Highlights of supportive care 2023

Dr Fontaine Medical oncologist

UZ Brussel

Highlights of supportive care 2023

- What about safety?
- Is it clinically meaningful for the patient?
- I have no disclosures except tickets for ESMO congress 2023, ESMO breast 2023, ESMO sarcoma congress 2023, SABCS 2023 and advisory board for Gilead 2023

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients
- Health education after breast cancer
- Safety and toxicity according to age, race and realworld data
- PRO outcome: utility?
- New anti emetic regimen

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients
- Health education after breast cancer
- Safety and toxicity according to age, race and realworld data
- PRO outcome: utility?
- New anti emetic regimen

Improved Uptake and Adherence to Prevention Medication with Use of Baby Tamoxifen in Patients at High Risk for Breast Cancer

Lauren F. Cornell, M.D.
Mayo Clinic, Jacksonville FL

Disclosure Information:

I have no financial relationships to disclose.

Objectives and methods

- Aims:
  1. Evaluate patient understanding of breast cancer risk and role of prevention medication with baby tamoxifen, including benefits, side effects, and risks after consultation with breast specialist
  2. Assess uptake, adherence, and tolerability of baby tamoxifen at 1 year in women at increased risk for breast cancer and those with DCIS in real world clinical setting
- Methods: Offered participation to women seen at the Mayo Clinic Breast Center in Minnesota or Florida who qualified for Prevention Medication(PM) due to:
  - ❑ DCIS
  - ❑ High risk intraepithelial lesions (IELs) including LCIS and/or AH,
  - ❑ Validated BRCAT or IBIS model calculation (BCRAT 5-year risk ≥ 3% or IBIS 10-year risk ≥ 8%)
  - All women received standard of care consultation with a breast specialist for discussion of PM rationale, benefits, side effects, and risks
  - Patients completed:
    - ❑ Baseline survey to assess understanding of their risk and role for PM
    - ❑ 1 year follow-up survey to assess adherence and tolerability

Results

- 41 patients consented for participation with 31 completing f/u at 1 year
  - 13 qualified based on BCRAT/IBIS calculation; 13 high-risk IELs; 5 DCIS
- **90% (n=37) reported good or complete understanding of BC risk after consultation**
- **73% (n=30) reported that availability of baby tamoxifen helped in their decision to consider PM**
- Of those who completed 1 yr f/u, 74% (n=23) reported taking baby tam after consultation
  - Those who initiated baby tam more likely to have DCIS or high risk IEL ($p<0.001$)
- **78% (n=18) of those who initiated baby tam were still taking medication at 1 year f/u**
  - Patients who continued baby tam at 1 year had higher estimated BC risk compared to those who discontinued (IBIS 10-yr risk 12.7% vs 7.6%, $p = 0.027$)
  - **Patients with DCIS or high risk IEL were more likely to continue medication at 1 year compared to those patients who qualified for PM based on calculated BCRAT/IBIS score (p=0.05)**
  - Of those who discontinued (n=5) all listed side effects as primary reason for discontinuation
    - hot flashes (n=2), night sweats (n=2), and fatigue (n=2)

Discussant

Current ASCO Guidelines for Breast Cancer Chemoprevention

Visvanathan K et al. JCO 2019;37:3152

- Multiple agents endorsed:
  - Premenopausal: tamoxifen 20 mg/day for 5 years (baby tam 5 mg/day for 3 years may be considered with caveats regarding lack of head-to-head comparison of 20 vs 5 mg)
  - Postmenopausal: tamoxifen 20 mg/day (5 mg/day incl baby tam as above), raloxifene 60 mg/day, exemestane 25 mg/day, anastrozole 1 mg/day – all for 5 years - choice depends on toxicity profile, patient preference
- RCTs show 50% or greater reduction in risk
- No head-to-head comparisons of different agents or durations
- Update has been persistently low – <5% of those offered chemoprevention start treatment - both patient and provider barriers have been identified – including toxicity concerns

Fertility preservation and assisted reproductive technologies in breast cancer patients interrupting adjuvant endocrine therapy to attempt pregnancy

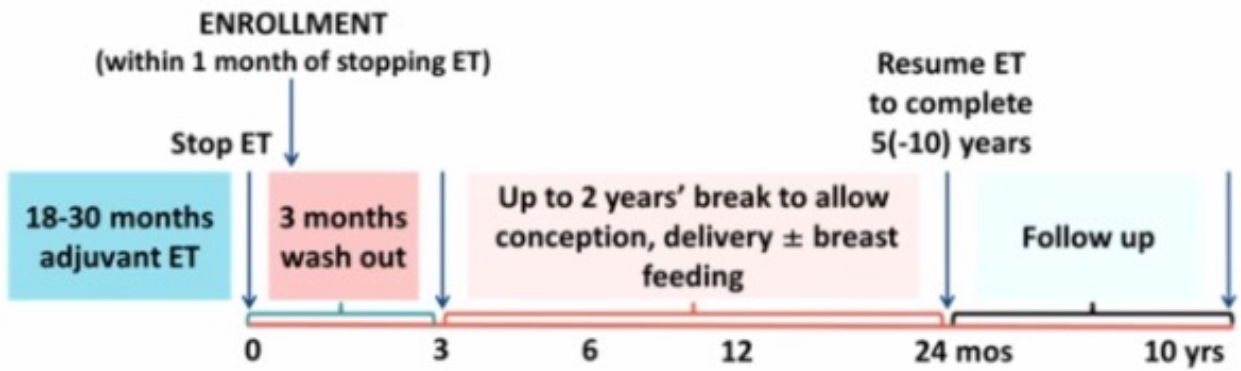
Results from the POSITIVE Trial
(IBCSG 48-14 / BIG 8-13 / Alliance A221405)

Hatem A. Azim Jr, MD, PhD
School of Medicine, Monterrey Institute of Technology, MX

On behalf of the POSITIVE Consortium

H. A. Azim Jr , S. M. Niman, A. H. Partridge, I. Demeestere, M. Ruggeri, M. Colleoni, C. Saura, C. Shimizu, A. B. Saetersdal, J. R. Kroep, A. Mailliez, E. Warner, V. F. Borges, F. Amant, A. Gombos, A. Kataoka, C. Rousset-Jablonski, S. Borstnar, J. Takei, J. E. Lee, J. M. Walshe, M. R. Borrego, H. C.F. Moore, C. Saunders, V. Bjelic-Radisic, S. Susnjar, F. Cardoso, N. J. Klar, T. Spanic, K. Ruddy, M. Piccart, L. A. Korde, A. Goldhirsch †, R. D. Gelber, O. Pagani, F. A. Peccatori

- Prospective, international, multicenter, investigator-initiated, single-arm trial



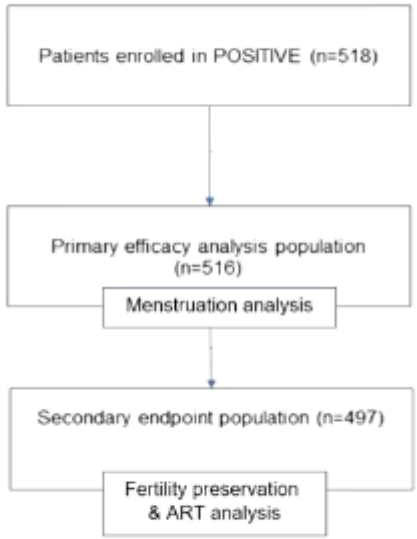
Endpoints

- **Primary**
  - Breast cancer free interval
- **Secondary**
  - Menstruation recovery
  - Use of assisted reproductive technology (ART)

