







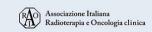


SESSIONE 10 - MAMMELLA: RADIOTERAPIA DOPO CHEMIOTERAPIA NEOADIUVANTE "Volumi e dosi"

27/11/2022 h 10.30-10.45

Dott.ssa Samantha Dicuonzo - Istituto Europeo di Oncologia – IRCCS- Milano











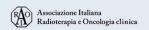


DICHIARAZIONE

Relatore: Dott.ssa Samantha Dicuonzo

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







JOURNAL OF CLINICAL ONCOLOGY

REVIE



Buchholz, 2008

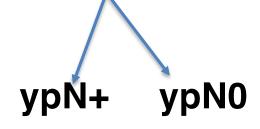
Statement of the Science Concerning Locoregional
Treatments After Preoperative Chemotherapy for Breast
Cancer: A National Cancer Institute Conference

is indicated for all patients treated with breast conservation. For patients treated with mastectomy, chest-wall and regional nodal radiation should be considered for those who present with clinical stage III disease or have histologically positive lymph nodes after preoperative chemotherapy. Additional prospective studies are needed to determine the value of postmastectomy radiation for patients with stage II breast cancer who have negative lymph nodes after chemotherapy.

cT3 N1, any cT4, any cN2, any cN3, ypN+

The unmet clinical need

cT1-2N1/cT3N0











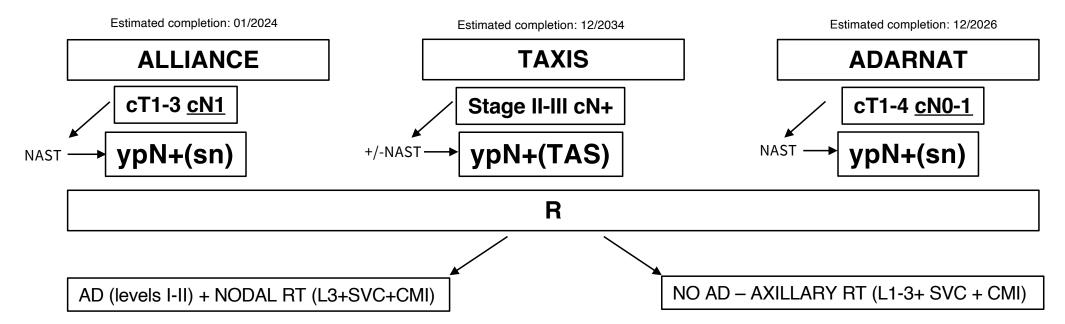
ypN+ after NAST







WAITING FOR...



Treatment will be given 5 days a week over 5-6 weeks -3d, imrt, proton-

50 Gy/25 fr or 50.4 Gy/28 fr 40 Gy/15 fractions







AIRO2022

XXXII CONGRESSO NAZIONALE AIRO XXXIII CONGRESSO NAZIONALE AIRB XII CONGRESSO NAZIONALE AIRO GIOVANI

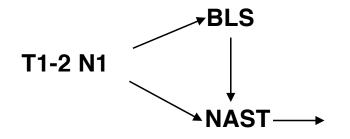
Radioterapia di precisione per un'oncologia innovativa e sostenibile

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

	conserving therapy	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 ALND1; cN1mi (SLNB), ≥1 risk factor*, or cN1 (SLNB), ≤2 macrometastases, no risk factor*; or if SLNB after primary chemotherapy and no ALND1; 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 ALND1: cN1 (SLNB), with s2 macrometastases and s1 risk factor*, or s2 macrometastases; or if SLNB after primary chemotherapy and no ALND1: 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†

Radiotherapy after breast Radiotherapy after



Breast surgery + AD or SN OR

Breast surgery alone in case of pre-BLS



Radiotherapy based on pathology findings

Low risk

Intermediate risk

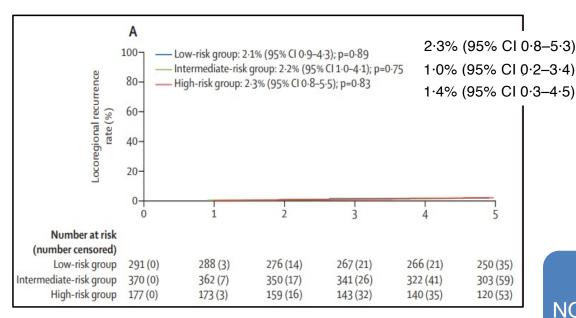
High risk







RAPCHEM: locoregional recurrence



13% NORMOFRACTIONATION

87% MODERATE HYPOFRACTIONATION (2,66 Gy schedule)

