Test genomici / Il trattamento dell'ascella dopo chemio-immunoterapia neoadiuvante

Laura Cortesi

I dati della Regione Emilia-Romagna

REGIONE EMILIA-ROMAGNA
Atti amministrativi
GIUNTA REGIONALE

Delibera Num. 1231 del 02/08/2021

Seduta Num. 37

Questo lunedì 02 **del mese di** agosto **dell' anno** 2021 **si è riunita in** video conferenza **la Giunta regionale con l'intervento dei Signori:**

1) Bonaccini Stefano	Presidente
2) Schlein Elena Ethel	Vicepresidente
3) Calvano Paolo	Assessore
4) Colla Vincenzo	Assessore
5) Corsini Andrea	Assessore
6) Felicori Mauro	Assessore
7) Lori Barbara	Assessore
8) Mammi Alessio	Assessore
9) Priolo Irene	Assessore
10) Salomoni Paola	Assessore

Regioni/P.A.	Popolazione Femminile residente	Tassi standardizzati di tumori alla mammella	Casi stimati di tumori alla mammella	Test attesi calcolati in base ai casi stimati di tumori alla mammella, alla stratificazione clinico patologica e ai fondi disponibili*	Fondi
Piemonte	2.216.159	174,2	4.400	822	1.643.938
Valle d'Aosta	63.913	191,2	150	28	56.043
Lombardia	5.115.227	188,1	10.000	1.868	3.736.223
Prov. Aut. Bolzano	269.052	169,2	400	75	149.449
Prov. Aut. Trento	277.511	169,2	600	112	224.173
Veneto	2.489.416	185	4.900	915	1.830.749
Friuli-Venezia Giulia	619.497	203,9	1.450	271	541.752
Liguria	794.455	174,3	1.650	308	616.477
Emilia-Romagna	2.290.338	178,6	4.500	841	1.681.300
Toscana	1.908.237	172,5	3.500	654	1.307.678
Umbria	450.271	159,3	800	149	298.898
Marche	776.981	163,1	1.300	243	485.709
Lazio	2.976.519	158,1	4.600	859	1.718.662
Abruzzo	662.198	144,8	1.000	187	373.622
Molise	152.563	144,8	250	47	93.406
Campania	2.927.527	140,5	4.050	756	1.513.171
Puglia	2.029.773	150,8	3.200	598	1.195.591
Basilicata	281.104	131,1	380	71	141.976
Calabria	966.378	124,3	1.300	243	485.709
Sicilia	2.504.348	148,7	3.800	710	1.419.765
Sardegna	819.925	151,7	1.300	243	485.709
Totale	**30.591.392**	**149,7**	**53.530**	**10.000**	**20.000.000**

Criteri identificati per l'accesso al test

Sulla base delle caratteristiche della popolazione testata negli studi e dei risultati ottenuti, si considerano elegibili al test predittivo multigenico le donne a **Rischio Intermedio**, ossia che non rientrano nelle categorie di rischio basso/alto indicate nell'All.2 del DM 18 maggio 2021:

Basso rischio: tutte le seguenti caratteristiche	**Alto rischio: almeno 4 delle seguenti caratteristiche**
G1	G3
T1 (a-b)*	T3-4
Ki 67<15%	Ki 67>30%
/ER>80%	ER<30%
N0	N positivo

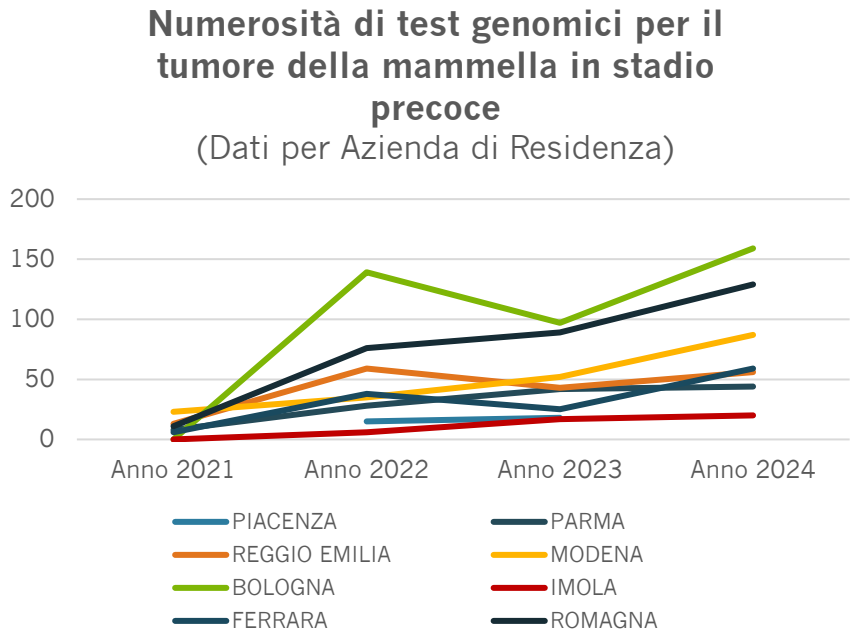
*per i T1a è sufficiente la presenza di 2 delle altre caratteristiche e sulla base delle quali il clinico riterrebbe incerta l'indicazione a chemioterapia adiuvante in aggiunta alla endocrinoterapia.

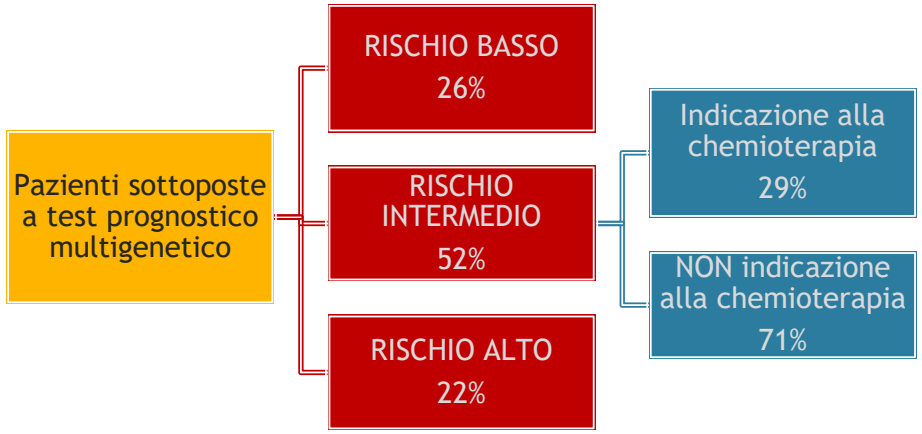
La stima delle pazienti della Regione Emilia-Romagna che potrebbero usufruire della prestazione è pari a circa 850 pazienti/anno con possibile **riduzione in circa il 50%-65% dei casi del ricorso a chemioterapia**.