Trial procedures

- At enrollment, all patients were asked to complete a menstrual diary for 2 years
- Information on use of fertility preservation **at diagnosis, prior to enrollment** was collected:
  - Ovarian stimulation for oocyte/embryo cryopreservation
  - GnRHa use during chemotherapy
  - Ovarian tissue cryopreservation
- Use of any ART modality **on study** was allowed (per physician/patient discretion) including:
  - Transfer of cryopreserved embryo
  - Ovarian stimulation for IVF
  - Intrauterine insemination
  - Clomiphene use
  - Embryo/egg donation

Trial enrollment and patient characteristics

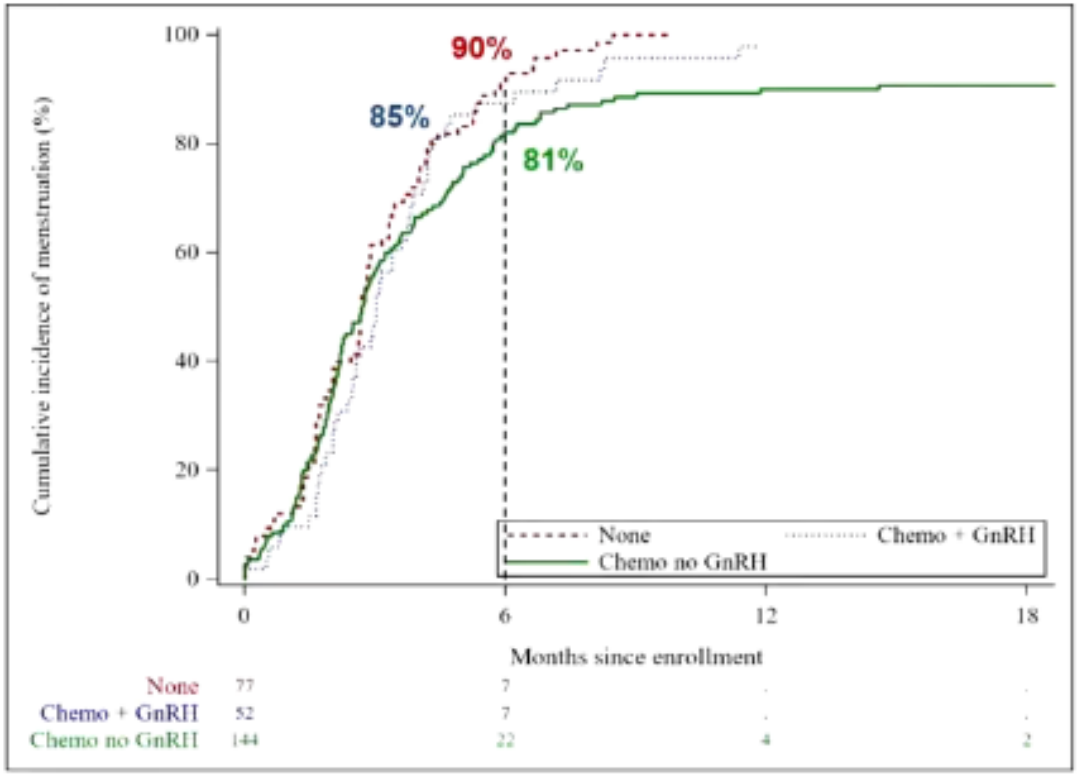


	Menstruation analysis population	FP & ART analysis population
Number	516	497
Age ≥ 35	339 (66%)	329 (66%)
Lymph node positive	174 (34%)	170 (34%)
Prior chemo	320 (62%)	308 (62%)
No prior live birth	387 (75%)	374 (75%)

FP: fertility preservation, ART: assisted reproductive technologies

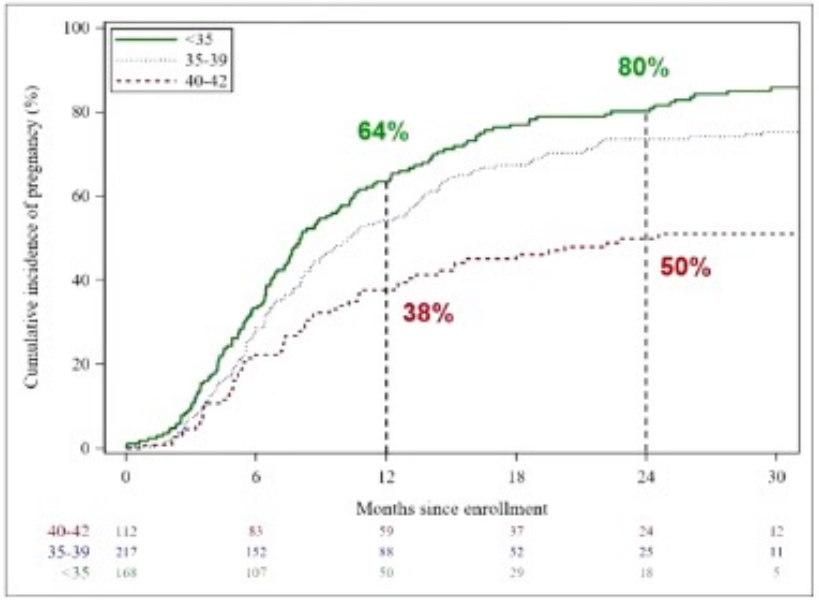
Menstruation recovery

- All 516 patients included in the 1ry analysis stopped ET within 1 month of study entry
- **273 patients (53%) reported amenorrhea at enrollment**
  - Of whom **255 patients (94%) recovered menses**



Time to pregnancy

368 patients (74%) reported at least one pregnancy



Multivariable Fine and Gray competing risk model	**sHR (95% CI)**
Chemo + GnRHa vs Chemo alone	1.29 (0.94 – 1.79)
None vs Chemo alone	1.05 (0.85 – 1.32)
35-39 vs <35	0.74 (0.59 – 0.93)
40-42 vs <35	0.40 (0.29 – 0.56)
SERM+OFS vs SERM only	0.94 (0.71 – 1.24)
AI+OFS vs SERM only	0.94 (0.67 – 1.33)
Prior birth: Yes vs No	0.94 (0.72 – 1.23)
Irregular vs Persistent amenorrhea	1.17 (0.85 – 1.63)
Normal vs Persistent amenorrhea	1.01 (0.78 – 1.32)

Fertility preservation and ART

- **Fertility preservation at BC diagnosis**
  - 252 / 497 (51%) underwent fertility preservation *
  - **179 (36%) ovarian stimulation for embryo/oocyte cryopreservation**
  - 67 (13%) GnRHa during chemotherapy
  - 30 (6%) ovarian tissue cryopreservation
- **ART use after enrollment**
  - 215 / 497 (43%) underwent ART on POSITIVE *
  - **80 (16%) ovarian stimulation for IVF**
  - **68 (14%) cryopreserved embryo transfer**
  - 37 (7%) intrauterine insemination
  - 19 (4%) clomiphene

* Some patients underwent more than 1 procedure

ART use and chance of pregnancy

Multivariate logistic regression model	OR (95% CI)
35-39 vs <35	0.50 (0.29 - 0.86)
40-42 vs <35	0.16 (0.08 - 0.29)
Ovarian stimulation for IVF after enrollment vs No ART	0.85 (0.48 - 1.50)
Cryopreserved embryo transfer * vs No ART	2.41 (1.17 - 4.95)
Other ART vs No ART	1.80 (0.92 - 3.57)
Chemotherapy + GnRHa vs Chemotherapy no GnRHa	1.41 (0.70 - 2.82)
None vs Chemotherapy without GnRHa	1.10 (0.70 - 1.75)

