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Supportive care in breast cancer

Brussels / Belgium / 27/01/2023

SAN ANTONIO BREAST CANCER SYMPOSIUM®

Mays Cancer Center UT Health San Antonio MD Anderson Cancer Center

AACR American Association for Cancer Research

SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM®

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LICENSED BY ENCORE MEDICAL EDUCATION

Disclosures

- <u>Consulting or Advisory role:</u>

  MSD, Eli Lilly, Astra Zeneca

- <u>Speaker Honoraria:</u>

  Eli Lilly, Astra Zeneca, MSD, Leopharma, Daichy Sankyo

- <u>Travel Support to Academic Meetings:</u>

  MSD, Pfizer, Roche, Gilead, Astra Zeneca, Eli Lilly

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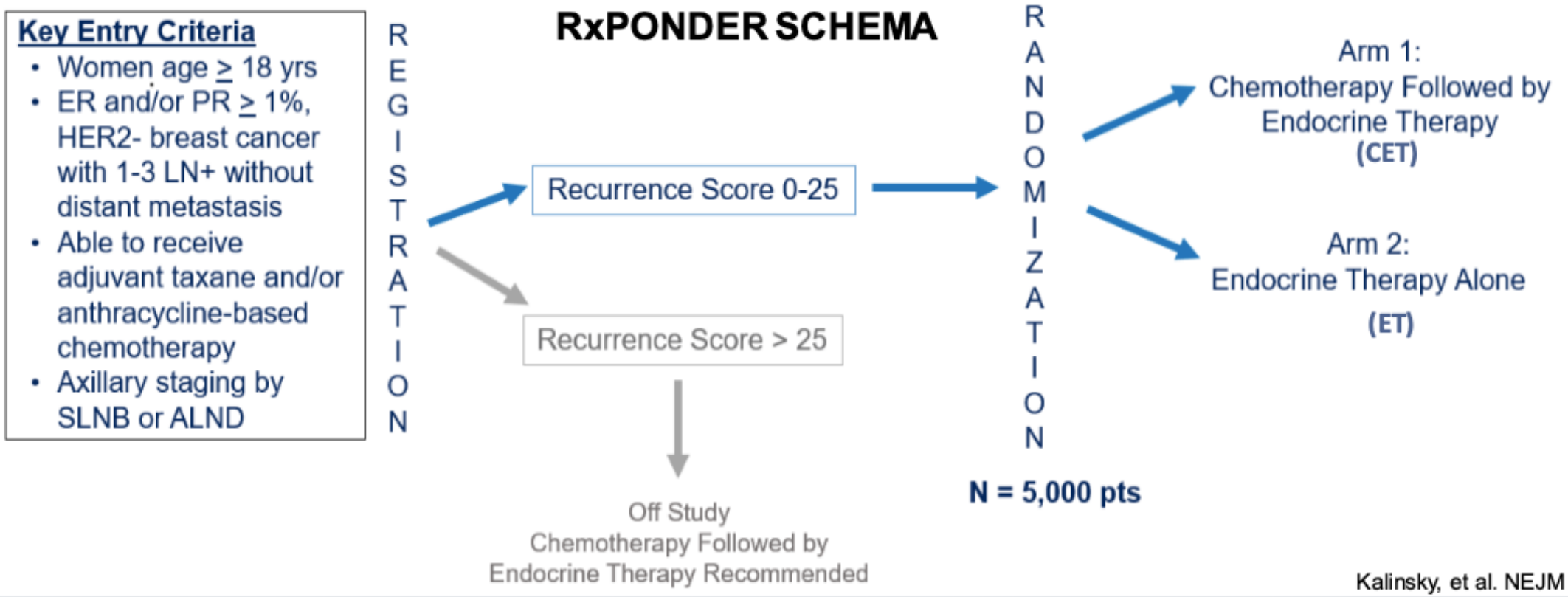
GS1-01: Race and Clinical Outcomes in the RxPONDER Trial: A Clinical Trial Rx for Positive Node, Endocrine Responsive Breast Cancer (SWOG S1007)

Presented by Yara Abdou

- RxPONDER: Clinical utility of the 21-gene RS in pts with HR+, HER2- breast cancer and 1-3 positive lymph nodes (1-3 LN+)



Kalinsky, et al. NEJM 2021

Race and clinical outcome in RxPonder

Background

- US Black women have 4% lower incidence of breast cancer compared to White women
- US Black women have 40% higher breast cancer mortality compared to White women

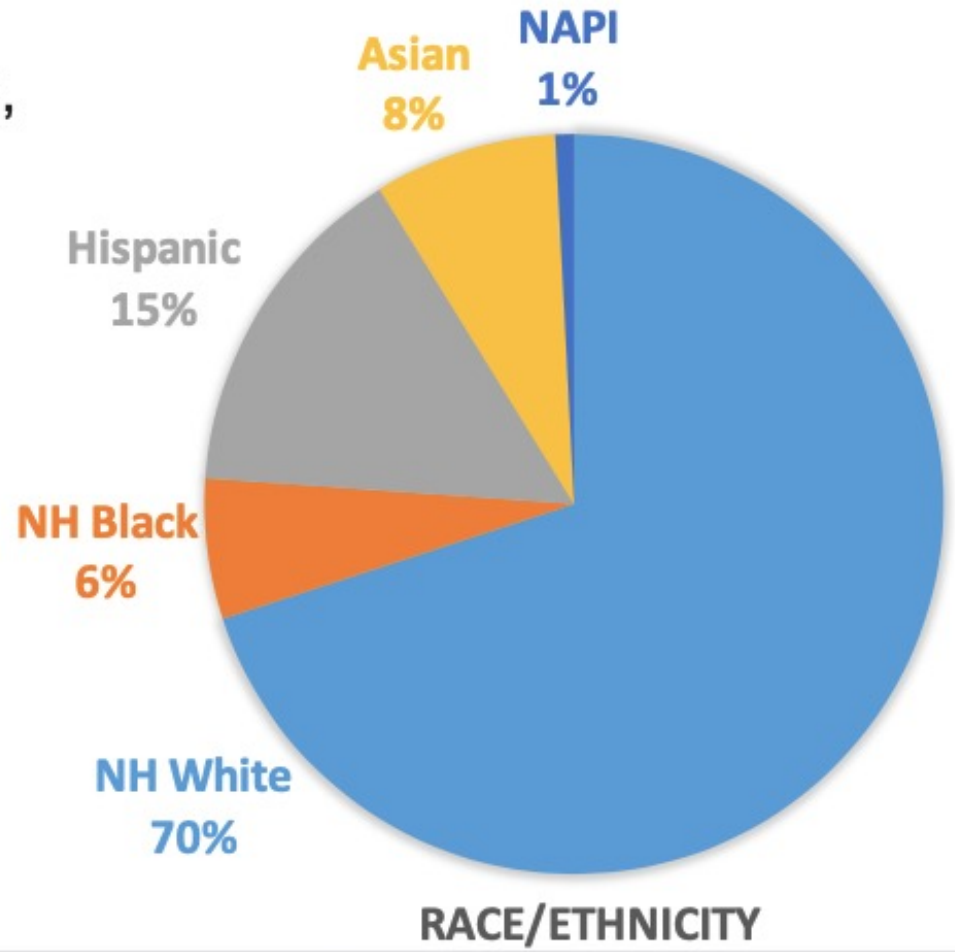
Objectives

- Evaluation of entire cohort by race for IDFS and DRFS
- Determine if race is independently prognostic
- Determine if race is predictive of treatment benefit

18.7% were excluded due to unreported race

A total of **4,048** women with HR+/HER2- BC, 1-3 LN+, RS ≤ 25 and known race/ethnicity were included:

- 2,833 Non-Hispanic (NH) White pts (70%)
- 248 NH Black pts (6.1%)
- 610 Hispanic pts (15.1%)
- 324 Asian pts (8.0%)
- 33 NAPI pts (0.8%)



Clinicopathologic characteristics by Race and Ethnicity

	NH White (n=2,833)	NH Black (n=248)	Asian (n=324)	NAPI (n=33)	Hispanic (n=610)
MEDIAN AGE (RANGE)	58 (28 – 87)	58 (18 – 86)	50 (28 – 76)	58 (42 – 74)	55 (28 – 79)
MENOPAUSAL STATUS					
Pre-menopausal	30%	23%	58%	27%	38%
Post-menopausal	71%	77%	42%	73%	62%
POSITIVE NODES					
1 node	66%	67%	73%	70%	65%
2 nodes	25%	22%	21%	24%	27%
3 nodes	9%	11%	6%	6%	9%
TUMOR SIZE					
T1	60%	55%	52%	64%	61%
T2	36%	41%	45%	36%	35%
T3	4%	3%	4%	0%	4%

Clinicopathologic characteristics by Race and Ethnicity

	NH White (n=2,833)	NH Black (n=248)	Asian (n=324)	NAPI (n=33)	Hispanic (n=610)
RECURRENCE SCORE					
0-13	42%	42%	42%	39%	43%
14-25	58%	58%	58%	61%	57%
HISTOLOGIC GRADE					
Low	27%	22%	14%	15%	27%
Intermediate	62%	60%	79%	64%	58%
High	10%	18%	7%	21%	14%
BODY MASS INDEX					
< 20	4%	2%	13%	4%	3%
20-24	27%	6%	47%	23%	24%
25-29	31%	29%	32%	35%	35%
30-34	21%	27%	6%	12%	22%
35+	18%	35%	2%	27%	16%

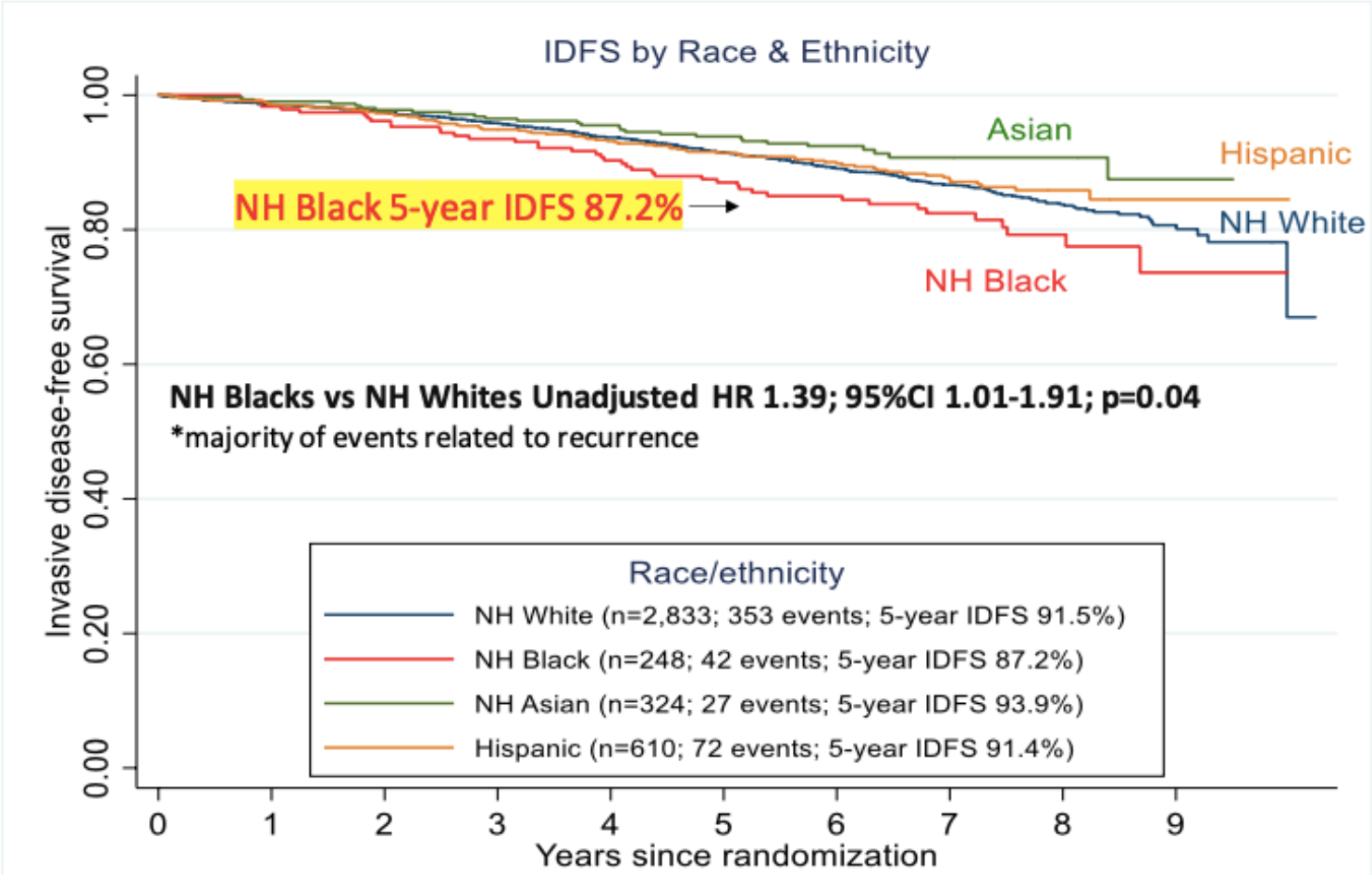
Treatment type by Non-Hispanic White or Black Race