Il monitoraggio dei test genomici nel carcinoma della mammella early

	2021	2022	2023	2024	2025
Piacenza	0	15	18	0	33
Parma	8	28	42	44	62
Reggio Emilia	13	59	43	56	104
Modena	23	35	52	87	130
Carpi	0	0	17	20	29
Bologna (Sant'Orsola e Bellaria)	0	139	97	159	209
Imola	0	6	17	20	0
Ferrara	6	38	25	59	40
Romagna (Forlì, Rimini, Ravenna)	11	76	89	129	200
	61 (7.2%)	386 (45.9%)	400 (47.5%)	473 (56.2%)	772 (92%)

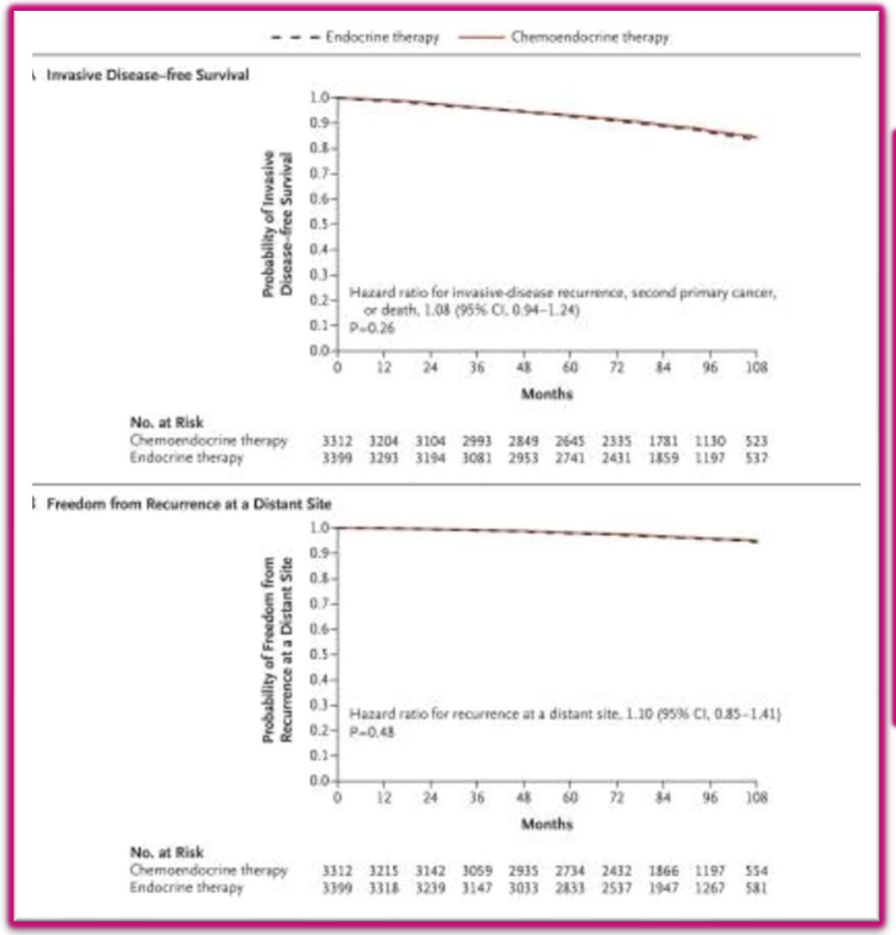
Il monitoraggio dei test genomici nel carcinoma della mammella early





Rete Oncologica ed Emato-oncologica
Regione Emilia-Romagna

Tailor(X): DRFS at 9 years



All patients

0–11	11–25	≥26
ET: 96.8%	ET: 94.5% CT: 95.0%	CT + ET: 86.8%

Young patients (≤50 yrs), n=2216

0–11	11–15	16–20	21–25	≥26
ET: 98.5%	ET: 97.2% CT+ET: 98.0%	ET: 93.6% CT+ET: 95.2%	ET: 86.9% CT+ET: 93.4%	CT+ET: 88.7%
		Δ 1.6 %	Δ 6.5 %	

Castration effect associated with cytotoxic therapy, rather than an effect in eradicating micrometastatic disease?

Sparano JA et a N Engl J Med. 2018 Jun 3;379(2):111–121.

Management of ER-positive: role of Gene Expression Assays in N0 disease:Tailor(X): DRFS at 12 years

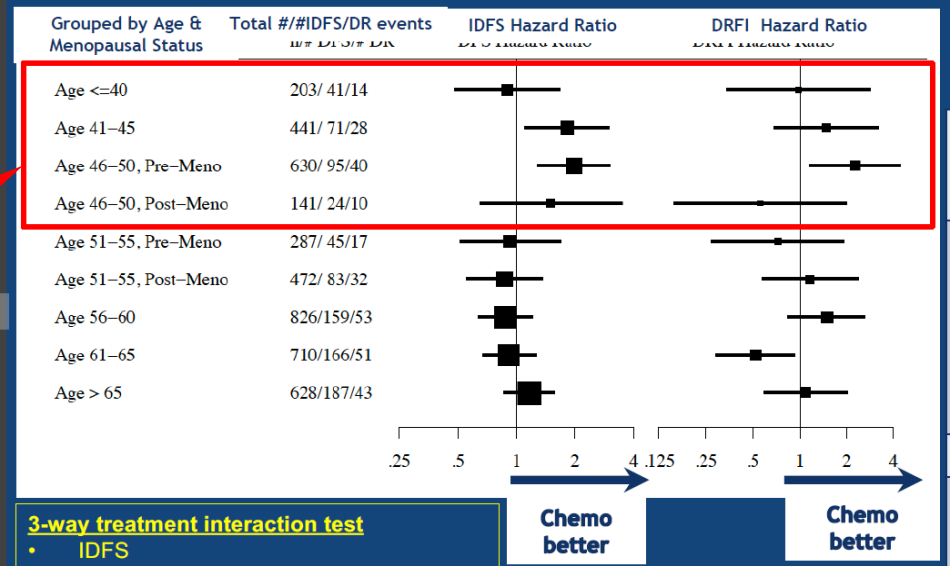
- Patients with N0 and an intermediate-risk RS of 11 to 25: no benefit from chemotherapy

- Potential benefit in younger patients (aged ≤50 years) with an RS of 16 to 25

Castration effect associated with cytotoxic therapy, rather than an effect in eradicating micrometasta tic disease?