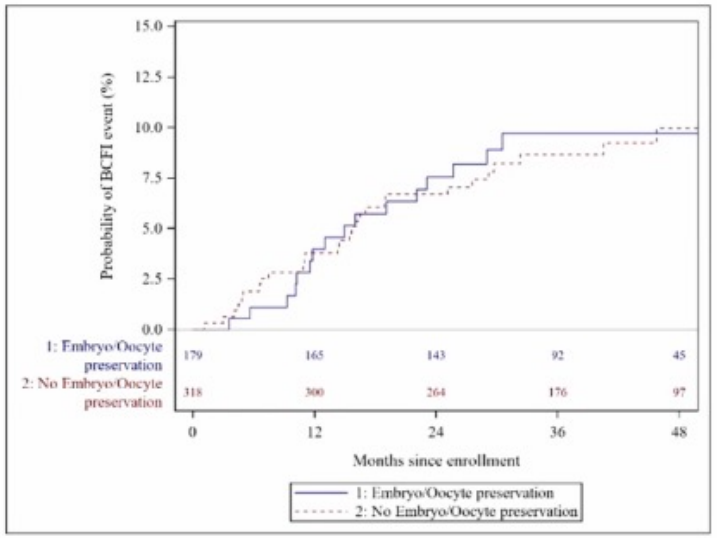
* 82% of patients reported at least 1 pregnancy

Ovarian stimulation and breast outcome

1) As part of embryo/oocyte cryopreservation
- at breast cancer diagnosis

At 3-years, BCFI-events cumulative incidence

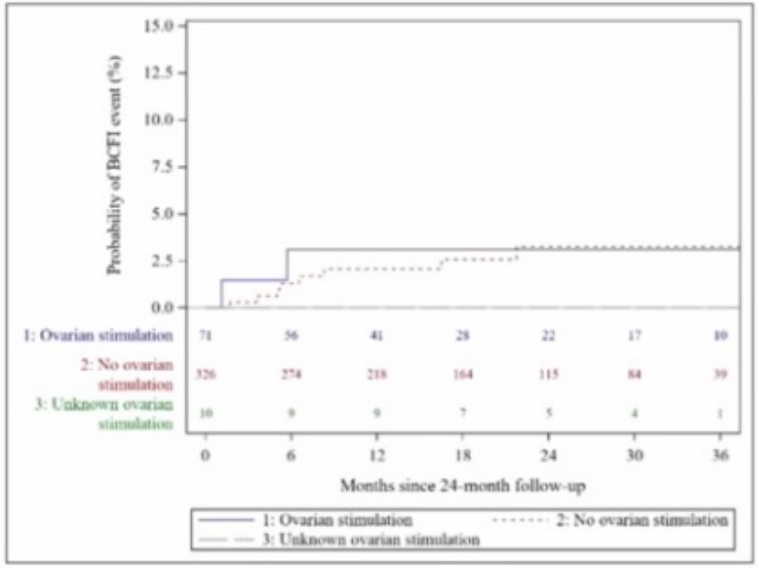
- **9.7%** (95% CI: 6.0% to 15.4%) for the 179 patients who underwent ovarian stimulation
- **8.7%** (95% CI: 6.0% to 12.5%) for the 318 patients who did not



ART and BC outcome

2) As part of ART - after enrollment

- **397 patients alive and BC free at 24-months (landmark analysis)**
  - 2 BC events amongst 71 patients in the ovarian stimulation group
  - 8 BC events amongst 326 patients in the non-ovarian stimulation group



Conclusions

- This is the largest prospective study to investigate fertility preservation and ART in patients with early HR+ BC who desired pregnancy
- More than 90% of women presenting with amenorrhea resumed menses, most during the first 6 months
- Young age was the main factor associated with shorter time to pregnancy
- Embryo/oocyte cryopreservation at BC diagnosis followed by embryo transfer after endocrine therapy interruption had higher pregnancy rates and was not associated with worse prognosis
- No increase in breast cancer events was observed in patients undergoing IVF on study albeit few events – longer follow-up is needed
- These data are of paramount importance for oncofertility counselling of young BC patients

Is pregnancy safe in pts with a BRCA mutation?

GS02-13: Pregnancy after Breast Cancer in Young Women with Germline *BRCA* Pathogenic Variants: Results from an International Cohort Study

Matteo Lambertini[1,2], Eva Blondeaux[3], Elisa Agostinetto[4], Anne-Sophie Hamy[5], Hee Jeong Kim[6], Antonio Di Meglio[7], Rinat Bernstein Molho[8], Florentine Hilbers[9], Katarzyna Pogoda[10], Estela Carrasco[11], Kevin Punie[12], Jyoti Bajpai[13], Michail Ignatiadis[4], Halle C.F. Moore[14], Kelly-Anne Phillips[15,16], Angela Toss[17], Christine Rousset-Jablonski[18], Fedro A. Peccatori[19], Tiphaine Renaud[20], Alberta Ferrari[21], Shani Paluch-Shimon[22], Robert Fruscio[23], Wanda Cui[15,16], Stephanie M. Wong[24], Claudio Vernieri[25], Kathryn J. Ruddy[26], Maria Vittoria Dieci[27,28], Alexios Matikas[29], Mariya Rozenblit[30], Cynthia Villarreal-Garza[31], Laura De Marchis[32], Lucia Del Mastro[1,2], Fabio Puglisi[33], Maria Del Pilar Estevez-Diz[34], Kenny A. Rodriguez-Wallberg[35,36], Bela Mrinakova[37], Sarah Meister[38], Luca Livraghi[39,40], Florian Clatot[41], Rinat Yerushalmi[42], Carmine De Angelis[43], Rodrigo Sánchez-Bayona[44], Icro Meattini[45], Natalia Cichowska-Cwalińska[46,47], Martine Berlière[48], Mahmoud Salama[49], Ugo De Giorgi[50], Amir Sonnenblick[51], Camila Chiodi[7], Young-Jin Lee[6], Camille Maria[5], Hatem A. Azim Jr.[31], Luca Boni[3], Ann H. Partridge[52]