Primary Treatment Type among Women Randomized to Chemotherapy

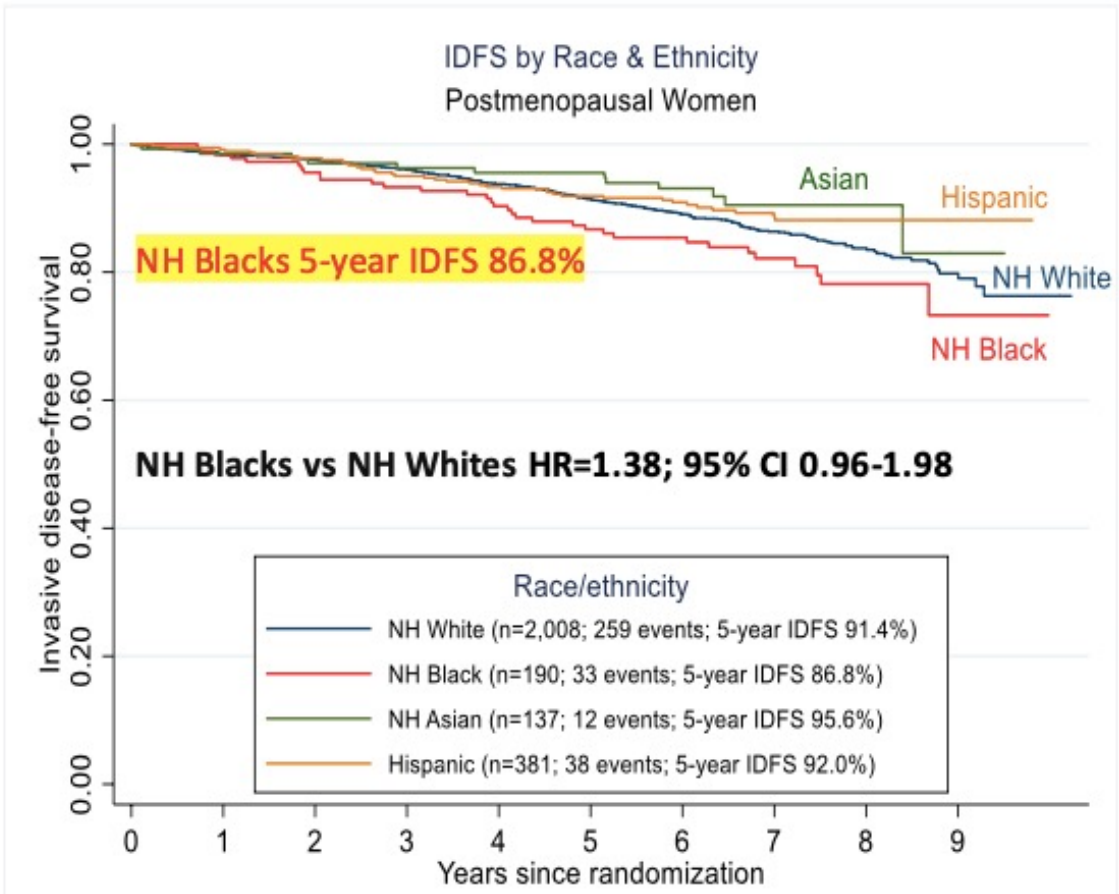
	Anthracycline +/- Taxane	Taxane/ cyclophosphamide
Premenopausal NH White	187 (53%)	168 (47%)
Premenopausal NH Black	9 (33%)	18 (67%)
Postmenopausal NH White	261 (33%)	537 (67%)
Postmenopausal NH Black	26 (32%)	55 (68%)

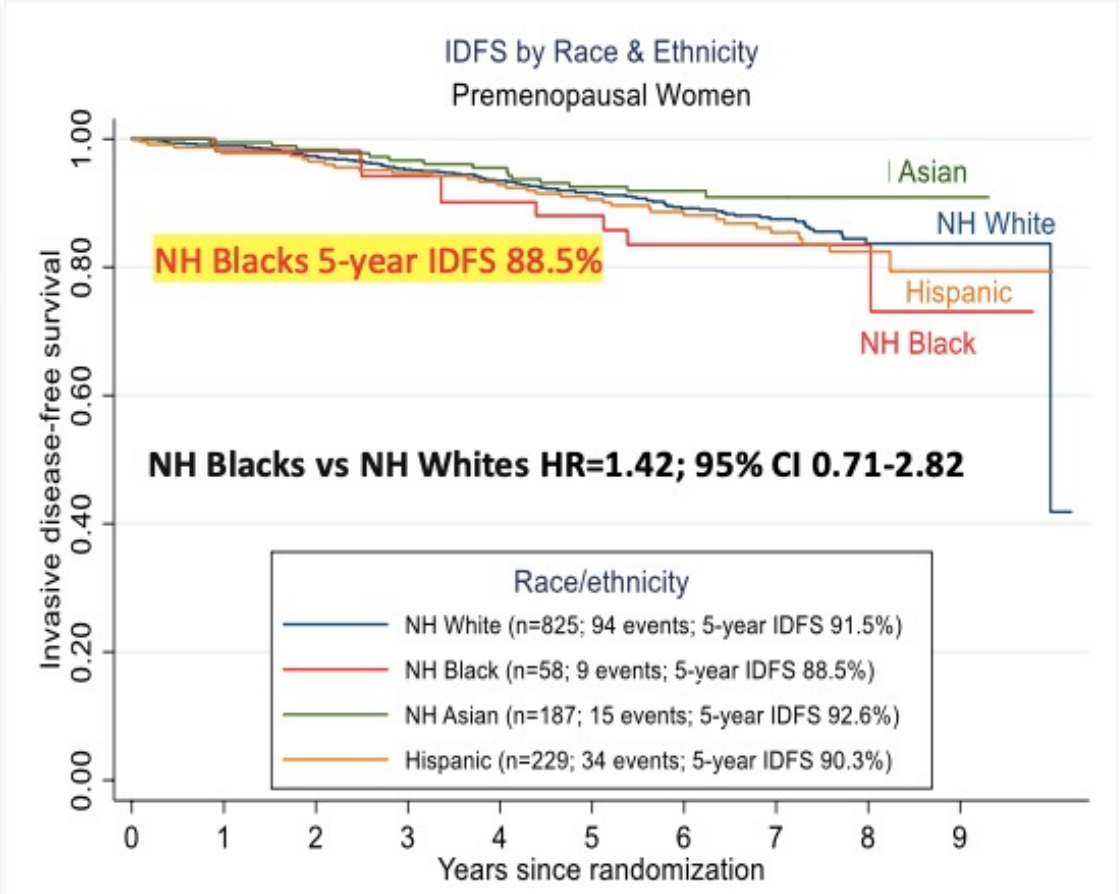
*Endocrine therapy selection was similar for NH White and Black Race (data not shown)

IDFS by Race and Ethnicity



IDFS by Race/Ethnicity and menopausal status





IDFS Multivariable Cox Regression for Race/Ethnicity

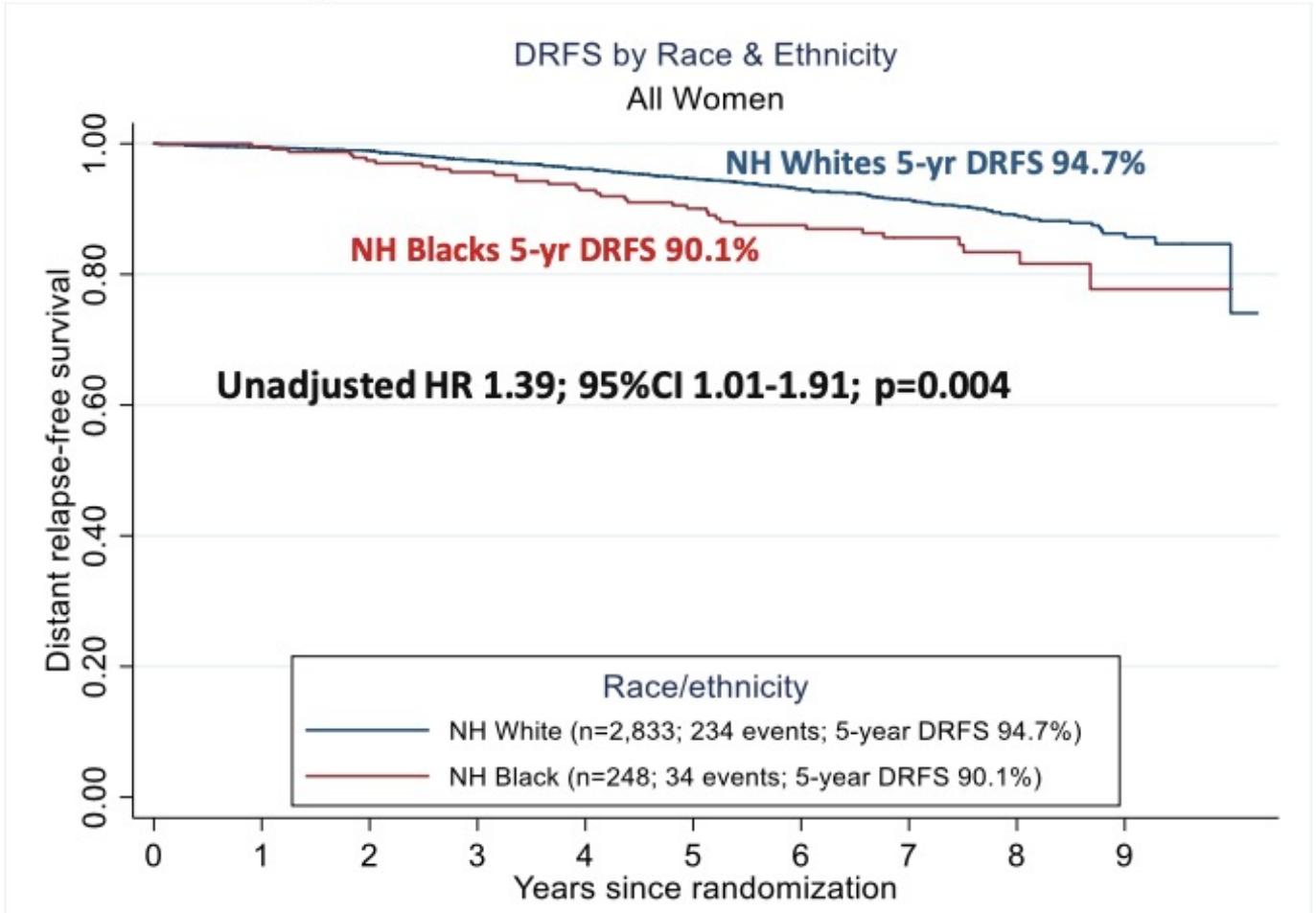
RACE	Adjusted Hazard Ratio (HR); 95% CI
NH Blacks vs NH Whites	HR=1.37; 95% CI 1.00-1.90; p=0.05
Asian vs NH Whites	HR=0.67; 95% CI 0.45-1.00; p=0.05
Hispanic vs NH Whites	HR=0.92; 95% CI 0.71-1.19; p=0.55

