AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

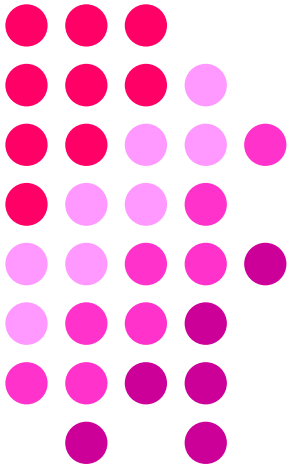
S.S. FORMAZIONE PERMANENTE E RAPPORTI CON L'UNIVERSITA'

REGIONE PIEMONTE

Evento Formativo Residenziale

CRPT: WORKSHOP AGLI ESTREMI DELLO SCREENING MAMMOGRAFICO

Novità e prospettive dalla 19° Conferenza di San Gallen sul tumore alla mammella



Alessandra Beano
SSD Oncologia Senologica

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Disclosures

- ***Research funding**: none.*
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- ***Advisor**: Astra Zeneca, Daiichi-Sankyo, Eisai, Gilead, Lilly, Menarini, Novartis, Roche, Seagen.*
- ***Travel grant**: Gentili, Gilead, Lilly, Novartis, Roche.*


SGBCC 2025
19TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE 2025
PRIMARY THERAPY OF PATIENTS WITH EARLY BREAST CANCER. EVIDENCE, CONTROVERSIES, CONSENSUS
12 - 15 MARCH 2025, VIENNA / AUSTRIA


NOW APPROVED
JOIN THE CONVERSATION ON SOCIAL MEDIA!
KISQALI

Breast cancer centre/unit and coordination

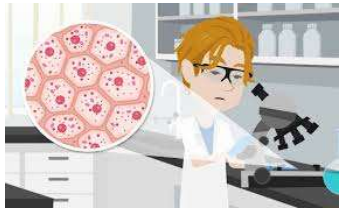
Minimum volume of 150 newly diagnosed early breast cancer cases a year and treating at least 50 metastatic breast cancer cases a year, coordinated by a core MDT member responsible for the multidisciplinary approach

EUSOMA
European Society of Breast Cancer Specialists

Core MDT

Radiology
At least 2 radiologists carrying out at least 1,000 mammographic exams (5,000 if participating in a centralised screening programme), 200 ultrasounds, 50 MRIs and 50 breast guided interventions a year.
At least 2 radiographers performing at least 1,000 mammograms each a year

Pathology
At least 2 pathologists each reporting on a minimum of 50 preoperative samples, 50 early resections and 25 metastatic breast cancer surgical specimens a year



Surgery
At least 2 breast surgeons carrying out primary surgery as first operator on at least 50 newly diagnosed breast cancers a year

Medical oncology
At least 2 medical oncologists each treating a minimum of 50 early and 25 metastatic breast cancer patients a year

Radiation oncology
At least 2 radiation or clinical oncologists each treating at least 50 early breast cancer patients a year. They must also have palliative treatment experience

Nursing
At least 2 breast care nurses working full time on breast cancer care seeing at least 50 early and 25 metastatic breast cancer patients a year

Extended MDT

- Psycho-oncology
- Geriatric oncology
- Oncology pharmacy
- Nuclear medicine
- Physiotherapy
- Plastic surgery
- Interventional radiology
- Self-image support
- Palliative care
- Clinical genetics
- Prevention

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[‡]

breast cancer. There is increasing recognition that the care of a breast cancer patient depends on highly individualized clinical features, including the stage at presentation, the biological subset of breast cancer, the genetic factors that may underlie breast cancer risk, the genomic signatures that inform treatment recommendations, the extent of response before surgery in patients who receive neoadjuvant therapy, and patient preferences. This customized approach to treatment requires integration of clinical care between patients and radiology, pathology, genetics, and surgical, medical and radiation oncology providers. It also requires a dynamic response from clinicians as they encounter accumulating clinical information at the time of diagnosis and then serially with each step in the treatment plan and follow-up, reflecting patient experiences and treatment response.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

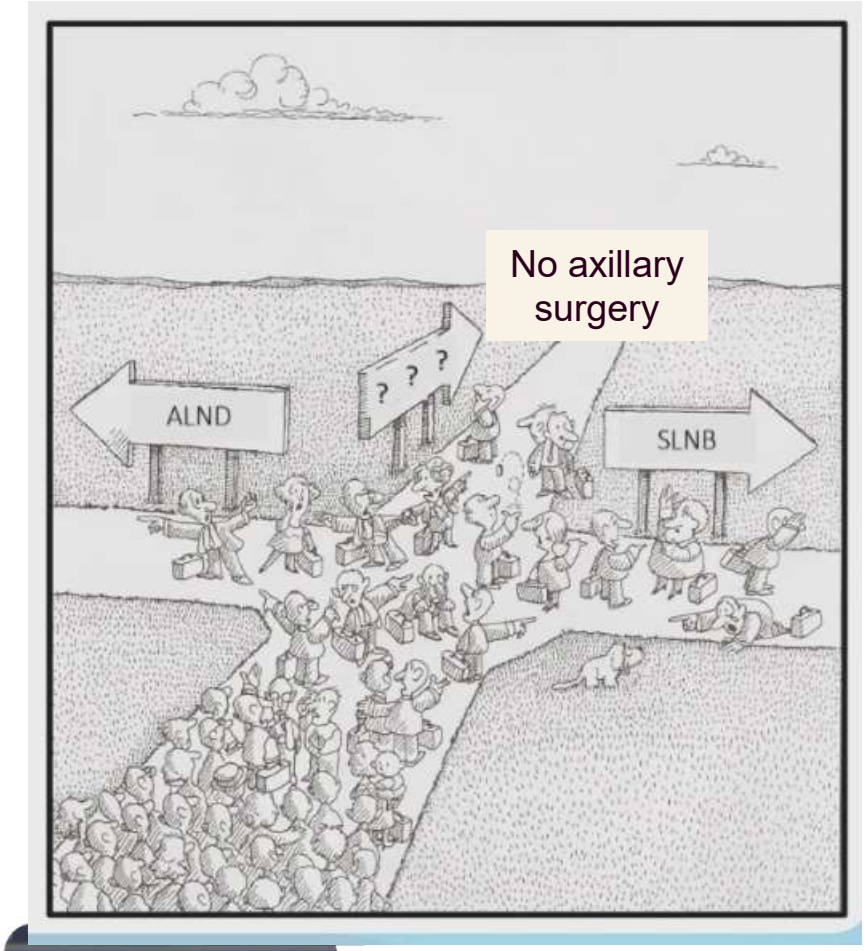
Understanding breast cancer complexity to improve patient outcomes: The St Gallen International Consensus Conference for the Primary Therapy of Individuals with Early Breast Cancer 2023

G. Curigliano[1,2*†], H. J. Burstein[3,4*†], M. Gnant[5,6], S. Loibl[7,8], D. Cameron[9], M. M. Regan[10], C. Denkert[11], P. Poortmans[12,13], W. P. Weber[14,15] & B. Thürlimann[16,17], St Gallen Consensus Conference Panelists 2023

treatment options. The emergence of more effective, innovative agents in both the preoperative (primary or neoadjuvant) and post-operative (adjuvant) settings has underscored the pivotal role of a multidisciplinary approach in treatment decision making, particularly when selecting systemic therapy for an individual patient. The importance of multidisciplinary discussions regarding the clinical benefits of interventions was explicitly emphasized by the consensus panel as an integral part of developing an optimal treatment plan with the 'right' degree of intensity and duration. The panelists focused on controversies surrounding the management of common ductal/no special type