[1]Department of Internal Medicine and Medical Specialties (DIMI), School of Medicine, University of Genova, Genova, Italy; [2]Department of Medical Oncology, U.O. Clinica di Oncologia Medica, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [3]Clinical Trial Unit, Epidemiologia Clinica, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [4]Department of Medical Oncology, Institut Jules Bordet and Université Libre de Bruxelles (U.L.B.), Brussels, Belgium; [5]Department of Medical Oncology, Université Paris Cité, Institut Curie, Paris, France; [6]Division of Breast Surgery, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [7]Département Médecine Oncologique, Gustave Roussy, Université Paris-Saclay, Villejuif, F-94805, France & INSERM U981, Villejuif, F-94805, France; [8]Susanne Levy Gertner Oncogenetics Unit, The Danek Gertner Institute of Human Genetics, Chaim Sheba Medical Center affiliated to Tel Aviv University, Tel Hashomer, Israel; [9]Department of Molecular Pathology, Netherlands Cancer Institute (NKI), Amsterdam, The Netherlands; [10]Department of Breast Cancer and Reconstructive Surgery, Maria Sklodowska-Curie National Research Institute of Oncology, Roentgena 5, 02-781 Warsaw, Poland; [11]Hereditary Cancer Genetics Unit, Medical oncology Department, Vall d'Hebron University Hospital, Vall d Hebron Institute of Oncology (VHIO), Barcelona, Spain; [12]Department of General Medical Oncology and Multidisciplinary Breast Center, Leuven Cancer Institute, University Hospitals Leuven, Leuven, Belgium; [13]Tata Memorial Centre, Homi Bhabha National Institute (HBNI), Mumbai, India; [14]Department of Medical Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland (OH), USA; [15]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [16]Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Victoria, Australia; [17]Department of Oncology and Haematology, Azienda Ospedaliero-Universitaria Policlinico di Modena, Italy; [18]Department of Surgery, Leon Berard Cancer Center, Lyon, France; [19]Gynecologic Oncology Department, European Institute of Oncology (IRCCS), Milan, Italy; [20]Cancer Genetics Unit, Bergonie Institute, Bordeaux, France; [21]Hereditary Breast and Ovarian Cancer (HBOC) Unit and General Surgery 3 - Senology, Breast Cancer Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy & University of Pavia, Italy; [22]Sharett Institute of oncology, Hadassah University Hospital & Faculty of Medicine, Hebrew University, Jerusalem, Israel; [23]UO Ginecologia, Department of Medicine and Surgery, University of Milan-Bicocca, IRCCS San Gerardo dei Tintori, Monza, Italy; [24]Stroll Cancer Prevention Centre, Jewish General Hospital, and McGill University Medical School, Montreal, Canada; [25]Medical Oncology Department, Breast Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [26]Department of Oncology, Mayo Clinic College of Medicine, Rochester (MN), USA; [27]Dipartimento di Scienze Chirurgiche, Oncologiche e Gastroenterologiche, Università di Padova, Padova, Italy; [28]Oncologia 2, Istituto Oncologico Veneto IRCCS, via Gattamelata 64, 35128 Padova, Italy; [29]Department of Oncology/Pathology, Karolinska Institute and Breast Center, Karolinska University Hospital, Stockholm, Sweden; [30]Smilow Cancer Hospital at Yale New Haven, New Haven (CT), USA; [31]Breast Cancer Center, Hospital Zambrano Hellion - TecSalud, Tecnológico de Monterrey, Monterrey, Mexico; [32]Division of Medical Oncology, Department of Radiological, Oncological and Pathological Sciences, "La Sapienza" University of Rome, Rome, Italy; [33]Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy; Department of Medicine, University of Udine, Udine, Italy; [34]Cancer Institute ICESP, Sao Paulo, Brazil; [35]Karolinska Institute, Department of Oncology-Pathology, Laboratory of Translational Fertility Preservation, [36]Karolinska University Hospital, Department of Reproductive Medicine, [37]1st Department of Oncology, Comenius University & St. Elisabeth Cancer Institute, Bratislava, Slovakia; [38]Breast Center, Dept. OB&GYN and CCC Munich, LMU University Hospital, Munich, Germany; [39]Azienda Ospedaliera "Papa Giovanni XXIII", Bergamo, Italy; [40]Nuovo Ospedale di Prato - Santo Stefano, Prato, Italy; [41]Centre Henri Becquerel, Rouen, France; [42]Davidoff Center, Rabin Medical Center, Petah Tikva, Tel-Aviv University, Tel-Aviv, Israel; [43]University of Naples "Federico II", Napoli, Italy; [44]Hospital Universitario 12 de Octubre, Madrid, Spain; [45]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy & Radiation Oncology Unit, Oncology Department, Florence University Hospital, Florence, Italy; [46]Department of Oncology and Radiotherapy, Medical University of Gdańsk, Gdańsk, Poland; [47]Early Phase Clinical Trials Centre, Medical University of Gdańsk, Gdańsk, Poland; [48]Cliniques Universitaires Saint-Luc UCL, Brussels, Belgium; [49]Oncofertility Consortium & Department of Obstetrics, Gynecology and Reproductive Biology, Michigan State University (MSU), East Lansing (MI), USA; [50]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola (FC), Italy; [51]The Oncology Division, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [52]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA.

SABCS
DECEMBER 5–9, 2023

Study design

- International, multicenter, hospital-based, retrospective cohort study

Key inclusion criteria

- Stage I - III invasive breast cancer
- Diagnosis between January 2000 and December 2020
- Age ≤ 40 years at diagnosis
- Known germline likely pathogenic or pathogenic variants in *BRCA1* and/or *BRCA2* genes

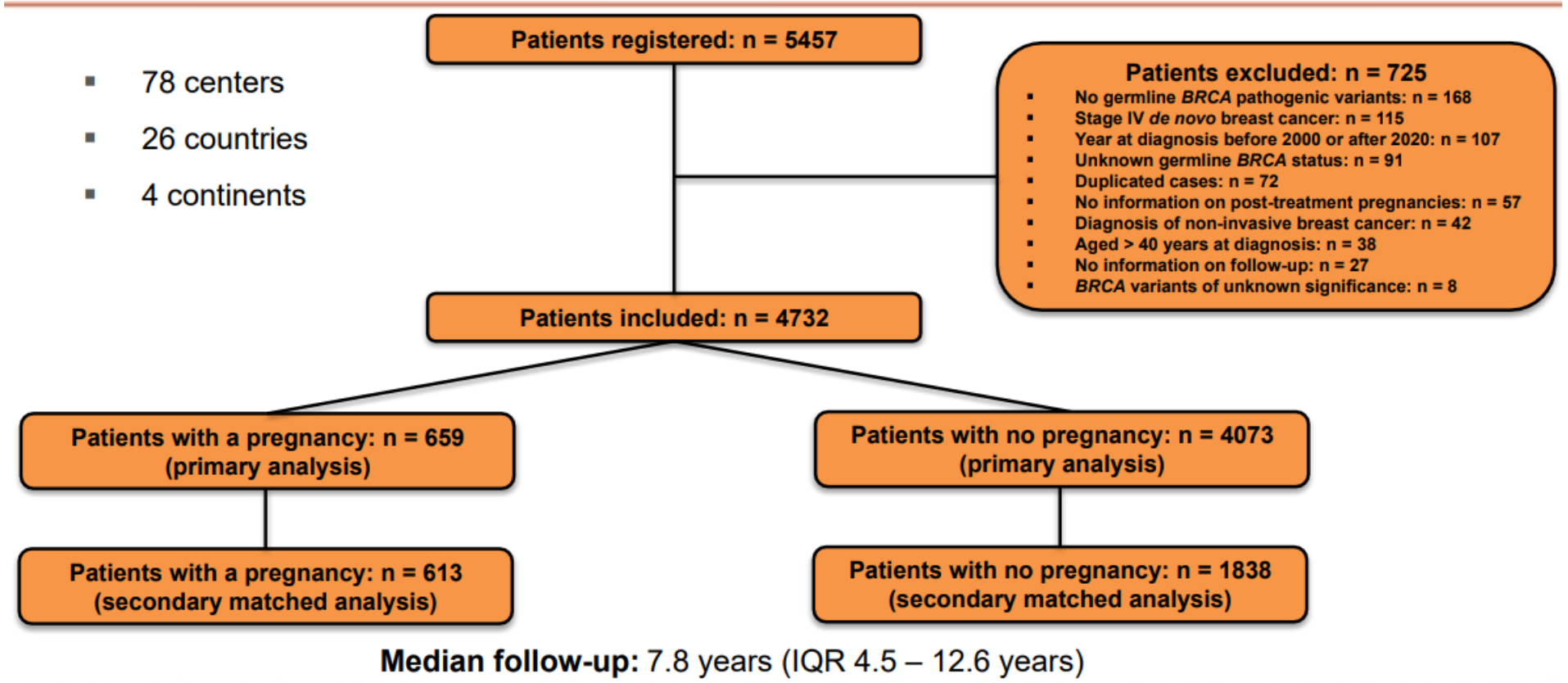
Key exclusion criteria

- Stage IV *de novo* breast cancer
- Lack of data on follow-up or post-treatment pregnancies
- History of ovarian cancer or other malignancies without prior breast cancer
- *BRCA* VUS or *BRCA* healthy carriers

Objectives of the study

- **Primary objectives** – To determine the cumulative incidence of pregnancy after breast cancer and its prognostic impact:
  - Cumulative incidence of pregnancy
  - Disease-free survival
- **Secondary objectives** – To determine the prognostic impact of pregnancy after breast cancer and reproductive outcomes:
  - Breast cancer-specific survival
  - Overall survival
  - Pregnancy, fetal and obstetric outcomes
- **Predefined subgroup analyses** – According to specific *BRCA* gene, hormone receptor status, HER2 status, exposure to chemotherapy and endocrine therapy