San Antonio Breast Cancer Symposium – December 6-10, 2022

TAILORx: Updated Analysis - Effect of Age, RS, and Clinical Risk on Chemotherapy Benefit (ITT Population)



3-way treatment interaction test
- IDFS
  - Chemo-Age-RS (p=0.007)
  - Chemo-Menopause-RS (p=0.06)
- DRFI
  - Chemo-Age-RS (p=0.43)
  - Chemo-Menopause-RS (p=0.26)

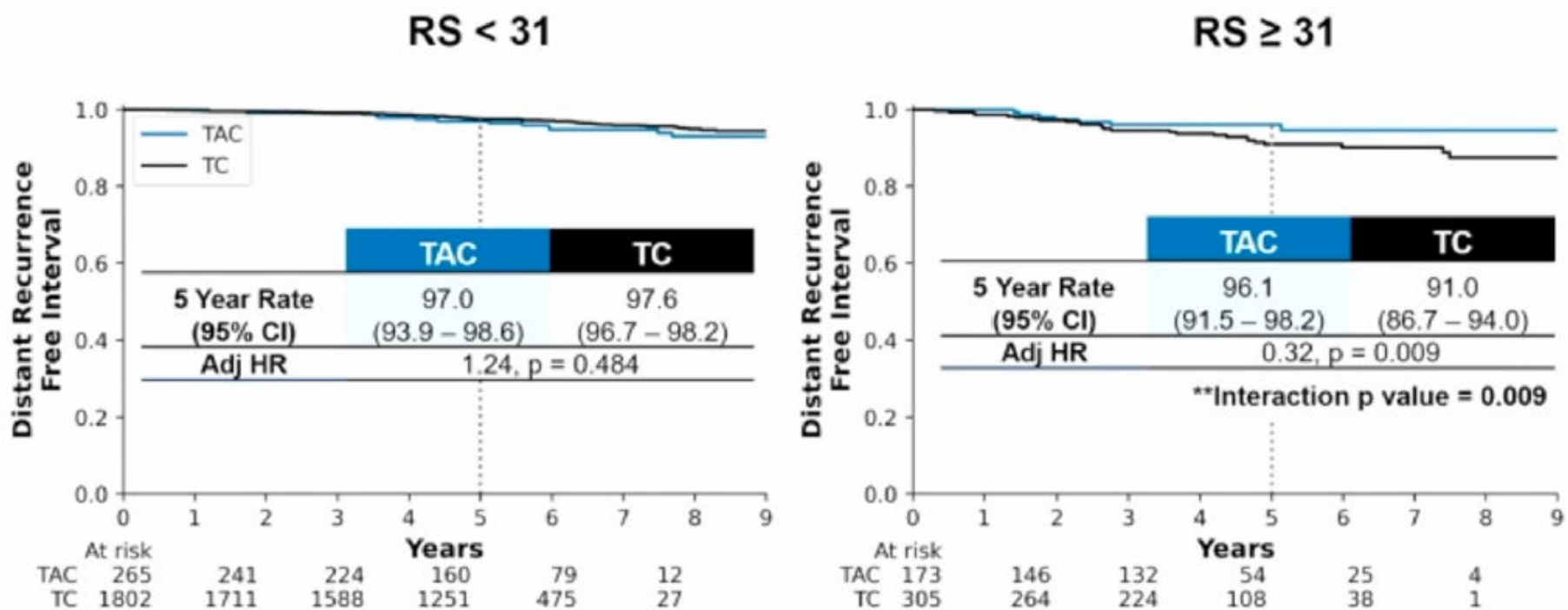
12-Year DRFI Rates in Age ≤ 50 Years & RS 16-25

	Estimated Absolute Chemo Benefit Not Stratified by Clinical Risk	Clinical Risk	No.	Estimated Absolute Chemo Benefit Stratified by Clinical Risk
RS 16-20 (N=886)	Δ +0.4% (±SE 2.1%)	Low	671 (76%)	Δ -0.5% (±SE 2.2%)
		High	215 (24%)	Δ +3.1% (±SE 5.4%)
RS 21-25 (N=476)	Δ +7.8% (±SE 3.4%)	Low	319 (67%)	Δ +5.9% (±SE 3.4%)
		High	157 (33%)	Δ +11.7% (±SE 7.2%)

Sparano JA et al. SABCS 2022;Abstract GS1-05.

SAN ANTONIO BREAST CANCER SYMPOSIUM

Primary Survival Outcome: Distant Recurrence-Free Interval at 5 years



*Adjusted hazard ratios controlling for age, ER/PR status, RS, tumor size, treatment received, and interaction of treatment with RS

Subgroup analysis : anthra benefit is seen if tumor > 2cm (HR:0.29 (0.10-0.87) regardless of menopausal status

MONARCH-E TRIAL

- HR+, HER2-,
- Node-positive,
- High risk early breast cancer

Cohort 1 (91% of patients)
≥4 positive ALN or 1-3 positive ALNs plus G3 and/or tumor ≥5cm

Cohort 2 (9% of patients)
1-3 positive ALNs, ki-67 ≥20%, G1-2, tumor size <5cm

N = 5637

R 1:1

- Abemaciclib + Endocrine Therapy
- Endocrine Therapy

- *Abemaciclib x 2 years*
- *ET for 3-8 years as clinically indicated in both arms*

Highly Awaited Data on Adjuvant CDK 4/6i Therapy: NATALEE Study

- Adult patients with HR+/HER2− EBC
- Prior ET allowed up to 12 mo
- **Anatomical stage IIA**[a]
  - **N0** with:
    - Grade 2 and evidence of high risk
      - Ki-67 ≥20%
      - Oncotype DX Breast Recurrence Score ≥26 ***or***
      - High risk via genomic risk profiling
    - Grade 3
  - **N1**
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

N=5101[b]

R 1:1[c]

- **Ribociclib** 400 mg/d 3 wk on/1 wk off for 3 y
- **NSAI** Letrozole or anastrozole[d] for ≥5 y **+ goserelin** in men and premenopausal women
- **NSAI** Letrozole or anastrozole[d] for ≥5 y **+ goserelin** in men and premenopausal women

Primary End Point
- iDFS using STEEP criteria

Secondary End Points
- Recurrence-free survival
- Distant disease–free survival
- OS
- PROs
- Safety and tolerability
- PK