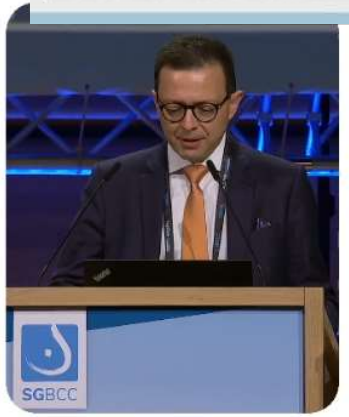
My MTD

- The axillary chaos
- The axillary dilemma:
  CDK4/6i in eBC
- Immunotherapy in eBC
- Early TNBC
- Hereditary BC

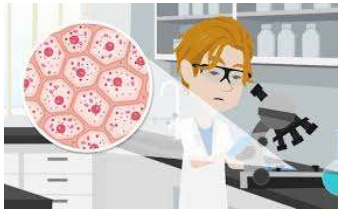


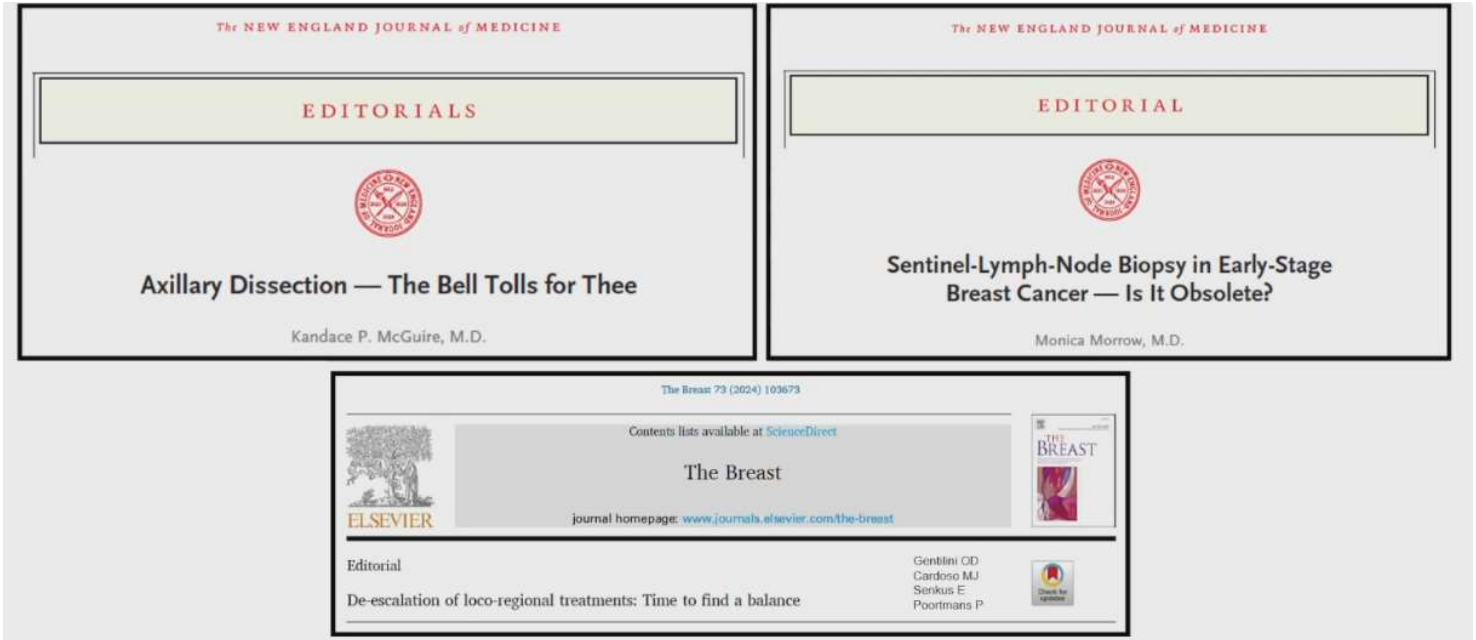
The axillary chaos…

…Now decision regarding the need and the time of adjuvant treatment are often based on biological characteristics (HR, Her2…) and genomic signatures.



Cicero Urban
Brazil





2023 and 2024 were "The Axilla's Years" with robust evidences from important clinical trials!

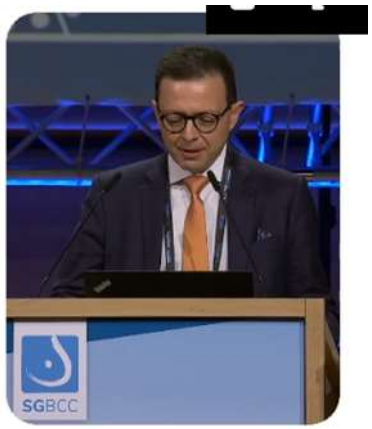
Cicero Urban
Brazil

From: «Who can avoid upfront SLNB and axillary surgery?»…

…To: «Who can not avoid upfront SLNB and axillary surgery?»

Are we ready for a world without upfront SNLB in clinically node negative breast cancer?

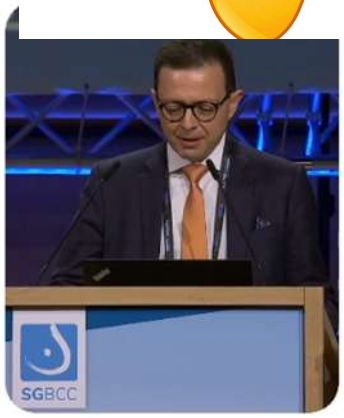
- But…
- De-escalation requires efforts in multidisciplinary decision making
- Risk of potential escalation of other modalities of treatment
- Standardization of information given to patients for shared decision making.



Cicero Urban
Brazil

- A reliable axillary US in fundamental for this new world.

Are we ready for a world without upfront SNLB in clinically node negative breast cancer?

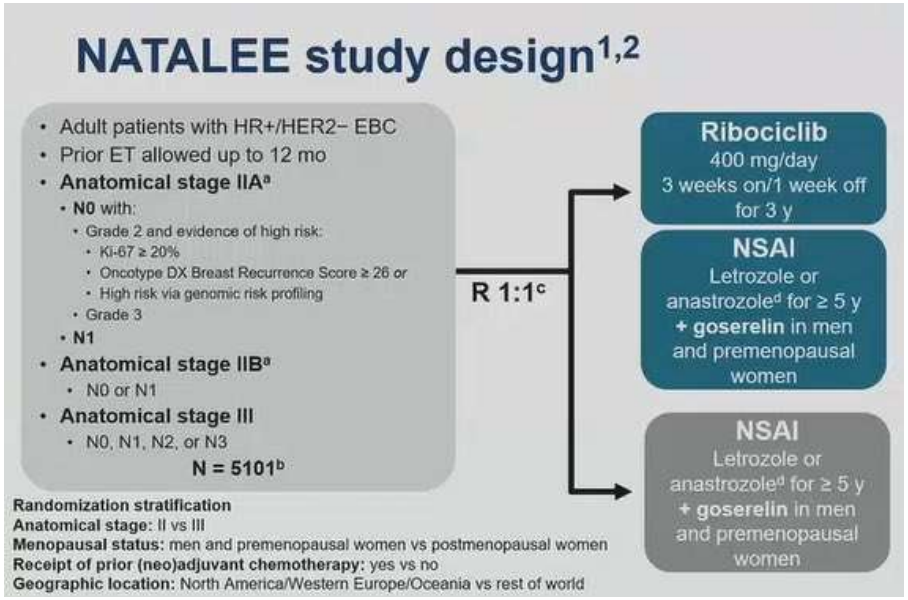


Cicero Urban
Brazil

- For 2025 an increasing impact of AUS on surgical, radiotherapy and systemic decisions.
- For the near future, we expect more decisions based on genomics and AI supplanting decisions based on anatomy.

- More data are needed for SLNB omission in invasive lobular carcinoma, luminal G3, T2, premenopausal patients, mastectomy and also in TN and Her2+ patients candidates to upfront surgery.