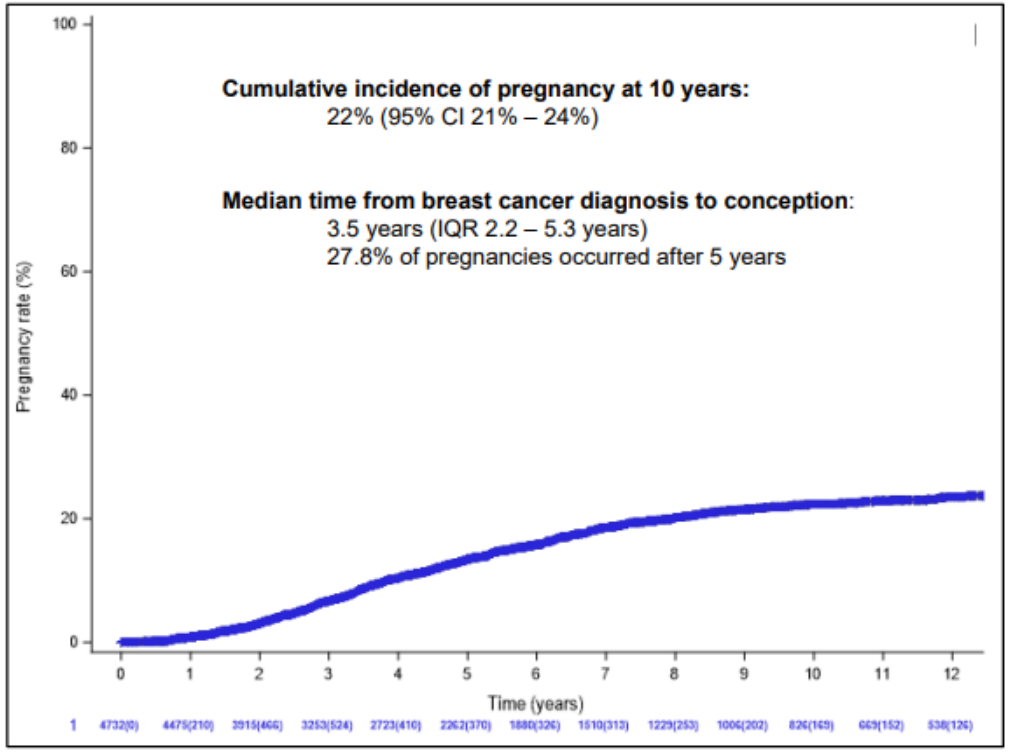
Participant flow



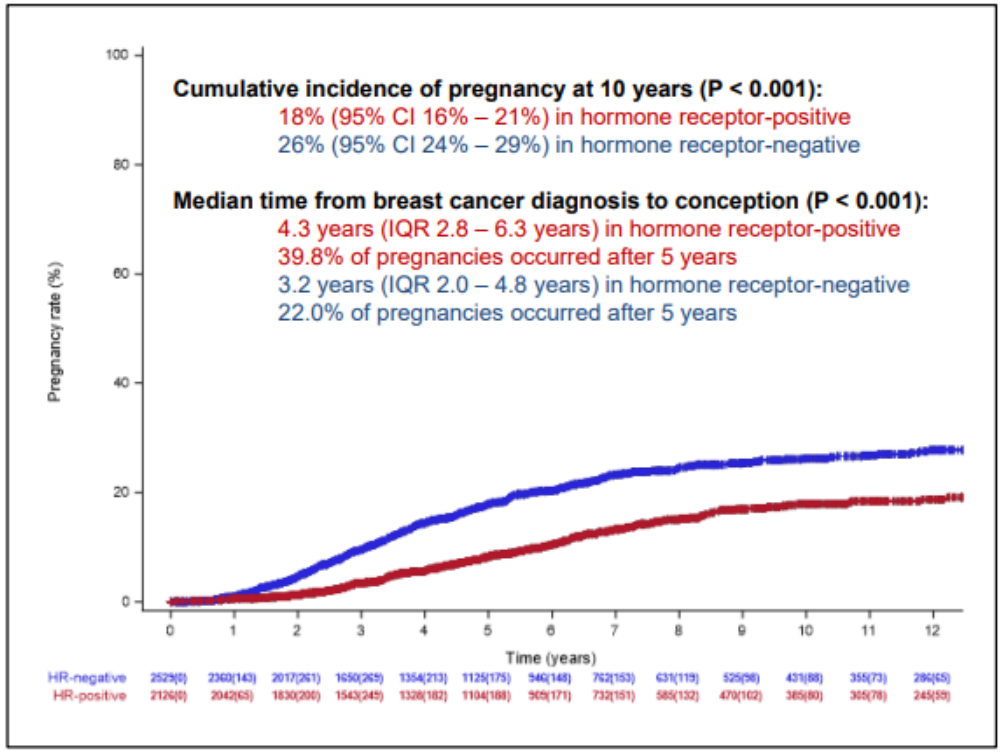
Median follow-up: 7.8 years (IQR 4.5 – 12.6 years)

Study results: incidence of pregnancy

Overall cohort



According to hormone receptor status



Study results: DFS

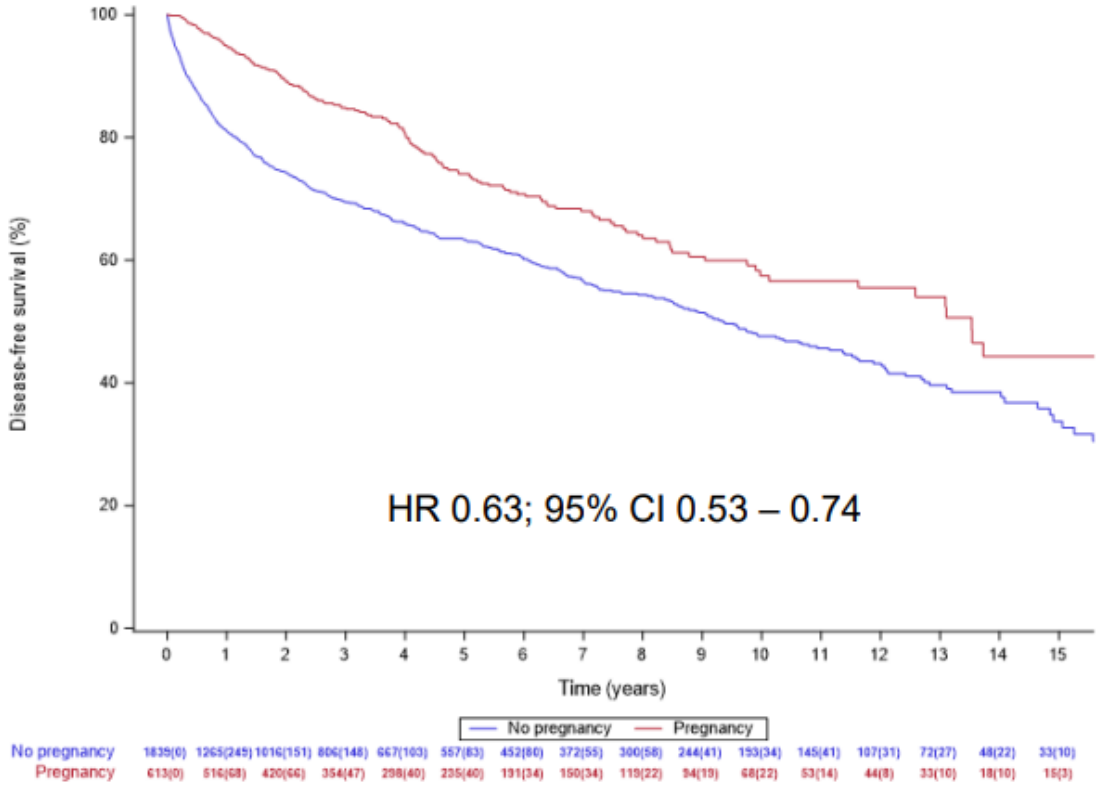
Primary analysis – Extended Cox model with occurrence of pregnancy as a time-varying covariate

