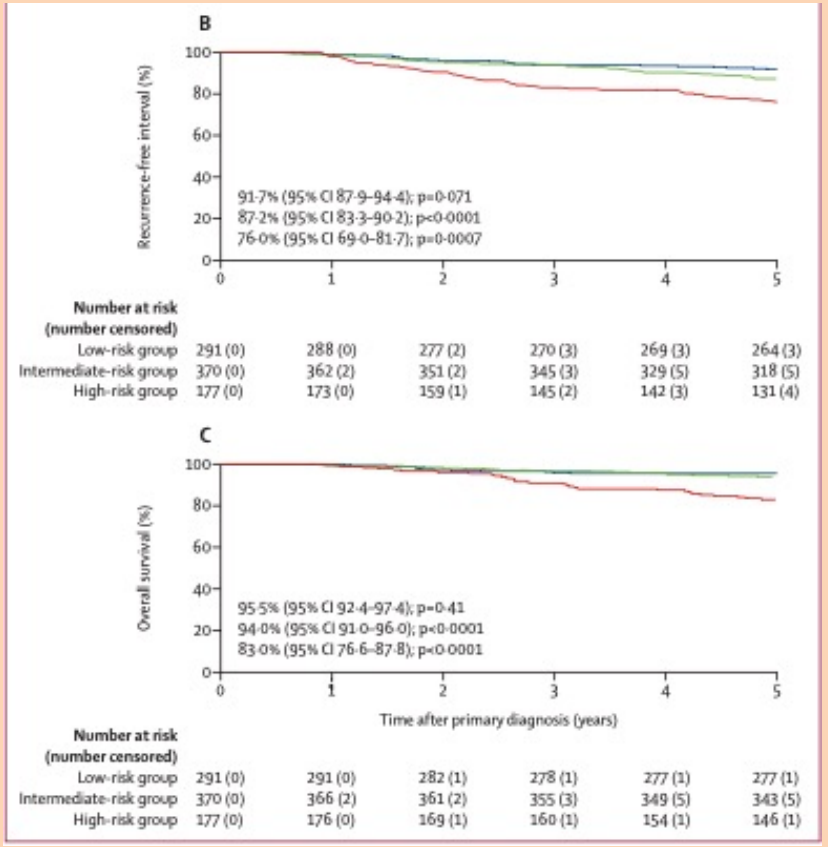


	Radiotherapy after breast conserving therapy	Radiotherapy after mastectomy
Low-risk group		
ypN0 (ALND)	Whole breast radiotherapy	..
If SLNB before primary chemotherapy and no ALND: cN1mi (SLNB), no risk factor*; or if SLNB after primary chemotherapy and no ALND: ypN0 (SLNB)	Whole breast radiotherapy	..
Intermediate-risk group		
ypN1 (ALND)	Whole breast radiotherapy	Chest wall radiotherapy
If SLNB before primary chemotherapy and no ALND†: cN1mi (SLNB), ≥1 risk factor*, or cN1 (SLNB), ≤2 macrometastases, no risk factor*; or if SLNB after primary chemotherapy and no ALND†: ypN1mi (SLNB), no risk factor*	Whole breast radiotherapy; in addition axilla level I and II†	Chest wall radiotherapy; in addition axilla level I and II†
High-risk group		
ypN2–3 (ALND)	Whole breast radiotherapy; axilla level III and IV	Chest wall radiotherapy; axilla level III and IV
If SLNB before primary chemotherapy and no ALND†: cN1 (SLNB), with ≤2 macrometastases and ≥1 risk factor*, or ≥3 macrometastases; or if SLNB after primary chemotherapy and no ALND†: ypN1mi (SLNB), ≥1 risk factor*, or ypN1 (SLNB)	Whole breast radiotherapy; axilla level III and IV; in addition axilla level I and II†	Chest wall radiotherapy; axilla level III and IV; in addition axilla level I and 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.