TB Boost: 54% patients

Radiotherapy

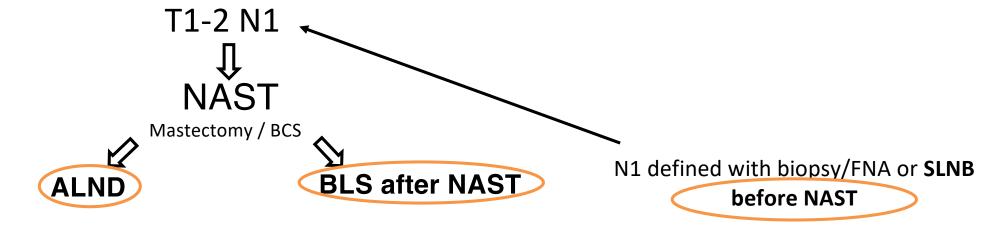
				- HR	
Radiotherapy		LII			:0-0001‡
According to study guideline	533 (64%)	181 (62%)	200 (54%)	152 (86%)	
Less than study guideline	90 (11%)	2 (1%)	63 (17%)	25 (14%)	
More than study guideline	214 (26%)	108 (37%)	106 (29%)	0	
Less or more than study guideline	1 (0%)	0	1 (0%)	0	







RAPCHEM: positive nodes pts (no ypN0)

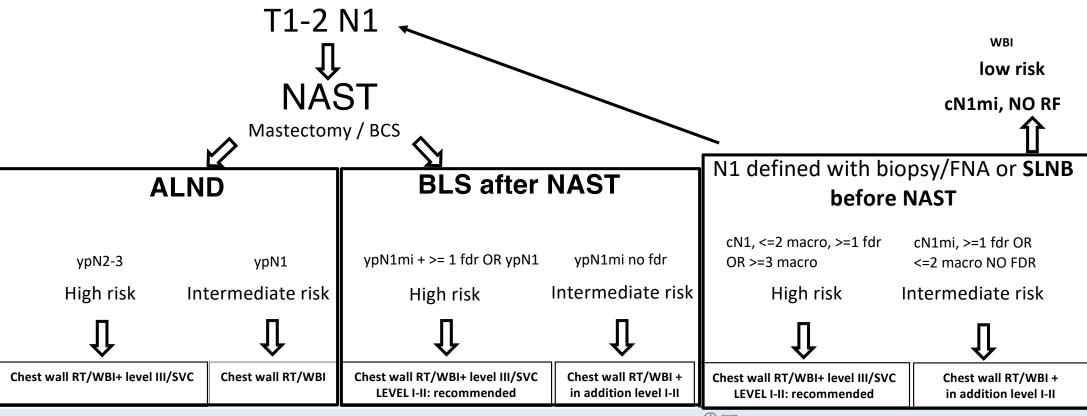








RAPCHEM: positive nodes pts (no ypN0)