Unadjusted HR 0.97; 95% CI 0.82 – 1.15
Adjusted HR* 0.99; 95% CI 0.81 – 1.20

Subgroup analyses	Multivariate HR* (95% CI)	P value for interaction
Specific *BRCA* gene		
BRCA1	0.80 (0.63 – 1.01)	0.007
BRCA2	1.55 (1.12 – 2.16)	
BRCA1 and *BRCA2*	4.49 (0.28 – 72.17)	
BRCA, unknown if 1 or 2	Not evaluable	
Hormone receptor status:		
ER and/or PR positive	1.30 (0.95 – 1.76)	0.009
ER and PR negative	0.76 (0.60 – 0.95)	
Unknown	0.28 (0.04 – 2.21)	
HER2 status:		
HER2 negative	0.61 (0.22 – 1.71)	0.08
HER2 positive	1.07 (0.87 – 1.31)	
Unknown	0.42 (0.17 – 1.02)	
Received chemotherapy:		
No	0.77 (0.39 – 1.52)	0.47
Yes	1.00 (0.82 – 1.23)	
Unknown	0.77 (0.39 – 1.52)	
Received endocrine therapy:		
No	0.85 (0.67 – 1.08)	0.01
Yes	1.55 (1.08 – 2.21)	
Unknown	0.13 (0.01 – 2.95)	

*Adjusted for: region, age, nodal status, hormone receptor status and type of breast surgery

Secondary matched analysis



Study results: secondary survival outcomes

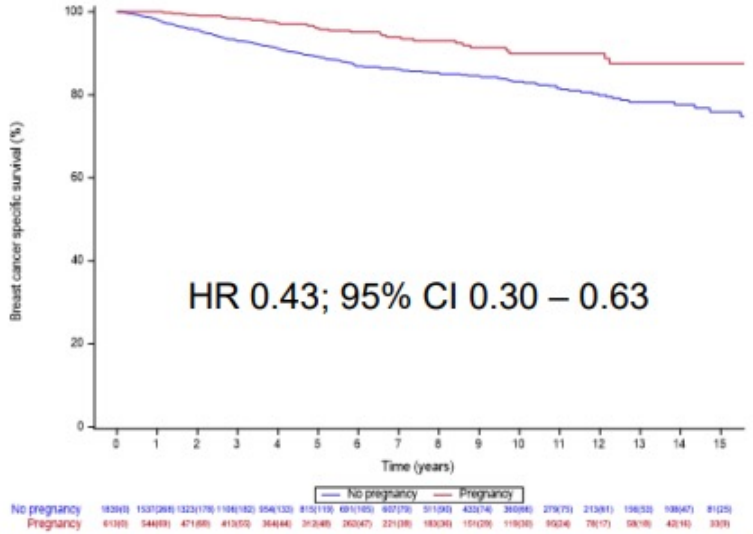
Breast cancer-specific survival

Extended Cox model:

Unadjusted HR 0.53; 95% CI 0.37 – 0.74

Adjusted HR* 0.60; 95% CI 0.40 – 0.88

Secondary matched analysis:



*Adjusted for: region, age, nodal status, hormone receptor status and type of breast surgery

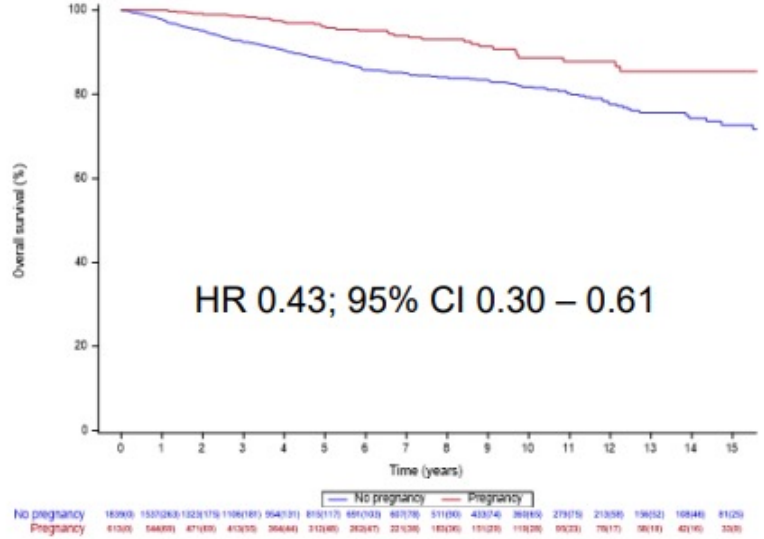
Overall survival

Extended Cox model:

Unadjusted HR 0.52; 95% CI 0.38 – 0.72

Adjusted HR* 0.58; 95% CI 0.40 – 0.85

Secondary matched analysis:



Conclusions

- This global study including 4732 young *BRCA* carriers from 78 centers worldwide provides reassuring evidence for the oncofertility counseling of young *BRCA* carriers interested in conceiving following diagnosis and treatment for breast cancer
- More than one out of five (22%) young *BRCA* carriers became pregnant within 10 years after a breast cancer diagnosis
- The rate of pregnancy, fetal and obstetric complications was low and in line with the expectations in a population of women with similar age and no history of breast cancer
- No detrimental prognostic effect of pregnancy after breast cancer was observed, particularly in *BRCA1* carriers

- **Conceiving after proper treatment and follow-up for breast cancer should not be contraindicated in young *BRCA* carriers**

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients

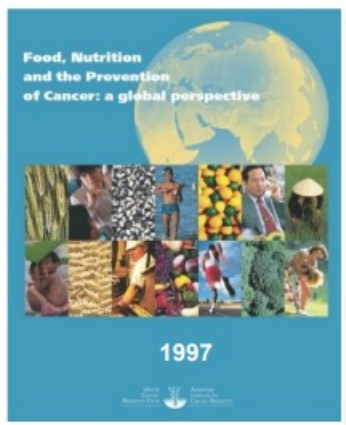
- Health education after breast cancer

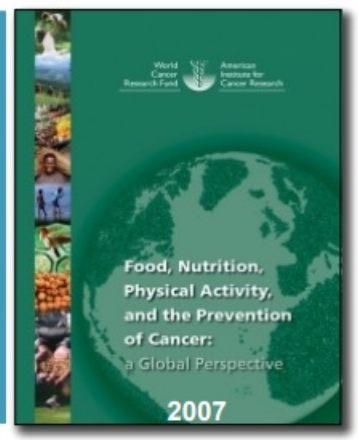
- Safety and toxicity according to age, race and realworld data

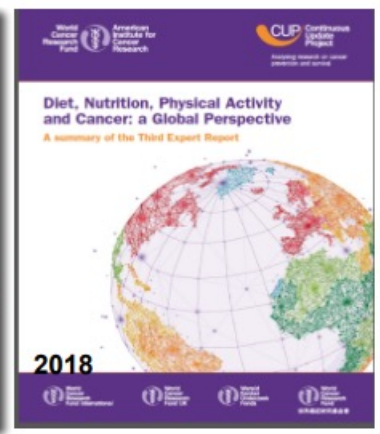
- PRO outcome: utility?
- New anti emetic regimen

Weight reduction and exercise

Practice changing?







Convincing Evidence:
12 Obesity-Associated Cancer Types

Is patient education after BC worthwhile?

