Multidisciplinary Care of Early Breast Cancer: Implementing Primary Systemic Therapy

Lee Schwartzberg MD, FACP

Chief, Medical Oncology/Hematology

Renown Health-Pennington Cancer Institute

Professor of Clinical Medicine

University of Nevada, Reno

Renown Health
Pennington
Cancer Institute

Disclosures

- Advisor/Consultant: AstraZeneca, Daiichi Sankyo, Novartis, Seagen, Spectrum, Napo, Genentech, Foundation Medicine, Coherus, GSK
- Speaker Bureau: AstraZeneca, Merck, Seagen, Daiichi Sankyo, Novartis

1993:
50 year old woman with palpable breast mass
Imaging: 3 cm mass in Left breast
Biopsy: Invasive cancer, NOS, poorly differentiated
ER+ PR+ by LBA; HER2 N/A; Ki-67 N/A

Total Mastectomy and axillary lymph node dissection:

Path: 4.2 x 4 cm IDC, 2/18 lymph nodes positive

Doxorubicin based adjuvant chemotherapy

Radiation x 5 weeks including all LNs + 1 week boost to chest wall/scar

Tamoxifen for 5 years

1993 Outcome

EFFICACY

- 30-40% chance of distant recurrence at 10 yrs

TOXICITY

- 35-40% chance of clinical lymphedema
- 10-20% chance of chronic chest wall pain/fibrosis
- 1-5% chance of cardiac disease

2023:
50 year old woman with palpable breast mass
Imaging: Mammo +US: 3 cm mass in Left breast, no palp LNs, sonographically neg
MRI: borderline LNs, 4 cm mass
US Biopsy: Invasive ductal ca, grade 3 ER+ 80% PR+ 10%;
HER2 3+; Ki-67 30%

Neoadjuvant TCHP; Clinical complete response by exam and imaging

Partial Mastectomy + SLNB

Path: pCR in breast and lymph nodes

Anti-HER2 Ab adjuvant therapy

Radiation to breast/level 1/2 lymph nodes 3 weeks

Aromatase inhibitor x 5 years

Outcome change over 30 years

1993

EFFICACY

- 30-40% chance of distant recurrence at 10 yrs

TOXICITY

- 35-40% chance of clinical lymphedema
- 10-20% chance of chronic chest wall pain/fibrosis
- 1-5% chance of cardiac disease

2023

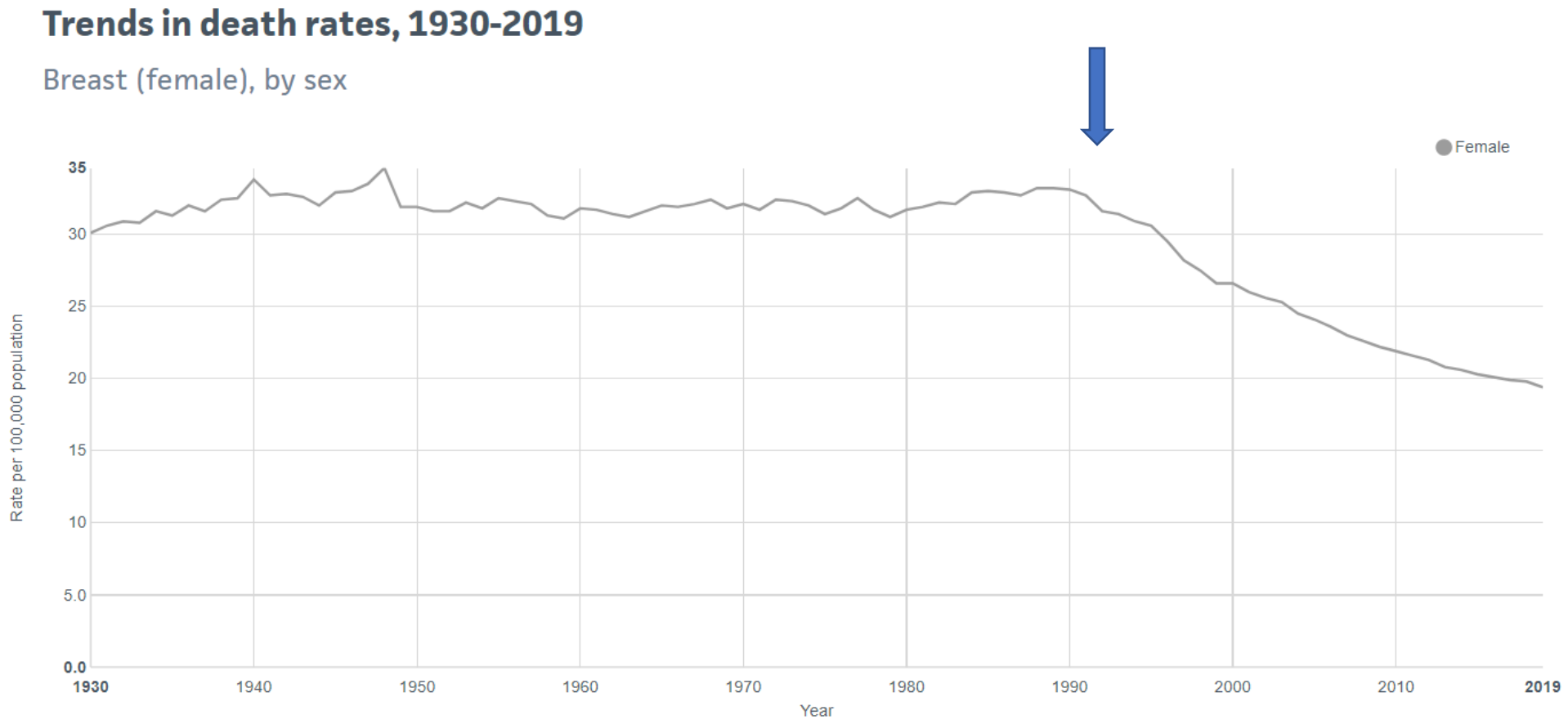
EFFICACY

- 5-10% chance of distant recurrence at 10 yrs

TOXICITY

- 5-10% chance of clinical lymphedema
- 3-5% chance of chronic chest wall pain/fibrosis
- 1-3% chance of cardiac disease

Breast cancer death rates have decreased 40% in past 30 years…
while interventions have reduced toxicity and side effects



DeSantis, CE et al; CA-A Cancer Journal for Clinicians 2019

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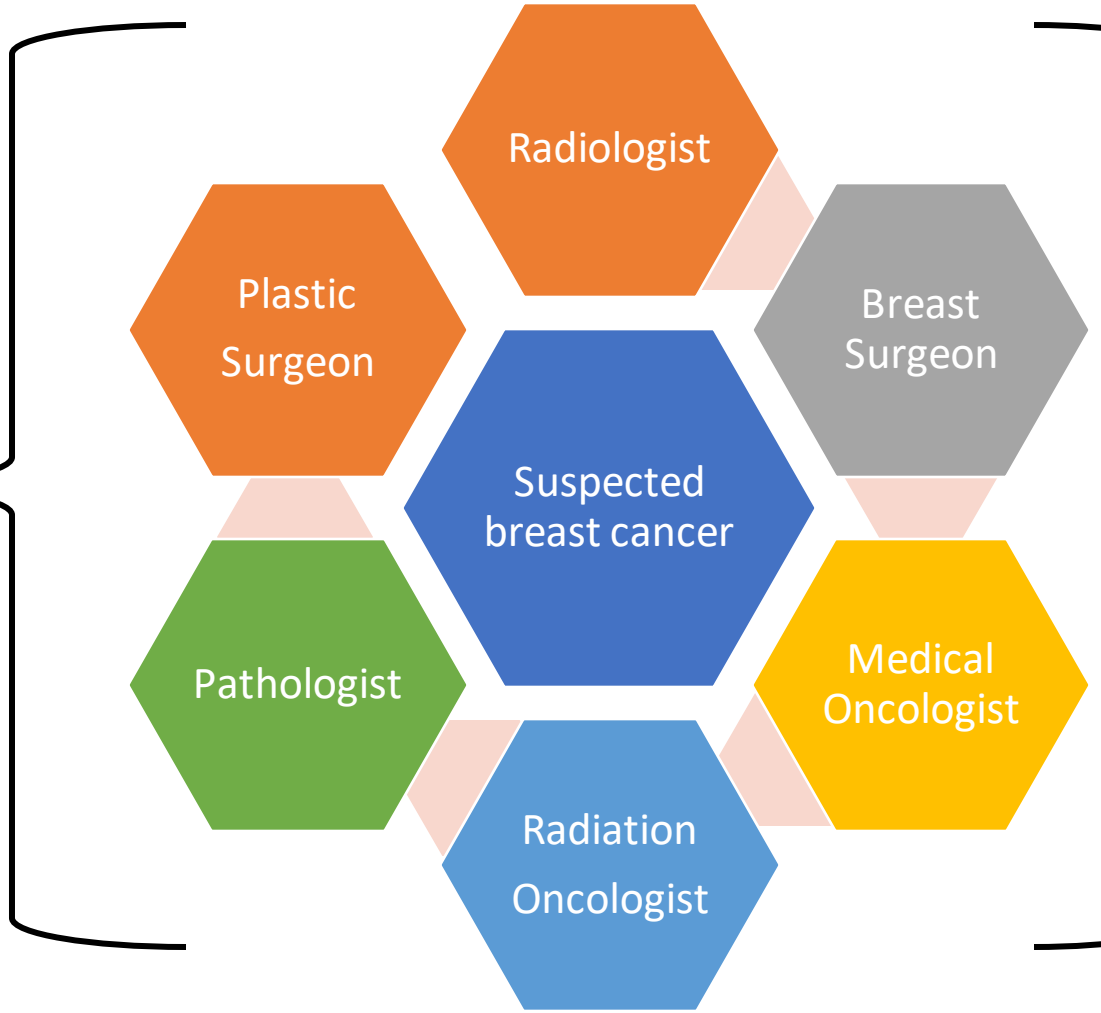
What led to this dramatic improvement?

1. Better and more screening
2. Better surgery
3. Better radiation therapy
4. Better understanding of the biology
5. Better systemic therapy (adjuvant and neoadjuvant)
6. Better multidisciplinary care

The multidisciplinary team for early breast cancer

Genetic Counselor



Nurse and/or Lay Navigator

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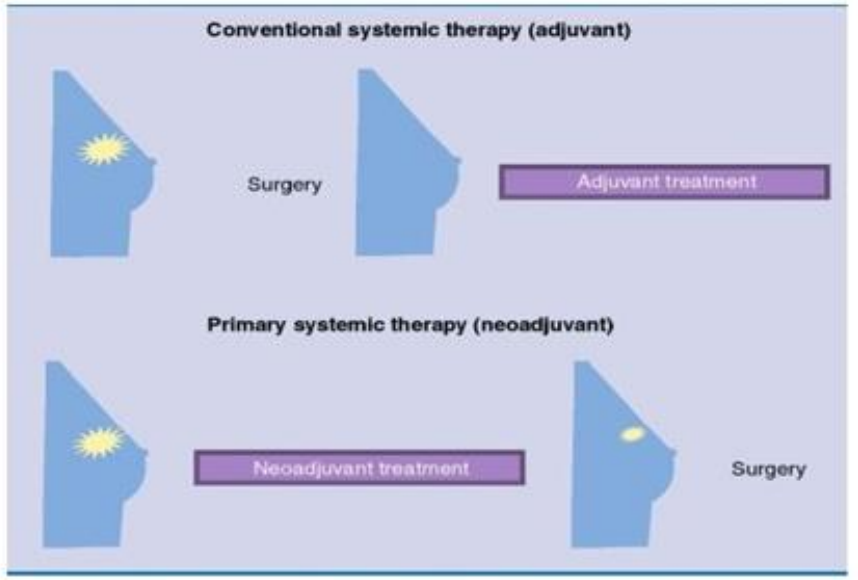
Why use Neoadjuvant Systemic Therapy?

- Traditional
  - Downstage disease, improve resectability and breast conservation
  - Reduce extent of axillary surgery
- Contemporary
  - Risk stratification to guide adjuvant therapy
  - Provide long-term prognostic information
  - Early assessment of novel agents/combinations
- Growing
  - Response/resistance biomarkers to optimize patient selection for available therapies
  - Pathological response-guided escalation and de-escalation clinical trials



Which EBC patients Should Be Considered for Preoperative Systemic Therapy for EBC?