Table 1: **Study guideline with risk groups based on locoregional recurrence risk, and locoregional radiotherapy recommendations**


A
Locoregional recurrence rate (%)
Low-risk group: 2·1% (95% CI 0·9–4·3); p=0·89
Intermediate-risk group: 2·2% (95% CI 1·0–4·1); p=0·75
High-risk group: 2·3% (95% CI 0·8–5·5); p=0·83
Number at risk (number censored)
Low-risk group 291 (0) 288 (3) 276 (14) 267 (21) 266 (21) 250 (35)
Intermediate-risk group 370 (0) 362 (7) 350 (17) 341 (26) 322 (41) 303 (59)
High-risk group 177 (0) 173 (3) 159 (16) 143 (32) 140 (35) 120 (53)


B
Recurrence-free interval (%)
91·7% (95% CI 87·9–94·4); p=0·071
87·2% (95% CI 83·3–90·2); p<0·0001
76·0% (95% CI 69·0–81·7); p=0·0007
Number at risk (number censored)
Low-risk group 291 (0) 288 (0) 277 (2) 270 (3) 269 (3) 264 (3)
Intermediate-risk group 370 (0) 362 (2) 351 (2) 345 (3) 329 (5) 318 (5)
High-risk group 177 (0) 173 (0) 159 (1) 145 (2) 142 (3) 131 (4)
C
Overall survival (%)
95·5% (95% CI 92·4–97·4); p=0·41
94·0% (95% CI 91·0–96·0); p<0·0001
83·0% (95% CI 76·6–87·8); p<0·0001
Time after primary diagnosis (years)
Number at risk (number censored)
Low-risk group 291 (0) 291 (0) 282 (1) 278 (1) 277 (1) 277 (1)
Intermediate-risk group 370 (0) 366 (2) 361 (2) 355 (3) 349 (5) 343 (5)
High-risk group 177 (0) 176 (0) 169 (1) 160 (1) 154 (1) 146 (1)

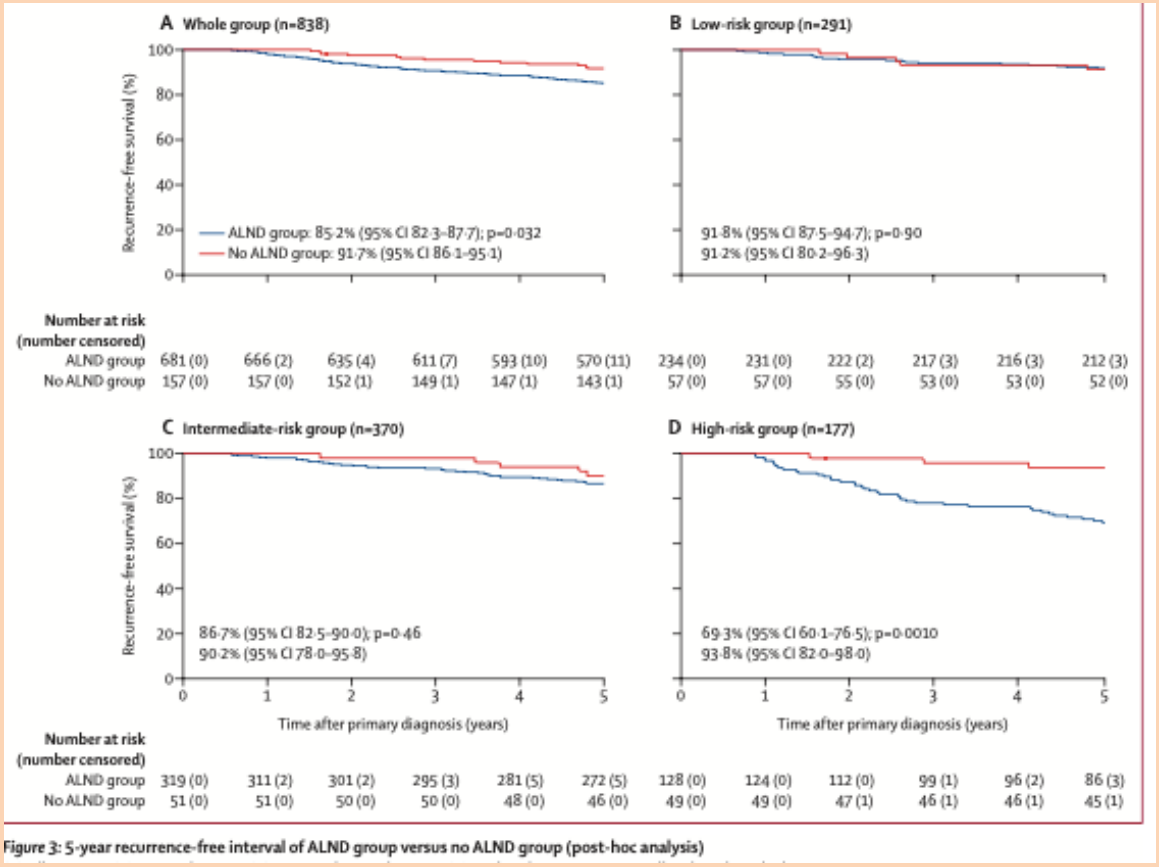


Figure 3: 5-year recurrence-free interval of ALND group versus no ALND group (post-hoc analysis)