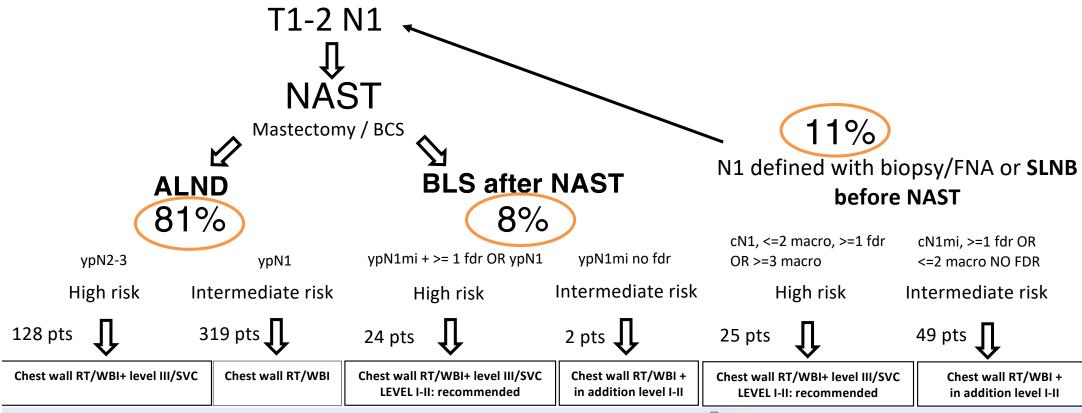








RAPCHEM: positive nodes pts (no ypN0)



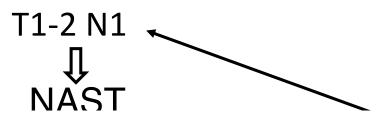








RAPCHEM: positive nodes pts (no ypN0)



Maybe results only for ALND-PTS????

ALNU 81%

ypN1

Intermediate risk High risk

128 pts

Chest wall RT/WBI+ level III/SVC

ypN2-3

319 pts **]**

Chest wall RT/WBI

ypN1mi + >= 1 fdr OR ypN1

High risk

Chest wall RT/WBI+ level III/SVC

LEVEL I-II: recommended

DLJ ailti NAJ

8%

Intermediate risk

vpN1mi no fdr

2 pts

Chest wall RT/WBI + in addition level I-II before NAST

cN1, <=2 macro, >=1 fdr

cN1mi, >=1 fdr OR OR >=3 macro <=2 macro NO FDR

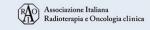
High risk

Intermediate risk

49 pts

Chest wall RT/WBI+ level III/SVC LEVEL I-II: recommended

Chest wall RT/WBI + in addition level I-II



24 pts



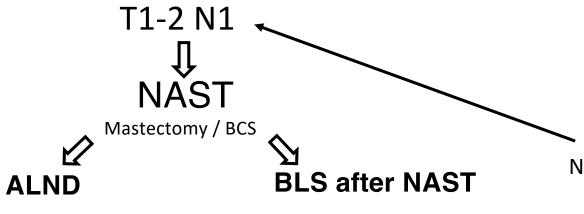


25 pts

Potentiale.

Radioterapia di precisione per un'oncologia innovativa e sostenibile

RAPCHEM: positive nodes pts (no ypN0)



N1 defined with biopsy/FNA or **SLNB**before NAST

ypN2-3

High risk

ypN1 Intermediate risk

Î

Chest wall RT/WBI+ level III/SVC

319 pts

ypN1mi + >= 1 fdr OR VPN1

ypN1mi no fdr

High risk Intermediate risk

CN1, =2 macro, >=1 fdr OR >=3 macro

cN1mi, >=1 fdr OR <=2 macro NO FDR

High risk

Intermediate risk

Chest wall RT/WBI

24 pts ...

Chest wall RT/WBI+ level III/SVC

LEVEL I-II: recommended

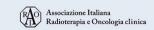
Chest wall RT/WBI + in addition level I-II

<u>1</u>1

Chest wall RT/WBI+ level III/SVC LEVEL I-II: recommended

oct wall PT/

Chest wall RT/WBI + in addition level I-II

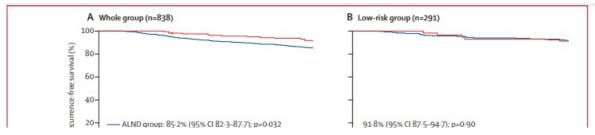




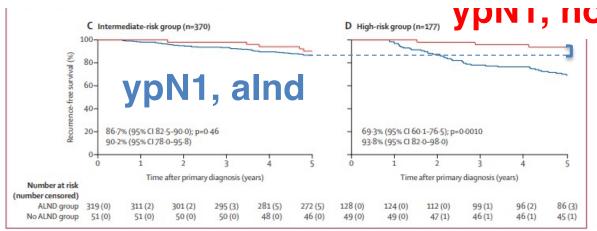




RAPCHEM: ypN1, impact of axillary surgery



Avoid ALND for ypN1????



cN1, no alnd









MESSAGE FROM RAPCHEM (ypN+)

Very low locoregional recurrence rates (less than 4% for the whole group and for each risk group)

It seems oncologically safe to de-escalate locoregional radiotherapy based on ypN status following ALND, in particular for ypN1 pts (maybe they could avoid ALND...)