Patients with HER2+ EBC who have a tumor ≥ 2 cm (T2) diameter or who have node-positive disease regardless of hormone receptor status should receive neoadjuvant chemotherapy with the addition of trastuzumab/pertuzumab

Patients with TNBC who have a tumor ≥ 2 cm (T2) diameter or who have node-positive disease should receive neoadjuvant chemotherapy with the addition of pembrolizumab

Patients with HR+HER2- EBC who are high-risk by age, tumor size, nodal status, and grade should consider neoadjuvant chemotherapy

Information to be discussed with the MDT when selecting patients for neoadjuvant therapy

Patient information and assessment of the disease

Patient Factors
- Age
- Clinical history (eg. comorbidities)
- Drug history (eg. concomitant medications)

Imaging
- Mammogram (size, M score)
- Ultrasound (size, U score)
- Axilla ultrasound (N score)

MRI

Core biopsy
- Type, grade, receptor status of the tumour (eg. HR, HER2)
- Axilla biopsy or fine needle aspiration

Definite indication for adjuvant systemic therapy

Additional considerations that should be in place at each MDT
- Definition of assessment criteria (eg. pCR definition)
- Protocols for testing and receiving timely results (eg. receptor status)

Purpose

What is the aim of NAC for this patient?
- Downstage breast tumour
- Downstage axilla
- Other (eg. logistical/ planning reasons, BRCA testing)

Management and treatment

Surgical and axillary management
- Current breast surgical plan
- Will the surgical plan change following NAC? (If so, provide alternative surgical plan, and which parameters trigger alternative plans)
- Current axillary plan
- Post-NAC sentinel lymph node biopsy or axillary node clearance
- Current adjuvant radiotherapy plan

Checklist
- Staging CT (if indicated)
- USS clip placement
- Surgical review planned
- Plan for imaging assessment of response

Outstanding issues
- Any outstanding issues should also be discussed

Critical Need:
Coordination between the surgeon, medical oncologist and radiologist during neoadjuvant therapy

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Modern Principles of Neoadjuvant Chemotherapy

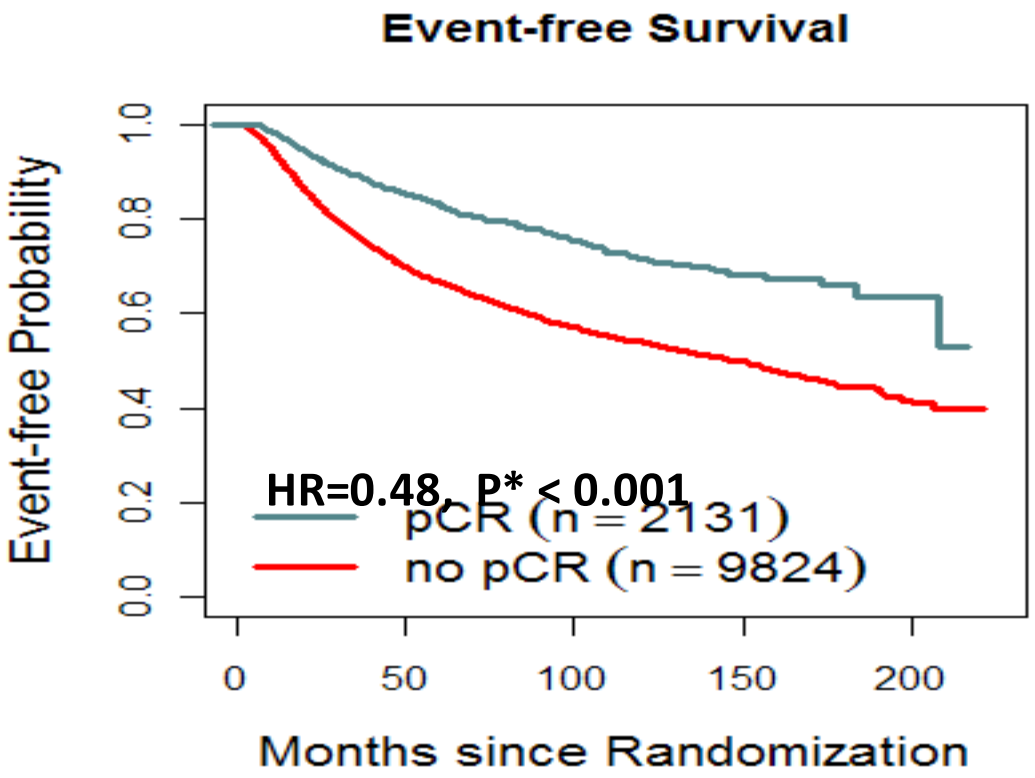
- Use the same chemotherapy before as would be used after
- Follow clinical response by examination and imaging
- Stop chemotherapy and proceed to surgery only if progression while on chemotherapy (<5%)
- Response guided chemotherapy for some?
- pCR is a surrogate for better long-term outcome on an individual patient basis

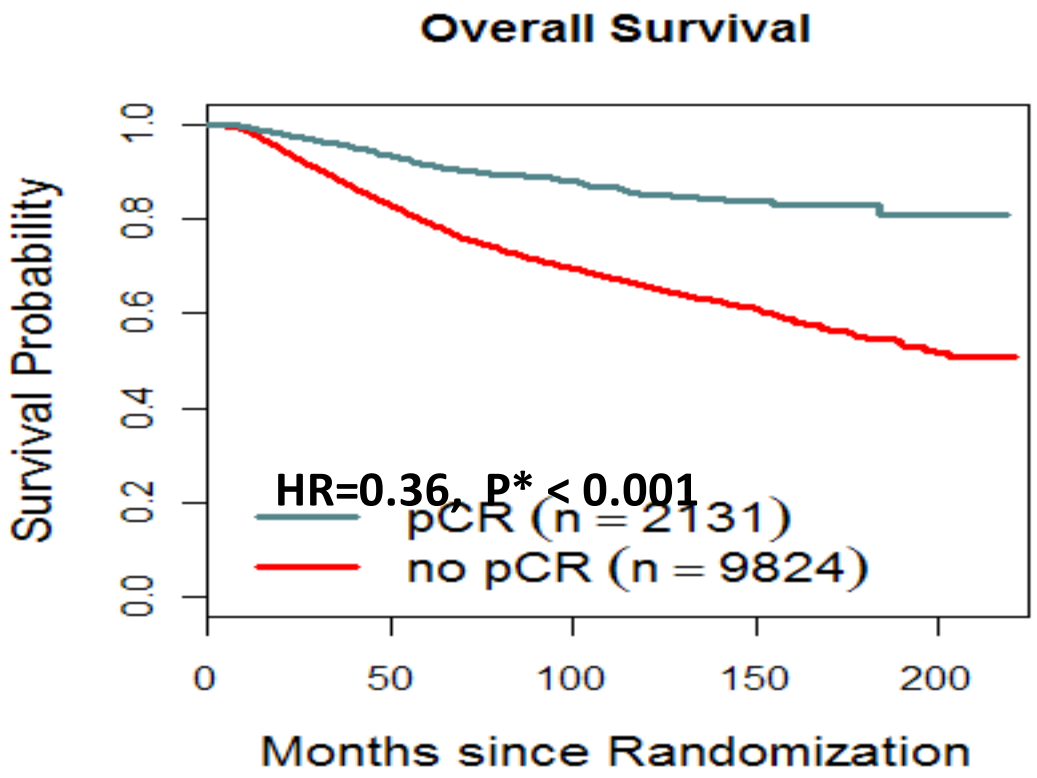
Pathologic Complete Response (pCR)
Primary goal of NACT in TNBC and HER2+ BC

- Definition: No invasive cancer in the breast or axillary lymph nodes (ypT0,ypN0)
  - Residual DCIS does not influence the definition
  - Caution: Multiple other definitions used in earlier studies

- Prognostic for long term outcome

Association of pCR on EFS and OS





pCR=ypT0/is ypN0

* Nominal p-value

Cortazar et al, Lancet 2014; 384: 164-72

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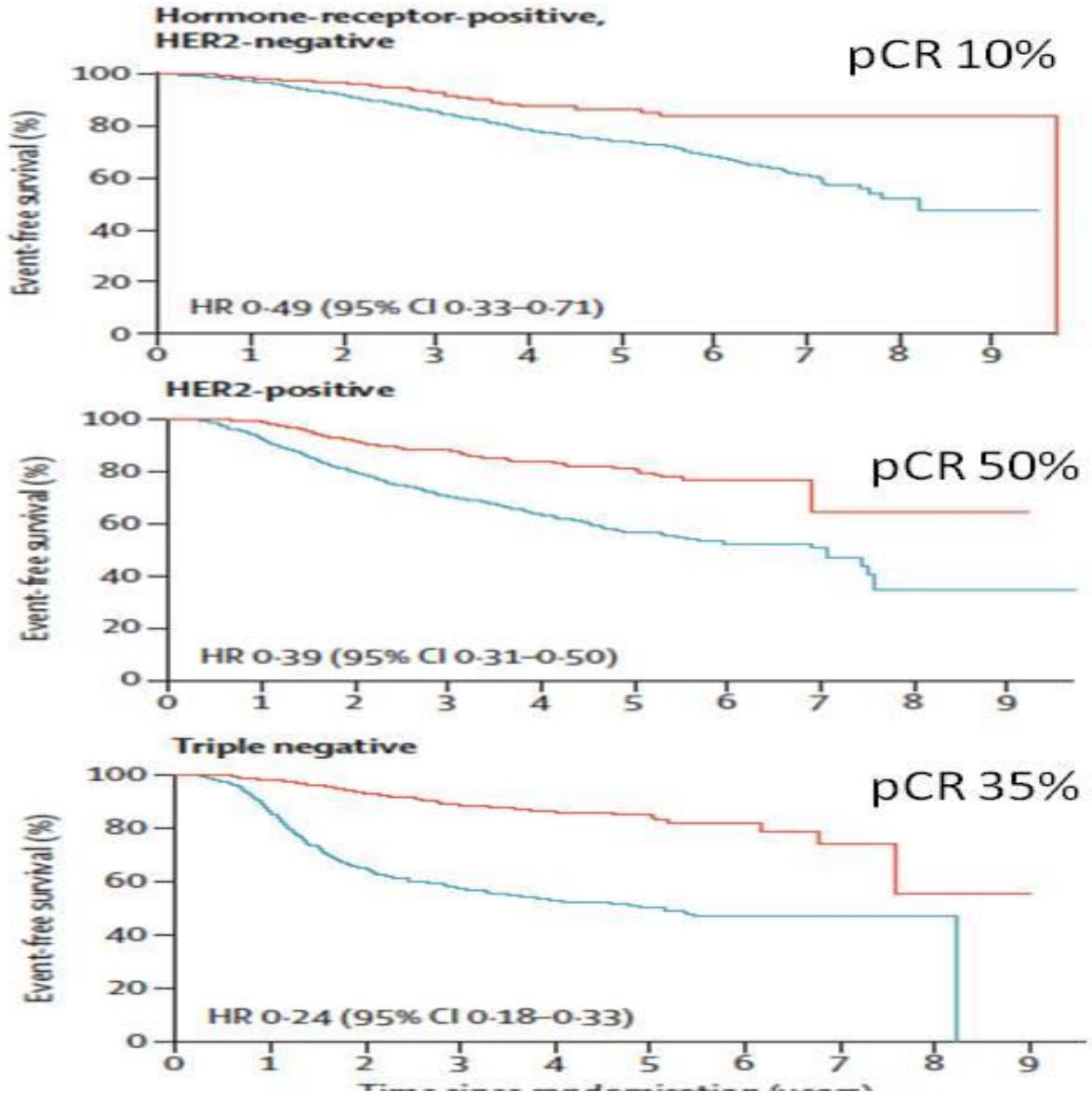
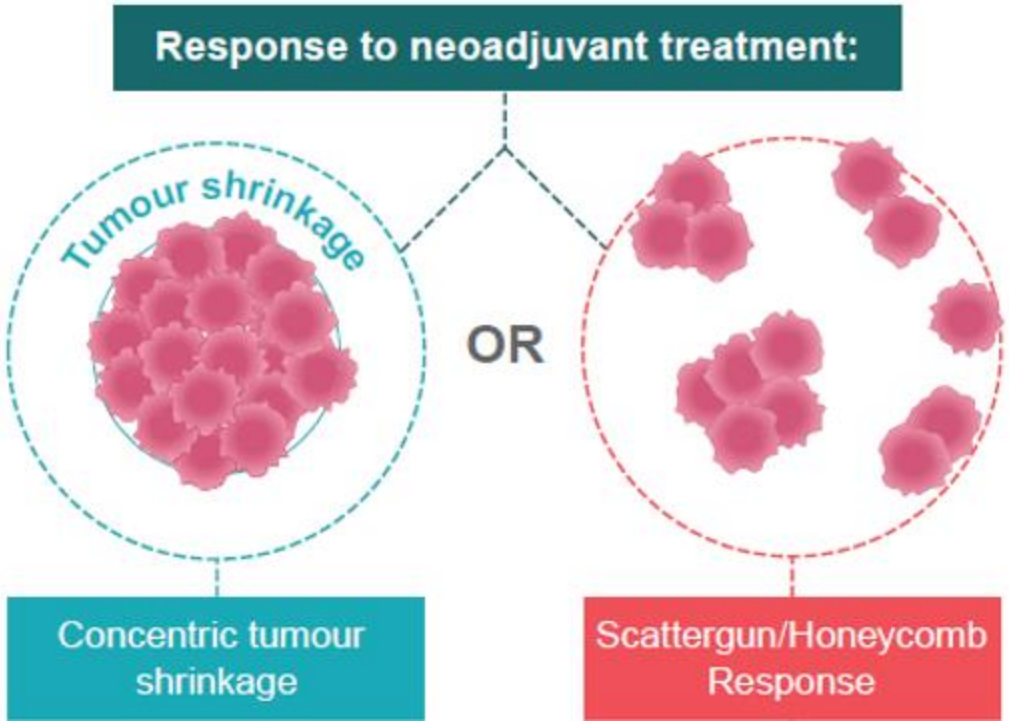
What the CTNeoBC meta-analysis tells us about pCR