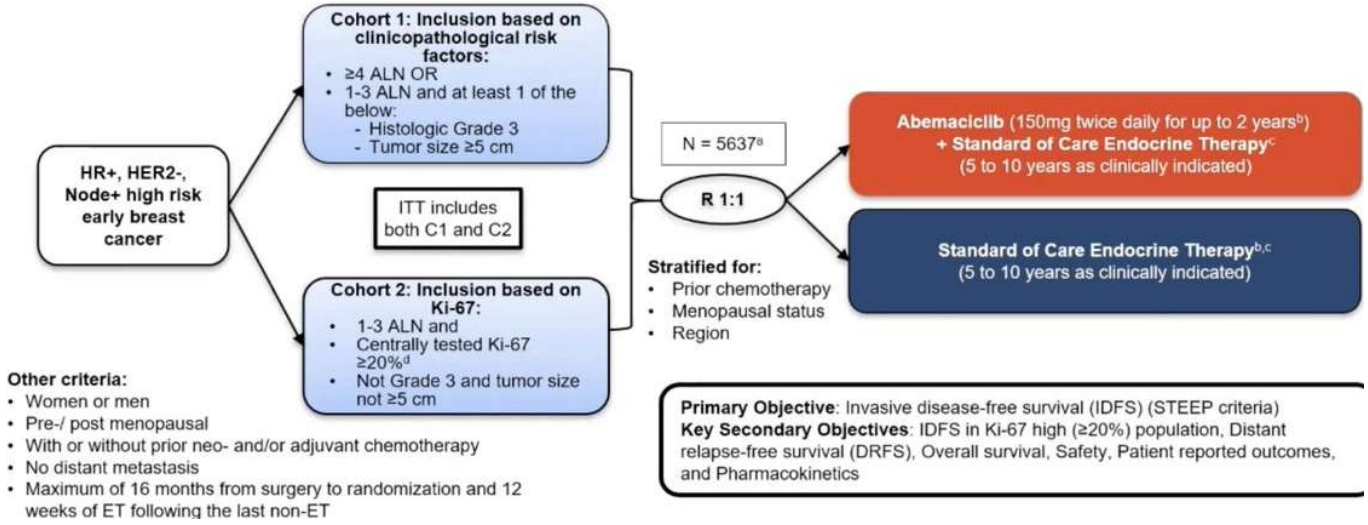
The axillary dilemma: adjuvant CDK 4/6 inhibitors in eBC



Intermediate/high risk

High risk

monarchE: study design



The axillary dilemma: adjuvant CDK 4/6 inhibitors in eBC

Question 8: Better based upon accurate estimates of risk of recurrence than on the eligibility criteria for the pivotal clinical trials?

253

Agree

A 233 92%

Disagree

B 20 7%

19TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE 2025

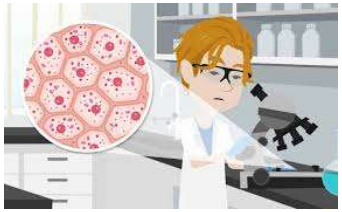
12 – 15 March 2025, Vienna / Austria

The selection of patients with intermediate risk ER+ breast cancers for adjuvant CDK46 inhibitors would be better based upon accurate estimates of risk of recurrence than on the eligibility criteria for the pivotal clinical trials (the Cameron/deMichele rule)

a. Agree 87.5%

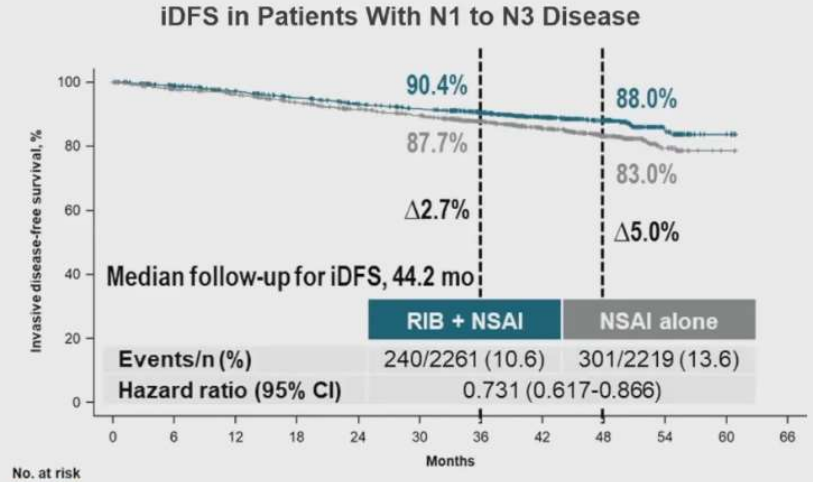
b. Disagree 12.5%

Total Votes : 64

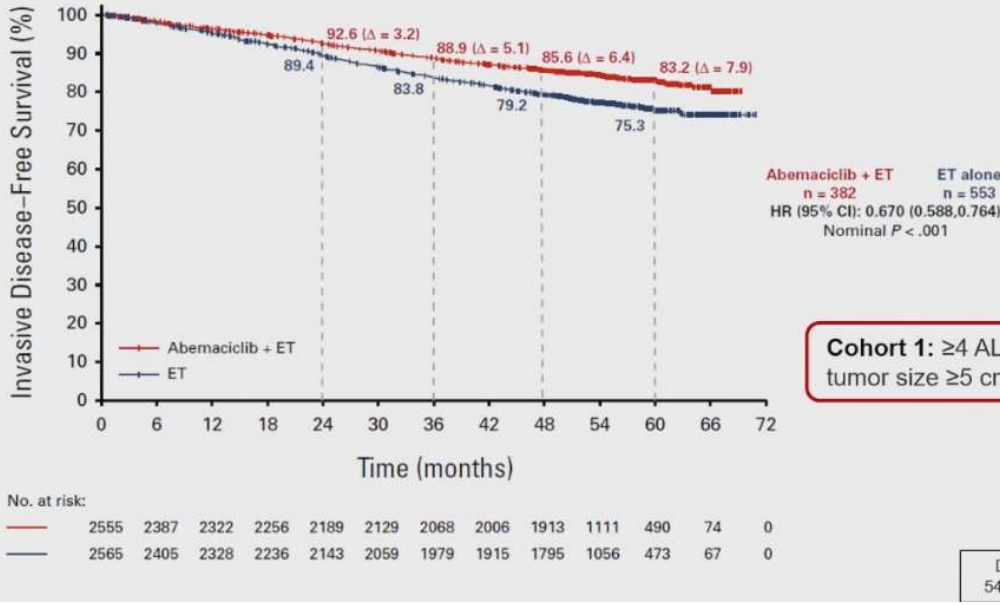


Adjuvant CDK 4/6 inhibitors in eBC

NATALEE: iDFS in node-positive EBC



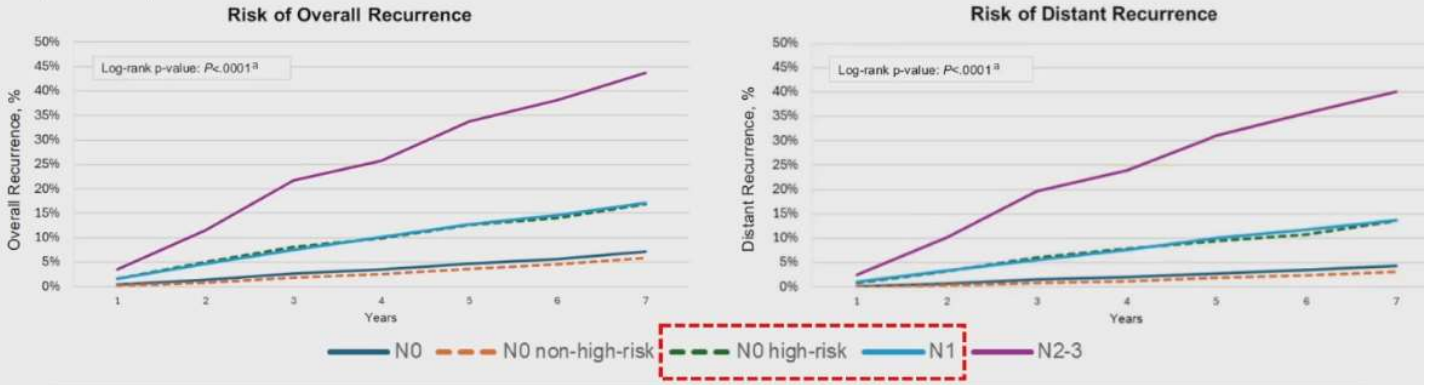
monarchE: iDFS in cohort 1



Adjuvant CDK 4/6 inhibitors in eBC

Real-world data (Flatiron) for patients with HR+/HER2− EBC to estimate ROR (N = 7564)