Effectiveness of 24-week mobile application based human coaching program for controlling weight, BMI and body composition in overweight/obese breast cancer survivors: Single-arm prospective cohort study

So-Youn Jung, MD. PhD
Center for Breast Cancer, National Cancer Center, Goyang, Republic of Korea

Disclosure Information

- Employee of: National Cancer Center, Republic of Korea
- This study was supported by a grant from National Cancer Center, Republic of Korea
- Acknowledgements: Breast cancer survivors in Korea, and Noom, Korea

SABCS
DECEMBER 5–9, 2023

Objectives and methods

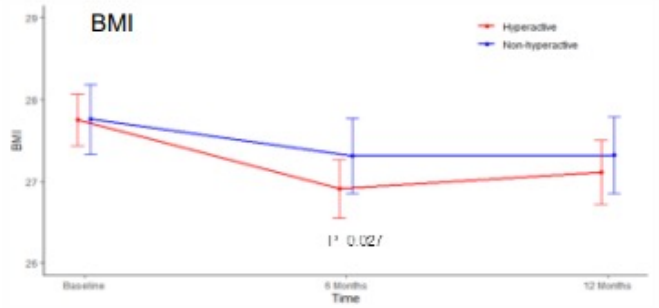
- Backgrounds: Overweight/obesity has been known as a prognostic factor for breast cancer recurrence and breast cancer related death.
- Objective: to develop 24-week mobile application based human coaching program and evaluate its efficacy in overweight/obese breast cancer survivors.
- Hypothesis: Hyperactive group using 24-week mobile application based human coaching program would reduce more than 0.8 of BMI in overweight/obese breast cancer survivors
- Study design:
  - a single-arm prospective study
  - 130 breast cancer survivors with BMI ≥25 were enrolled
  - 24-week program: diet-,exercise-, and psychology-based contents with trained human coach
  - Outcome: weight, BMI, lipid level, bioimpedance, and Quality of Life (QoL) at baseline, 6 month and 12month follow-up in hyperactive group who joined more than 16 weeks

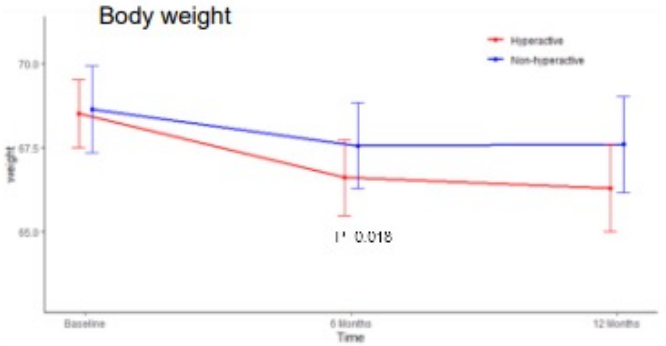
Results

- 101 participants (77.7%) and 93 participants (71.5%) completed 6 month and 12 month follow-up
- In hyperactive group (68/101, 67% at 6 month and 61/101, 60.4% at 12 month), body weight and BMI reduced significantly at 6 month and maintained at 12 month without the yo-yo effect.

Variables, mean (SD)	Hyperactive (N=61)			6months-Baseline		12months-Baseline		12months-6month	
	Baseline	6mon	12 mon	mean diff (95%CI)	P*	mean diff (95%CI)	P*	mean diff (95%CI)	P*
Weight (kg)	68.52(7.88)	66.61(8.78)	66.3(10.25)	-1.91(-2.65, -1.17)	<.0001	-2.22(-3.67, -0.77)	0.0034	-0.31(-1.79, 1.17)	**0.6778**
BMI (kg/m²)	27.75(2.45)	26.91(2.8)	27.11(3.08)	-0.84(-1.16, -0.53)	<.0001	-0.64(-1.05, -0.23)	0.0026	0.2(-0.12, 0.53)	**0.2159**
Triglycerides	174.02(92.65)	132.02(69.74)	135.72(65.26)	-42(-63.67, -20.33)	0.0003	-38.3(-58.54, -18.05)	0.0004	3.7(-11.89, 19.3)	0.6364
HDL-cholesterol	55.77(13.49)	57.79(13.03)	57.57(14.04)	2.02(-0.54, 4.58)	0.1203	1.8(-1.01, 4.61)	0.2040	-0.21(-2.51, 2.09)	0.8536
LDL-cholesterol	109.64(35.16)	109.02(32.92)	107.8(34.99)	-0.62(-7.42, 6.17)	0.8551	-1.84(-9.77, 6.1)	0.6452	-1.21(-6.65, 4.22)	0.6569
SMM(kg)	23.81(3.08)	24.73(3.99)	24.23(3.21)	0.92(0.28, 1.56)	0.0059	0.42(-0.09, 0.92)	0.1034	-0.5(-1.23, 0.23)	0.1749
BFM(kg)	25.06(5.28)	21.79(6.75)	23.04(7.2)	-3.27(-4.5, -2.04)	<.0001	-2.02(-3.17, -0.87)	0.0009	1.25(-0.19, 2.7)	0.0886
PBF(%)	36.39(4.72)	32.36(7.53)	33.78(6.85)	-4.03(-5.7, -2.36)	<.0001	-2.61(-4.08, -1.13)	0.0008	1.42(-0.5, 3.34)	0.1434
WHR	0.88(0.07)	0.82(0.08)	0.87(0.07)	-0.05(-0.08, -0.03)	<.0001	-0.01(-0.02, 0.01)	0.4013	0.04(0.02, 0.07)	0.0019
VFA(cm2)	111.68(35.05)	88.12(39.47)	102.45(43.44)	-23.56(-33.62, -13.5)	<.0001	-9.23(-16.72, -1.73)	0.0167	14.33(3.33, 25.33)	0.0115

* Paired T test





Conclusions

- This study demonstrated that 24-week mobile application based human coaching program is beneficial for controlling body weight, BMI, TG and body composition in bioimpedance for overweigh/obsess breast cancer survivors.
- However, it would be not enough to maintain some parts of improved body composition (WHR, VFA).
- In addition, further randomized study need to demonstrate the effect of 24-week mobile application based human coaching program compared to conventional education.

The Breast Cancer Weight Loss Trial

3136 Participants

Key Eligibility*

- Stage II-III Breast Cancer
- HR+/HER-2- or TNBC
- Diagnosed w/in past 14 months
- Completed with surgery and any chemotherapy and/or radiation
- BMI ≥ 27 kg/m2

Randomize

- **Health Education + 2-year Telephone-Based Weight Loss Intervention**
- **Health Education Alone**

*Patients planning on taking medications for the purpose of weight loss and/or undergoing a surgical weight loss procedure within 2 years were not eligible

Ligibel et al. npj Breast Cancer. 2017

The Breast cancer Weight Loss trial

Impact of weight and body composition in BC

% Weight Change at 12-months (SD).

	Control (n=1173)	WLI (n=1220)	P value*
Overall	+0.8 (6.4)	-4.8 (7.9)	P <0.0001
Menopausal status			
Premenopausal	+1.4 (6.6)	-3.3 (7.8)	P <0.0001
Postmenopausal	+0.5 (6.3)	-5.9 (7.8)	P < 0.0001
Race/Ethnicity			
Black	+2.1 (5.9)	-1.6 (7.1)	P <0.0001
Hispanic	+1.0 (6.6)	-3.2 (6.3)	P <0.0001
Non-Black/non-Hispanic	+0.7 (6.4)	-5.4 (8.0)	P <0.0001
HR Status			
HR+	+0.8 (6.3)	-5.0 (7.5)	P < 0.0001
HR-	+1.0 (6.7)	-3.7 (8.0)	P < 0.0001

*Kruskal-Wallis test.

J Clin Oncol 41, 2023 (suppl 16; abstr 12001)

Can lifestyle be practice changing?