- **pCR is a reliable prognostic marker**
  - Individual patients with pCR have superior outcomes
- **Definition matters: Eradication of invasive cancer from breast + nodes sufficient**
  - Residual DCIS not prognostically important
- **Subtype matters: Magnitude of difference in outcome between pCR+ and no pCR differs between subgroups**



Cortazar et al, Lancet 2014; 384: 164-72

Response to NACT is heterogeneous

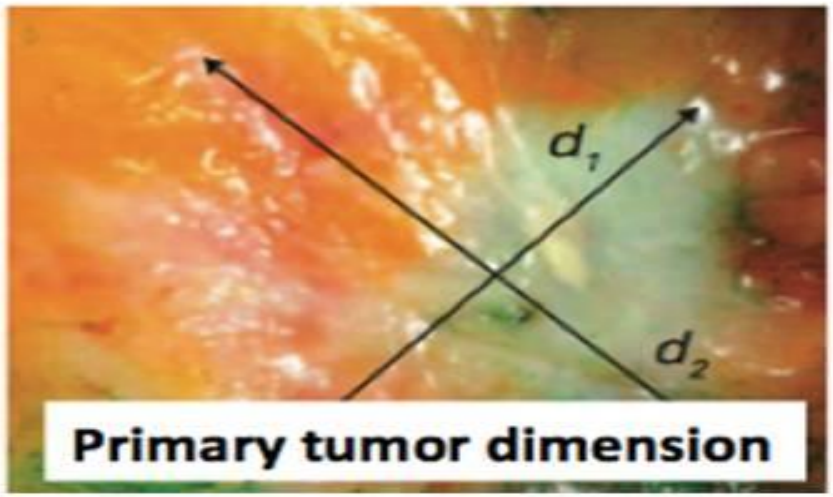


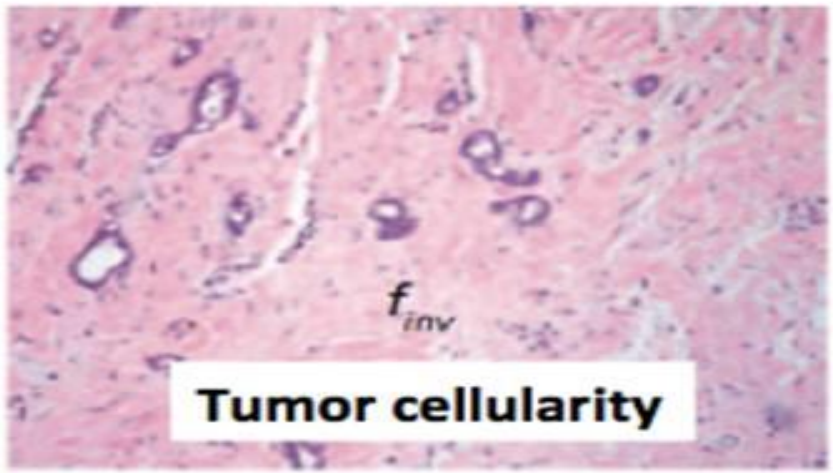
Traditional staging by TNM after NACT (yp T, yp N)
doesn't represent prognosis well

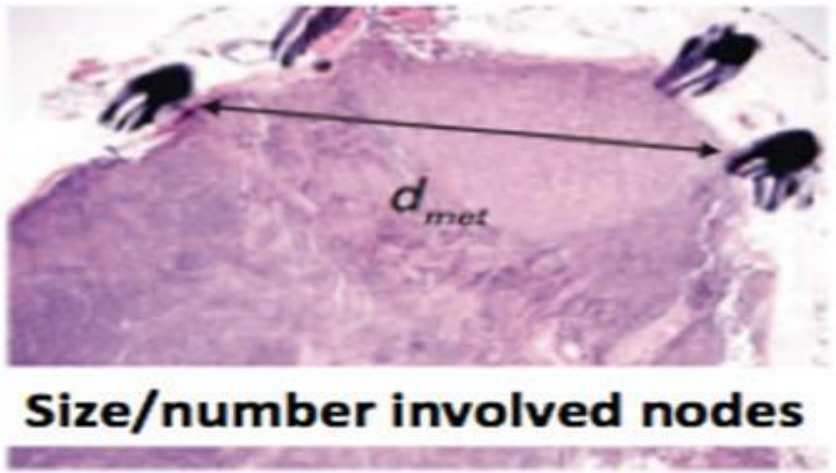
Can we do better to sort patients who need additional therapy?

Residual Cancer Burden (RCB) as an alternative neoadjuvant biomarker

Method to quantify residual disease ranging from pathological complete response to extensive residual disease.





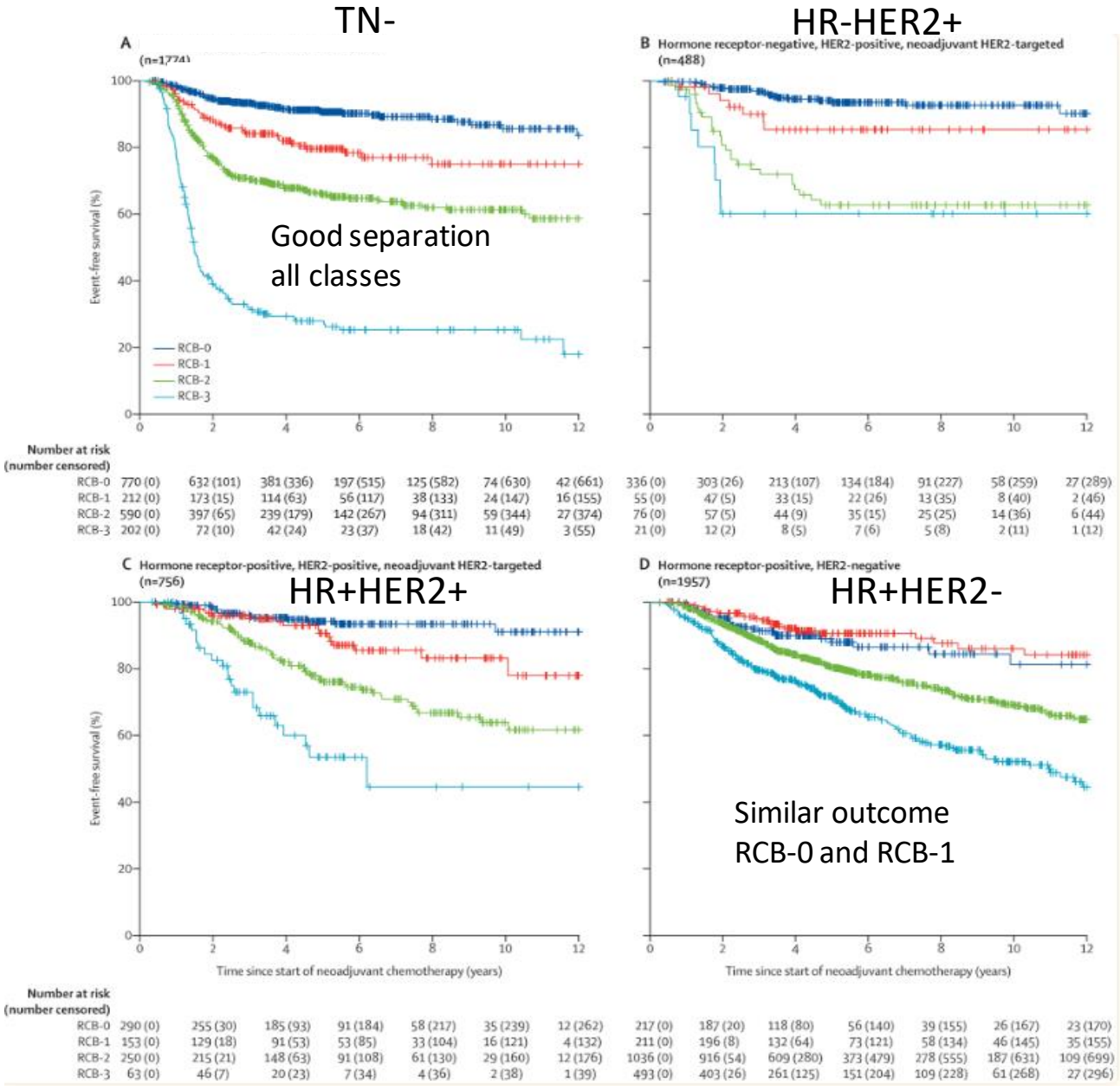


Highly reproducible:

- Concordance correlation coefficient = 0.931 (0.908–0.949).
- Overall accuracy = 0.989.
- Kappa coefficient for overall agreement = 0.583 (0.539–0.626).

Symmans et al. J Clin Oncol. 2007; Peintinger, Modern Pathology, 2015

RCB in 5161 patients: Prognosis varies by subtype



Yau, C et al. Lancet Onc 2022

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Neoadjuvant Chemotherapy for TNBC

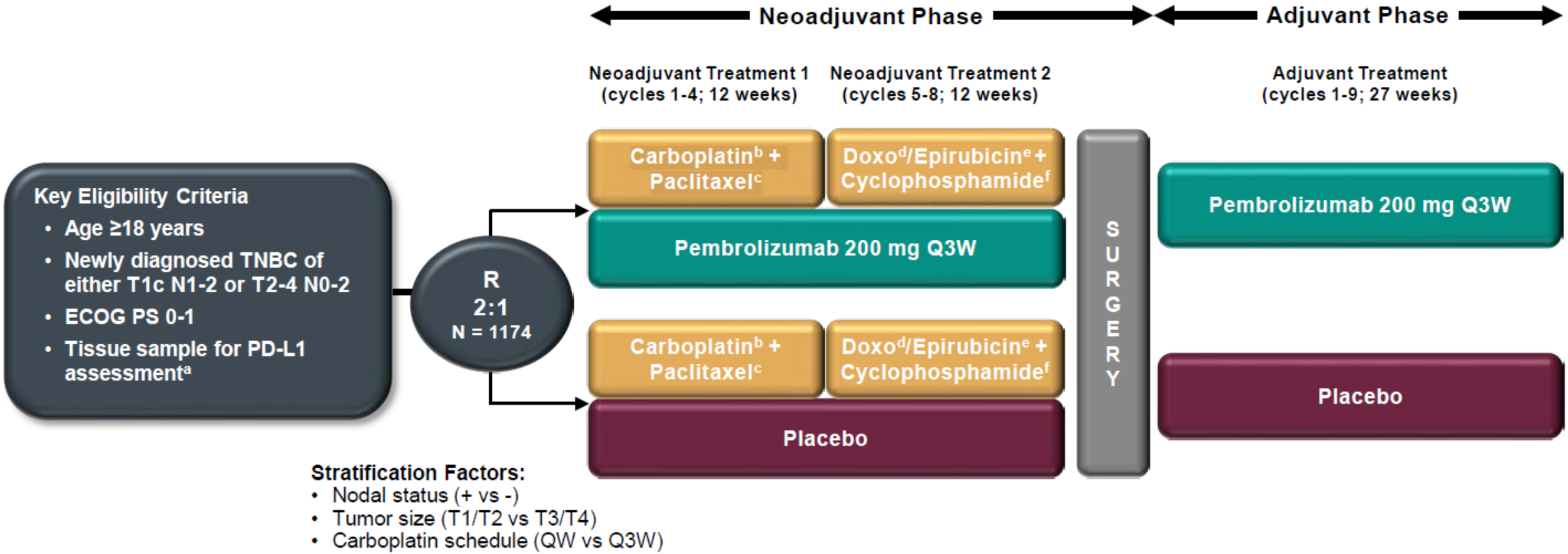
No targeted therapies available

- Anthracycline and Taxanes give best response
- Dose density
- Addition of carboplatin improves pCR and EFS

Recent advances

- TNBC is more immune-activated (increased TILs); implications for Immune therapy

KEYNOTE-522 Study Design (NCT03036488)