- The N0 non-high-risk group had significantly lower overall ROR and distant ROR vs the N0 high-risk (*P*<.0001) and N1 (*P*<.0001) groups
- The N0 high-risk and N1 groups were not statistically different in overall (*P*=.617) or distant (*P*=.438) ROR rates



N0 high-risk was defined by NATALEE trial inclusion criteria: node-negative T2 disease ([grade 2 with high genomic risk or Ki-67 ≥20%] or grade 3), T3, or T4

EBC, early breast cancer; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; N, node; ROR, risk of recurrence; T, tumor

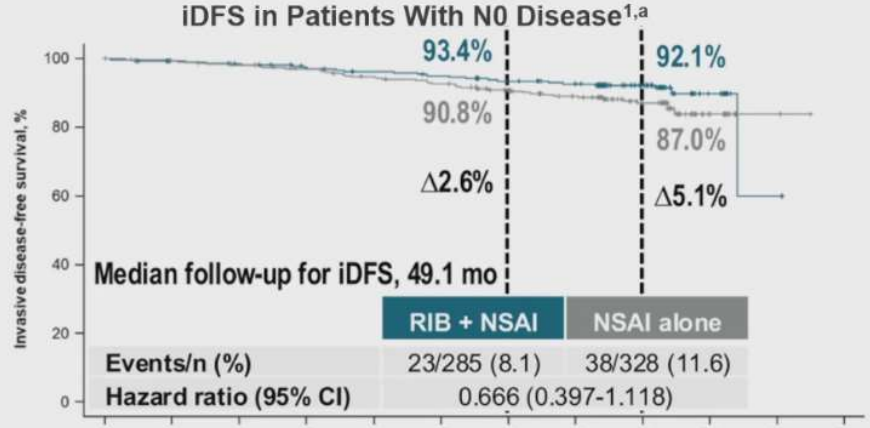
Nadia Harbeck
Germany

Adjuvant CDK 4/6 inhibitors in eBC

NATALEE: iDFS in high-risk N0 EBC

- RIB + NSAI improved iDFS over NSAI alone in high-risk N0 EBC[1]
- In the control arm, the 3- and 4-year iDFS rates underscore the risk of recurrence and unmet need in NATALEE patients with N0 disease who are treated with current SOC[1]

iDFS in Patients With N0 Disease[1,a]