Exploratory End Points
- Locoregional recurrence–free survival
- Gene expression and alterations in tumor ctDNA/ctRNA samples

Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
Receipt of prior (neo)adjuvant chemotherapy: yes vs no
Geographic location: North America/Western Europe/Oceania vs rest of world

Comparison of NATALEE and MONARCH-E population

Accademia di Senologia "Umberto Veronesi" – Inveruno

N0 not allowed in monarchE

AJCC Anatomical Staging[1]	TN (M0)	NATALEE[2,3]	monarchE[4]
Stage IIA	T0N1	✓	Only if grade 3 or Ki-67 ≥20%
	T1N1	✓	Only if grade 3 or Ki-67 ≥20%
	T2N0	Only if G3 or G2 with Ki-67 ≥20% or high genomic risk[a]	✗
Stage IIB	T2N1	✓	Only if grade 3 or Ki-67 ≥20%
	T3N0	✓	✗
Stage IIIA	T0N2	✓	✓
	T1N2	✓	✓
	T2N2	✓	✓
	T3N1	✓	✓
	T3N2	✓	✓
Stage IIIB	T4N0	✓	✗
	T4N1	✓	Only if tumor size ≥5 cm or grade 3 or Ki-67 ≥20%
	T4N2	✓	✓
Stage IIIC	Any TN3	✓	✓

In monarchE, relatively few patients with stage II were allowed:
- N1 allowed only if grade 3 or Ki-67 ≥20%

In monarchE, within stage III,
- N0 not allowed (in IIIB)
- N1 (whether in IIIA or IIIB) allowed only if tumor size ≥5 cm, grade 3, or Ki-67 ≥20%

lidERA Breast Cancer study design

A global, randomized, open-label, multicenter Phase III trial

SAN ANTONIO BREAST CANCER SYMPOSIUM

Key eligibility criteria
- Participants with ER+, HER2-negative early breast cancer
- Stage I–III disease (anatomical)
  - pN0 and pT > 1 cm with Grade 3, or Ki67 ≥ 20%, or high score on genomic assay,* or pT4N0
  - Node-positive
- Pre- or post-menopausal†
- Breast cancer surgery within 12 months
- (Neo)adjuvant chemotherapy if indicated

Stratification factors
- Risk: Medium-‡ vs high-risk§ Stage I–III breast cancer
- Region: USA/Canada/Western Europe vs Asia–Pacific vs RoW
- Previous chemotherapy: No vs yes
- Menopausal status: Pre-menopausal vs post-menopausal

At least 5-year treatment duration | **5-year follow-up**

N = 4170

R 1:1

- Giredestrant (30 mg PO QD)
- SOC ET: Tamoxifen/anastrozole/letrozole/exemestane

Long-term follow-up

Primary endpoint
- IDFS (excluding second primary non-breast cancer)

Key secondary endpoints
- DFS, DRFI, IDFS (including second primary non-breast invasive cancer with exception of non-melanoma skin cancers and *in situ* carcinomas of any site), LRRFI, OS, safety

Giredestrant is currently also being investigated in combination with abemaciclib in the adjuvant setting (lidERA Breast Cancer substudy 1)

Enrollment: August 2021 to September 2023. Up to 12 weeks of ET ± CDK4/6i were allowed. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. * OncotypeDx ≥ 26 or high-risk Mammaprint.
† Pre-menopausal patients on aromatase inhibitors or giredestrant had to receive ovarian function suppression with an approved luteinizing hormone-releasing hormone agonist. ‡ Medium risk: pN0 and primary tumor > 1 cm with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or high score on genomic assay [if available]) and pN1 with low-risk biologic features (Grade 1/2 and Ki67 < 20% and tumor ≤ 5 cm and low score on genomic assay [if available]). § High risk: pT4, or pN2, or pN3 and pN1 with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or tumor > 5 cm, or high score on genomic assay [if available]).
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DFS, disease-free survival; DRFI, distant recurrence-free interval; ER+, estrogen receptor-positive; ET, endocrine therapy; IDFS, invasive disease-free survival; LRRFI, locoregional recurrence-free interval; OS, overall survival; PO, orally; QD, once daily; R, randomization; RoW, rest of the world; SOC, standard-of-care.
ClinicalTrials.gov number: NCT04961996. Adapted from Geyer CE, *et al.* ASCO 2023 (TPS616), with permission.

Presented by: Aditya L. Bardia, MD.

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- Previous chemotherapy: No vs yes
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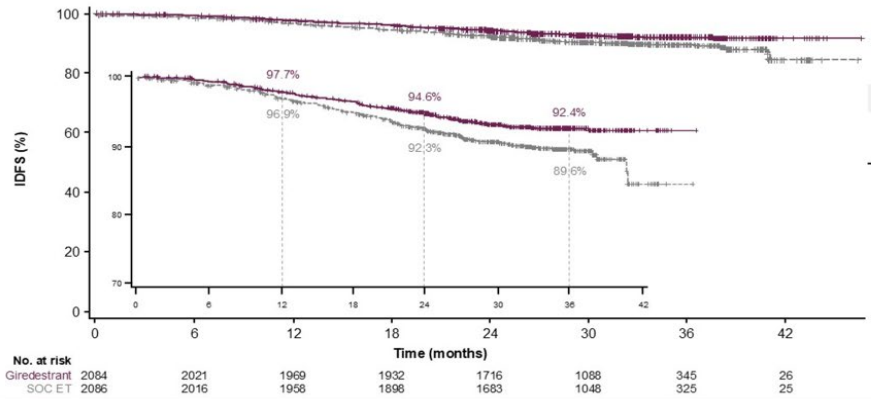
ClinicalTrials.gov number: NCT04961996. Adapted from Geyer CE, *et al.* ASCO 2023 (TPS616), with permission.

lidERA Breast Cancer

Primary endpoint: IDFS



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	140 (6.7)	196 (9.4)
Stratified HR (95% CI)	0.70 (0.57, 0.87); **p = 0.0014***	

Median follow-up: 32.3 months

Statistically significant and clinically meaningful improvement in IDFS:
Giredestrant reduced the risk of invasive disease recurrence or death by 30% compared with SOC ET

Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively. * Log-rank (2-sided). p-value boundary for IDFS interim analysis was 0.0217 (2-sided). AI, aromatase inhibitor; CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival; SOC, standard-of-care.