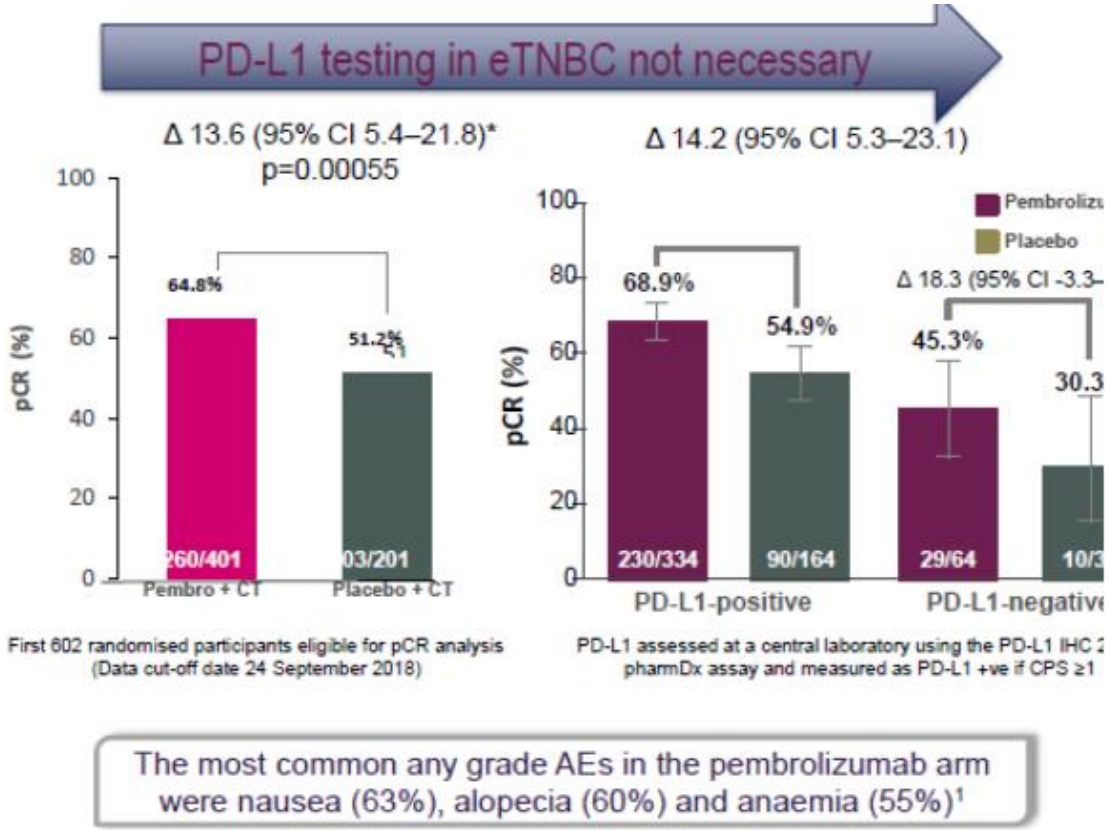
Stratification Factors:
- Nodal status (+ vs -)
- Tumor size (T1/T2 vs T3/T4)
- Carboplatin schedule (QW vs Q3W)

Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

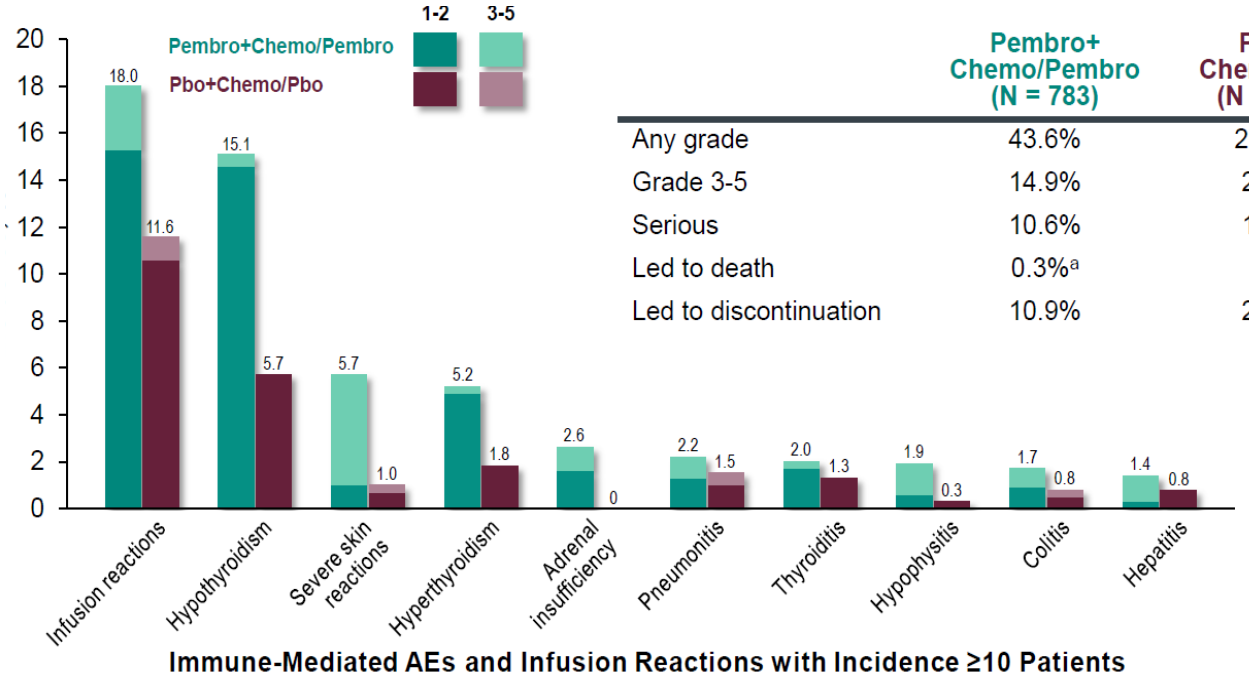
Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

Schmid P, ESMO Virtual Plenary 2021

KN-522 Response and Toxicity



The most common any grade AEs in the pembrolizumab arm were nausea (63%), alopecia (60%) and anaemia (55%)[1]



	Pembro+ Chemo/Pembro (N = 783)	Pbo+ Chemo/Pbo (N = 389)
Any grade	43.6%	21.9%
Grade 3-5	14.9%	2.1%
Serious	10.6%	1.3%
Led to death	0.3%[a]	0
Led to discontinuation	10.9%	2.6%

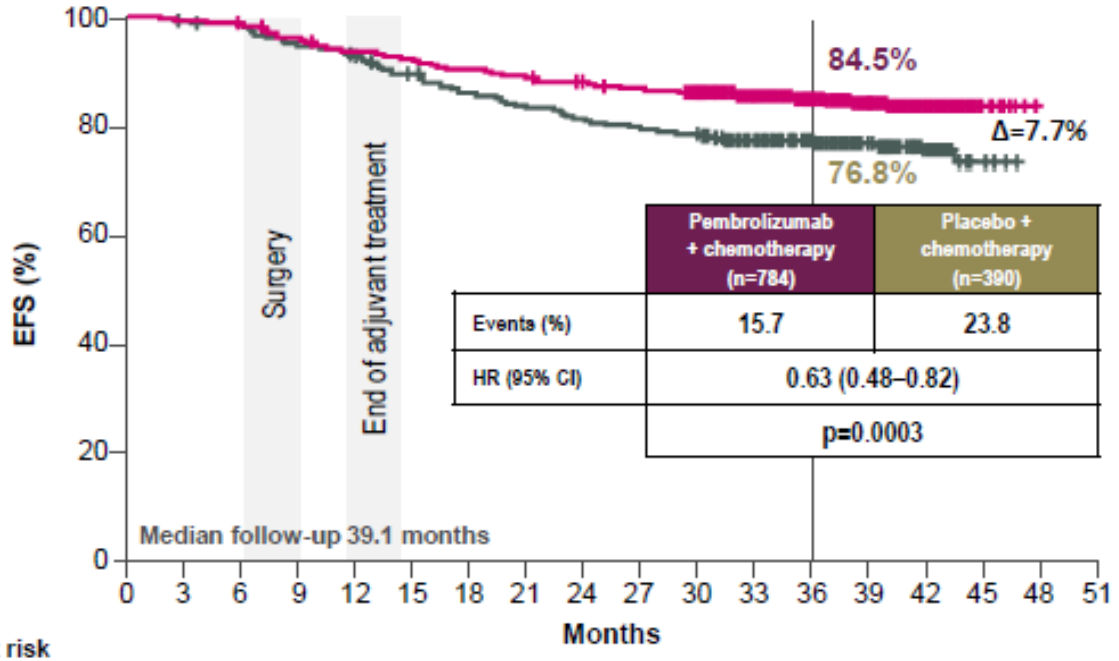
Immune-Mediated AEs and Infusion Reactions with Incidence ≥10 Patients

Schmid P, ESMO Virtual Plenary 2021, Schmid P NEJM 2022

KEYNOTE-522: EFS at IA4

KEYNOYTE-522[1] (IA4)
Pembrolizumab + CT vs placebo + CT in early TNBC

EFS in KEYNOTE-522 (IA4)[1]

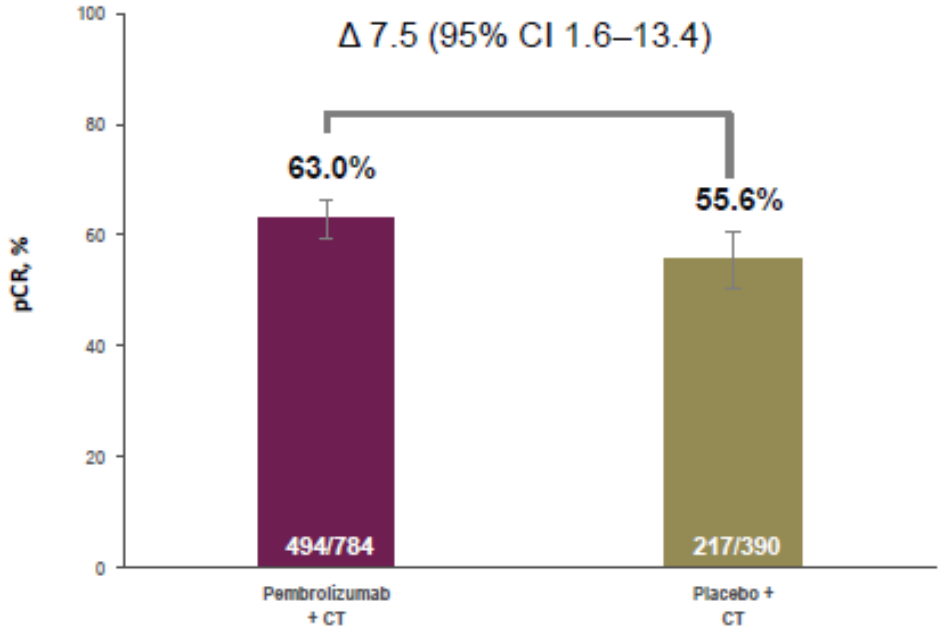


No. at risk

Pembrolizumab + CT	784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
Placebo + CT	390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0

KEYNOYTE-522 (IA3)*[2]
Pembrolizumab + CT vs placebo + CT in early TNBC

pCR in KEYNOTE-522 (IA3)[2]



All 1174 participants in ITT
(Data cut-off date 23 March 2020, median follow-up 26 months)

1. Schmid P, et al. Presented at ESMO Virtual Plenaries; 15–16 July 2021. Abstract VP7-2021. 2. Schmid P et al. New Engl J Med 2022 3. Pembrolizumab ODAC Briefing Document For Public Release. BLA 125514 Supplement-089. February 2021.

Neoadjuvant Therapy for HER2+ disease

- Anthracycline + taxane based chemotherapy
- Trastuzumab added significantly
- Pertuzumab added benefit (pCR and EFS) to chemo + trastuzumab
- Non-anthracycline regimens give equal results to anthracycline with less cardiac toxicity

Pivotal Studies on Neoadjuvant Trastuzumab/Pertuzumab for Patients With HER2+ EBC

Open-Label Phase II NeoSphere Study: Neoadjuvant Trastuzumab/Pertuzumab[1]

Chemo-naive women with HER2+ EBC (operable or LA/inflammatory); primary tumor > 2 cm (N = 417)

TH x 4 cycles (n = 107)	SURGERY	**FEC Q3W x 3** **Trastuzumab Q3W for 1 yr**
THP x 4 cycles (n = 107)		**FEC Q3W x 3** **Trastuzumab Q3W for 1 yr**
HP x 4 cycles (n = 107)		**Docetaxel Q3W x 4 → FEC Q3W x 3** **Trastuzumab Q3W for 1 yr**
TP x 4 cycles (n = 96)		**FEC Q3W x 3** **Trastuzumab Q3W for 1 yr**

Primary endpoint: pCR in breast (ITT)