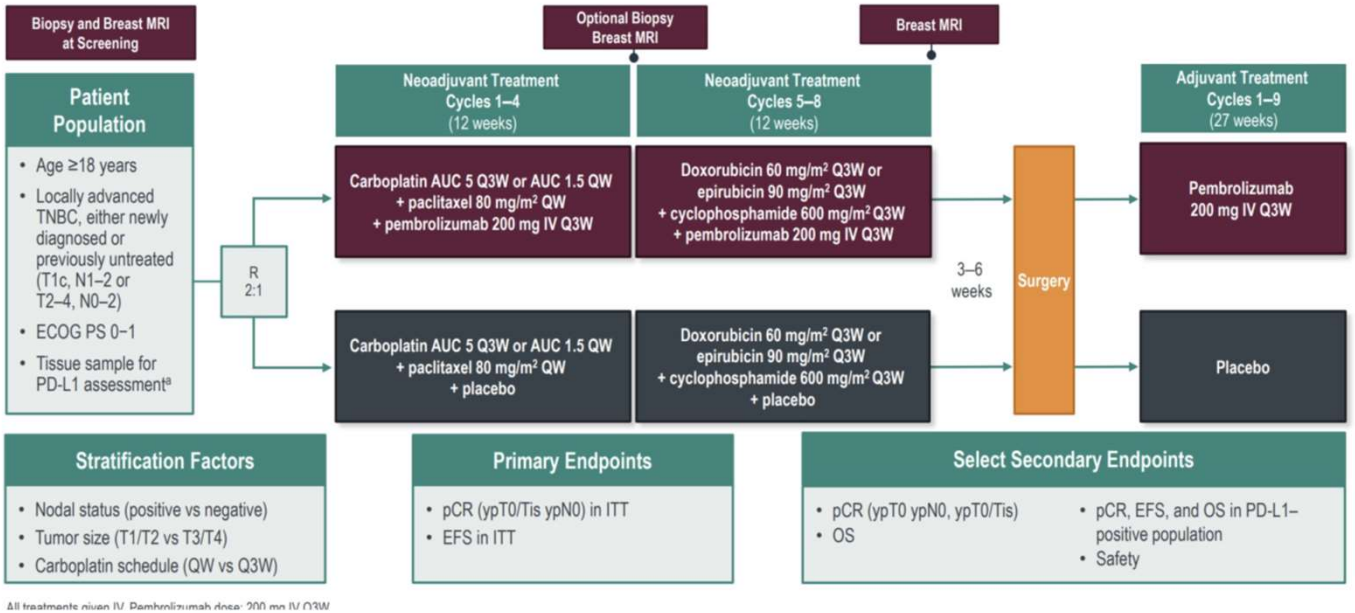


Data cutoff: April 29, 2024
44.2-month median iDFS follow-up

Nadia Harbeck
Germany

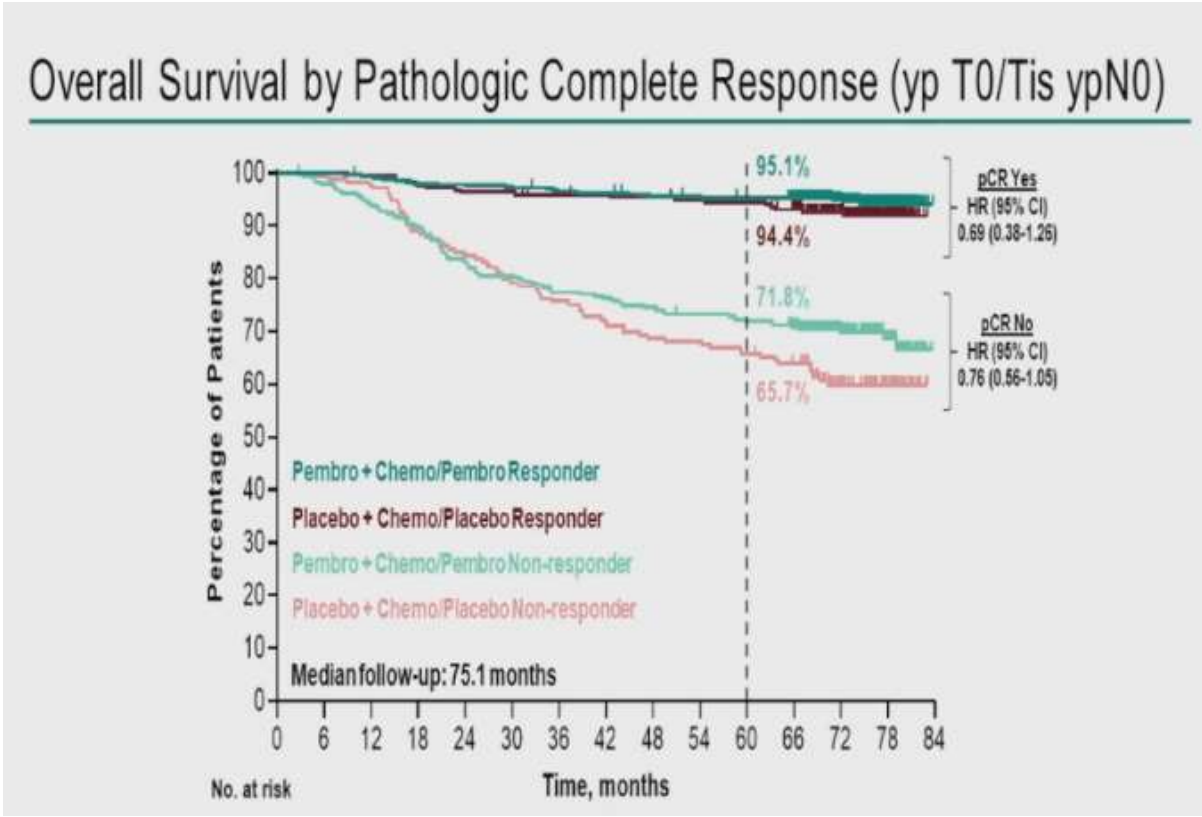
Immunotherapy in eBC

KEYNOTE-522 Study Design[1–3]

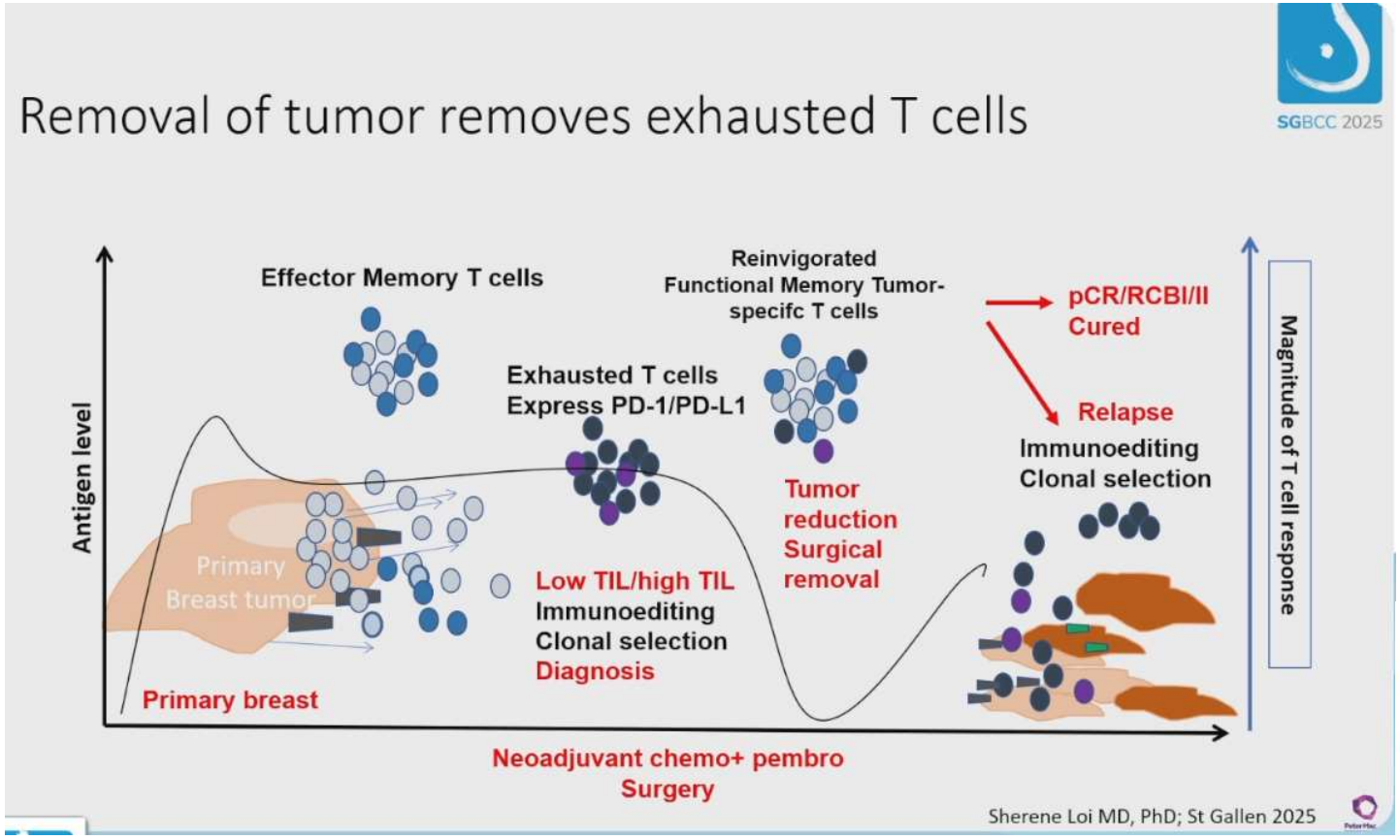


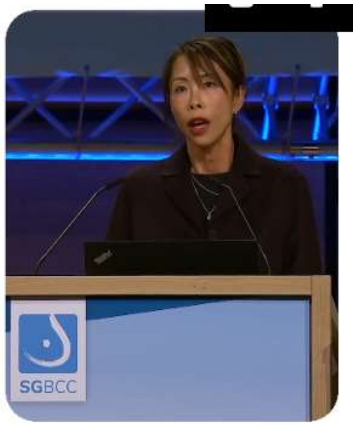
All treatments given IV. Pembrolizumab dose: 200 mg IV Q3W