HR adjusted for RS, treatment arm, menopausal status, age, and grade

RACE	Adjusted Hazard Ratio (HR); 95% CI
NH Blacks vs NH Whites	HR=1.21; 95% CI 0.81-1.82; p=0.35
Asian vs NH Whites	HR=0.74; 95% CI 0.48-1.13; p=0.17
Hispanic vs NH Whites	HR=0.98; 95% CI 0.74-1.29; p=0.87

HR adjusted for RS, treatment arm, menopausal status, age, grade and BMI

DRFS by NH White and Black Race



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DRFS Multivariable Cox Regression

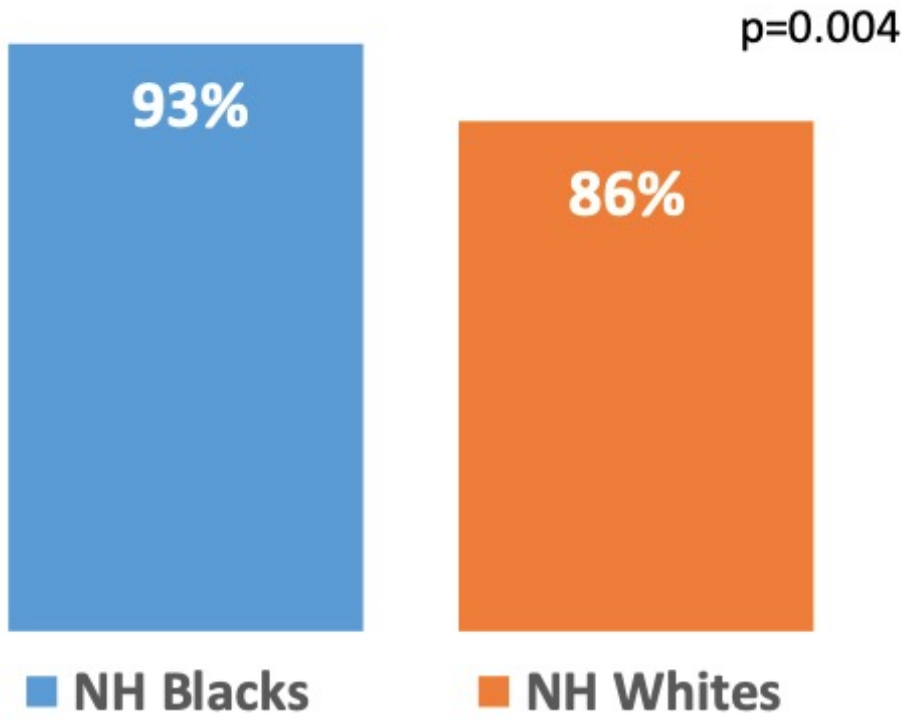
RACE	Adjusted Hazard Ratio (HR); 95% CI
NH Blacks vs NH Whites	HR=1.71; 95% CI 1.19-2.45; p=0.004

HR adjusted for RS, treatment arm, menopausal status, age, and grade

RACE	Adjusted Hazard Ratio (HR); 95% CI
NH Blacks vs NH Whites	HR=1.31; 95% CI 0.81-2.10; p=0.27

HR adjusted for RS, treatment arm, menopausal status, age, grade and BMI

Accepted Treatment Assignment



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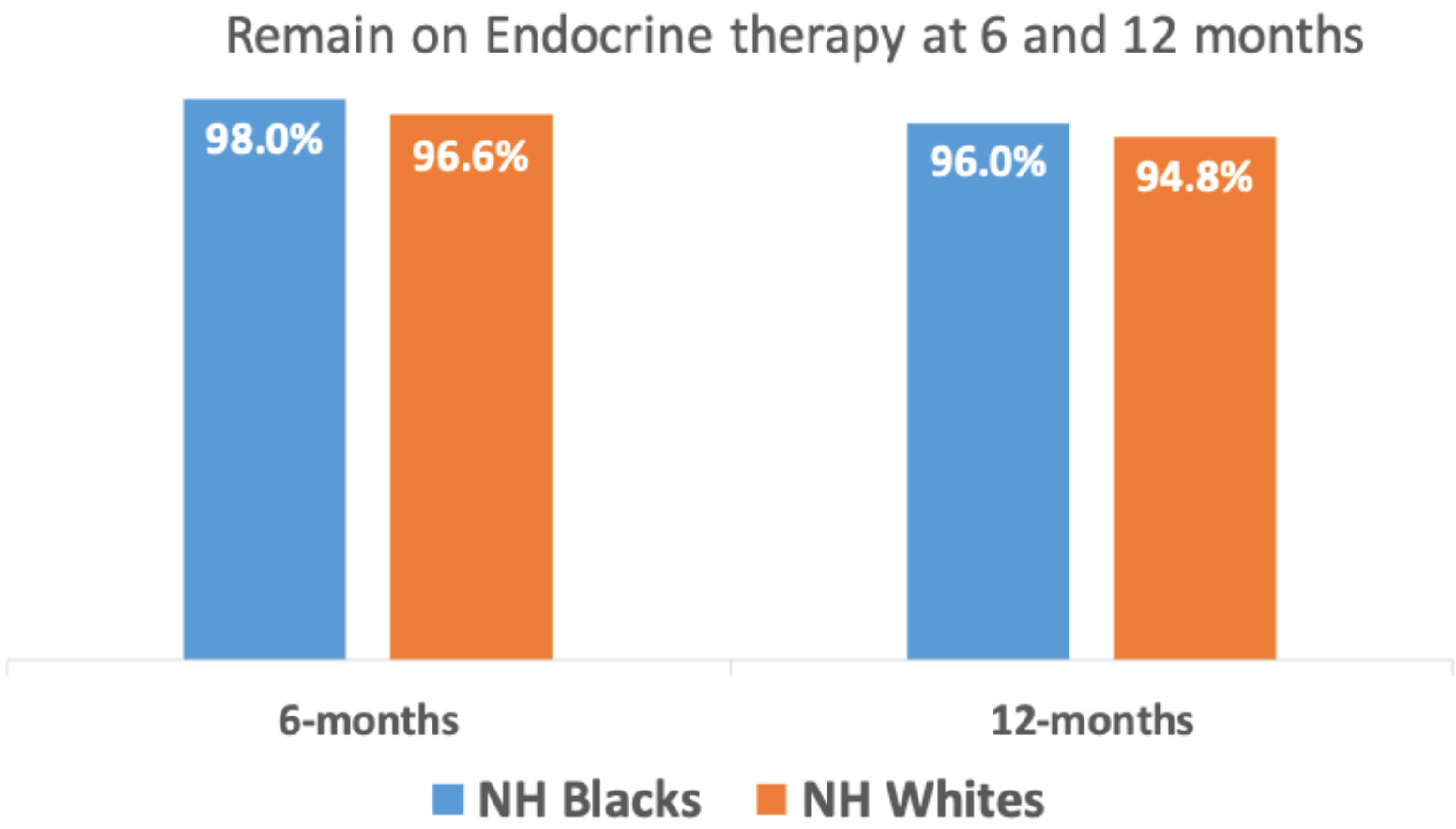
Endocrine Therapy Adherence



Take home message:

Definitive conclusions about racial differences in treatment beneft cannot be made due to the limited number of events in the NH Black cohort!

Outcome differences are less likely attributable to lack of treatment compliance within the first year.

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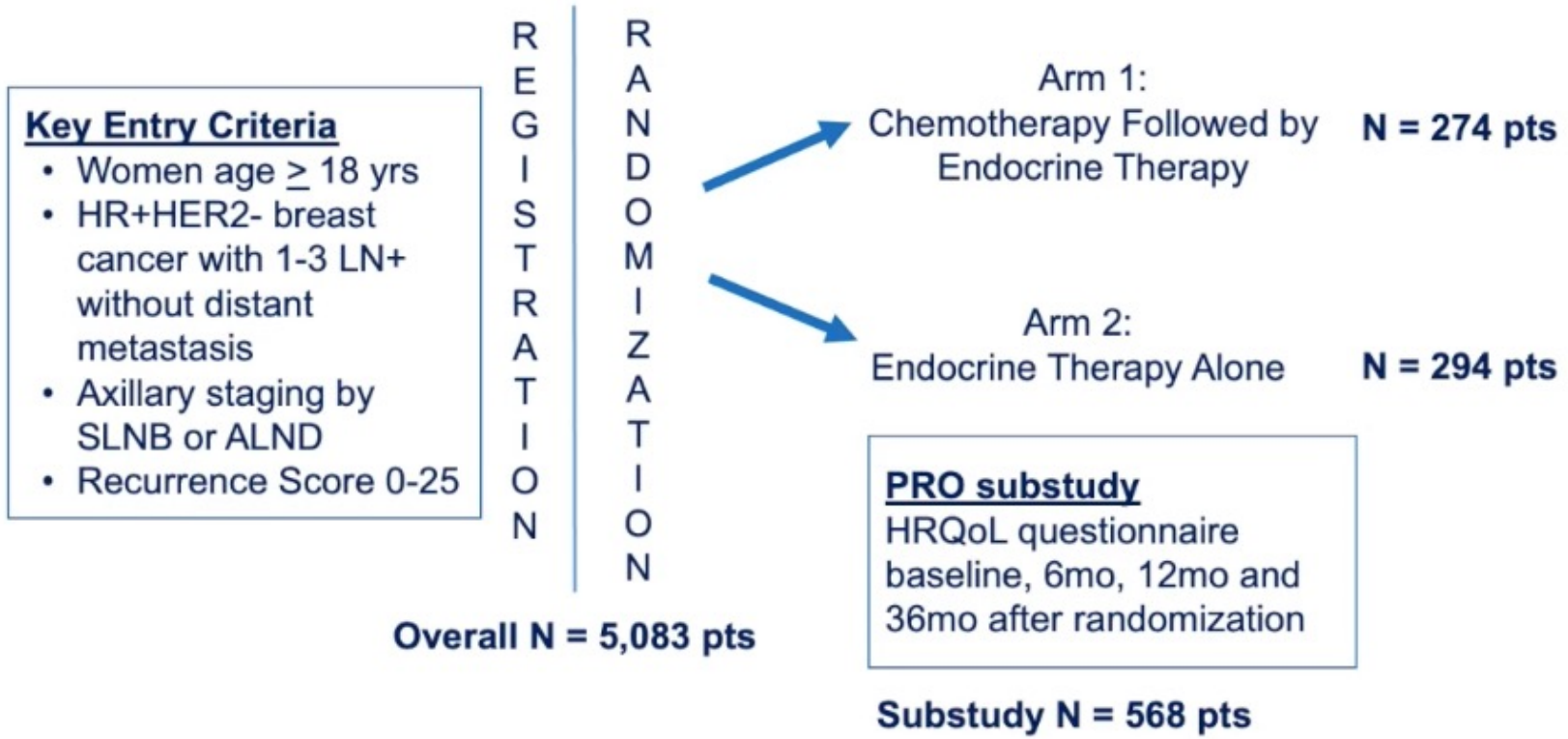
GS1-04: Patient-reported Cognitive Impairment in women participating in the Rx PONDER trial (SWOG S1007) by menopausal status