Risk Score

One of the stratification factors (with region, prior chemo, menopause)

Medium risk:

- **pN0 (> 1 cm) with high-risk biology - Grade 3, Ki67 ≥ 20%, or high genomic score**
- **pN1 with low-risk biology - Grade 1/2 + Ki67 < 20% + tumor ≤ 5 cm (+ low genomic score if done)**

High risk: **70% in this category**

- **pT4, pN2, or pN3**
- **pN1 with high-risk biology - Grade 3, Ki67 ≥ 20%, tumor > 5 cm, or high genomic score**

4: PROTOCOL OVERVIEW

Study design

Key Inclusion Criteria

- ER+ (>10%) HER2- Early BC
- Intermediate-high or high risk of recurrence
  - T4, ≥ 2LN, T1c-T3 N0 or 1 LN and G3, high genomic risk or Ki-67 ≥ 20%
- Completed definitive locoregional therapy (surgery with or without radiotherapy), with or without (neo)adjuvant chemotherapy
- No evidence of invasive disease
- ECOG PS 0-1

Randomization 1:1

Arm A
Standard ET
(AI or TAM +/- OFS*)
+/- abemaciclib**
N=2,750

Arm B
Camizestrant 75 mg/daily
(+/- OFS)**
+/- abemaciclib**
N=2,750

Primary endpoint
IBCFS (STEEP)

Secondary endpoints
IDFS, DRFS, OS

*pre-peri-menopausal women and men will receive LHRH (for women mandatory in both arms, for men with AI only)
**Patients receiving Abemaciclib will be capped at a planned 30% of total population. Abemaciclib can only be prescribed in countries with regulatory approval for the broadened indication in High Risk Early Breast Cancer*

Stratification factors

• Risk of recurrence	High[a]	Intermediate-high[b]
• Menopausal status	Pre, Peri, Men	Post
• Planned use of abemaciclib	Yes	No

[a] **High-risk definition – LN affected**
- 1+N, pT1c-T3 with one of the following: Grade 3 or Ki67-high or high-risk genomic signature *or*
- 1+N, T4 *or*
- ≧ 2+N, any T

[b] **Intermediate-high risk definition – No LN affected**
- N0, pT1c-T3 with one of the following: Grade 3 or Ki67-high or high-risk genomic signature *or*
- N0, T4

CAMBRIA-2

Fortrea

Linfonodo sentinella positivo: Ascella e ruolo dell'Oncotype

1) Gestione dell'ascella (PDTA Emilia-Romagna)

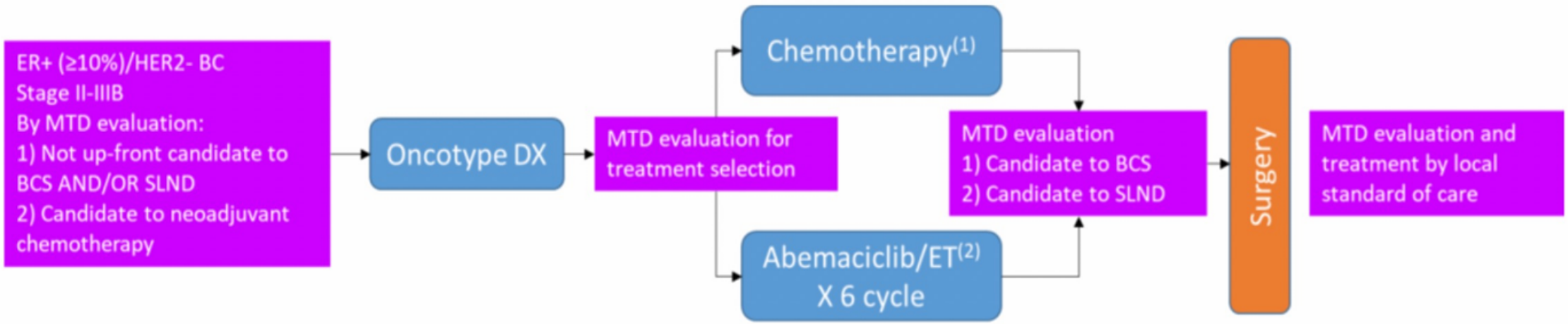
- Basata su criteri Z0011
- 1–2 LS positivi + chirurgia conservativa + RT → NO dissezione se
  T2 fino a 3 cm
  pz. Post-menopausa
  No estensione extracapsulare
  Luminali
- Oncotype NON influenza la decisione chirurgica

VIOLET trial

E. Munzone et al (Italy)
Sponsor: Fondazione Veronesi

A Pragmatic Phase II Study to Optimize Neoadjuvant Treatment and Surgical De-escalation in HR+/HER2− Early Breast Cancer Using Oncotype DX and Abemaciclib

Trial Schema **150 pts; 10 centers**



The primary objectives

1 to determine the proportion of patients with ER+ (≥10%)/HER2- EBC in whom NAC can be replaced by NET plus abemaciclib based on the results of the ODX RS (biopsy) and according to the MDT decision.
2 to evaluate the proportion of patients undergoing breast conservative surgery and/or sentinel node biopsy.

De-escalation of Axillary Surgery in Patients With cN+ Disease Based on Response to NAC

Nodal pCR

(cN+ → ypN0)

Likelihood of nodal pCR

Surgical staging techniques

Outcomes after ALND omission

Ongoing trials

Residual nodal disease

(cN+ → ypN+)