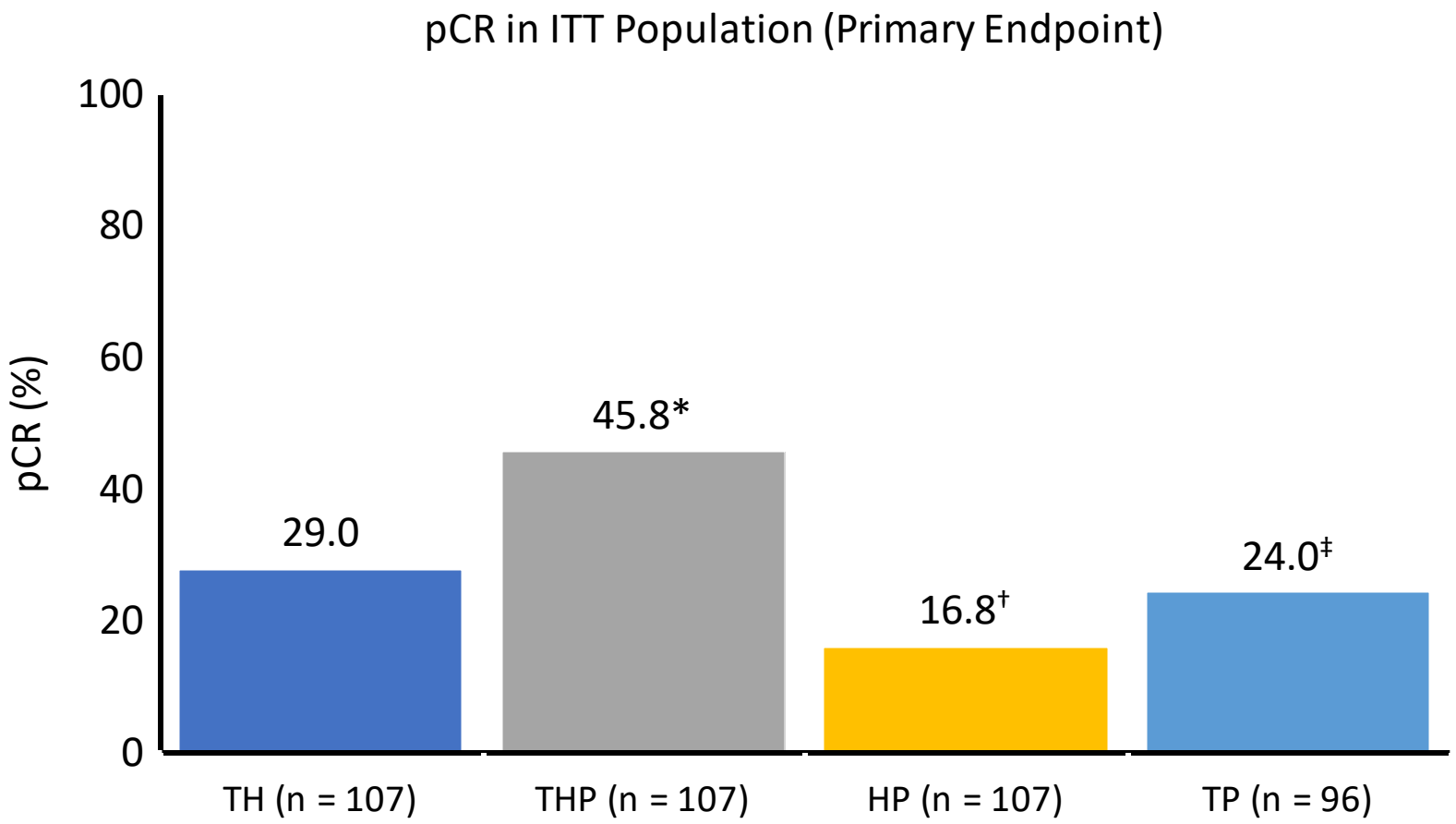
Phase II TRYPHAENA Cardiac Safety Study: Dual HER2 Targeting ± Anthracycline Tx[2]

Patients with operable, LA/inflammatory BC (N = 225)

FEC + HP x 3 cycles → **THP** x 3 cycles	**pCR assessed at surgery**	**Adjuvant tx to complete 1 yr of** trastuzumab →	Primary endpoint: Cardiac safety
FEC x 3 cycles → THP x 3 cycles			
TCHP x 6 cycles			

1. Gianni. Lancet Oncol. 2012;13:25. 2. Schneeweiss. Ann Oncol. 2013;24:2278.

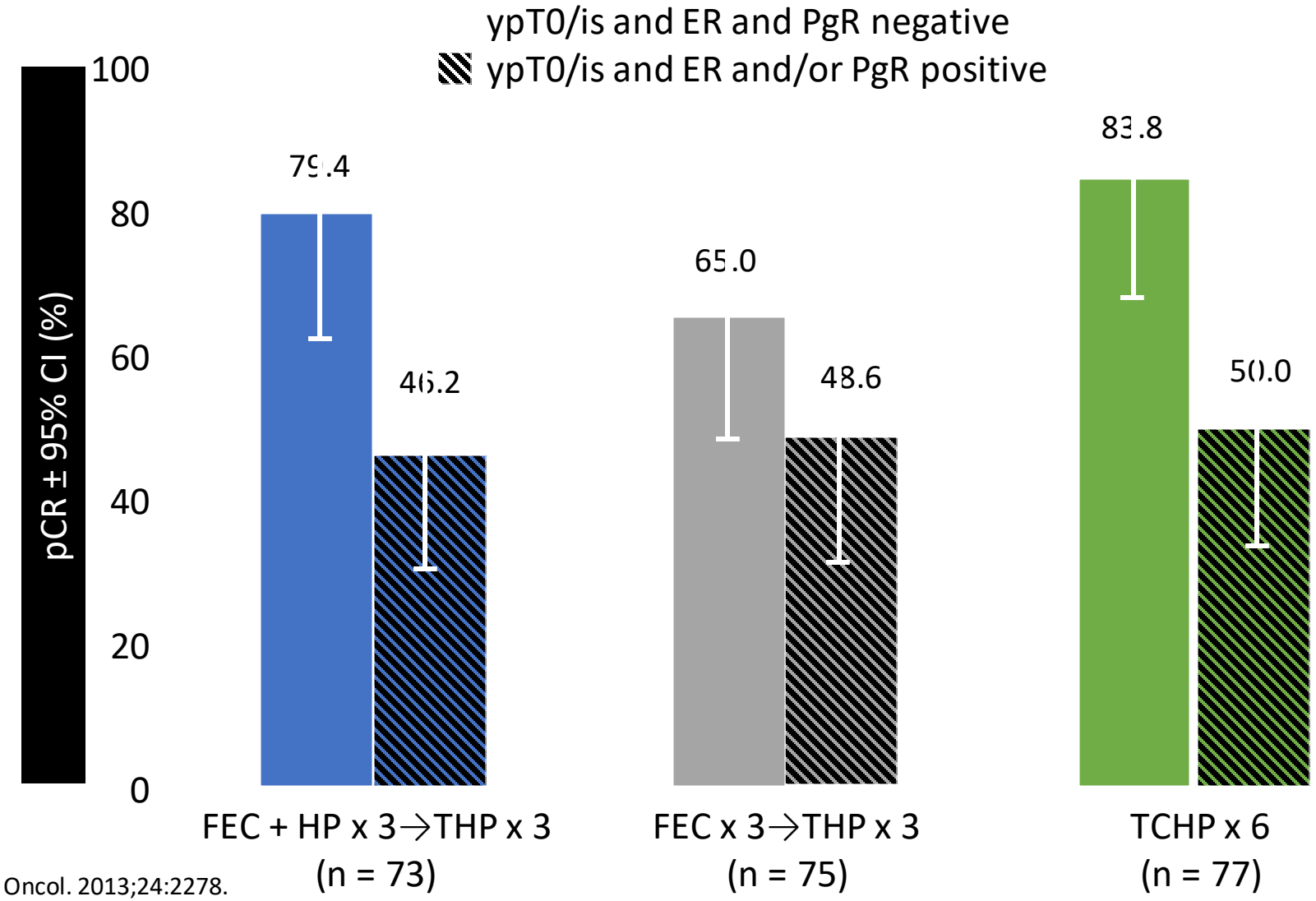
NeoSphere: Neoadjuvant Trastuzumab/Pertuzumab + CT Increases pCR Rates



P values vs TH: **P* = .0141; †*P* = .0198; ‡*P* = .003.

Gianni. Lancet Oncol. 2012;13:25.

TRYPHAENA: pCR (ypT0/is) by ER/PgR Status



Schneeweiss. Ann Oncol. 2013;24:2278.

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What to do about locoregional therapy after primary systemic therapy?

- Breast conservation vs. mastectomy?
- ALND vs. post-neoadjuvant SLNB?
- Radiation to RNIs or not?

  Post mastectomy RT?

Approach to Lumpectomy After Neoadjuvant Therapy

- Remove any suspicious clinical or radiologic findings
- Generous sample of “normal” breast tissue
- It is **NOT** necessary to remove the entire volume of tissue initially occupied by tumor

Sentinel Lymph Node Biopsy After Neoadjuvant Therapy
A Practical Approach

- Clinically node negative
  - SLN biopsy after NAC
  - Intraoperative Frozen Section of SLN
  - cALND for failed mapping
  - cALND for any positive LN including micrometastatic disease
  - Radiation tx decisions made with combination of pre-tx factors and final path status (nodes, breast)

MDACC Experience
Clipping the node for SLN after NAC

- **Clipped node +/- SLN to reflect the status of the nodal basin in all-comers undergoing NAC**

	N	Node +	pCR (%)	FNR (%)
Clipped node	191	120	37%	4.2% (95%CI 1.4-9.5)
SLN	118	74	37%	10.1% (95%CI 4.2-19.8)
SLN + clipped node	118	74	37%	1.4% (95%CI 0.03-7.3)

Also noted clipped node was not a SLN in 23% of pts

⟶ *"Targeted Axillary Dissection"*

Caudle AS et al JCO 2016;34(10):1072-8,
King T, SABCS 2016

Sentinel Lymph Node Biopsy After Neoadjuvant Therapy

- Clinically node positive (N1) converts to node negative
  - SLN biopsy after NAC w/ dual mapping agents
  - If node not clipped, remove at least 3 SLN,
  - If node clipped, clipped node + SLNs
  - Intraoperative frozen section of all nodes removed
  - cALND for
    - failed mapping
    - fewer than 3 SLN (or failure to retrieve clipped node)
    - any positive LN including micrometastatic disease/ITCs *(unless on trial)*

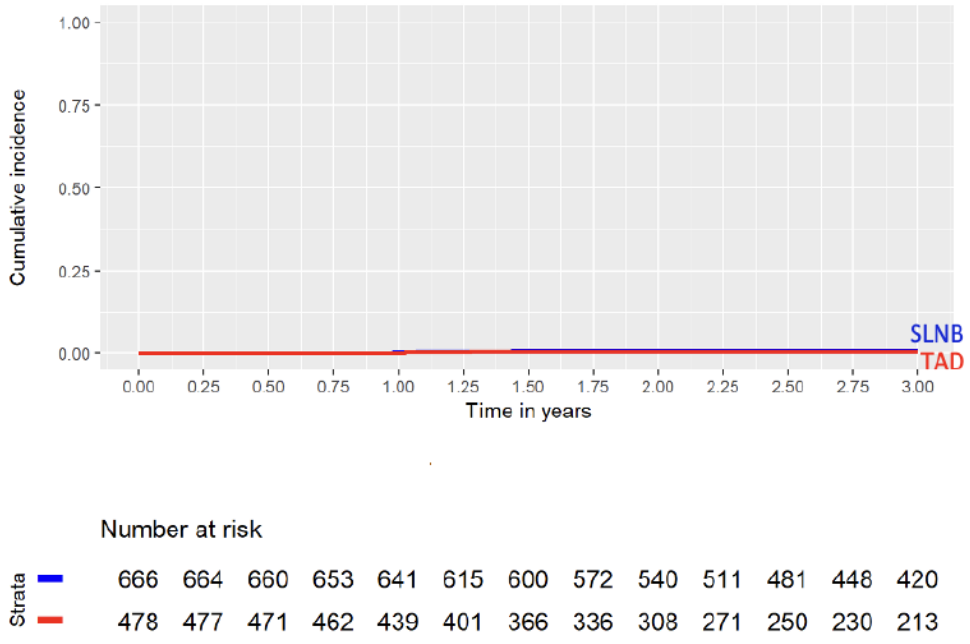
} To reduce FNR

Observational Trial of TAD vs. SLNB after NACT in cN+ pts

N= 1144

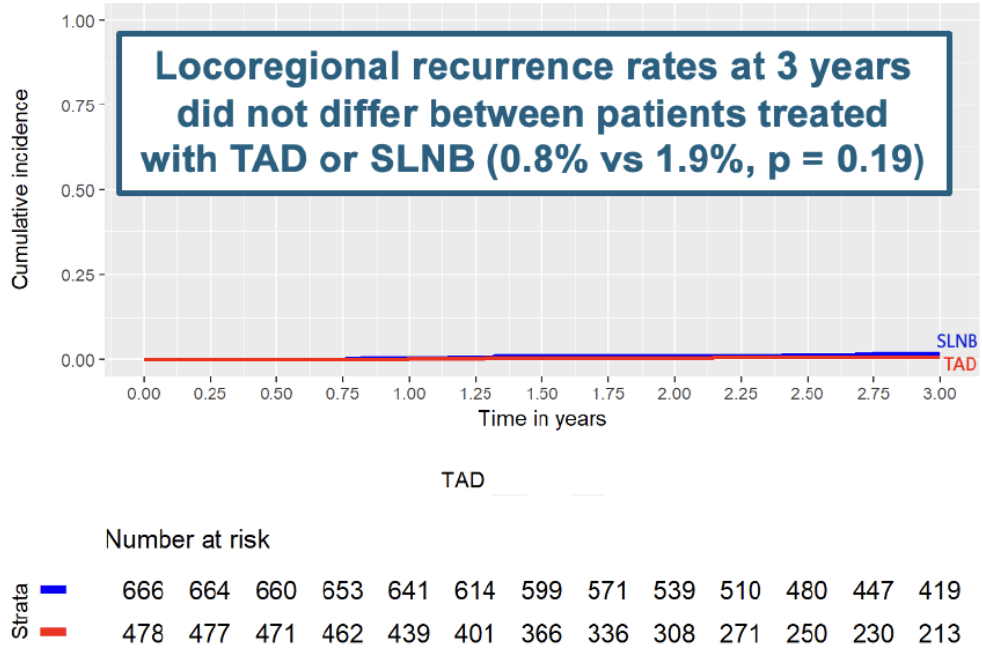
3 years median f/u

3-year rate of any axillary recurrence TAD vs SLNB (0.5% vs 0.8%, p = 0.55)