Presented by Irene Kang

RxPONDER Schema and PRO Substudy

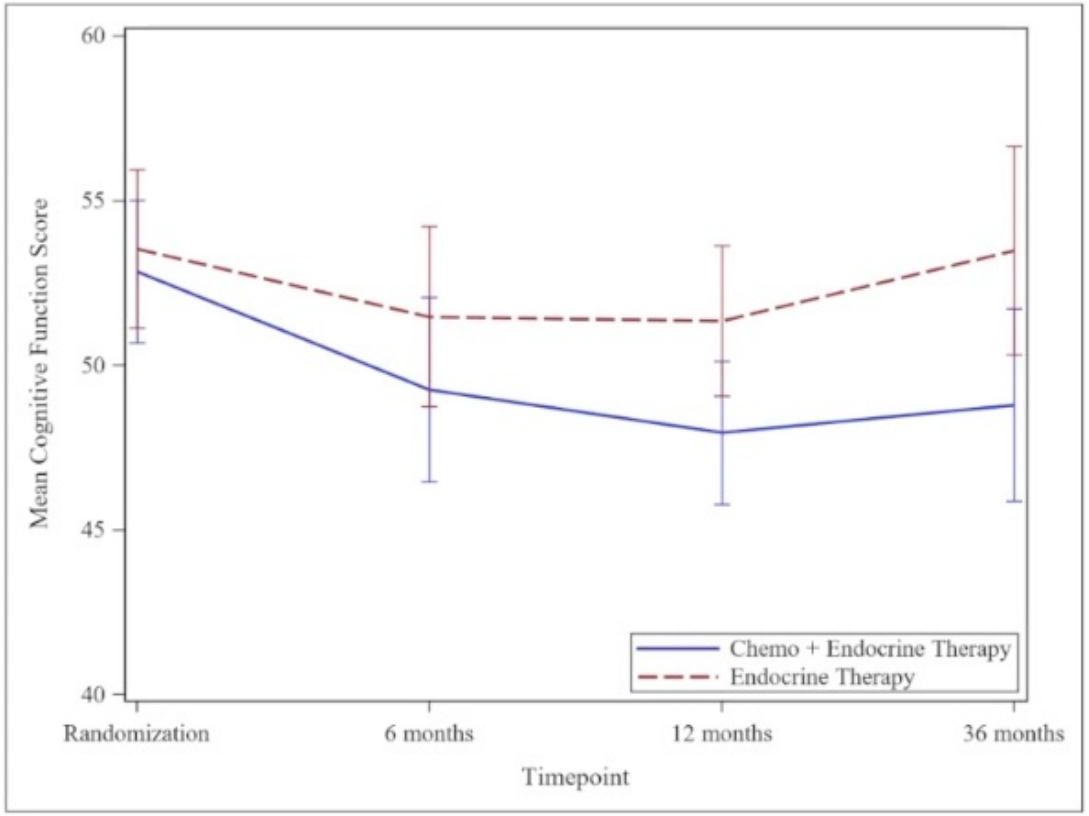


ALND = Axillary Lymph Node Dissection, SLNB = Sentinel Lymph Node Biopsy,
PRO = Patient Reported Outcomes, HRQoL = Health-related Quality of Life

RxPONDER PRO Substudy

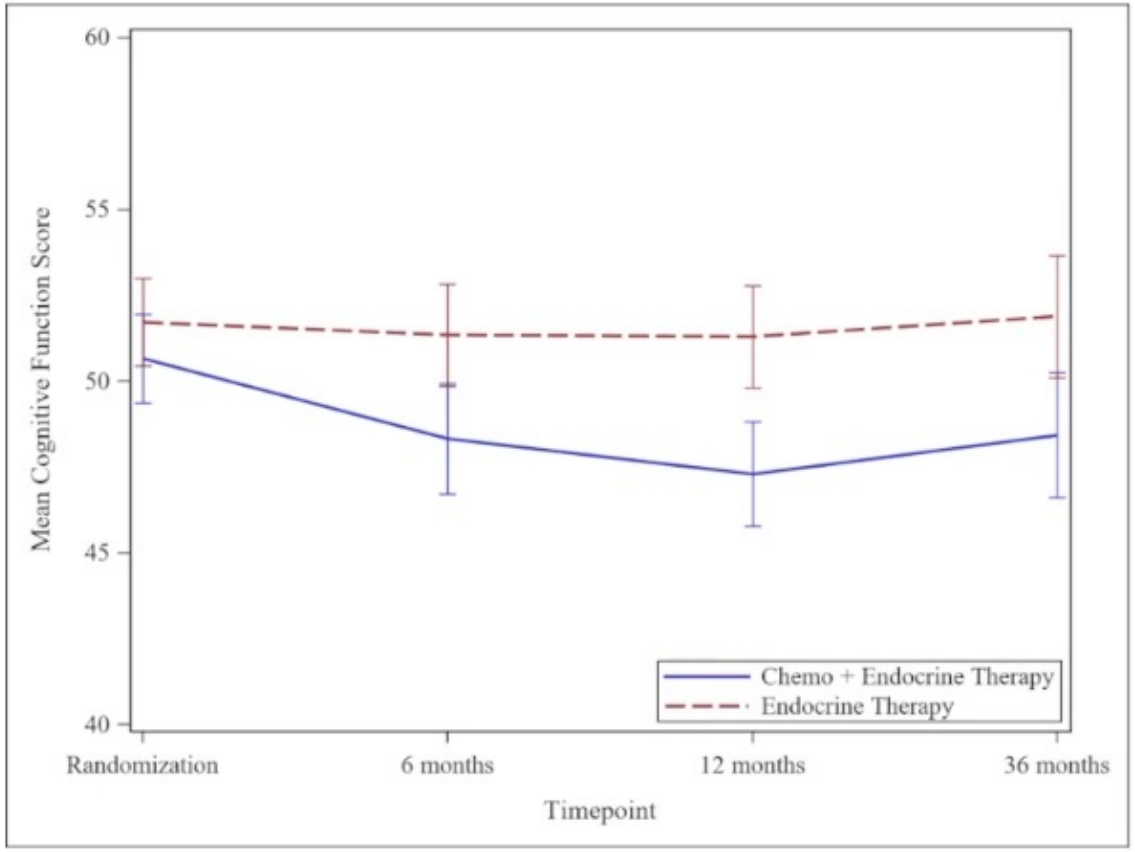
- Consecutive English-speaking US patients invited to participate from Feb 2011- Dec 2012 (goal n=500)
- HRQOL questionnaires at baseline (after randomization), and 6 mo, 12 mo, 36 mo
  - PROMIS Cognitive Function Concerns – 8 selected questions
  - Also PROMIS Anxiety & Fatigue, and EQ-5D
- Primary endpoint: Mean cognitive function score by treatment arm and menopausal status
  - T-scores: reference population with mean score 50, SD 10
  - Higher score = better cognitive function
  - Change of 3 units is clinically meaningful (0.3 SD)
- Analysis:
  - Intent to treat
  - Generalized estimating equations (GEE) model was fit to the three follow-up timepoints adjusting for baseline score, treatment arm and timepoint
  - Change from baseline and Odds of clinically meaningful worse cognitive function

Mean Cognitive Function Score: Premenopausal



Total n=139				
CET	65	43	44	36
ET	74	55	56	39

Mean Cognitive Function Score - Postmenopausal



Total n=429					
	CET	209	159	149	122
	ET	220	184	182	137

Comparisons of Mean Cognitive Function Score by menopausal status

Menopausal status	Treatment Arm	Timepoint				Longitudinal mean score difference
		Randomi-zation	6 months	12 months	36 months	
Premenopausal	CET	52.8	49.3	48.0	48.8	-3.02 (p=0.01)
	ET	53.2	51.5	51.4	53.5	
Postmenopausal	CET	50.7	48.3	47.3	48.4	-2.36 (p<0.003)
	ET	51.7	51.3	51.3	51.9	

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Take home message:

- C + ET has greater negative effect on CRCI compared to ET alone in both pre- and postmenopausal women

- CRCI seems to persist over time in a significant proportion of patients

Cave: These findings deviate from an analysis of CRCI in patients of the TAILORx trial:

”Adjuvant CT+E is associated with significantly greater CRCI compared with E at 3 and 6 months. These differences abated over time, with no significant differences observed at 12 months and beyond”

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GS4-09 Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIVE breast cancer: Primary Results from the POSITIVE Trial (IBCSG 48-14 / BIG 8-13)

Presented by Ann Partridge

Key question / Primary endpoint

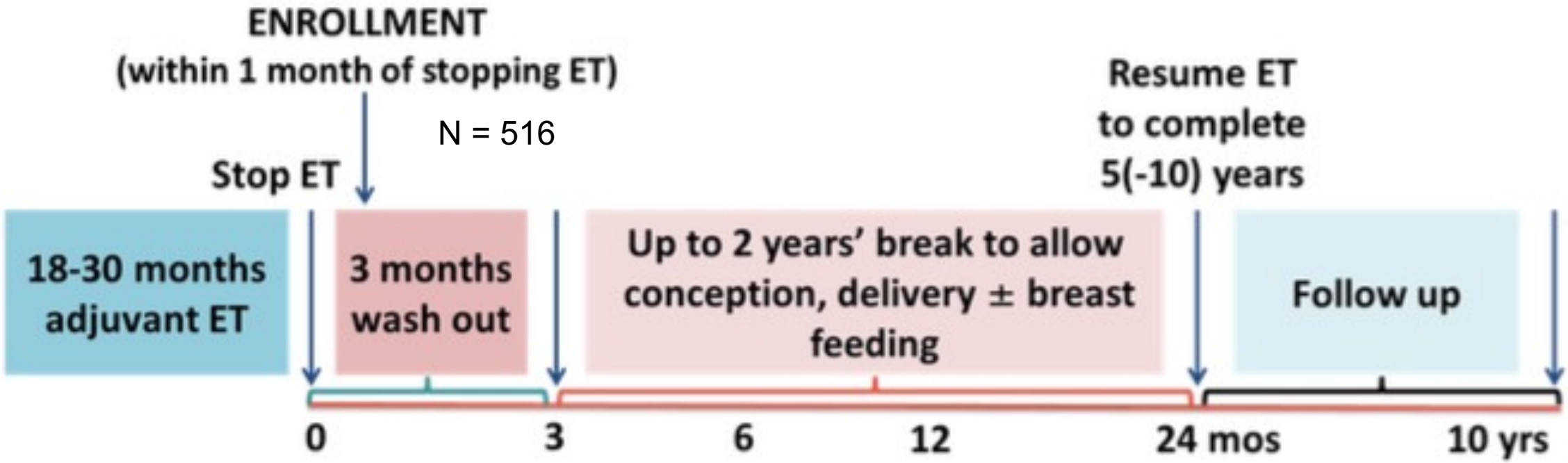
- Is it safe, from a BC relapse perspective, to temporarily interrupt ET to attempt pregnancy?
- **Breast cancer-free interval (BCFI)** = time from enrollment (after 18-30 months of ET) to the first ipsilateral / locoregional / contralateral invasive disease or distant recurrence

Eligibility criteria

- Premenopausal women wishing to become pregnant
- Age ≤ 42 years at study entry
- At least 18 months and no more than 30 months of prior adjuvant ET for stage I-III HR+ BC
- Prior neo/adjuvant chemotherapy ± fertility preservation allowed
- No clinical evidence of recurrence