Likelihood of + nodes at ALND

Patient selection for omission of ALND & real-world outcome data

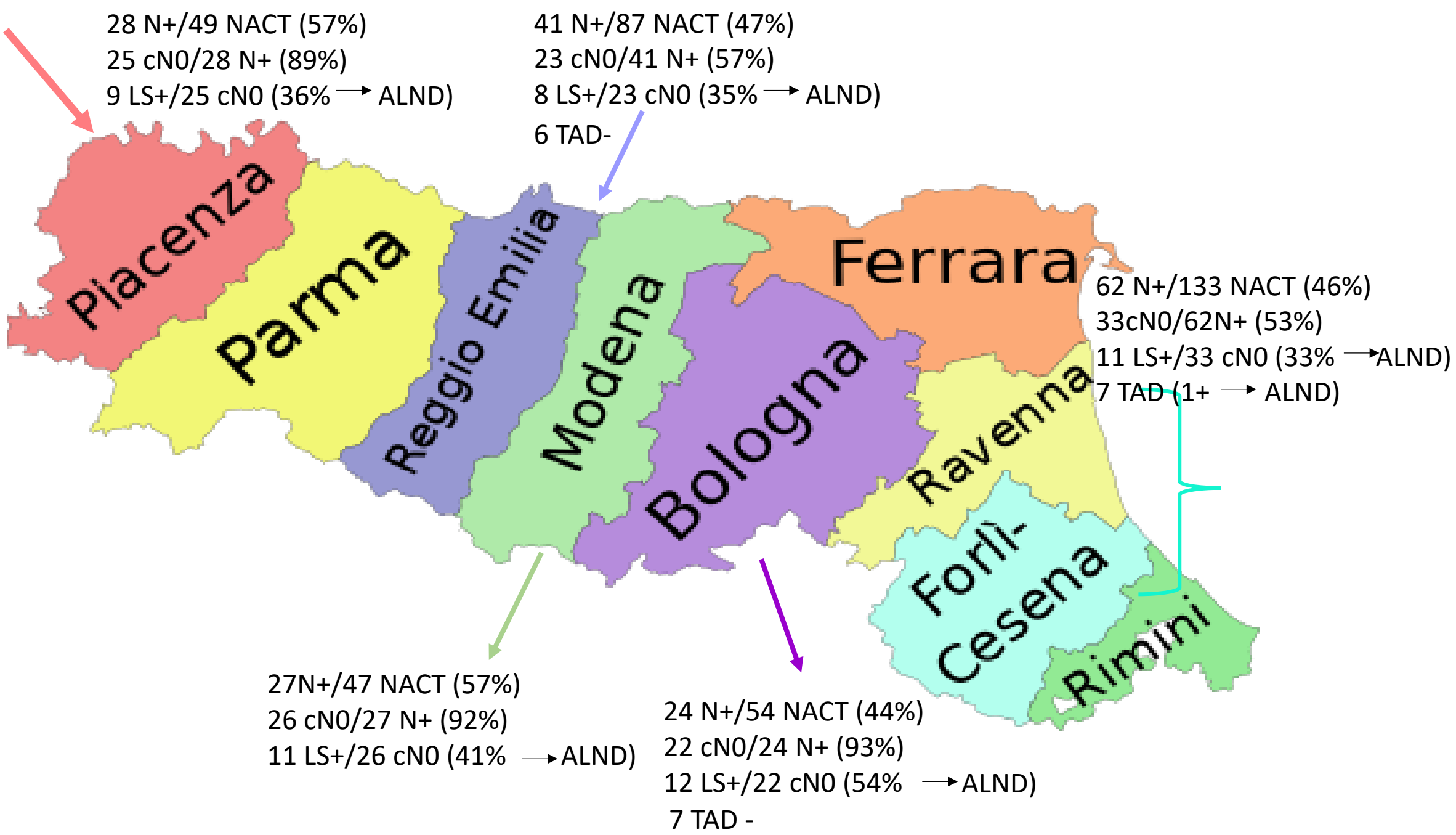
Ongoing trials

Axillary Staging Techniques in Patients With cN+ Disease Undergoing NAC

Technique	FNR
SLNB	*11.9-14.2%*
dual tracer	*5-11%*
>3 SLNs	**4.9-9.1%**
MARI	**7%**
TAD	**2-7%**

in cN+ patients undergoing NAC, the surgical staging technique needs to be optimized to reduce the FNR

Boughey J et al. JAMA 2013
Kuehn T et al. Lancet Oncol 2013
Boileau JF et al. J Clin Oncol 2015
Classe JM et al. Breast Cancer Res Treat 2019
Donker M et al. Ann Surg 2015
Caudle AS et al. J Clin Oncol 2016
Siso C et al. Eur J Surg Oncol 2023


28 N+/49 NACT (57%)
25 cN0/28 N+ (89%)
9 LS+/25 cN0 (36% → ALND)
41 N+/87 NACT (47%)
23 cN0/41 N+ (57%)
8 LS+/23 cN0 (35% → ALND)
6 TAD-
Piacenza
Parma
Reggio Emilia
Modena
Bologna
Ferrara
Ravenna
Forlì-Cesena
Rimini
62 N+/133 NACT (46%)
33cN0/62N+ (53%)
11 LS+/33 cN0 (33% → ALND)
7 TAD (1+ → ALND)
27N+/47 NACT (57%)
26 cN0/27 N+ (92%)
11 LS+/26 cN0 (41% → ALND)
24 N+/54 NACT (44%)
22 cN0/24 N+ (93%)
12 LS+/22 cN0 (54% → ALND)
7 TAD -

Axillary Recurrence After Omission of ALND in cN+ → ypN-

Study	Inclusion period	ypN0 (no ALND)	Axillary RT	Median Follow-Up (months)	Axillary Recurrence Rate
NEOSENTITURK MF-1803	2019-2023	341	100%	39	0.3%
OPBC/OMA study (11 countries)	2013-2020	1146	81%	42	1%
MSKCC	2014-2019	234	70%	40	0.4%
McGill University	2013-2018	60	71%	36	0%
NEOSENTITURK MF-1802	2004-2018	211	100%	36	0%
Mayo Clinic	2009-2019	159	78%	34	0.7%
European Institute of Oncology	**2000-2015**	**123**	**35%**	**110**	**1.6%**
Italian National Cancer Institute	**2007-2021**	**132**	**0%**	**100**	**0 %**

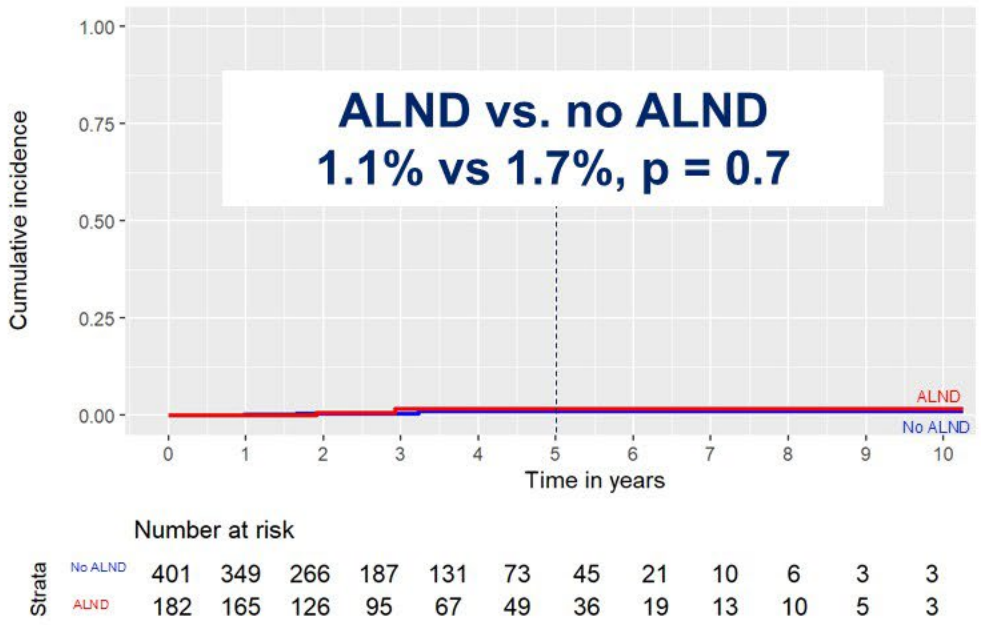
No benefit of ALND in patients who downstage to ypN0 with NAC