Moderate hypofractionation also after NAST



BUT

No toxicity data

In each risk group, the actual sample size treated according to the study guideline was smaller than required based on the power calculation

Single arm









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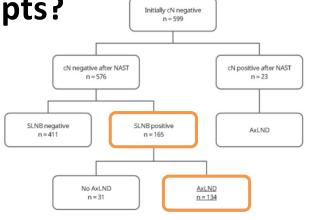
Original Article

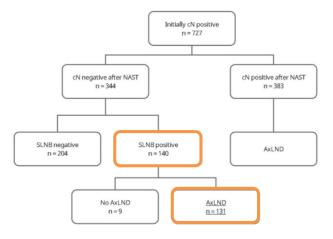
Predictors of positive axillary non-sentinel lymph nodes in breast cancer patients with positive sentinel lymph node biopsy after neoadjuvant systemic therapy



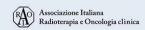
But.....Is SLNB safe after NAST for ypN1(sn) pts?

Maria Cristina Leonardi a, Camilla Arrobbio a,b,1, Sara Gandini c, Stefania Volpe a,b,*, Francesca Colombo a,b, Eliana La Rocca a.b, Viviana Galimberti d, Sabrina Kahler-Ribeiro-Fontana d, Cristiana Fodor a, Samantha Dicuonzo^a, Damaris Patricia Rojas^a, Maria Alessia Zerella^a, Anna Morra^a, Emilia Montagna^e, Marco Colleoni e, Giovanni Mazzarol f, Laura Lavinia Travaini g, Mattia Zaffaroni a, Paolo Veronesi b,d, Roberto Orecchia h, Barbara Alicia Jereczek-Fossa a,b





265 women











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Original Article

Predictors of positive axillary non-sentinel lymph nodes in breast cancer patients with positive sentinel lymph node biopsy after neoadjuvant systemic therapy





165/265 pts had additional positive non SLNs in axilla (62.3%) after NAST

cN1 pts (131/265) had greater incidence of other positive non-SLNs at AxLND (n = 93,71%)

Variables significantly associated with positive non SLNs at MVA

age (p = 0.025, risk increased as age increased)

initial clinical axillary status (p = 0.002, positive versus negative is directly associated with positive non-SLNs) SLN ECE (p < 0.001, present versus absent is directly associated with positive non SLNs) ratio of positive SLNs/total SLNs excised (p = 0.016, the higher the ratio the higher the risk)

If simultaneous combination of all the four high-risk features \rightarrow amount of positive non-SLNs in the I, II and III levels was to 78.9%, 79% and 63.2%, respectively

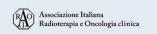








ypN0 after NAST







WAITING FOR...

Estimated completion: 08/2028

NSABP B-51/RTOG 1304

cT1-3 <u>cN1</u> ypN0(SN/ALND)

BCS

MASTECTOMY

R

R

1a WBI+ boost

2a nothing

1b WBI+ boost + RNI

2b CW+ RNI

3D-IMRT 25 fractions

Estimated completion: 02/2030

ATNEC

cT1-3 cN1
s
T
ypN0(SN)

R

Axillary treatment (RT or ALND)

NO Axillary treatment Estimated completion: 06/2025

OBSERB

cT1-3 <u>cN1</u>

S
ycN0(radiological)



SLNB

RNI









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

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 ALNDT: cN1mi (SLNB), ≥1 risk factor*, or cN1 (SLNB), ≥2 macrometastases, no risk factor*; or if SLNB after primary chemotherapy and no ALNDT: 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: cNI (SLNB), with ≈2 macrometastases and ≈1 risk factor*, or ≈3 macrometastases; or if SLNB after primary chemotherapy and no ALND: ypNImi (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†

Radiotherapy after breast

conserving therapy

Radiotherapy after

	→ BLS
T1-2 N0-1	
	NAST——

Breast surgery + AD or SN OR

Breast surgery alone in case of pre-BLS



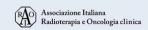
Radiotherapy based on pathology findings