Quale approccio in pz cN0 con LNs positivo/i dopo terapia sistemica neoadiuvante

Chirurgia ± Radioterapia *vs* Radioterapia

retrospective data show that patients with residual cancer in sentinel nodes including micrometastases[38] have a substantial risk of additional nodal metastases in axillary nodes. Real-world data from the National Cancer Database

Moo, Ann Surg Oncol 2018

The Alliance A011202 (NCT01901094) trial

Designed to determine optimal management of the axilla in cT1-T3N1 breast cancer patients with positive SLN following NAT

Randomization:
ALND + RT to the breast/chest wall, undissected axilla, supraclavicular nodes and internal mammary nodes
vs
no further axillary surgery but RT to the breast/chest wall, full axilla including levels I, II, III, supraclavicular nodes and internal mammary nodes

Primary endpoint: invasive breast cancer recurrence-free survival

The British ATNEC trial is a prospective multicenter randomized trial that will include 2,465 T1–3 N1 breast cancer patients treated with NACT. Patients undergo BCS or mastectomy and TAD with SLNB. At least 3 nodes have to be removed. Patients with 1–2 positive post-NACT SLNs will be randomized to undergo RT or ALND. Patients with ypN0 status will receive either RT or ALND in one arm and no further regional treatment in the second arm. Endpoint is DFS at 5 years.

The Swiss TAXIS trial is a prospective multicenter randomized trial with a planned accrual of 1,500 patients within 5.4 years. Breast cancer patients with stage II/III disease confirmed in the primary tumor and the lymph nodes (cN1, ycN1) are eligible for the study. Patients are treated either with primary surgery or NACT. They are randomized to undergo ALND or the exclusive resection of clinically apparent disease (excision of suspicious clipped nodes) with consecutive RT to the axilla. Endpoint is DFS after 5 years.

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Short communication

NEONOD 2: Rationale and design of a multicenter non-inferiority trial to assess the effect of axillary surgery omission on the outcome of breast cancer patients presenting only micrometastasis in the sentinel lymph node after neoadjuvant chemotherapy

Corrado Tinterri [a], Giuseppe Canavese [a], Paolo Bruzzi [b], Beatrice Dozin [b,*]

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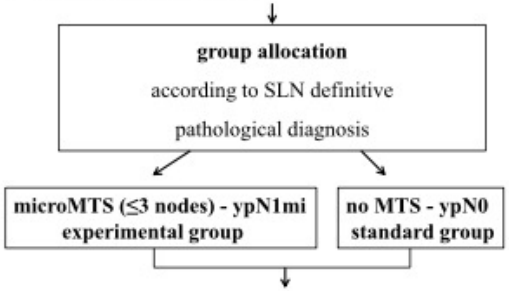
[b] U.O. Epidemiologia Clinica, IRCCS Ospedale Policlinico San Martino, Genova, Italy

NEONOD 2 trial

- age ≥18 - ≤ 75 y
- cT1-T2-T3 unifocal invasive breast cancer
- pre-NAC positive axilla (cN+, ultrasound/microcytology)
- post-NAC negative axilla (cN-, ultrasound/microcytoloy)
- BCS or mastectomy
- SLNB and SLN evaluation



- no ALND
- hormonal/biological therapies
- WBI ± boost (if BCS)
- chest wall RT ± boost (if mastectomy)
- no irradiation at axillary level

Fig. 1. NEONOD 2 trial: study design.
NAC, neoadjuvant chemotherapy; BCS, breast conserving surgery; SLNB, sentinel lymph node biopsy; SLN, sentinel lymph node; MTS, metastasis; ALND, axilaary
lymph node dissection; WBI, whole breast irradiation; RT, radiotherapy.

AGENDA

RT in pazienti con:

- 1-2 LNs positivo/i, non sottoposte a ALND
- 1-3 linfonodi positivi dopo ALND

RT su linfonodi mammari interni

RT dopo terapia sistemica neoadiuvante e chirurgia

Frazionamento della dose

RT ultra-ipofrazionata e irradiazione linfonodi regionali

A sub-study tested ultra-hypo-fractionation in patients requiring RT to:

1. axillary or suvraclavicular lymph nodes after sentinel node biopsy
2. levels 3 - 4 after axillary dissection

Primary endpoint: safety

Interim analysis at 2-3 years' follow-up: no differences in arm or shoulder adverse effects after 26 Gy in 5 fractions and 40 Gy in 15 fractions