Cabioglu N et al. JAMA Surg 2025
Montgna G et al. JAMA Oncol 2024
Barrio AV et al. JAMA Oncol 2021
Kahler-Ribeiro S et al. Eur J Surg Oncol 2021
Cabioglu N et al. Eur J Surg Oncol 2021
Piltin MA et al. Ann Surg Oncol 2020
Wong SM et al. Ann Surg Oncol 2021
Martelli G et al. Ann Surg Oncol 2025

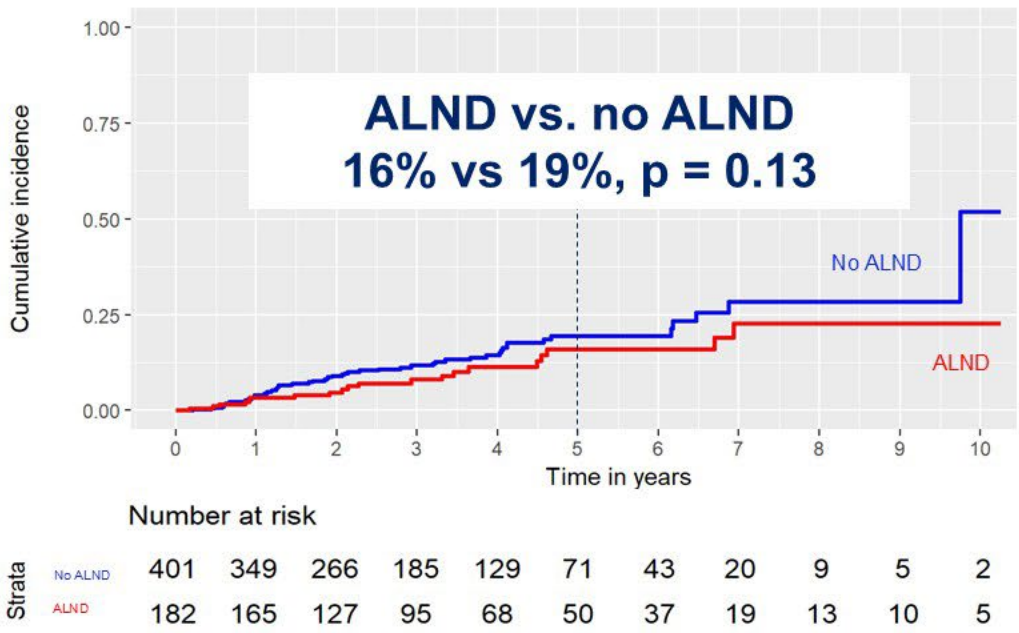
Qualità globale delle prove	Raccomandazione clinica	Forza della raccomandazione
Molto bassa	In pazienti cN1 prima della terapia sistemica neoadiuvante, e con successiva negativizzazione clinico-radiologica post-terapia, può essere presa in considerazione l'omissione dello svuotamento ascellare nel caso 1 o più linfonodi sentinella, eventualmente identificati con doppio tracciante e/o con clip, risultino negativi[229–233,235]	**Condizionata a favore**
COI: nessun conflitto dichiarato		

Are Nodal ITCs After NAC an Indication for Axillary Dissection?
The OPBC-05/ICARO study

5-year rate of isolated axillary recurrence



5-year rate of any (locoregional or distant) invasive recurrence



ALND omission is safe in selected ypN0i+ patients

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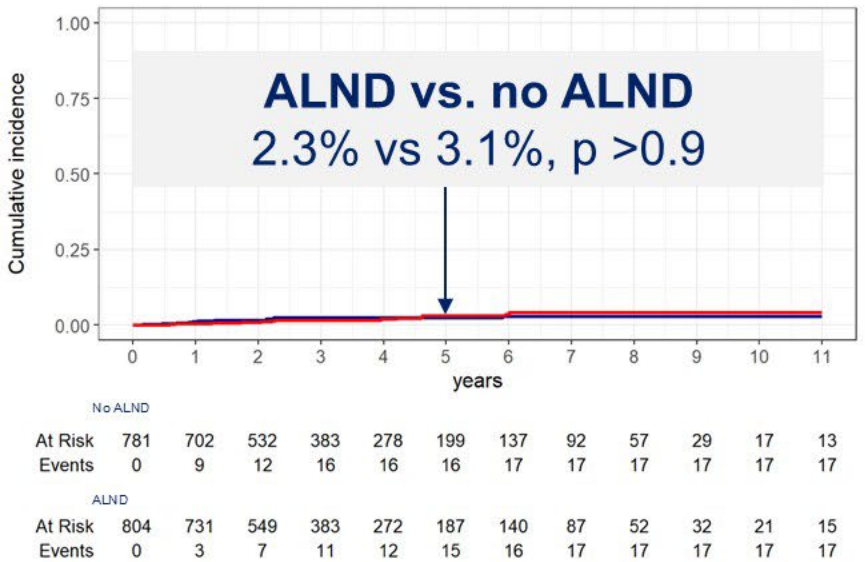
ONCOPLASTIC BREAST CONSORTIUM