Low risk

Intermediate risk

High risk

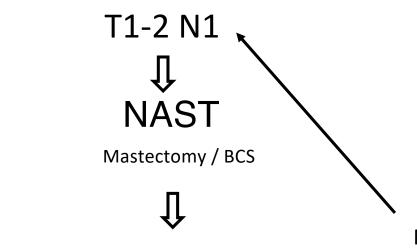








RAPCHEM: negative nodes pts (ypN0)



ALND

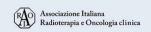
ypN0

BLS after NAST ypN0

N1 defined with biopsy/FNA or **SLNB before NAST**

cN1mi, NO RF

ONLY WBI



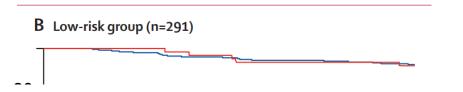






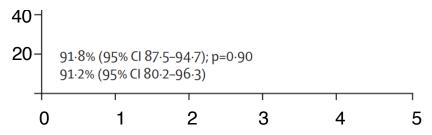
RAPCHEM: negative nodes pts (ypN0)

Recurrence-free survival (%)



ALND group

Avoid ALND and RNI for ypN0????



Time after primary diagnosis (years)







MESSAGE FROM RAPCHEM (ypN0)

Very low locoregional recurrence rates: 2.1% for the low risk group

It seems oncologically safe to de-escalate locoregional radiotherapy based on ypN status following ALND, also for ypN0 pts (maybe they could avoid ALND...and RNI)



BUT

No toxicity data

In each risk group, the actual sample size treated according to the study guideline was smaller than required based on the power calculation

Single arm







But.....Is SLNB safe after NAST for ypN0(sn) pts?

Sentinel-lymph-node biopsy in patients with breast cancer

() before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minchwitz, Valentina Nekliudova, Sabine Schmatladh, Peter Schrenk, Annette Staebler, Michael Untch

JAMA Oncology | Brief Report

Nodal Recurrence in Patients With Node-Positive Breast Cancer Treated With Sentinel Node Biopsy Alone After Neoadjuvant Chemotherapy—A Rare Event

CONCLUSIONS AND RELEVANCE This cohort study found that in patients with cN1 disease rendered cNO with NAC, with 3 or more negative SLNs with SLNB alone, nodal recurrence rates were low, without routine nodal clipping. These findings potentially support omitting ALND in such patients.

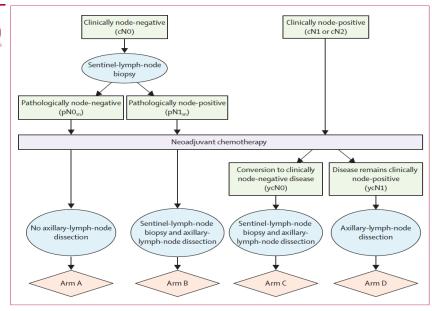


Figure 1: SENTINA trial design

> 2 Sentinel-lymphnodes

Arm B (n=64) Arm C (n=226) Overall false-negative rate (n/N; 95% CI) 51.6% (33/64; 38.7-64.2) 14.2% (32/226; 9.9-19.4) False-negative rate, according to number of sentinel nodes removed 1 66.7% (16/24) 24.3% (17/70) 2 18.5% (10/54) 53.8% (7/13) 3 50.0% (5/10) 7.3% (3/41) 4 50.0% (3/6) 0.0% (0/28) 5 18.2% (2/11) 6.1% (2/33)







BOLOGNA, 25-27 NOVEMBRE

PALAZZO DEI CONGRESSI



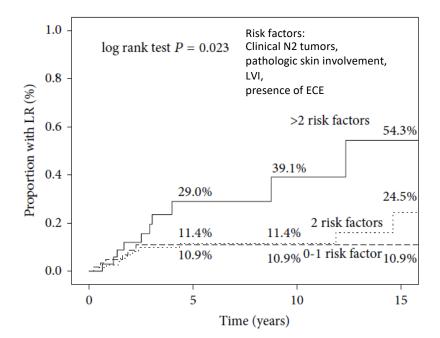


RT after NAST: TO DO OR NOT TO DO?