Overall cumulative incidence
- 3 year – **0.65%** (0.29-1.3)
- 5 year – 1.0% (0.49-2.0)

Locoregional recurrence rates at 3 years did not differ between patients treated with TAD or SLNB (0.8% vs 1.9%, p = 0.19)



Overall cumulative incidence
- 3 year – **1.5%** (0.83-2.4)
- 5 year – 2.7% (1.6-4.1)

Montagma, SABCS 2022

Post NAC Trials of Axillary Management

ALLIANCE A11202 Schema

Clinical T1-3 N1 M0 BC

Neoadjuvant Chemotherapy

BCT or Mastectomy
Sentinel Lymph Node Surgery

SLN Negative

SLN Positive

Randomization

ALND ⊕
Breast/chest wall and nodal XRT (no Axillary RT)

No further axillary surgery.
Breast/chest wall and nodal XRT (incl. Axilla)

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

Clinical T1-3 N1 M0 BC

Axillary nodal involvement
(FNA or core needle biopsy)

Neoadjuvant chemo (+ Anti-HER-2 therapy for HER-2 neu ⊕ pts)

Definitive surgery with histologic documentation of **negative axillary nodes** (by axillary dissection or by SLNB ± axillary dissection

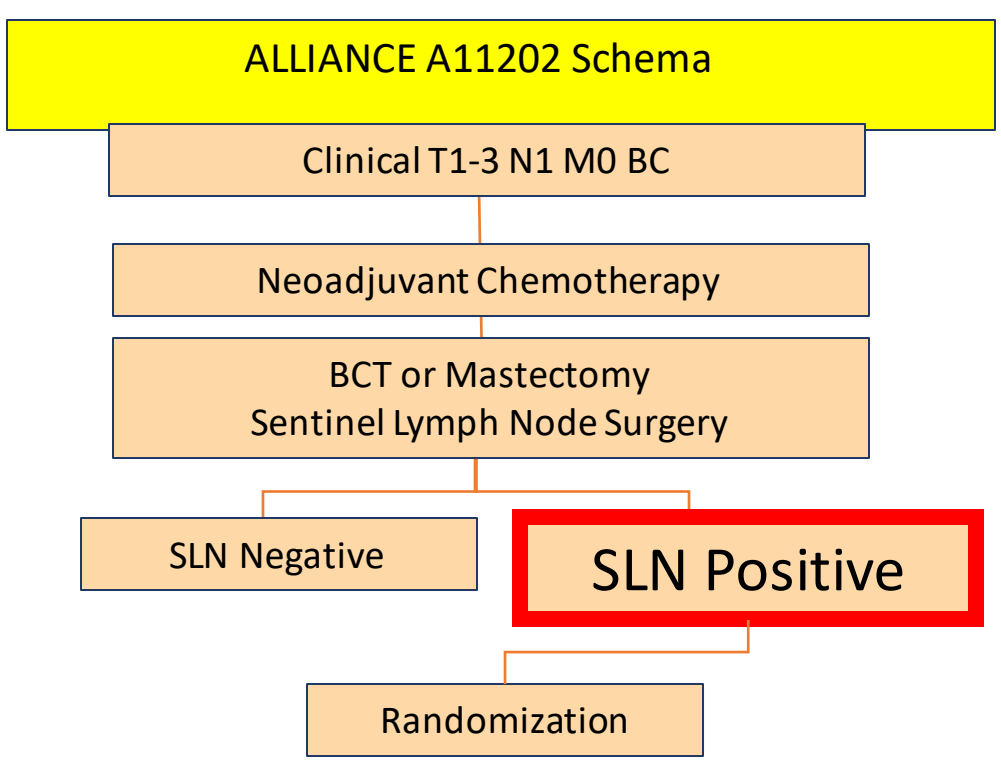
Stratification
Type of surgery (mastectomy vs lumpectomy)
ER status (+ vs -), HER-2 status (+ vs -)
pCR in breast (yes vs no)

Randomization

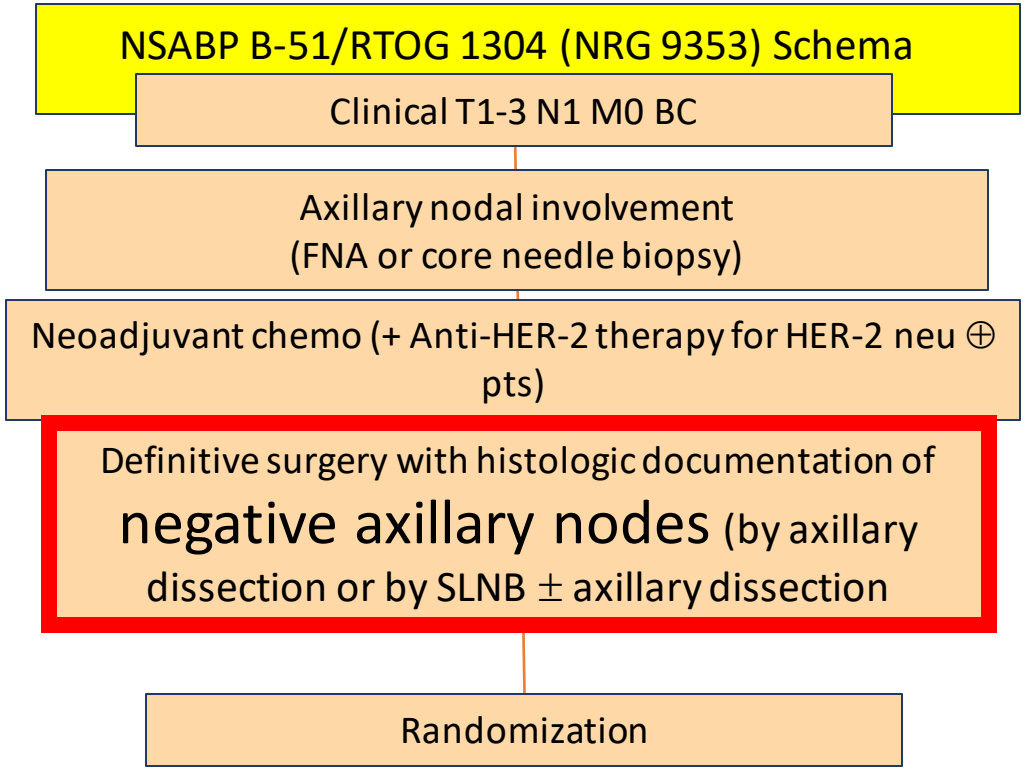
No Regional Nodal XRT
with breast XRT if BCS &
No chest wall XRT if mastectomy

Regional Nodal XRT
with breast XRT if BCS
and chest wall XRT if mastectomy

Post NAC Trials of Axillary Management



Can axillary RT replace ALND ?



Can response to NAC be used to select patients who do not need PMRT or extended nodal RT?

Adjuvant therapy after neoadjuvant therapy: For non-pCR patients

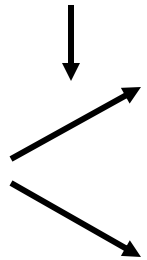
- HER2+: Additional anti-HER2 therapy (T-DM1)
- TNBC: Continue Pembro if by KN-522 +/-capecitabine
- HR+HER2-: Endocrine therapy + abemaciclib
- BRCA 1/2+: Olaparib

KATHERINE: Trastuzumab Emtansine vs Trastuzumab as Adjuvant Therapy for HER2+ EBC

- International, randomized, open-label phase III study

Stratified by clinical stage, HR status, single vs dual neoadjuvant HER2-targeted therapy, pathologic nodal status after neoadjuvant therapy

Patients with HER2+ EBC (cT1-4/N0-3/M0) **who had residual invasive disease in breast or axillary nodes** after neoadjuvant chemotherapy plus HER2-targeted therapy* at surgery
(N = 1486)



T-DM1† 3.6 mg/kg IV Q3W x 14 cycles
(n = 743)

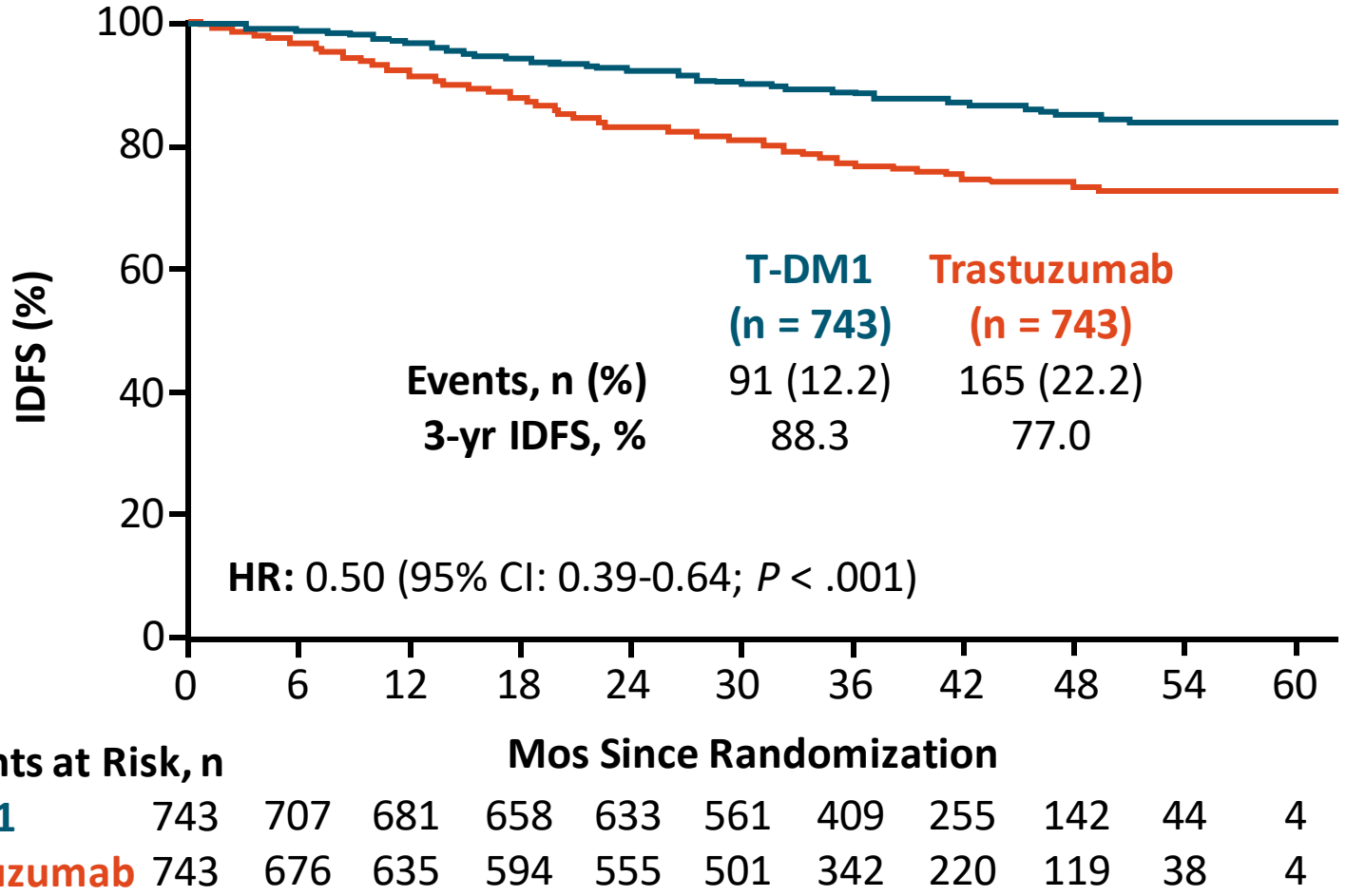
Trastuzumab 6 mg/kg IV Q3W x 14 cycles
(n = 743)

Randomization occurred within 12 wks of surgery; **radiotherapy and/or endocrine therapy given per local standards**. *Minimum of 9 wks taxane and trastuzumab. †Patients who d/c T-DM1 for toxicity allowed to switch to trastuzumab to complete 14 cycles.