POSITIVE trial: prospective single-arm design

≤ 46 BCFI events after 1600 patient-years of FU = SAFE



12/2014 - 12/2019

116 centres

20 countries

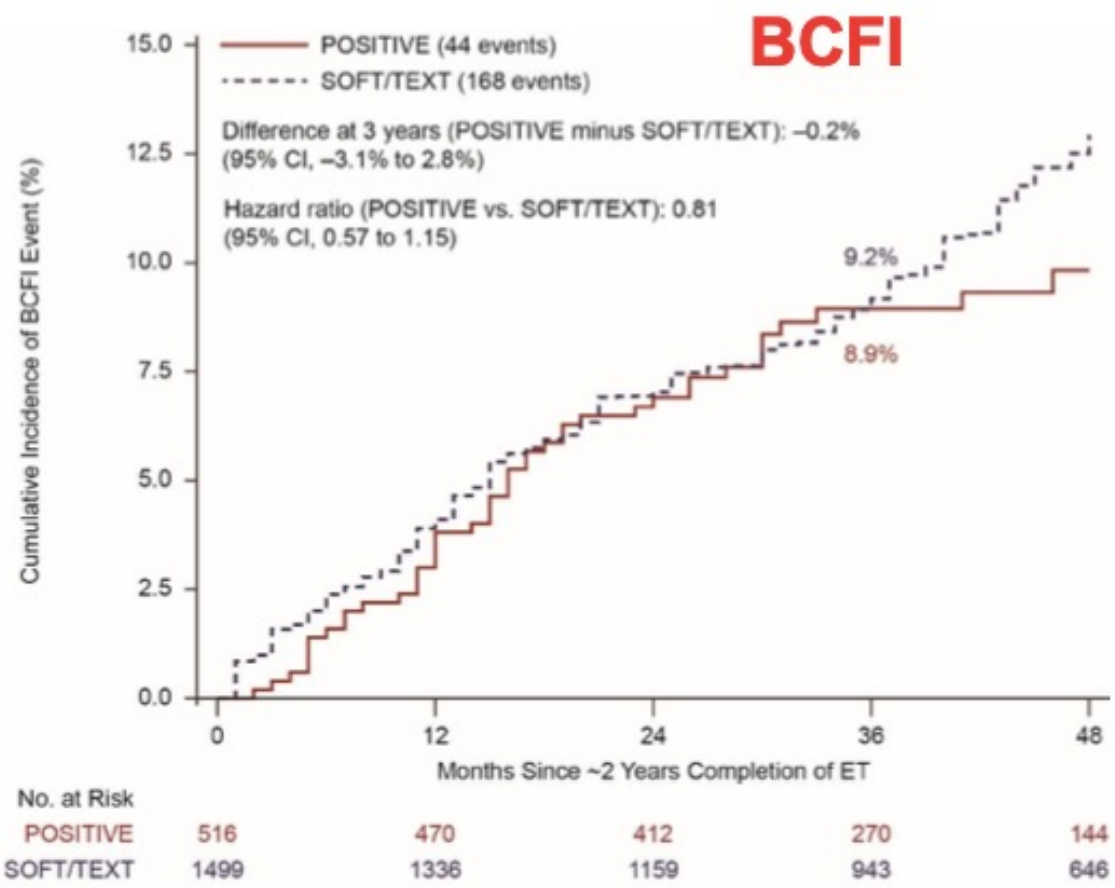
POSITIVE trial – patient characteristics

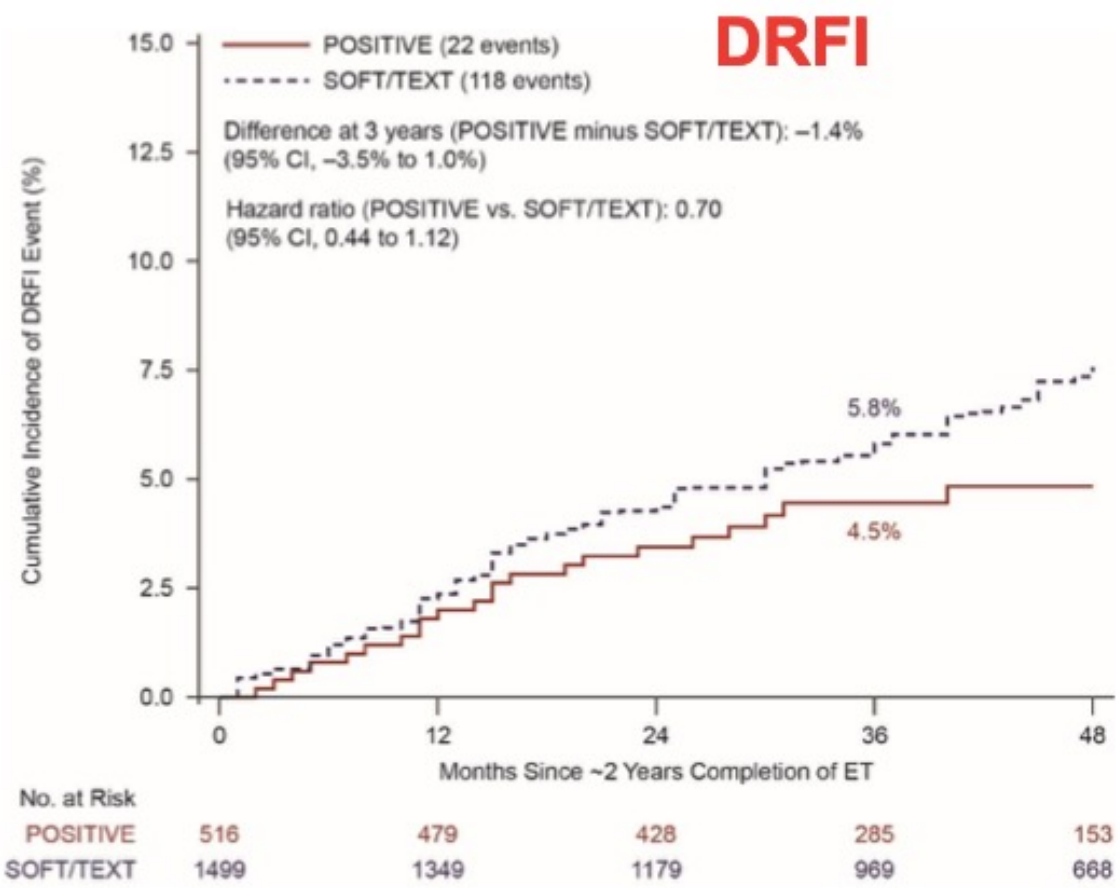
	N	%
	516	**100**
Age at enrollment ***Median 37 years (range 27-43 years)***		
<35	177	34%
35-39	221	**43%**
40-42	118	23%
Number of prior births		
0	387	**75%**
1	107	21%
≥ 2	22	4%
TNM stage		
I	242	**47%**
II	240	**47%**
III	31	6%
Unknown	3	1%

	N	%
	516	**100**
Endocrine therapy prior to enrollment ***Median duration: 23.4 months***		
SERM alone	215	**42%**
SERM+OFS	184	**36%**
AI+OFS	82	16%
Other	35	7%
Prior (neo-)adjuvant chemotherapy		
None	196	38%
Yes	320	**62%**
Breast surgery		
Mastectomy	233	45%
Breast conserving procedure	283	55%

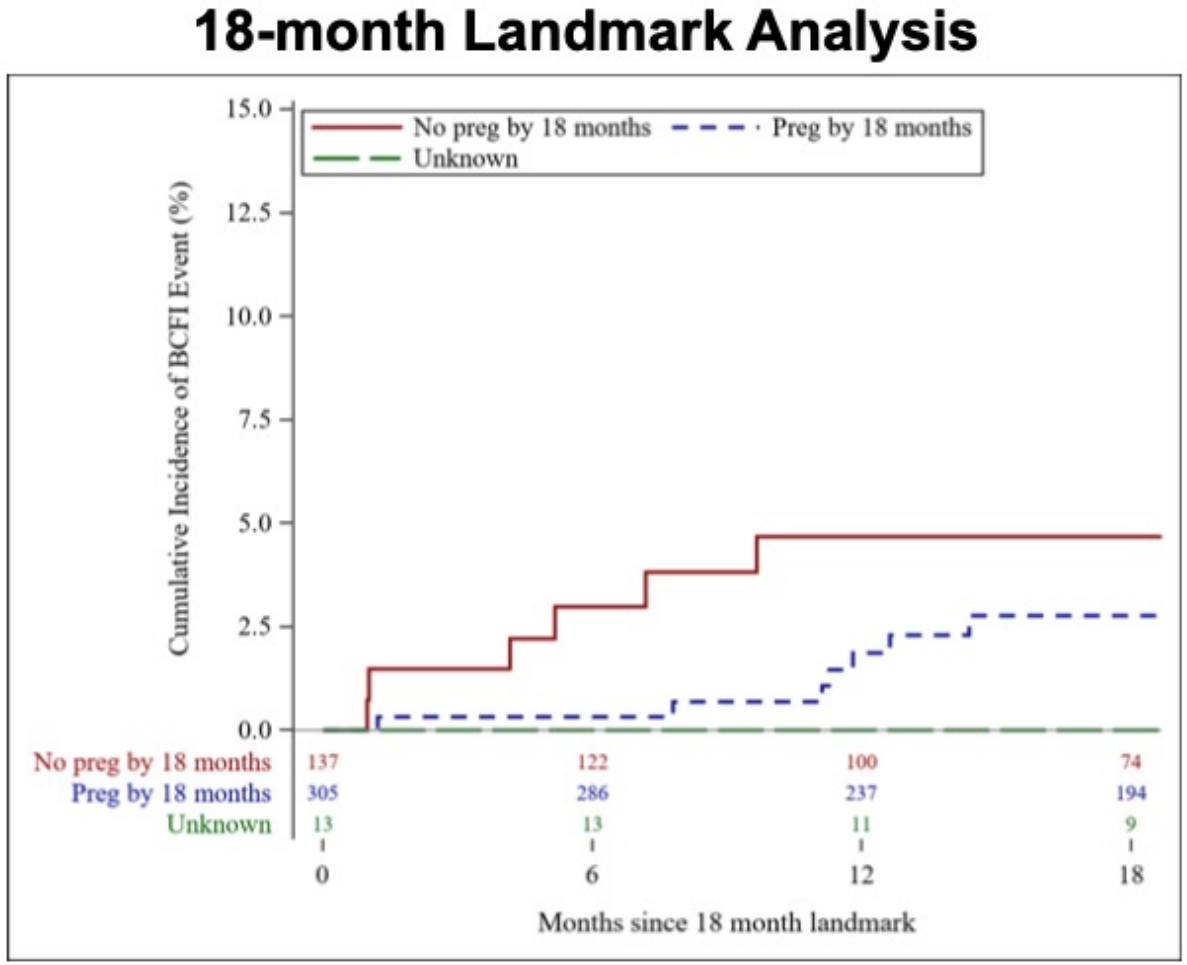
Partridge AH et al. Breast 2021;59:327-338.
DOI: 10.1016/j.breast.2021.07.021

POSITIVE - results





POSITIVE – pregnant versus non-pregnant analysis



Time-dependent Cox Models

BCFI hazard ratios

(pregnant vs. not pregnant):

0.55 (95% CI: 0.28 to 1.06) – univariable

0.53 (95% CI: 0.27 to 1.04) – multivariable*

* including age, BMI, lymph node status, prior chemo, and prior AI

POSITIVE – pregnancy outcomes

	N	% of 497	% of 368
Secondary endpoint population	497	100%	
At least one on trial pregnancy	368	**74%**	100%
At least one live birth (full-term or preterm)	317	**64%**	**86%**
At least one miscarriage	93	19%	25%
At least one elective abortion	16	3%	4%
At least one stillbirth/neonatal death	1/1	0.2% / 0.2%	0.3% / 0.3%

Note: 110 women had more than one pregnancy, and may contribute information to more than one row

- **Delivery**
  - Vaginal 66%
  - Cesarean section 34%
- **Pregnancy complications**
  - 11% of pregnancies
  - Most common:
    Hypertension/preeclampsia 3%
    Diabetes 2%