Risk Factors

Clinical Study

Postmastectomy Radiotherapy for Locally Advanced Breast Meattini 2014 Cancer Receiving Neoadjuvant Chemotherapy

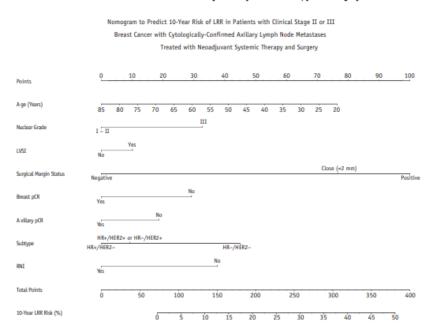


Nomogram to Predict 10-Year Risk of LRR in Patients with Clinical Stage II or III

Breast Cancer with Cytologically-Confirmed Axillary Lymph Node Metastases

Treated with Neoadjuvant Systemic Therapy and Surgery

Stecklein 2018













RT after NAST: TO DO OR NOT TO DO?

Risk Factors

Original Research

Factors predictive of locoregional recurrence following neoadjuvant chemotherapy in patients with large operable or locally advanced breast cancer: An analysis of the EORTC 10994/BIG 1-00 study

Final; Multivariate Fine and Gray model

HR (95% CI) 2-sided p-Value (Gray test)

Potential predictive factors

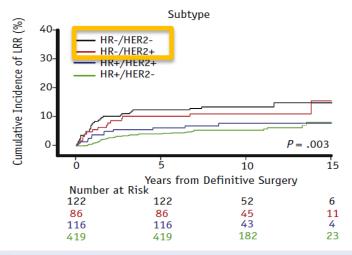
Breast cancer subtype/trastuzumab

Luminal A	1.00
Luminal B (HER2–)	2.29 (0.76-6.97)
HER2+ Trastu-	6.26 (2.81-13.93)
HER2+ Trastu+	3.37 (1.10-10.34)
Triple negative	6.44 (2.83–14.69)
Unknown	2.28 (0.93-5.63)

Clinical Investigation

Long-Term Impact of Regional Nodal Irradiation in Patients With Node-Positive Breast Cancer Treated With Neoadjuvant Systemic Therapy

Shane R. Stecklein, MD, PhD,* Minjeong Park, PhD,† Diane D. Liu, MS,† Janeiro J. Valle Goffin, MD,‡ Abigail S. Caudle, MD, MS,† Elizabeth A. Mittendorf, MD, PhD,* Carlos H. Barcenas, MD, MSc,† Sarah Mougalian, MD,† Wendy A. Woodward, MD, PhD,* Vicente Valero, MD,† Aysegul A. Sahin, MD,† Wei T. Yang, MD,† and Simona F. Shaitelman, MD, EdM*







< 0.0001





PALAZZO DEI CONGRESSI





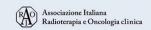
SPECIAL ARTICLE

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. Thürlimann³, W. P. Weber⁴, P. Poortmans⁵, M. M. Regan¹, H. J. Senn⁶, E. P. Winer¹ & M. Gnant⁷, Panelists of the St Gallen Consensus Conference[‡]

¹Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA; ²European Institute of Oncology, University of Milan, Milan, Italy; ³Cantonal Hospital, St. Gallen; ⁴University of Basel, Basel, Switzerland; ⁵University of Antwerp, Antwerp, Belgium; ⁶St. Gallen Oncology Conferences (Foundation SONK), St. Gallen, Switzerland; ⁷Medical University of Vienna, Vienna, Austria

... the Panel recommended against RNI in women with triple-negative or HER2-positive tumors, presenting with T2 stage tumors but a clinically negative axilla, who achieve a pCR to neoadjuvant treatment. However, the 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







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Radioterapia di precisione per un'oncologia innovativa e sostenibile

RT after NAST: is it possible to reduce toxicity?(1)

nautotherapy and Oncology 137 (2019) 139-100

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journal homepage: www.thegreenjournal.com



Original Article

ESTRO ACROP consensus guideline for target volume delineation in the setting of postmastectomy radiation therapy after implant-based immediate reconstruction for early stage breast cancer