- Primary endpoint: IDFS
- Secondary endpoints: distant recurrence-free survival, OS, safety

Geyer. SABCS 2018. Abstr GS1-10. von Minckwitz. NEJM. 2019;380:617.

KATHERINE: IDFS



First IDFS Event, %	T-DM1	T
Any	12.2	22.2
Distant recurrence	10.5*	15.9†
Locoregional recurrence	1.1	4.6
Contralateral breast cancer	0.4	1.3
Death without prior event	0.3	0.4

CNS events: *5.9% vs †4.3%.

von Minckwitz. NEJM. 2019;380:617.

OlympiA: Trial schema

- Local genetic testing or on-study central screening
  (Myriad Genetics Inc.)
- Germline pathogenic or likely pathogenic *BRCA1/2* mutation
- HER2–negative (hormone receptor–positive or TNBC)
- Stage II-III Breast Cancer or lack of PathCR to NACT

Neoadjuvant Group
- *TNBC:* non-pCR
- *Hormone receptor–positive:* non-pCR and CPS+EG score ≥ 3

≥ 6 cycles Neoadjuvant Chemotherapy → Surgery → +/- Radiotherapy

Adjuvant Group
- *TNBC:* ≥ pT2 or ≥ pN1
- *Hormone receptor–positive:* ≥ 4 positive lymph nodes

Surgery → ≥ 6 cycles Adjuvant Chemotherapy → +/- Radiotherapy

1:1 Randomization N=1836

Olaparib 300 mg twice daily for 1 year

Placebo twice daily for 1 year

Primary End Point
- Invasive disease-free survival (IDFS) by STEEP system[1]

Secondary End Points
- Distant disease-free survival[1] (DDFS)
- Overall survival[1] (OS)
- BRCA1/2 associated cancers
- Symptom / Health related QoL
- Safety

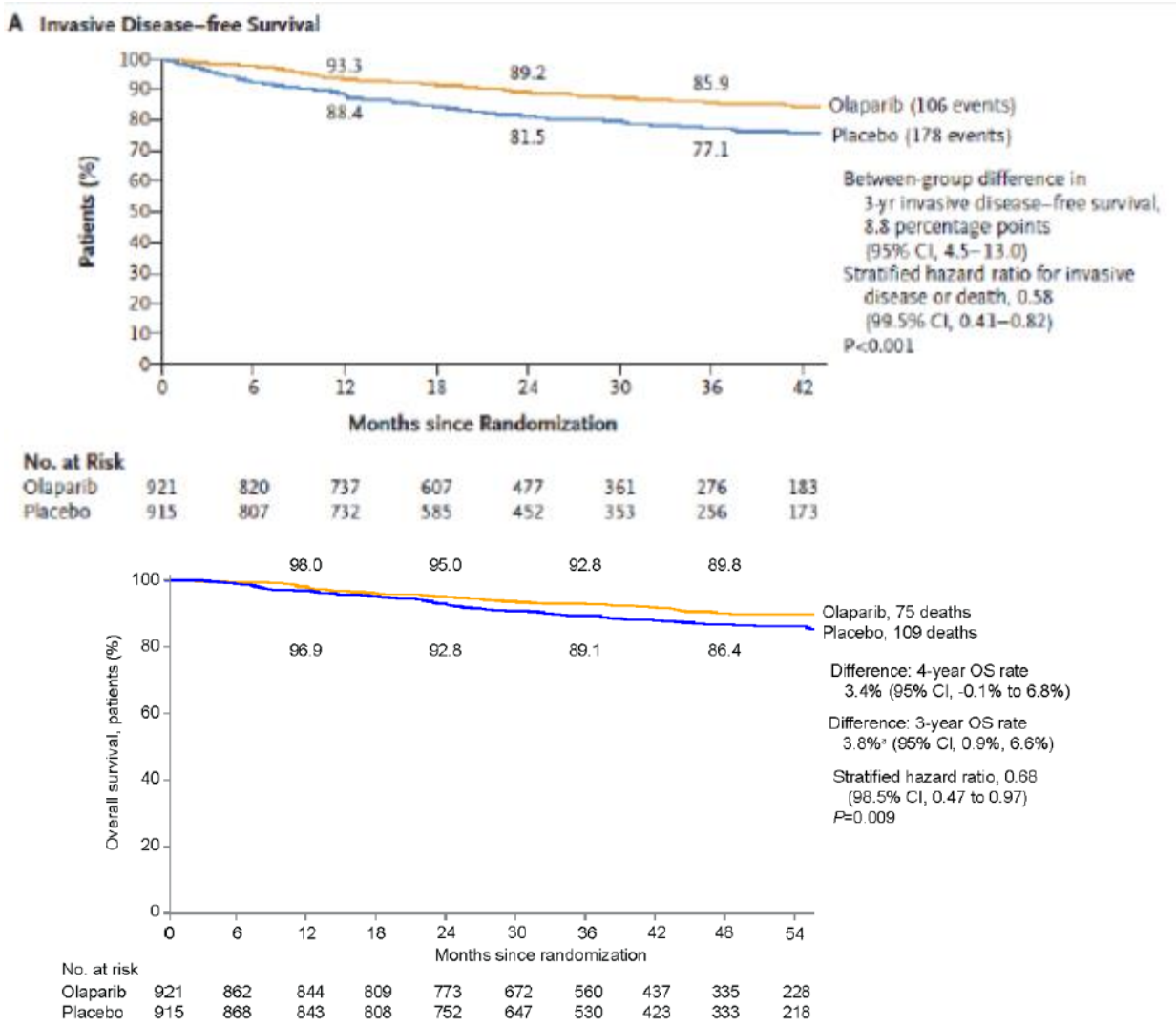
Stratification Factors
- Hormone receptor–positive vs. TNBC
- Neoadjuvant vs. adjuvant
- Prior platinum-based chemotherapy (yes vs. no)

Concurrent Adjuvant Therapy
- Endocrine therapy
- Bisphosphonates
- No 2nd Adjuvant Chemotherapy

Hormone receptor +ve defined as ER and/or PgR positive (IHC staining ≥ 1%)
Triple Negative defined as ER and PgR negative (IHC staining < 1%)
[1]Hudis CA, J Clin Oncol 2007

Presented By: Andrew Tutt MB ChB PhD FMedSci
The Institute of Cancer Research and Kings College London

OlympiA: Results



8.8% absolute Improvement At 3 years

3.4% absolute improvement at 4 years

- All HER 2- patients with less than pCR to NACT should be tested for BRCA 1/2 germline mutations
- Combinations of IO/Olaparib, Olaparib/endocrine are feasible

Tutt, A NEJM 2021;Geyer, C et. al Ann Onc Sept 2022

MonarchE Update: Adjuvant Abemaciclib after NACT/adjuvant for high-risk HR+HER2-

monarchE Study Design (NCT03155997)

HR+, HER2-, node positive high-risk EBC
- Women or men
- Pre-/postmenopausal
- With or without prior neo- and/or adjuvant chemotherapy
- No metastatic disease
- Maximum of 16 months from surgery to randomization and 12 weeks of ET following the last non-ET

Cohort 1: High risk based on **clinical pathological features**
- ≥4 ALN OR
- 1-3 ALN and at least 1 of the below:
  - Grade 3 disease
  - Tumor size ≥5 cm

Cohort 2: High risk based on **Ki-67**
- 1-3 ALN and
- Ki-67 ≥20% and
- Grade 1-2 and tumor size <5 cm

Stratified for:
- Prior chemotherapy
- Menopausal status
- Region

R 1:1
N = 5637

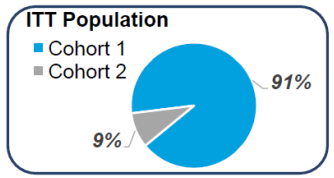
On-study treatment period
2 years

Abemaciclib
(150mg twice daily)
+
Endocrine Therapy: AI or tamoxifen

Endocrine Therapy: AI or tamoxifen

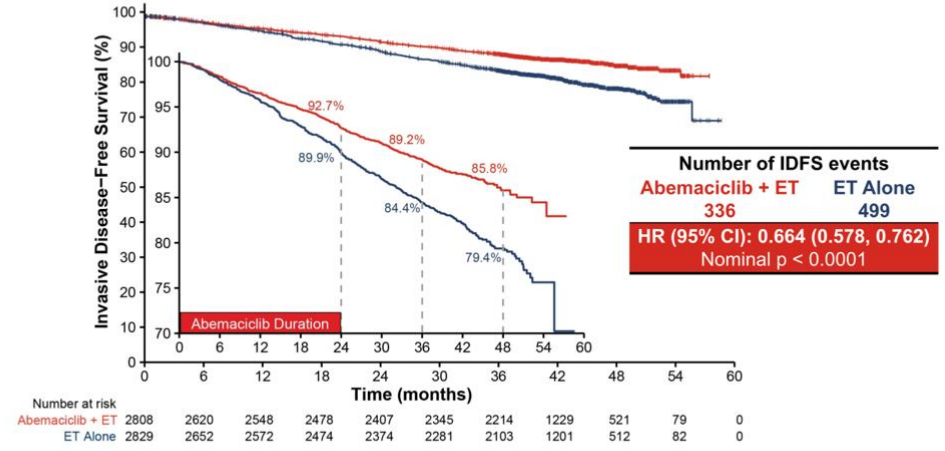
Follow-up period
Endocrine Therapy
3-8 years as clinically indicated

Primary Objective: IDFS
Secondary Objectives: IDFS in high Ki-67 populations, DRFS, OS, Safety, PK, PRO



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

IDFS Benefit in ITT Persists Beyond Completion of Abemaciclib



33.6% reduction in the risk of developing an IDFS event with an increase in absolute benefit in IDFS 4-year rates (6.4%) compared to 2-and 3-year IDFS rates (2.8% and 4.8% respectively)

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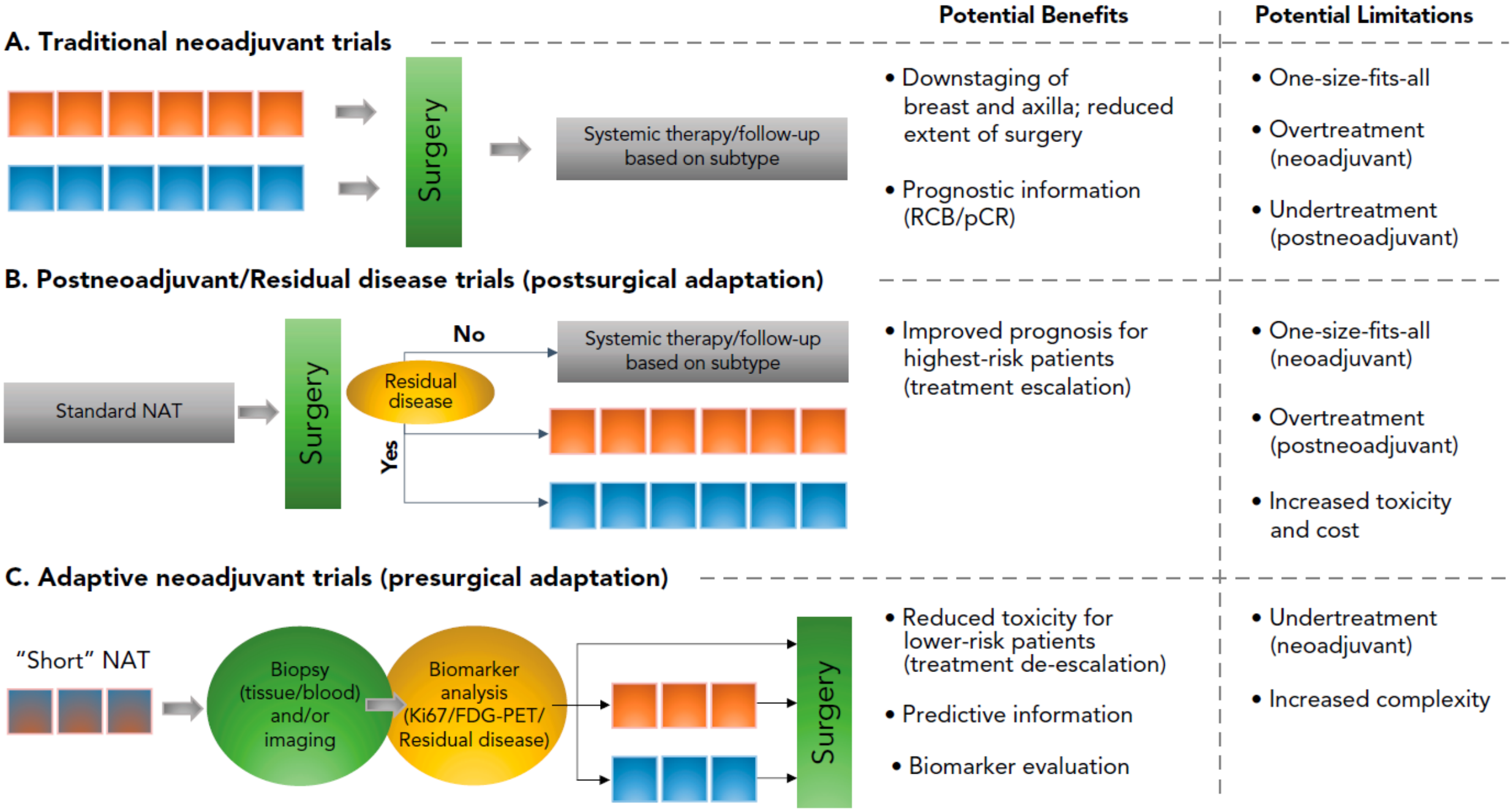
Johnston SRD, et. al. San Antonio Breast Cancer Symposium 2022