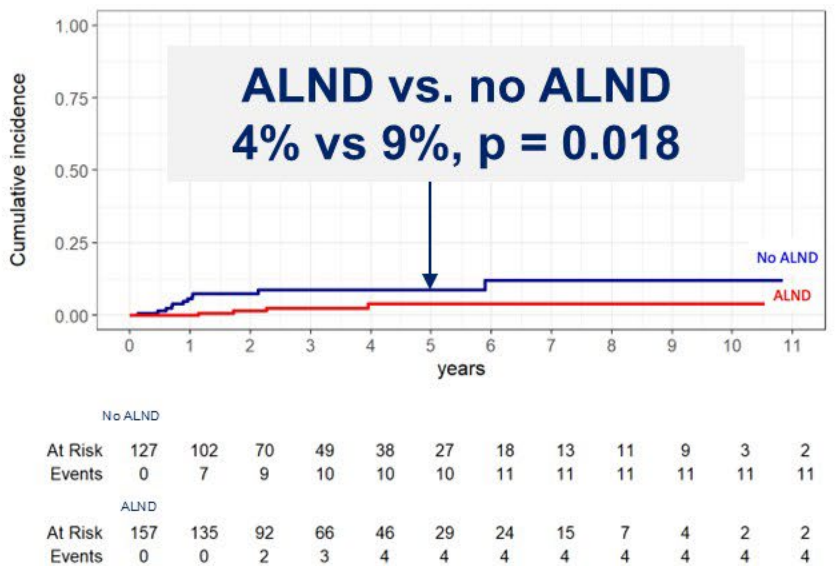
Association of ALND With Oncological Outcomes in ypN1mic Patients After NAC: The OPBC-07/microNAC study

5-year rate of any axillary recurrence full cohort



No ALND												
At Risk	781	702	532	383	278	199	137	92	57	29	17	13
Events	0	9	12	16	16	16	17	17	17	17	17	17
ALND												
At Risk	804	731	549	383	272	187	140	87	52	32	21	15
Events	0	3	7	11	12	15	16	17	17	17	17	17

5-year rate of any axillary recurrence TNBC cohort



No ALND												
At Risk	127	102	70	49	38	27	18	13	11	9	3	2
Events	0	7	9	10	10	10	11	11	11	11	11	11
ALND												
At Risk	157	135	92	66	46	29	24	15	7	4	2	2
Events	0	0	2	3	4	4	4	4	4	4	4	4

ALND omission is safe in selected ypN1mic patients – caution with TNBC!!

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ONCOPLASTIC BREAST CONSORTIUM

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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,*]

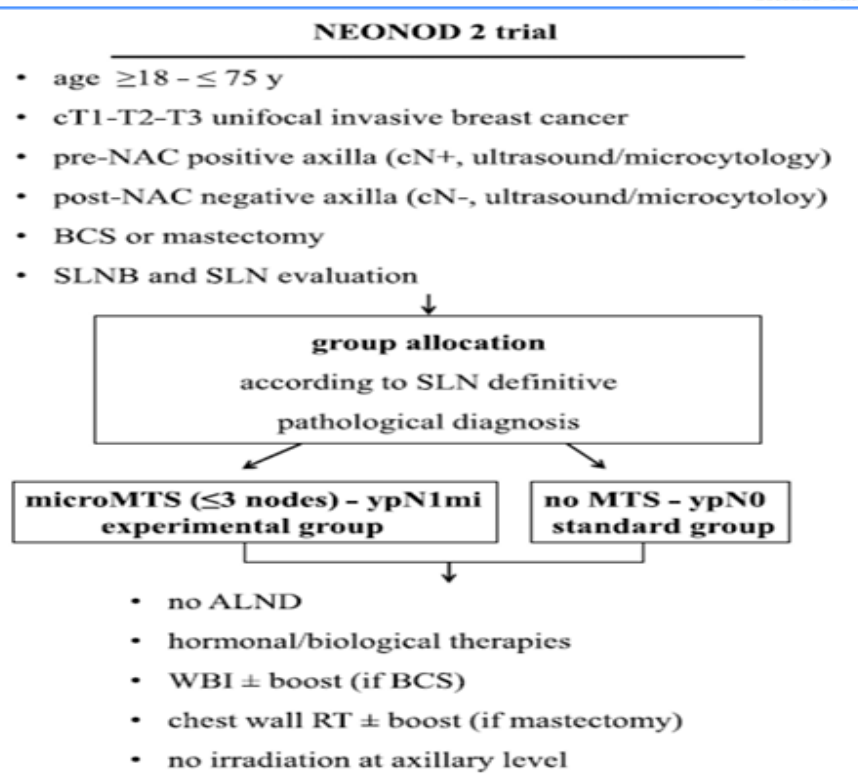

Fig. 1. NEONOD 2 trial: study design.
NAC, neoadjuvant chemotherapy; BCS, breast conserving surgery; SLNB, sentinel lymph node biopsy; SLN, sentinel lymph node; MTS, metastasis; ALND, axilaary
lymph node dissection; WBI, whole breast irradiation; RT, radiotherapy.

Table 1
Enrollment criteria.

Inclusion
A. Before surgery (clinical evaluation)
• Age ≥ 18 and ≤ 75 years
• Infiltrating breast carcinoma (cytology/core biopsy)
• Tumor size cT1-cT2-cT3 (ultrasound/mammography)
• Positive axillary nodes (cN+) at presentation (clinical visit, ultrasound and possibly cyto-microhistology)
• Neoadjuvant chemotherapy (NAC) undergone (anthracycline/taxane based) followed by SLNB
• Axillary nodes downstaged to clinically negative (cN-) after NAC (clinical visit, ultrasound and possibly cyto-microhistology)
• No previous infiltrating breast carcinoma
• No distant metastases (M0)
• Signed and dated written informed consent
B. Intra-operative or post-surgery (definitive pathological diagnosis)
B1. Inclusion in the experimental group
✓Infiltrating breast carcinoma
✓Tumor size pT1-pT2-pT3
✓Micrometastases (>0.2 mm-≤2 mm, ypN1mi) in up to 3 SLNs
B.2 Inclusion in the standard group
✓Infiltrating breast carcinoma
✓Tumor size pT1-pT2-pT3
✓Absence of metastasis (ypN0) or ITC (ypN0(i+) in the SLN
Exclusion
• Ongoing pregnancy or breast-feeding
• Inflammatory breast cancer
• In situ breast carcinoma
• Concomitant contralateral breast carcinoma
• Comorbidity, chronic life-threatening disease or psychological conditions precluding the compliance to a regular follow-up
• Previous neoplasm within the 3 years preceding inclusion (except for in situ carcinoma of the cervix, basalioma, squamous cell carcinoma or non melanoma skin carcinoma
SLNB, sentinel lymph node biopsy; NAC, neoadjuvany chemotherapy; SLN, sentinel lymph node; ITC, isolated tumor cell

Conclusioni

- 44-57% N+ all’esordio
- Downstaging cN+/cN0: 53%-93%
- **LS+(TAD+):35%-54%**

- **Ancora alto tasso di cFNR**
- **Vere risposte linfonodali (ypN0):46%-65%**

Grazie per l'Attenzione!!