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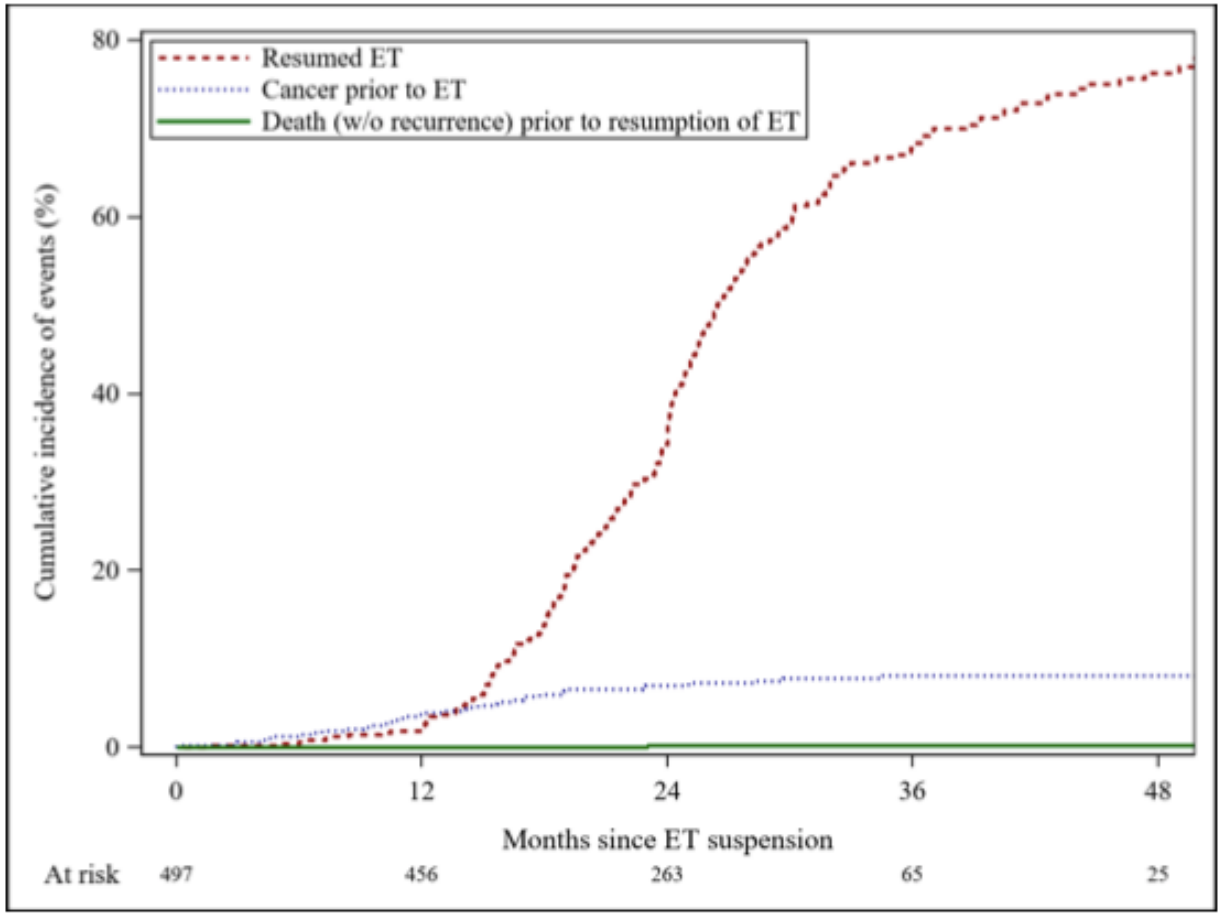
POSITIVE – offspring outcomes

- 350 live births for the 317 women who had at least 1 live birth
- 335 singleton births and 15 sets of twins (365 offspring)
- 62% of 317 women reported breastfeeding

	N	%
Total offspring	365	100%
Low birth weight (<2500g)		
Yes	29	8%
No	**334**	**92%**
Missing/Unknown	2	0.5%
Birth defects		
Yes	8	2%
No	**350**	**96%**
Missing/Unknown	7	2%

POSITIVE – ET resumption



Cumulative incidences at 48 months:

- 8% had cancer recurrence/death before resuming ET
- 76% resumed ET
- 15% had not yet resumed ET

79% of women disease-free at 2 years who have not yet resumed ET reported continuing pursuit of pregnancy, active/recent pregnancy or breastfeeding at most recent follow-up.

Take home messages:

- Temporary interruption of ET to attempt pregnancy among women who desire pregnancy does not impact short-term disease outcomes

What about abemaciclib?

- Follow-up to 2029 planned to monitor ET resumption and disease outcomes

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Educational Session :
Breast Cancer and Cardiovascular Toxicity: What an Oncologist Needs to Know

Presented by Susan Dent

Scope of the problem

More than antracyclines and Her2-targeted therapy…

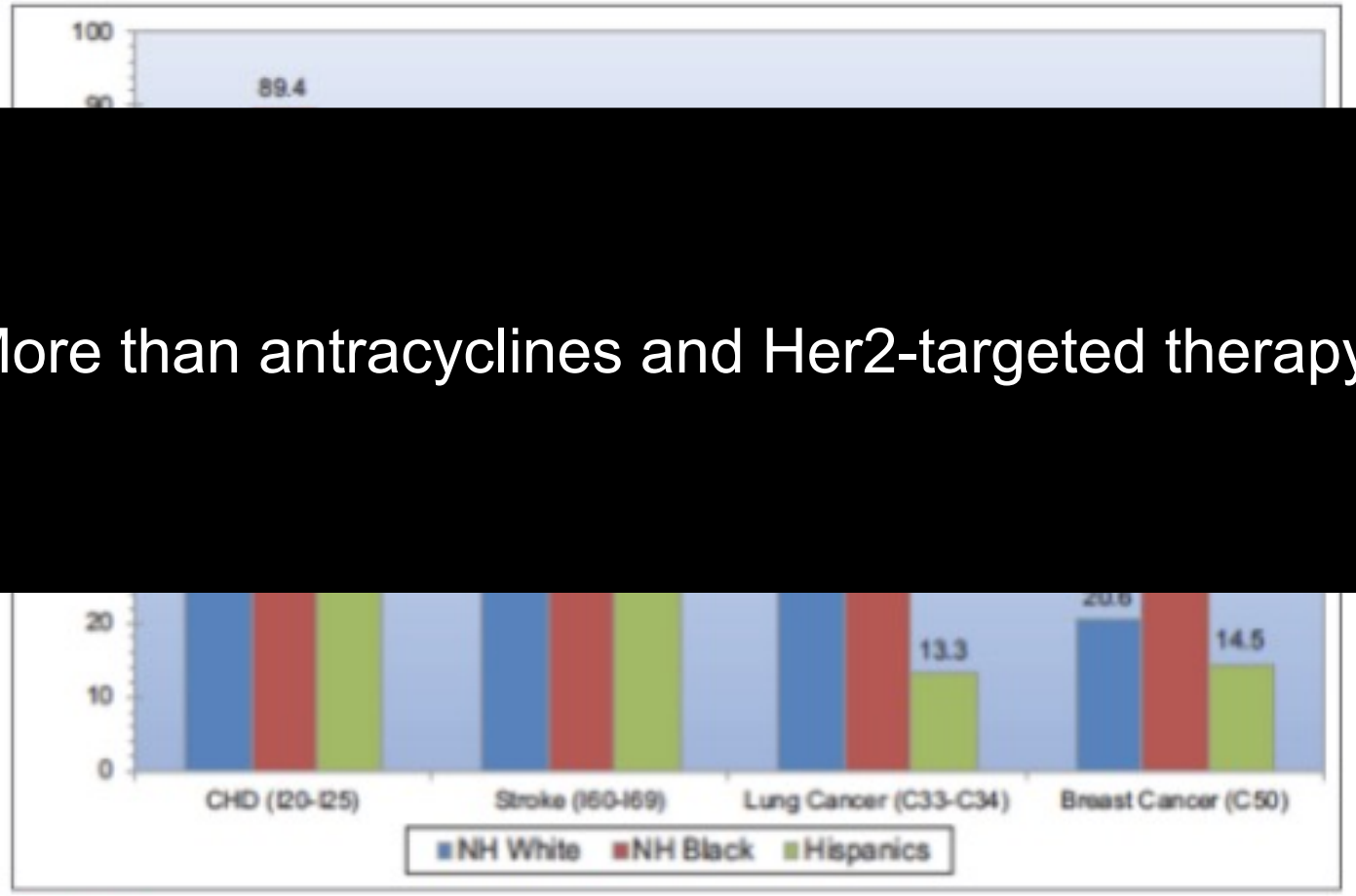
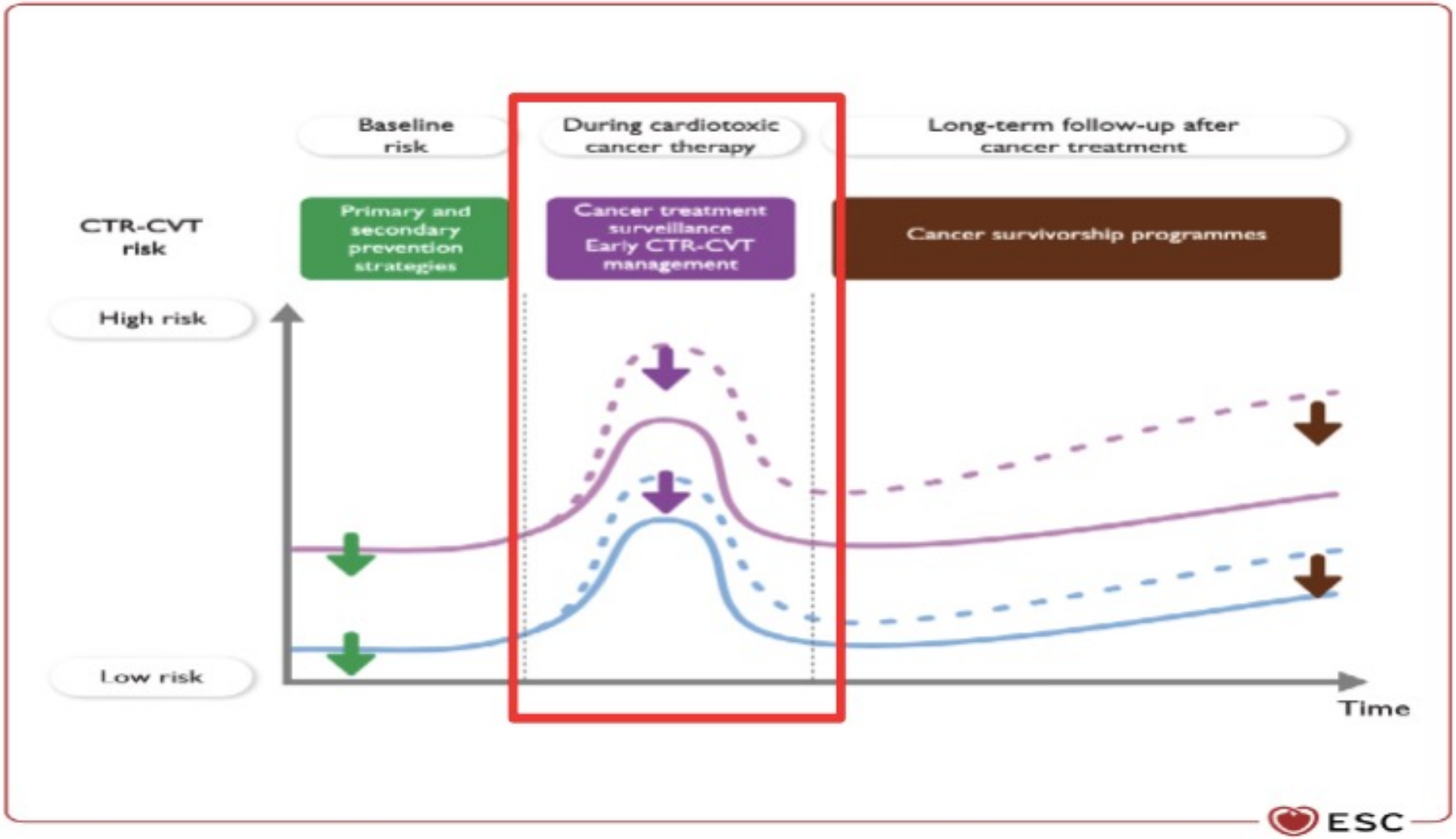


Figure 1. **Rates of cardiovascular disease and breast cancer in women.** Age-adjusted mortality rates

Cardiovascular risk in patients with cancer



QT prolongation with Ribociclib

- **ML-2, -3,-7** all grade QTc AE's in 7 % on ribociclib and ET vs 2 % with ET alone
- Permanent discontinuation of ribociclib/placebo due to QTc < 1 %
- **ML-7:** greater increase in mean QTc from baseline with Tamoxifen (**not recommended with Ribociclib)**
- **Note**: clinical trials excluded patients on other QT prolonging medications