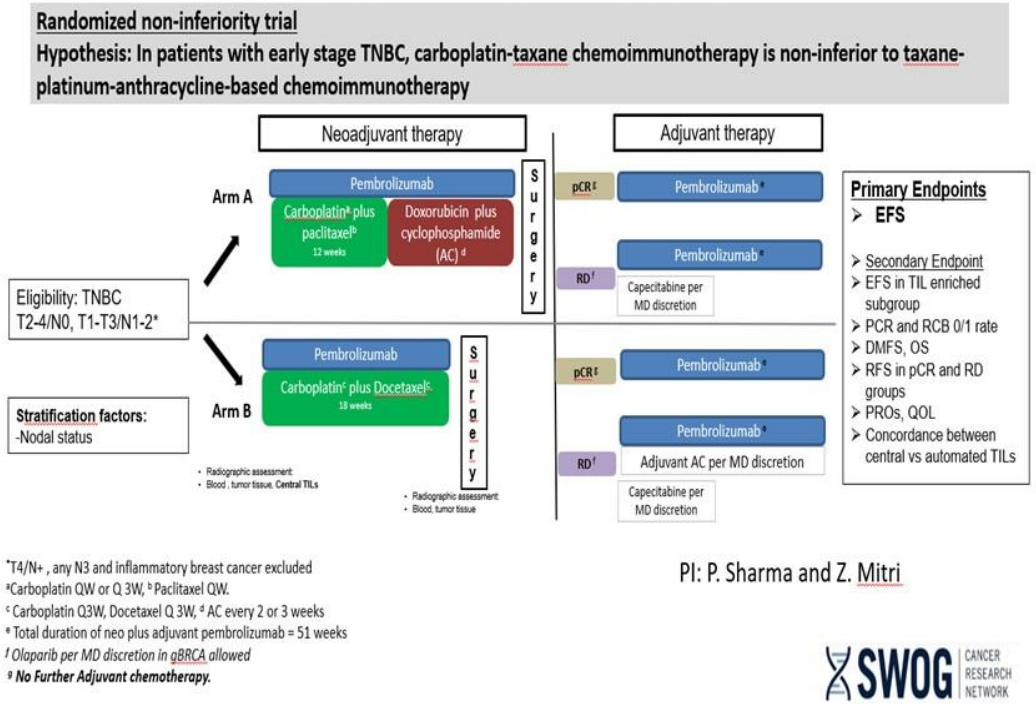
Renown Health
Pennington
Cancer Institute


Potential Benefits
Potential Limitations
A. Traditional neoadjuvant trials
Surgery
Systemic therapy/follow-up based on subtype
• Downstaging of breast and axilla; reduced extent of surgery
• Prognostic information (RCB/pCR)
• One-size-fits-all
• Overtreatment (neoadjuvant)
• Undertreatment (postneoadjuvant)
B. Postneoadjuvant/Residual disease trials (postsurgical adaptation)
Standard NAT
Surgery
Residual disease
No
Yes
Systemic therapy/follow-up based on subtype
• Improved prognosis for highest-risk patients (treatment escalation)
• One-size-fits-all (neoadjuvant)
• Overtreatment (postneoadjuvant)
• Increased toxicity and cost
C. Adaptive neoadjuvant trials (presurgical adaptation)
"Short" NAT
Biopsy (tissue/blood) and/or imaging
Biomarker analysis (Ki67/FDG-PET/ Residual disease)
Surgery
• Reduced toxicity for lower-risk patients (treatment de-escalation)
• Predictive information
• Biomarker evaluation
• Undertreatment (neoadjuvant)
• Increased complexity

Neoadjuvant chemo-immunotherapy for TNBC
Treatment optimization

- Treatment de-escalation: Do all patients need 4-drug poly-chemotherapy when immunotherapy is part of neoadjuvant systemic therapy?
  - I-SPY 2.2: Ongoing arms assessing novel agents/combinations to allow early de-escalation
  - Chemotherapy de-escalation: S2212 (SCARLET)
- Treatment escalation: Early identification of patients unlikely to achieve optimal response with standard neoadjuvant treatment
  - Tissue, Imaging +/- Machine learning/AI, Circulating biomarkers (ctDNA)
  - Neoadjuvant testing of novel more effective therapies
- Preferential immunotherapy response biomarkers

Shorter anthracycline-free Chemoimmunotherapy Adapted to pathological Response in Early TNBC (SCARLET)



*T4/N+ , any N3 and inflammatory breast cancer excluded
[a]Carboplatin QW or Q 3W, [b] Paclitaxel QW.
[c] Carboplatin Q3W, Docetaxel Q 3W, [d] AC every 2 or 3 weeks
[e] Total duration of neo plus adjuvant pembrolizumab = 51 weeks
[f] *Olaparib per MD discretion in gBRCA allowed*
[g] ***No Further Adjuvant chemotherapy.***

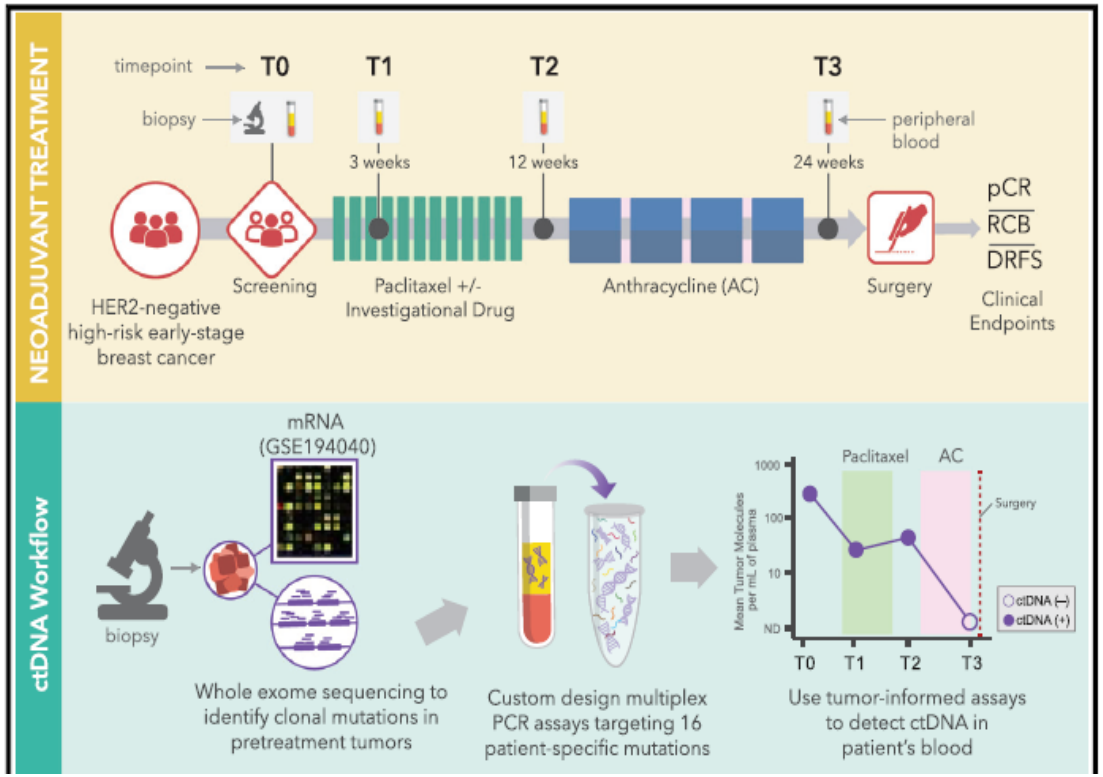
PI: P. Sharma and Z. Mitri

SWOG CANCER RESEARCH NETWORK

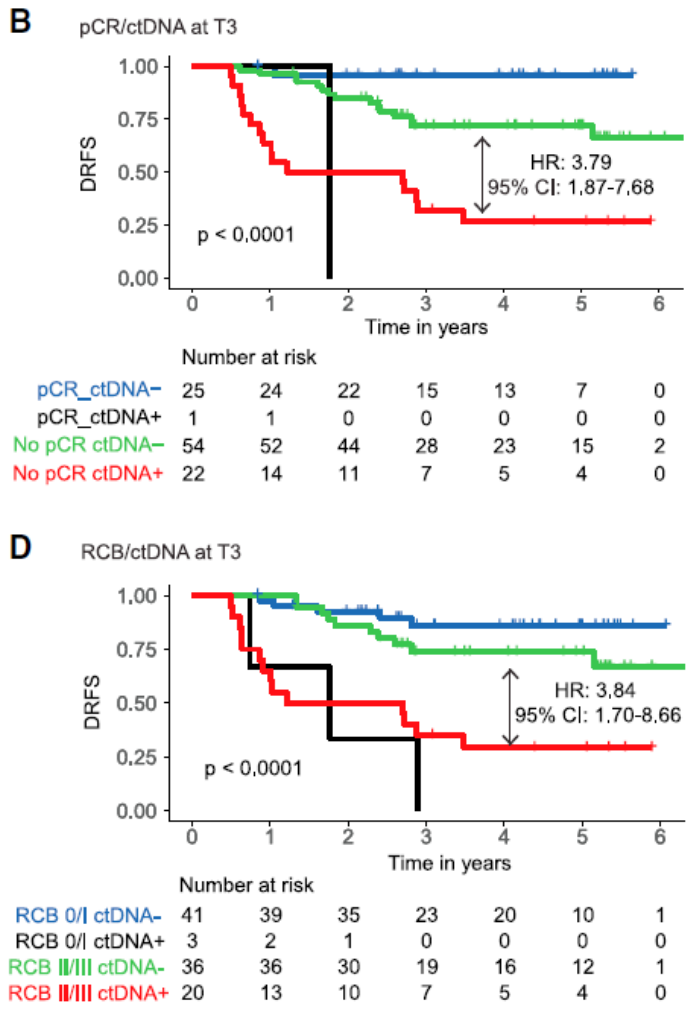
"True optimization is the revolutionary contribution of modern research to decision processes."
George Dantzig

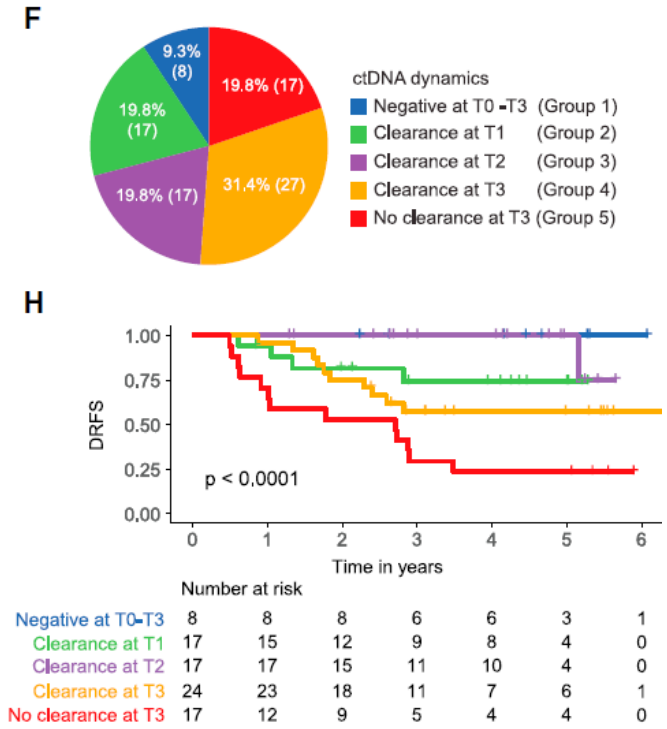
Improving Neoadjuvant/adjuvant chemotherapy through sequential ctDNA

I-SPY2 Samples



TNBC





Magbuana MJ, et al Cancer Cell June 2023

Conclusions

- Treatment for early-stage breast cancer has evolved substantially and improves survival with less toxicity
- Multidisciplinary planning before treatment essential for best outcomes
- Primary systemic therapy indicated for many TNBC and HER2+ cancers
- pCR is a reliable surrogate marker for outcome
- Less than pCR requires systemic adjuvant therapy based on biomarkers
- Local therapy is modified based on treatment response
- New approaches (IO, ADCs) will continue to improve outcomes

THANK YOU!