Orit Kaidar-Person ^{a.*,1}, Birgitte Vrou Offersen ^{b.1}, Sandra Hol ^c, Meritxell Arenas ^d, Cynthia Aristei ^e, Celine Bourgier ^c, Maria Joao Cardoso ^g, Boon Chua ^h, Charlotte E. Coles ^l, Tine Engberg Damsgaard ^J, Dorota Gabrys ^k, Reshma Jagsi ^l, Rachel Jimenez ^m, Anna M. Kirby ⁿ, Carine Kirkove ^o, Youlia Kirova ^p, Vassilis Kouloulias ^q, Tanja Marinko ^r, Icro Meattini ^s, Ingvil Mjaaland ^t, Gustavo Nader Marta ^{u,v}, Petra Witt Nystrom ^w, Elzbieta Senkus ^x, Tanja Skyttä ^y, Tove F. Tvedskov ^z, Karolien Verhoeven ^{aa}, Philip Poortmans ^{ab}

Table 2

Indications for including a volume posterior to the implant in the CTVp_chestwall.

Partial inclusion in retro-pectoral implant positioning: in case of the presence of adverse factors and/or if the tumour was localised in areas within the breast close to the dorsal fascia that was not covered by the initial position of the major pectoral muscle: separate volume (blue volume in Fig. 4B)

Complete inclusion in pre-pectoral implant positioning: in case of the presence of adverse factors (blue in Fig. 4C) Adverse prognostic tumour characteristics include:

Large primary breast cancer (pT3) treated by mastectomy and IRR-

Locally advanced breast cancer (LABC) with non-pathological complete response to primary systemic therapy

invasion of the major pectoral muscle and/or the chest wall

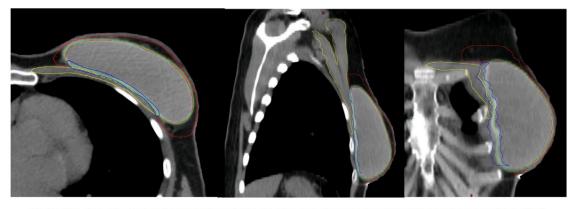


Fig. 4c. CTVp_chestwall with a ventral (red) and dorsal (blue) part in cases with a prepectoral implant (green). Pectoral muscles (yellow).









RT after NAST: is it possible to reduce toxicity?(2)

FULL PAPER

Comparison of two radiation techniques for the breast boost in patients undergoing neoadjuvant treatment for breast cancer

¹MARIA C DE SANTIS, MD, ²LUIGIA NARDONE, MD, ¹BARBARA DILETTO, MD, ²ROBERTA CANNA, MD, ¹MICHELA DISPINZIERI, MD, ³LORENZA MARINO, MD, ¹LAURA LOZZA, MD and ²VINCENZO VALENTINI, PhD

IOERT as anticipated tumor bed boost during breast-conserving surgery after neoadjuvant chemotherapy in locally advanced breast cancer—Results of a case series after 5-year follow-up

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Breast Care

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Targeted Intraoperative Radiotherapy Tumour Bed Boost during Breast-Conserving Surgery after Neoadjuvant Chemotherapy

Javant S. Vaidva Jeffrey S. Tobias

Technical note

Post-chemotherapy target volumes are safe as boost volume for intact breast radiotherapy in locally advanced breast cancer*

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Original article

Is tumor bed boost necessary in patients who achieved ypCR following neoadjuvant chemotherapy and breast conserving therapy? (KROG 12-05 and 16-16)

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Conclusions

Based on available data, postoperative RT after NAST

Clinical Stage III: ok for N2-N3

Clinical Stage II (T3N1?):

	RAPCHEM	ST GALLEN/ BUCHOLZ/ETC
YPN1 ALND	WBI/PMRT NO RNI	WBI/PMRT RNI
YPN1 SLNB	WBI/PMRT RNI	=

Maybe not ready for de-escalation?

Ongoing randomized trials awaited/new translational perspectives

YPN0 BLS	ONLY WBI NO PMRT NO RNI	RT for high risk pts (TN, HER2) from St.Gallen

Maybe ready for de-escalation according the risk factor only if sn 3 or more?

ESTRO contouring: why not?

Hypofractionation: why not?









THANK YOU