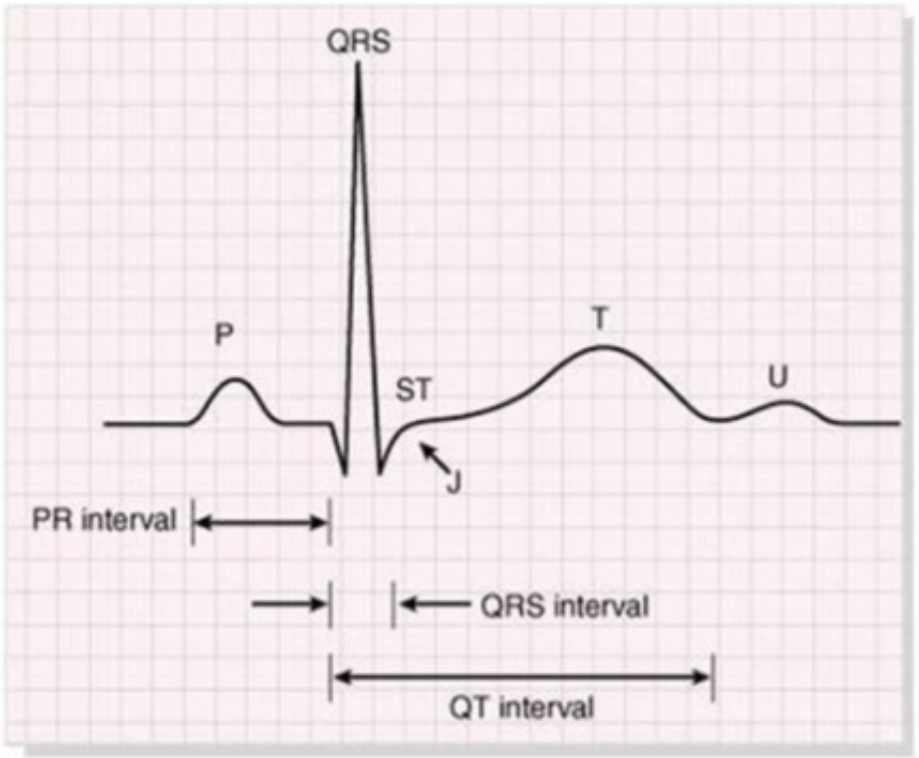
Generic Name	Brand Names (Partial List)	Drug Class	Therapeutic Use	PubMed Search	Risk Category
Osimertinib	Tagrisso	Anti-cancer	Cancer (EGFR pos. NSC Lung cancer)	LINK	
Oxaliplatin	Eloxatin	Anti-cancer	Cancer	LINK	
Panobinostat	Farydak	Histone deacetylase inhibitor	Cancer, Multiple myeloma	LINK	
Pazopanib	Votrient	Anti-cancer	Cancer (renal cell, sarcoma)	LINK	
Ribociclib	Kisqali	Anti-cancer	Cancer (breast)	LINK	
Romidepsin	Istodax	Histone deacetylase inhibitor	Cancer (lymphoma)	LINK	
Sorafenib	Nexavar	Anti-cancer	Cancer (liver, renal cell, metastatic thyroid)	LINK	
Sunitinib	Sutent	Anti-cancer	Cancer (GIST, renal cell, pNET)	LINK	
Tamoxifen	Nolvadex(discontinued 6/13), Istubal, Valodex	Anti-cancer	Cancer (breast)	LINK	
Tipiracil and Trifluridine	Lonsurf	Anti-cancer	Cancer (Metastatic colorectal)	LINK	

Showing 31 to 40 of 44 entries (selected from 263 total entries) First Previous 1 2 3 4 5 Next Last

Crediblemeds.org

Burris H et al Br J Cancer 2021

European Society of Cardiology Cardio-Oncology Guidelines: Recommendations for Monitoring with CDK 4/6 inhibitors



Corrected QT interval using Fridericia correction is recommended

Recommendation Table 18 — Recommendations for baseline risk assessment and monitoring during cyclin-dependent kinase 4/6 inhibitor therapy

Recommendations	Class[a]	Level[b]
QTc[c,d] monitoring is recommended at baseline and 14 and 28 days in all patients with cancer receiving ribociclib.[361,365,367,368]	I	A
QTc[c,d] monitoring is recommended in patients treated with ribociclib with any dose increase.[361,365,367,368]	I	B
QTc[c] monitoring should be considered in patients treated with palbociclib or abemaciclib who have a baseline QTc above the normal range[c] or other conditions that may prolong the QTc interval.[e]	IIa	C

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QTc, corrected QT interval; QTcF, corrected QT interval using Fridericia correction.
[a]Class of recommendation.
[b]Level of evidence.
[c]QT interval using Fridericia correction (QTcF = QT/$\sqrt[3]{RR}$) is the preferred method in patients with cancer. Upper 99% limit of normal for QTc values in the general population are 450 ms for men and 460 ms for women.[369]
[d]According to the European Medicines Agency: (1) ribociclib should be interrupted when QTcF > 480 ms; (2) if QTcF prolongation resolves to <481 ms, resume treatment at the same dose level; (3) if QTcF ≥ 481 ms recurs, interrupt dose until QTcF resolves to <481 ms and then resume ribociclib at next lower dose level.
[e]See *Section 6.4.2* and *Table 8*.

Lyon A et al, EHJ, 2022

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Immune Checkpoint Inhibitor-related Cardiotoxicity

Types of Cardiotoxicity	Incidence*
Myocarditis	0.09% to 2.4%
Pericarditis	<1% to 2%
Pericardial Effusion	2%
Cardiac Arrhythmia	4%
Myocardial Infarction	<1% to 2%
Heart Failure	0.4%
Takotsubo Cardiomyopathy	Rarely reported
Cardiac Arrest	Rarely reported

*Varies with molecule used and method of treatment (monotherapy/combination)

Temporal Emergence of Myocarditis

- Median Onset: 30 days
- Within first 15 days, particularly if combination therapy
- Late CV events (>90 days) = non-inflammatory HF, HTN, progressive atherosclerosis
- Rate of fatality in myocarditis = 50%
- In fatal myocarditis, 93% received one or two doses

Anatol J Cardiol 2020; 24: 68-75
Lancet Oncol 2018;19:1579–1589.

Baseline Risk Assessment and Monitoring

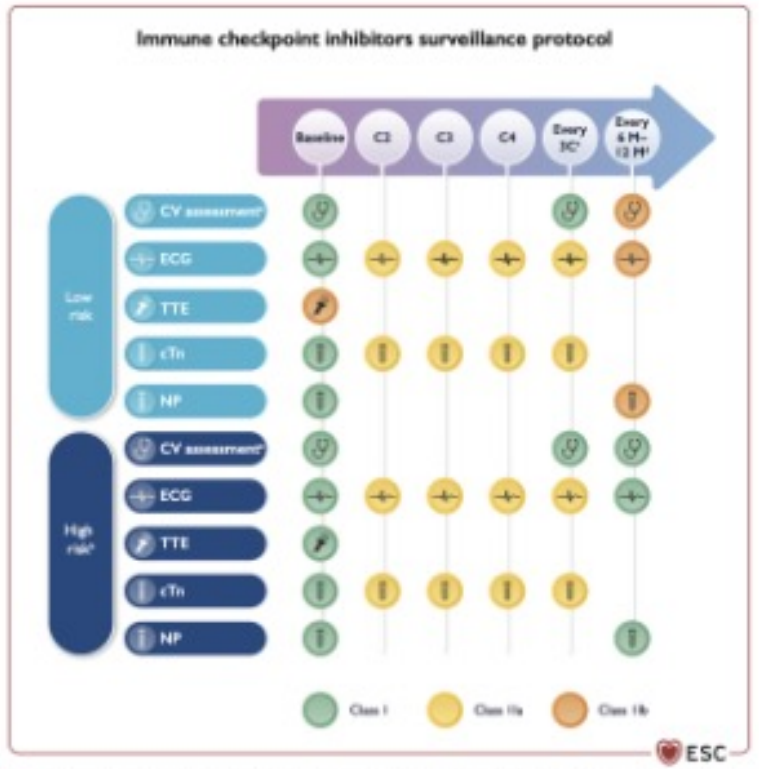


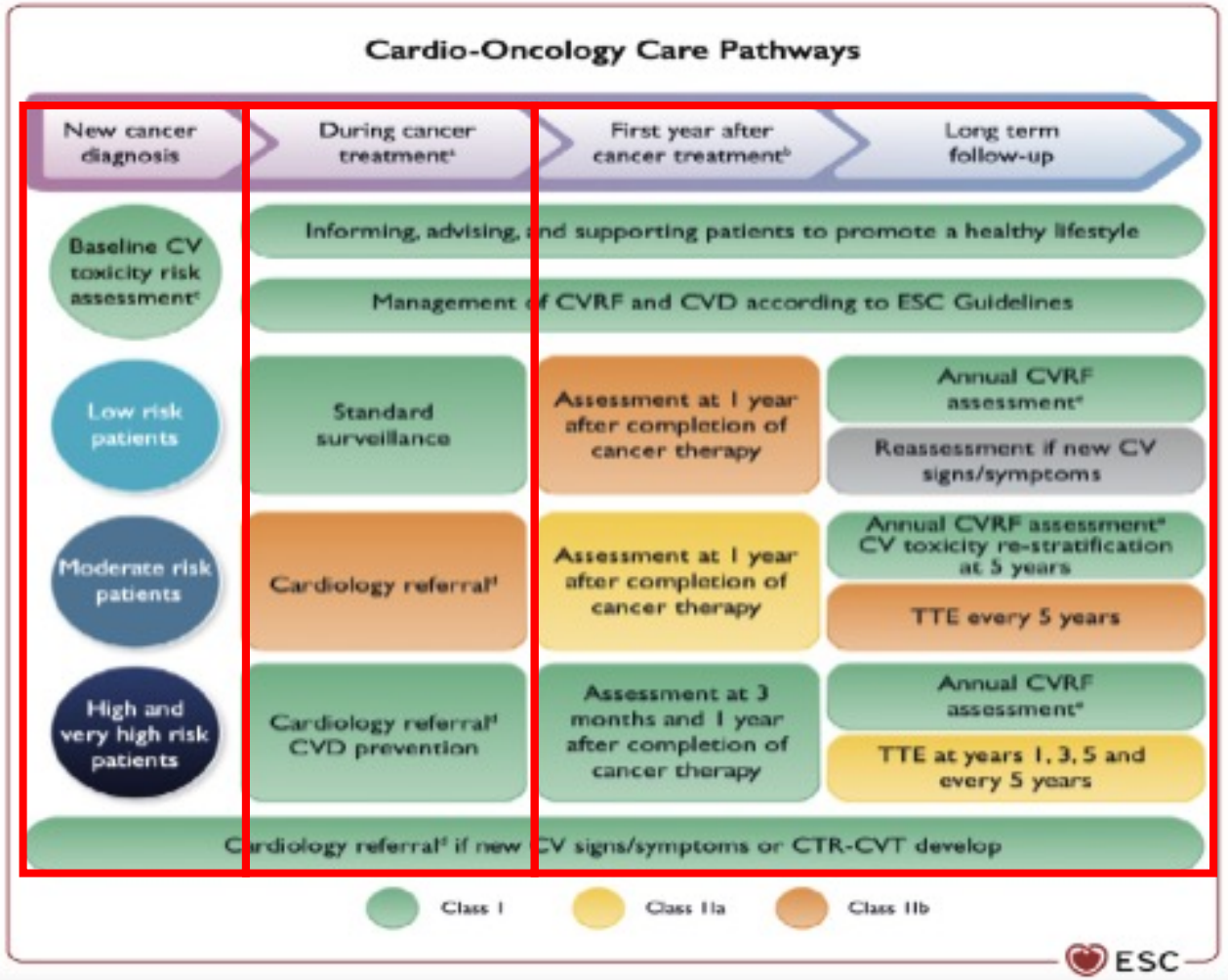
Figure 10 Cardiovascular surveillance in patients treated with immune checkpoint inhibitors. BNP, B-type natriuretic peptide; BP, blood pressure; C, chemotherapy cycle; cTn, cardiac troponin; CV, cardiovascular; CVD, cardiovascular disease; CTRCD, cancer therapy-related cardiac dysfunction; ECG, electrocardiogram; HbA1c, glycated haemoglobin; ICI, immune checkpoint inhibitors; M, months; NP, natriuretic peptides (including BNP and NT-proBNP); NT-proBNP, N-terminal pro-B-type natriuretic peptide; TTE, transthoracic echocardiography. [a]Including physical examination, BP, lipid profile, and HbA1c. [b]Dual ICI, combination ICI-cardiotoxic therapy, ICI-related non-CV events, prior CTRCD or CVD. [c]Every three cycles until completion of therapy to detect subclinical ICI-related CV toxicity. [d]In patients who require long-term (>12 months) ICI treatment.