Immunotherapy in eBC



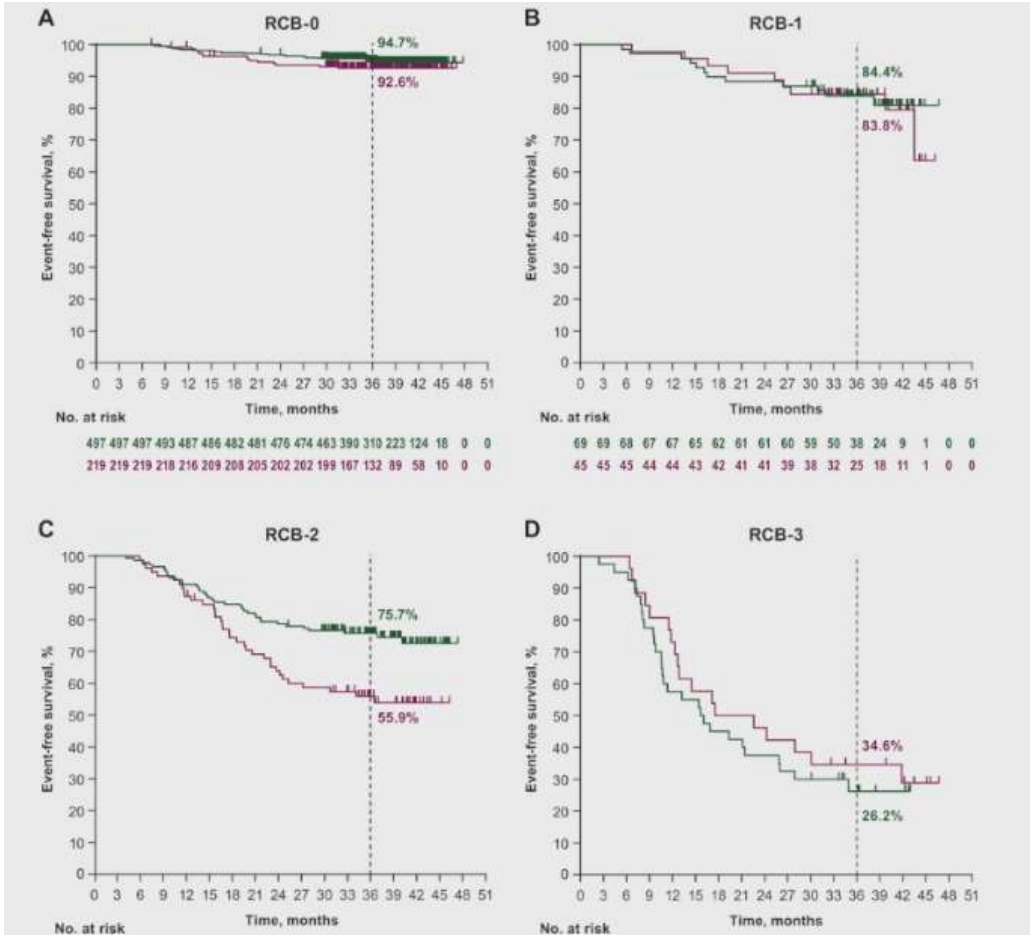
Immunotherapy in eBC





Sherene Loi
Australia

Immunotherapy in eBC



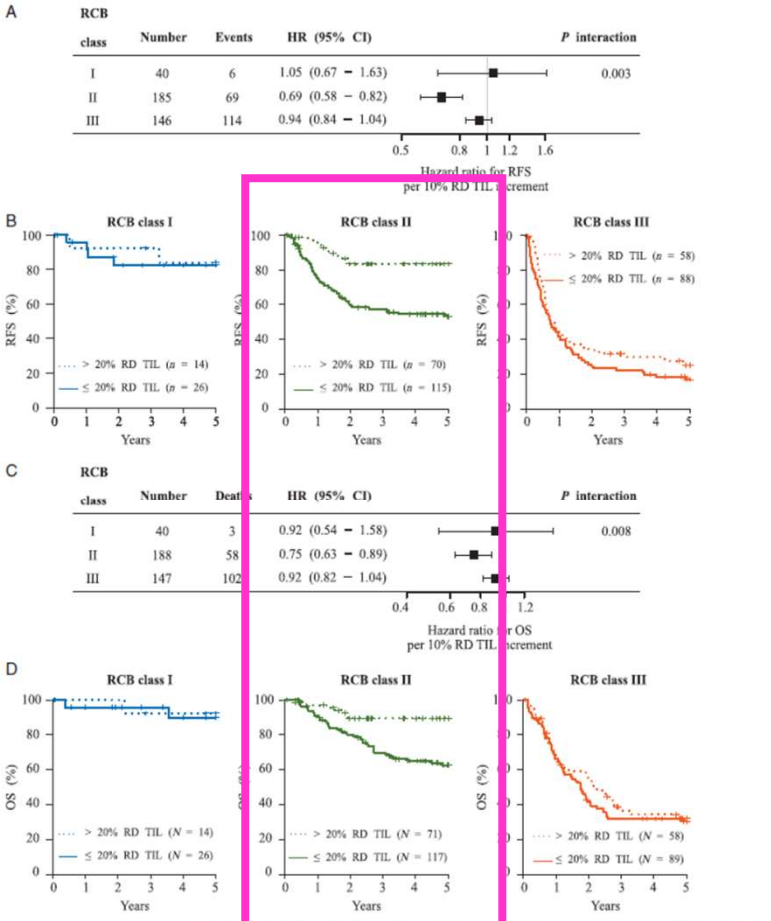


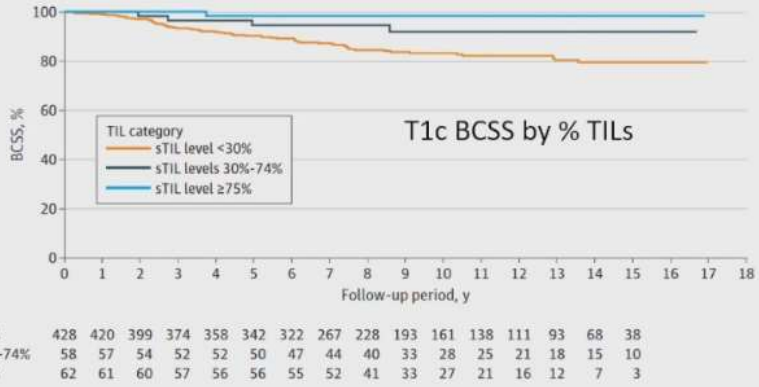
Figure 2. Prognostic interactions between RCB class and RD TILs. The forest plots demonstrate the prognostic association of RD TILs by RCB class for recurrence-free survival (A) and for overall survival (C). The interaction P value was obtained using a likelihood ratio test. Kaplan–Meier curves demonstrating survival by a TIL level cut-off value of 20% for RCB class I, II, and III are shown for both recurrence-free survival (B) and overall survival (D). HR, hazard ratio; 95% CI, 95% confidence intervals; RFS, recurrence-free survival; OS, overall survival.

Adjuvant treatment for all TN eBC?

10 Year BCSS by TILS

TILs	<30%	30-74%	≥75%
All stage I	87%	94% HR 0.38 (95% CI 0.17-0.87)	93% HR 0.50 (95% CI 0.25-1.00)
T1a/b	92%	97% HR 0.41 (95%CI, 0.10-1.73)	89% HR 1.37 (95% CI, 0.62-3.05)
T1c	83%	91% HR 0.40 (95%CI, 0.15-1.10)	98% HR 0.09 (95% CI, 0.01-0.68)

C sTIL cutoff at <30%, 30%-74%, and ≥75%



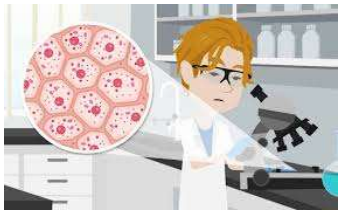
No. at risk

sTIL level <30%	428	420	399	374	358	342	322	267	228	193	161	138	111	93	68	38
sTIL levels 30%-74%	58	57	54	52	52	50	47	44	40	33	28	25	21	18	15	10
sTIL level ≥75%	62	61	60	57	56	56	55	52	41	33	27	21	16	12	7	3

Geurts et al (Kok), JAMA Onc 2024

Hope S. Rugo
USA

Adjuvant treatment for all TN eBC?



- CT recommended for:
  - All pT1c N0
  - Most pT1b N0
  - Highly selected young patients with smaller tumors AND high risk features

- CT is not recommended for:
  - Most pT1a
  - Low grade good prognosis rare s

- Stratifying treatment based on TILs

Hereditary BC

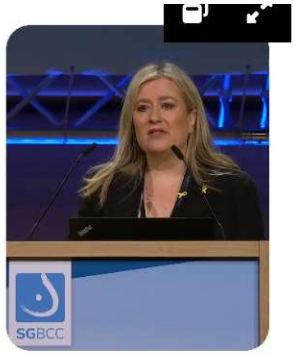
Introduction

Approximately 5-10% of breast cancers (BC) are associated with a germline pathogenic variant (PV) or likely-PV (L/PV) in one of several genes

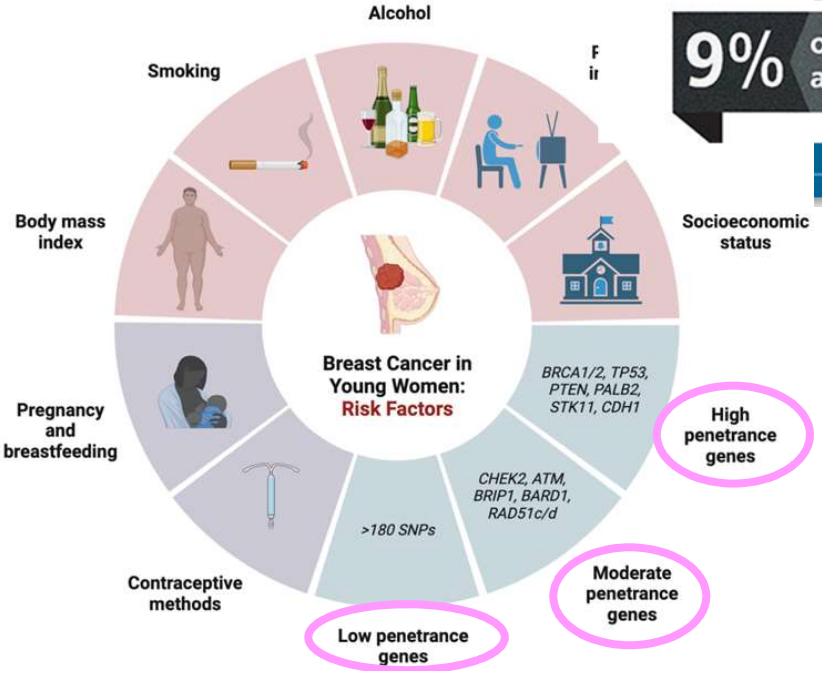
Most common germline PVs associated with BC – *BRCA1* & *BRCA2*