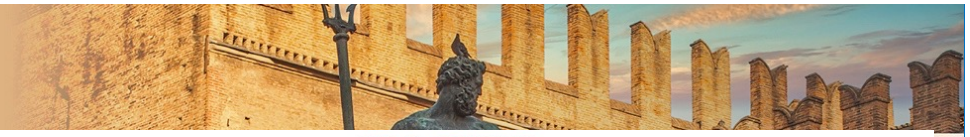
Definitive assessment of non-inferiority will, however, be available only at the 5 year analysis

CONCLUSIONI

Incertezze rimangono nel trattamento radiante delle stazioni linfonodali, alcune legate all' impiego della biopsia del LNs e a nuove indicazioni di terapia sistemica

Potrà la radiomica aiutare nella scelta terapeutica?

BIOPSIA VIRTUALE



Hindawi
Contrast Media & Molecular Imaging
Volume 2022, Article ID 6729473, 10 pages
https://doi.org/10.1155/2022/6729473

WILEY | Hindawi

Research Article

Preoperative Prediction of Axillary Lymph Node Metastasis in Breast Cancer Based on Intratumoral and Peritumoral DCE-MRI Radiomics Nomogram

Ying Liu,[1] Xing Li,[2] Lina Zhu,[2] Zhiwei Zhao,[2] Tuan Wang,[2] Xi Zhang,[2] Bing Cai,[2] Li Li,[2] Mingrui Ma,[3] Xiaojian Ma,[3] and Jie Ming[2,4]

Hindawi
Computational and Mathematical Methods in Medicine
Volume 2022, Article ID 1507125, 12 pages
https://doi.org/10.1155/2022/1507125

Hindawi

Research Article

Radiomic Signature Based on Dynamic Contrast-Enhanced MRI for Evaluation of Axillary Lymph Node Metastasis in Breast Cancer

Yanqiu Tang,[1] Lin Chen,[2] Yating Qiao,[3] Weifeng Li,[4] Rong Deng,[2] and Mengdi Liang[1]

Original Article

Development of the prediction model based on clinical-imaging omics: molecular typing and sentinel lymph node metastasis of breast cancer

Xian Wang[1,2^], Xueyang Wang[2,3], Yanjun Zhang[1], Dekang Zhang[3], Zhou Song[1], Qingyu Meng[1], Yunjian Li[4], Chunxi Wang[1]

EBioMedicine 69 (2021) 103460

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Research paper

Magnetic resonance imaging radiomics predicts preoperative axillary lymph node metastasis to support surgical decisions and is associated with tumor microenvironment in invasive breast cancer: A machine learning, multicenter study

Yunfang Yu[a,1], Zifan He[a,1], Jie Ouyang[b,1], Yujie Tan[a,1], Yongjian Chen[c], Yang Gu[a], Luhui Mao[a], Wei Ren[a], Jue Wang[a], Lili Lin[a], Zhuo Wu[a], Jingwen Liu[a], Qiyun Ou[a], Qiugen Hu[c], Anlin Li[d], Kai Chen[a], Chenchen Li[a], Nian Lu[f], Xiaohong Li[d], Fengxi Su[a], Qiang Liu[a], Chuanmiao Xie[f,*], Herui Yao[a,*]

Systematic Review Article

Radiomics And Artificial Intelligence In Predicting Axillary Lymph Node Metastasis In Breast Cancer: A Systematic Review.

Author(s): Abdullah S. Eldaly, Francisco R. Avila, Ricardo A. Torres-Guzman, Karla Maita, John P. Garcia, Antonio J. Forte* and Luiza Palmieri Serrano

DOI: 10.2174/1573405618666220822093226

Conclusion: The results of radiomics and artificial intelligence in predicting ALNM are promising. However, validation as a substitute to SLNB requires more substantial evidence from large randomized trials.

CONCLUSIONI

Nella scelta terapeutica necessaria una stretta collaborazione tra oncologo radioterapista e chirurgo

L'oncologo radioterapista deve saper comprendere e gestire i nuovi scenari, che prevedono e prevederanno l'impiego di nuovi farmaci

Il vantaggio legato al trattamento radiante non è lo stesso in tutti i sottogruppi di pazienti

Il carcinoma della mammella non è un'unica malattia, ma un insieme di forme eterogenee, ciascuna con una propria prognosi

CONCLUSIONI

La scelta del miglior approccio terapeutico, che possa garantire il controllo di malattia, senza inficiare il risultato con la tossicità legata al trattamento, dovrà sempre più essere basata su fattori biomolecolari e sull'analisi dei profili genici

PRECISION MEDICINE