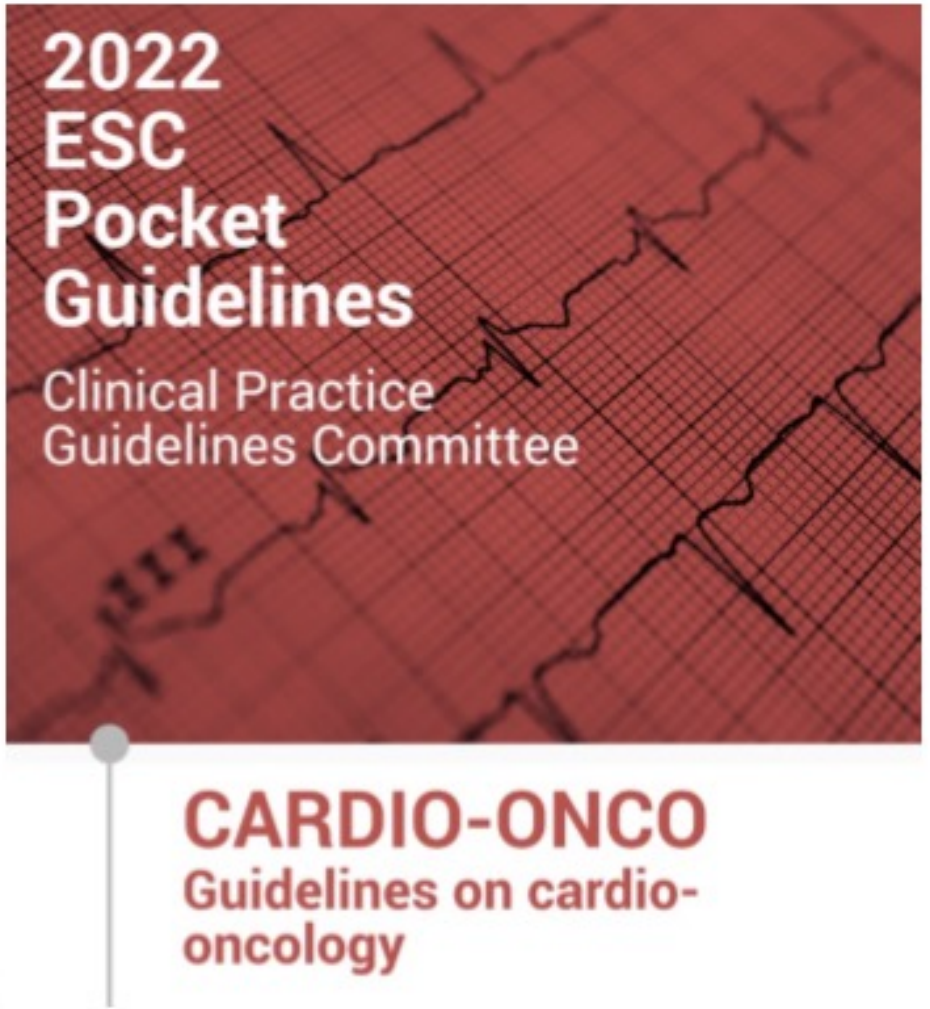
Lyon A et al, EHJ 2022

Recommendation Table 15 — Recommendations for baseline risk assessment and monitoring during immunotherapy

Recommendations	Class[a]	Level[b]
ECG, NP, and cTn measurements are recommended in all patients before starting ICI therapy.[333]	I	B
Baseline echocardiography is recommended in high-risk patients[c] before starting ICI therapy.[333]	I	B
Baseline echocardiography may be considered in all patients before starting ICI therapy.	IIb	C
Serial ECG and cTn measurements should be considered before ICI doses 2, 3, and 4, and if normal, reduce to every three doses until completion of therapy to detect subclinical ICI-related CV toxicity.[333]	IIa	B
CV assessment[d] is recommended every 6–12 months in high-risk patients[c] who require long-term (>12 months) ICI treatment.[321–323,335,336]	I	C
CV assessment[d] may be considered every 6–12 months in all patients who require long-term (>12 months) ICI treatment.	IIb	C

ESC Guideline on Cardio- Oncology





Lyon et al, European Heart Journal 2022

Take home messages:

- Baseline ECG for all CDK 4/6i
- Baseline cardial risk stratification determines follow-up strategy

Reading tip: ESC guidelines cardio-oncologie ☺

OFFICIAL

best of SABCS

Poster Spotlight Discussion
Symptom Management and Associated Toxicities

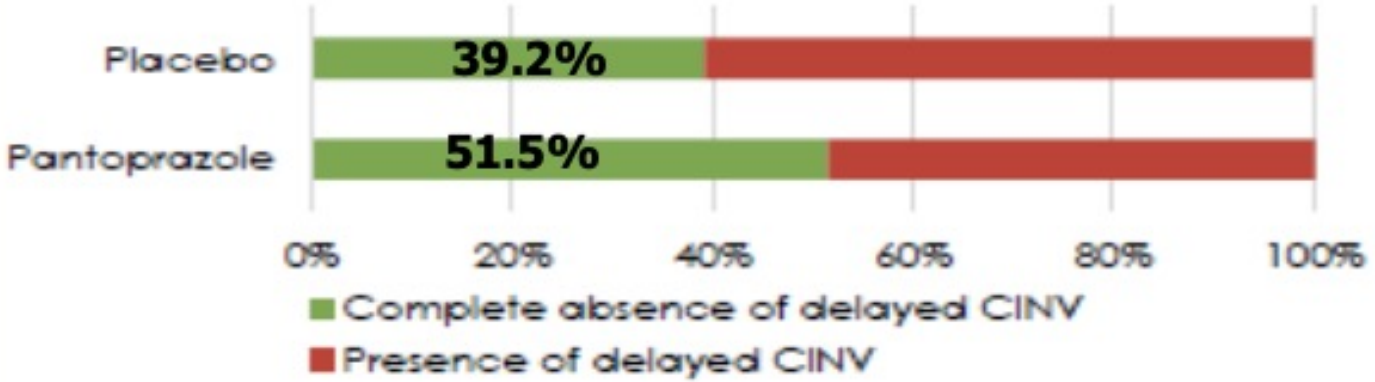
Presented by Ines Vaz Luis

- **PD8 01 PantoCIN: Pantoprazole's** effectiveness as prophylaxis against **delayed Chemotherapy-Induced Nausea and Vomiting (CINV)** in patients receiving adjuvant or neoadjuvant breastcancer chemotherapy. Wewala et al.

METHODS	
Study type	▪ Doubled-blinded crossover trial
Patient population	▪ 160 patients with early breast cancer receiving adjuvant or neo-adjuvant chemotherapy (AC, FEC, TC – moderate or high emetic risk). Patients treated with 3 agents anti-emetic regimen +/-Olanzapine
Intervention	▪ Pantoprazole 40mg D1-D5
Primary objective	▪ To determine whether pantoprazole can reduce the incidence of delayed CINV in patients receiving chemotherapy for early breast cancer
Statistical analyses	▪ Intention to treat analyses. The significance level for all analyses is set at 0.025 (one-sided). Assumptions: Baseline risk of delayed CINV in the study population is 50% and that Placebo would reduce this to 45% and the within person correlation was 0.6, N=155 patients will have 80% power to detect a statistically significant effect (one-sided α (type 1) error of 0.025) of Pantoprazole

- **PD8 01 PantoCIN: Pantoprazole's** effectiveness as prophylaxis against **delayed Chemotherapy-Induced Nausea and Vomiting (CINV)** in patients receiving adjuvant or neoadjuvant breastcancer chemotherapy. Wewala et al.

RESULTS



OR=2.2, 95% CI (1.2 - 4.1)

p-value=0.01

Patient preferences
50.4% preferred pantoprazole
25.2% preferred placebo
based on amount of nausea, heartburn and vomiting in the delayed phase

No significant difference in:
Vomiting
Breakthrough Antiemetic Use
Adverse Event

https://www.riskcinv.org

Recommendation

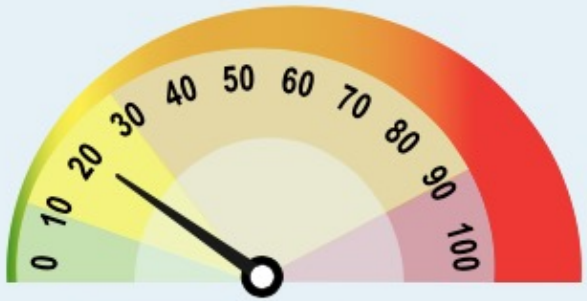
CINV RISK ASSESSMENT

Based on **MASCC/ESMO** emetogenicity level & CINV risk assessment, your patient has additional risk factors which predispose them to CINV. These should be considered when selecting their antiemetic treatment.

5-HT_3 RA or DEX or DOP

Chemotherapy Emetogenicity Level*

10 - 30%: Low Emetogenic

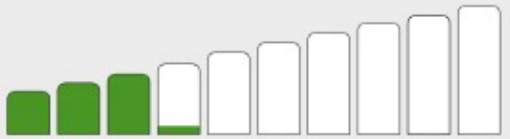


Based on MASCC/ESMO Guidelines, the emetogenicity level of the regimen is related to the highest emetogenic agent selected.

Chemotherapy: 5-Fluorouracil

No additional antiemetic is needed.

Patient Emetogenicity Risk Profile



31.2%
Low Risk

- Age is under 60
- Expecting to develop CINV
- Morning sickness history
- <7 hours sleep before chemotherapy
- Non-prescribed treatments taken after previous cycle

*Indicates the risk of emesis in absence of antiemetic prophylaxis.

- **PD8 04** The role of Yoga as a complementary therapy in women undergoing treatment for breast cancer: A randomized controlled trial. Nair et al.

METHODS	
Study type	▪ Randomized controlled trial
Patient population	▪ 850 women with non-metastatic breast cancer during and after standard treatment, were randomized to yoga and conventional exercise (YCE) versus conventional exercise only (CE).
Intervention	▪ YCE versus CE only.
Primary endpoint	▪ Disease-free survival

- **PD8 04** The role of Yoga as a complementary therapy in women undergoing treatment for breast cancer: A randomized controlled trial. Nair et al.

RESULTS

Median follow-up 80 months: YCE VS. CE

- DFS 80% vs 76.7% (HR= 0.85, 95% CI= 0.64-1.14, p=0.28)
- OS 85.4% vs 83.1% (HR= 0.86, 95%CI = 0.61-1.21, p=0.38)

- Improved physical (p=0.043) and emotional function (0.017), fatigue (p=0.002), pain (p=0.031), appetite loss (< 0.001) arm symptoms (0.035) and systemic therapy side effects (0.036) reduced at 6-9mo in YCE, mostly persisted over time

Take home messages:

- Pantoprazole 40 mg on day 1-5 significantly reduced the incidence of delayed CIN (not vomiting)

- Yoga in combination with conentional exercise did not affect DFS nor OS compared to conventional exercise

BUT: improved physical function, emotional function, fatigue, pain, ….
(and the effect persisted over time)