What we find in terms of hereditary predisposition genes including prevalence will depend on where we look (age, subtype, stage, ethnicity, family history)

Initial high threshold for guidelines reflected factors that have changed over time including - cost, clinical utility, guidelines & measures for screening & risk-reduction



Shani Paluch-Shimon
Israel



9% of all breast cancers diagnosed before the age of 40 are attributable to mutations in **BRCA1 or BRCA2** genes

Low incidence
Unexpected finding
CHALLENGES OF DIAGNOSING BREAST CANCER IN YOUNG WOMEN
Dense breast tissue
Lack of regular screening programs

Hereditary BC

Guidelines

SGBCC 2025

Majority of international guidelines still focus on risk-adapted approach: age, family history, triple negative breast cancer, ancestry

Some international guidelines also recommend testing of patients eligible for PARP inhibitors

The American Society of Breast Surgeons recommend testing ALL women with a personal history of breast cancer

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2025
Hereditary Cancer Testing Criteria

NCCN Guidelines Index
Table of Contents
Discussion

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST CANCER SUSCEPTIBILITY GENES
(Genes such as *BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11,* and *TP53.* See GENE-A)[a,f,g,h,i]

Testing is clinically indicated in the following scenarios:

- See General Testing Criteria on CRIT-1.
- Personal history of breast cancer with specific features:
  - ≤50 y
  - Any age:
    - Treatment indications
      - To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting[j,k] (NCCN Guidelines for Breast Cancer)
      - To aid in adjuvant treatment decisions with olaparib for high-risk,[l] HER2-negative breast cancer[l]
    - Pathology/histology
      - Triple-negative breast cancer
      - Multiple primary breast cancers (synchronous or metachronous)[m]
      - Lobular breast cancer with personal or family history of diffuse gastric cancer (NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric)
    - Male breast cancer
    - Ancestry: Ashkenazi Jewish
  - Any age (continued):
    - Family history[n]
      - ≥1 close blood relative[o] with ANY:
        - breast cancer at age ≤50 y
        - male breast cancer
        - ovarian cancer
        - pancreatic cancer
        - prostate cancer with metastatic,[p] or high- or very-high-risk group (Initial Risk Stratification and Staging Workup in NCCN Guidelines for [redacted] Cancer)
      - [redacted] cases of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer

- Family history criteria: unaffected; or affected but does not meet above criteria
  - Individual with a first- or second-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making).[q]
  - Individuals who have a probability >5% of a *BRCA1/2* P/LP variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk).[r]

Criteria met → GENE-1

If testing criteria not met, consider testing criteria for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

CARCINOMA MAMMARIO IN STADIO PRECOCE — **LINEE GUIDA 2023** — AIOM

1. **Pazienti con caratteristiche cliniche associate a un'aumentata probabilità di variante patogenetica (VP) di BRCA1/2, indipendentemente dalla storia familiare:**
2. **Pazienti senza caratteristiche cliniche associate a un'aumentata probabilità di VP BRCA, eleggibili a trattamenti specifici in caso di VP germinale:**

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Identification of germline mutations informs disease management and follow-up; patients with *gBRCA1/2m* and other PVs may opt for different locoregional breast cancer management and contralateral surgical prophylaxis, and warrant more intensive risk-reducing measures for other malignancies such as ovarian cancer.[1] High-risk patients with *gBRCA1/2m* may be candidates for adjuvant therapy with a poly (ADP-ribose) polymerase (PARP) inhibitor.

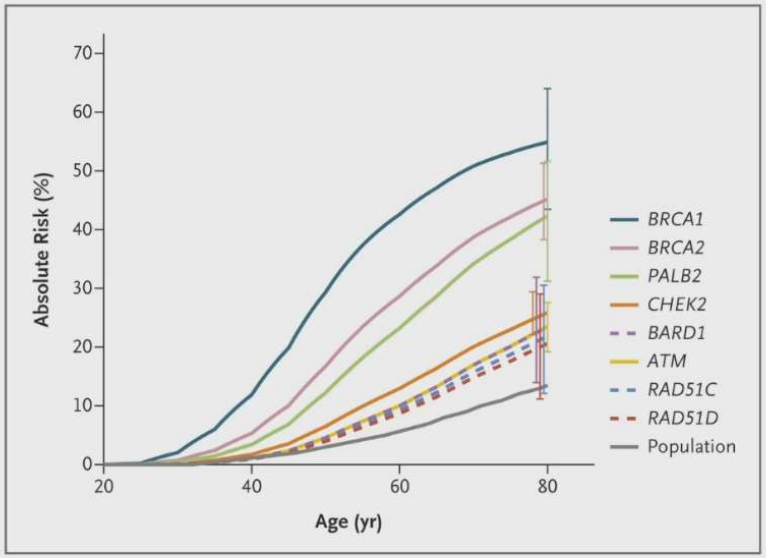
Germline testing for PVs in *BRCA1/2* should be offered for patients who meet the respective national criteria and for those who are candidates for adjuvant olaparib therapy.[20,21]

Hereditary BC

Breast Cancer Risk

The NEW ENGLAND JOURNAL of MEDICINE

(Breast Cancer Association Consortium, 2021)



Kelly Metcalfe
Canada

SGBCC 2025

Hereditary BC

Guidelines based testing will miss some PV carriers

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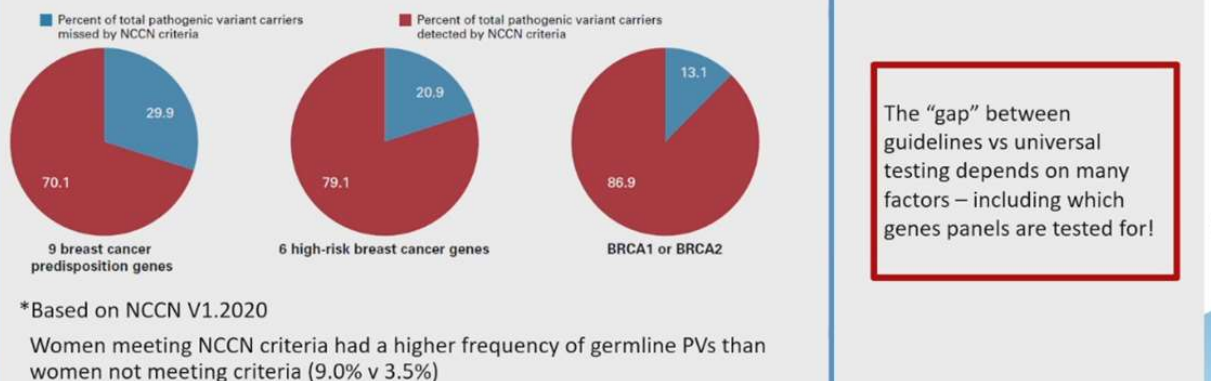

*Based on NCCN V1.2020

Women meeting NCCN criteria had a higher frequency of germline PVs than women not meeting criteria (9.0% v 3.5%)

The "gap" between guidelines vs universal testing depends on many factors – including which genes panels are tested for!

Other studies have shown that "out-of-guideline" detection changed clinical management including in women >65yro

PV=pathogenic variant

Yadav et al, JCO, 2020; Whitworth et al, 2022, JAMA Network Open, 2022

Shani Paluch-Shimon
Israel

SGBCC 2025

Hereditary BC

GS1-08: Association between Risk-reducing Surgeries and Survival in Young *BRCA* Carriers with Breast Cancer: Results from an International Cohort Study

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center

AACR American Association for Cancer Research

	N (%) n = 5290
Region:	
Latin America/South America	271 (5.1)
Australia/Oceania	179 (3.4)
Northern Europe	741 (14.0)
Eastern Europe	316 (6.0)
North America	629 (11.9)
Southern Europe	2059 (38.9)
Asia	1088 (20.6)
Africa	7 (0.1)
Income:	
High income	4584 (86.7)
Low-middle income	706 (13.4)
Age at diagnosis, median (IQR) years	35.0 (31.0-38.0)
Age at diagnosis:	
≤ 30 years	1105 (20.9)
31-35 years	1929 (36.5)
36-40 years	2256 (42.6)
Timing of *BRCA* testing	
Tested before or at diagnosis	2581 (48.8)
Tested after diagnosis	2411 (45.6)
Unknown date of *BRCA* testing	298 (5.6)

	N (%) n = 5290
Specific *BRCA* gene	
BRCA1	3361 (63.5)
BRCA2	1891 (35.7)
BRCA1 and *BRCA2*	31 (0.6)
BRCA, unknown if 1 or 2	7 (0.1)
Tumor size:	
T1 (≤ 2 cm)	1929 (36.5)
T2 (>2 – ≤ 5 cm)	2411 (45.6)
T3 (> 5 cm) - T4	719 (13.6)
Unknown	231 (4.4)
Nodal status:	
N0	2708 (51.2)
N1	1758 (33.2)
N2 – N3	643 (12.6)
Unknown	181 (3.4)
Tumor subtype:	
Luminal-like	1898 (35.9)
TNBC	2596 (49.1)
HER2-positive	377 (7.1)
Unknown	419 (7.9)
Chemotherapy use:	
Yes	4860 (91.8)
No	401 (7.6)
Unknown	29 (0.5)

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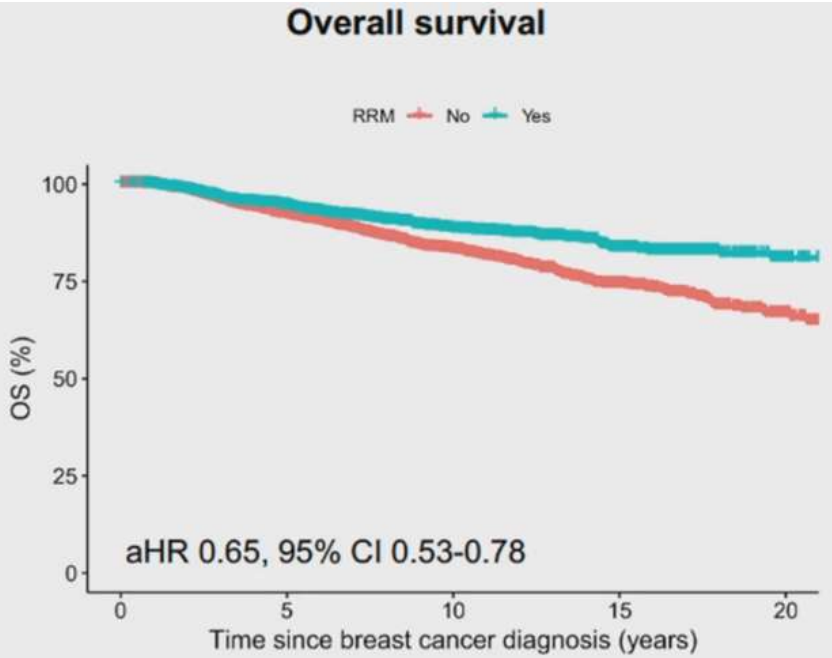
AACR American Association for Cancer Research

Lambertini et al. 2024

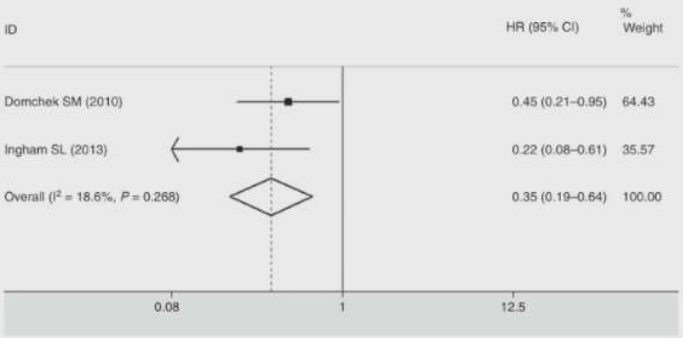


Hereditary BC

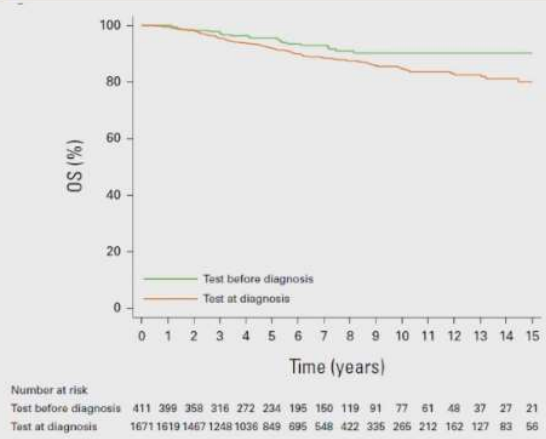
How important is the impact of cascade testing?

SGBCC 2025

RRSO saves lives in unaffected *BRCA1/2* carriers



Knowing *BRCA* status ***prior*** to diagnosis is associated with a better outcome for BC



RRSO= Risk-reducing salpingo-ophorectomy ; BC=breast cancer

Li et al, Clin Cancer Res 2016; Hadar et al, JAMA Oncology, 2020;Lubinski, JAMA Oncology, 2024; Lambertini, JCO, 2025

Shani Paluch-Shimon
Israel

SGBCC 2025

...and the last 2 suggestions...

19TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE 2025

12 – 15 March 2025, Vienna / Austria

Oncofertility Counseling is Mandatory As soon as Possible after Diagnosis

ESMO

ANNALS OF ONCOLOGY

SPECIAL ARTICLE

Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines†

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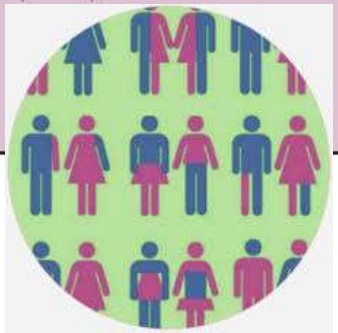
- All cancer patients of reproductive age should receive complete oncofertility counselling **as early as possible** in the treatment planning process, **irrespective of the type and stage of disease** [III, A]
- As there is no absolute threshold of exposure to anticancer therapies that determines gonadal failure and infertility, **every patient** should be considered as being at **potential risk of developing treatment-related gonadotoxicity** [V, A]

Lambertini M et al, Ann Oncol 2020;31(12):1664

Matteo Lambertini
Italy

Transgender (TG) and nonbinary (NB) persons		
Knowledge about the risks of breast/gynecological cancers in TG and NB persons receiving gender-affirming hormone therapy is limited. Even less information exists regarding TG/NB individuals with known genetic predisposition. Cancer registries should include TG/NB identities, and further education and research should be implemented to fill the gap in information and counseling in this population.	Expert opinion	100%



...grazie per l'attenzione!