Randomized Trial of Exercise and Nutrition on Chemotherapy Completion and Pathologic Complete Response in Women With Breast Cancer: The Lifestyle, Exercise, and Nutrition Early After Diagnosis Study

Tara Sanft, MD[1,2]; Maura Harrigan, RD, MS, CSO[3]; Courtney McGowan, RD, CSO[3]; Brenda Cartmel, PhD[2,3]; Michelle Zupa, BS[3]; Fang-Yong Li, MS[3]; Leah M. Ferrucci, PhD[2,3]; Leah Puklin, MPH[3]; Anlan Cao, BS[3]; Thai Hien Nguyen, MPH[3]; Marian L. Neuhouser, PhD[4]; Dawn L. Hershman, MD[5]; Karen Basen-Engquist, PhD[6]; Beth A. Jones, PhD[2,3]; Tish Knobf, PhD[2,7]; Anees B. Chagpar, MD, MPH[1,2]; Andrea Silber, MD[1,2]; Anna Tanasijevic, MPH[8]; Jennifer A. Ligibel, MD[8]; and Melinda L. Irwin, PhD, MPH[2,3]

DOI https://doi.org/10.1200/JCO.23.00871

Methods

- 173 stage I-III pts

- R to ***usual care*** or ***intervention*** with ***exercise*** and ***nutrition advice***
- Primary objectives: RDI and pCR

TABLE 5. Effect of Intervention Versus UC on RDI and pCR Among Women Receiving Neoadjuvant Chemotherapy by Study Arm (N = 72)

Variable	Intervention	UC	*P*
Overall	N = 40	N = 32	
RDI continuous, mean ± SD	92.0% ± 12.1%	89.3% ± 11.6%	.34
Dose reductions, skip, and/or toxicity delays, No. (%)	20 (50)	19 (63)	.43
pCR, No. (%)	21 (53)	9 (28)	.037
HR+ and HER2−	N = 10	N = 12	
RDI, mean ± SD	96.0% ± 7.2%	90.6% ± 9.1%	.16
Dose reductions and/or toxicity delays, No. (%)	5 (40)	9 (75)	.19
pCR, No. (%)	3 (30)	0 (0)	.08
TNBC	N = 16	N = 10	
RDI, mean ± SD	89.2% ± 13.0%	84.6% ± 13.9%	.40
Dose reductions and/or toxicity delays, No. (%)	9 (56)	8 (80)	.48
pCR, No. (%)	11 (69)	3 (30)	.05
HER2+	N = 14	N = 10	
RDI, mean ± SD	92.4% ± 12.3%	92.6% ± 12.6%	.98
Dose reductions and/or toxicity delays, No. (%)	6 (43)	3 (30)	.52
pCR, No. (%)	7 (50)	6 (60)	.63

Weight reduction and exercise

Practice changing? ***Yes***

Effects of a structured and individualized exercise program on fatigue and health-related quality of life in patients with metastatic breast cancer: the multinational randomized controlled PREFERABLE-EFFECT study

Anne May[1], Anouk Hiensch[1], Johanna Depenbusch[2,3], Martina Schmidt[2,3], Evelyn Monninkhof[1], Mireia Pelaez[4], Dorothea Clauss[5], Philipp Zimmer[5,6], Jon Belloso[4], Mark Trevaskis[7], Helene Rundqvist[8], Joachim Wiskemann[3,9], Jana Muller[3,9], Carlo Fremd[2,3], Renske Altena[8], Joanna Kufel-Grabowska[10], Rhode Bijlsma[1], Lobke van Leeuwen-Snoeks[11], Daan ten Bokkel-Huinink[12], Gabe Sonke[13], Bruce Mann[14], Prudence Francis[15], Gary Richardson[16], Isabel Álvarez[17], Wolfram Malter[19], Elsken Van der Wall[1], Neil Aaronson[13], Elżbieta Senkus[10], Ander Urriticoechea[4], Eva Zopf[7,16], Wilhelm Bloch[5], Martijn Stuiver[13], Yvonne Wengström[8], Karen Steindorf[2,3]

(1) University Medical Center Utrecht, Utrecht, Utrecht University, Netherlands; (2) German Cancer Research Center (DKFZ); (3) National Center for Tumor Diseases (NCT) Heidelberg, Germany; (4) OSID-Onkologikoa, Osakidetza;(5) German Sport University Cologne, Germany; (6) TU Dortmund University, Germany; (7) Australian Catholic University; (8) Karolinska Institutet, Sweden; (9) Heidelberg University Hospital; (10) Medical University of Gdańsk; (11) Diakonessenhuis Utrecht, Netherlands; (12) Alexander Monro Hospital, Netherlands; (13) Netherlands Cancer Institute, Netherlands; (14) The Royal Melbourne Hospital, Parkville, Victoria, Australia; (15) Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia;(16) Cabrini, Australia; (17) Hospital Universitario Donostia-BioDonostia. GEICAM Spanish Breast Cancer Group, Spain; (19) Universitätsklinikum Köln, Germany

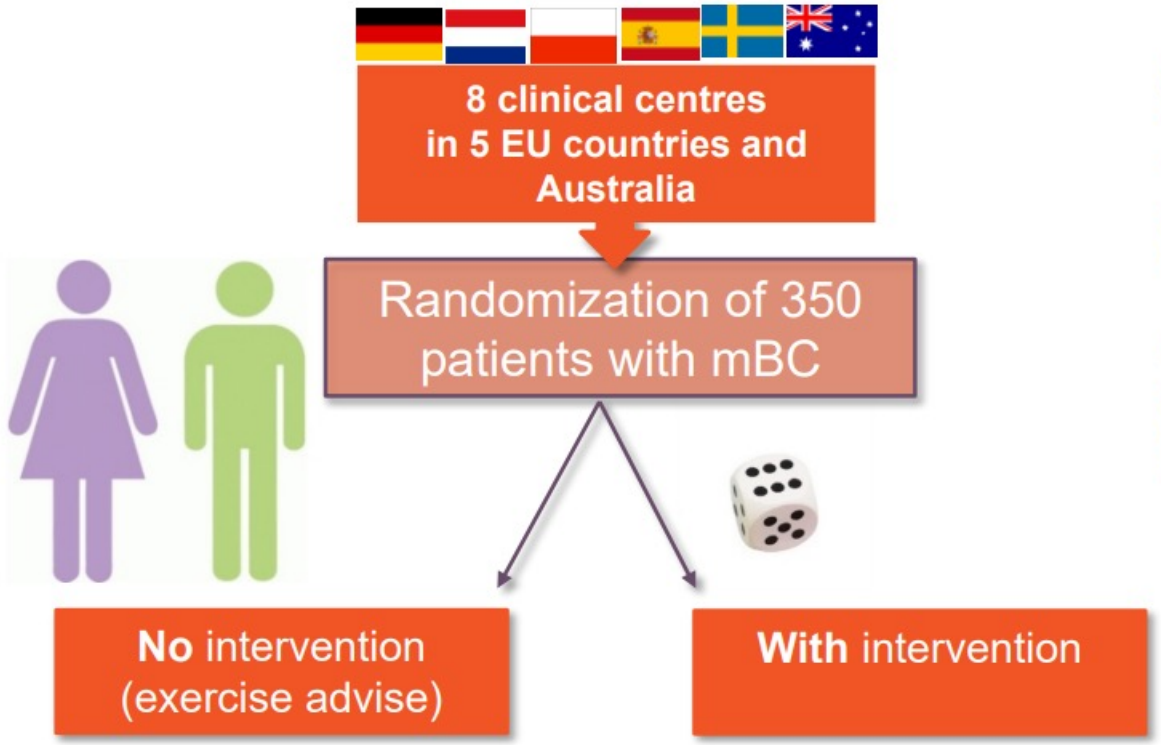
SABCS
DECEMBER 5–9, 2023

Aim of the trial

To investigate the effects of supervised and individualized exercise in patients with metastatic breast cancer on fatigue and quality of life.

PREFERABLE

Study design



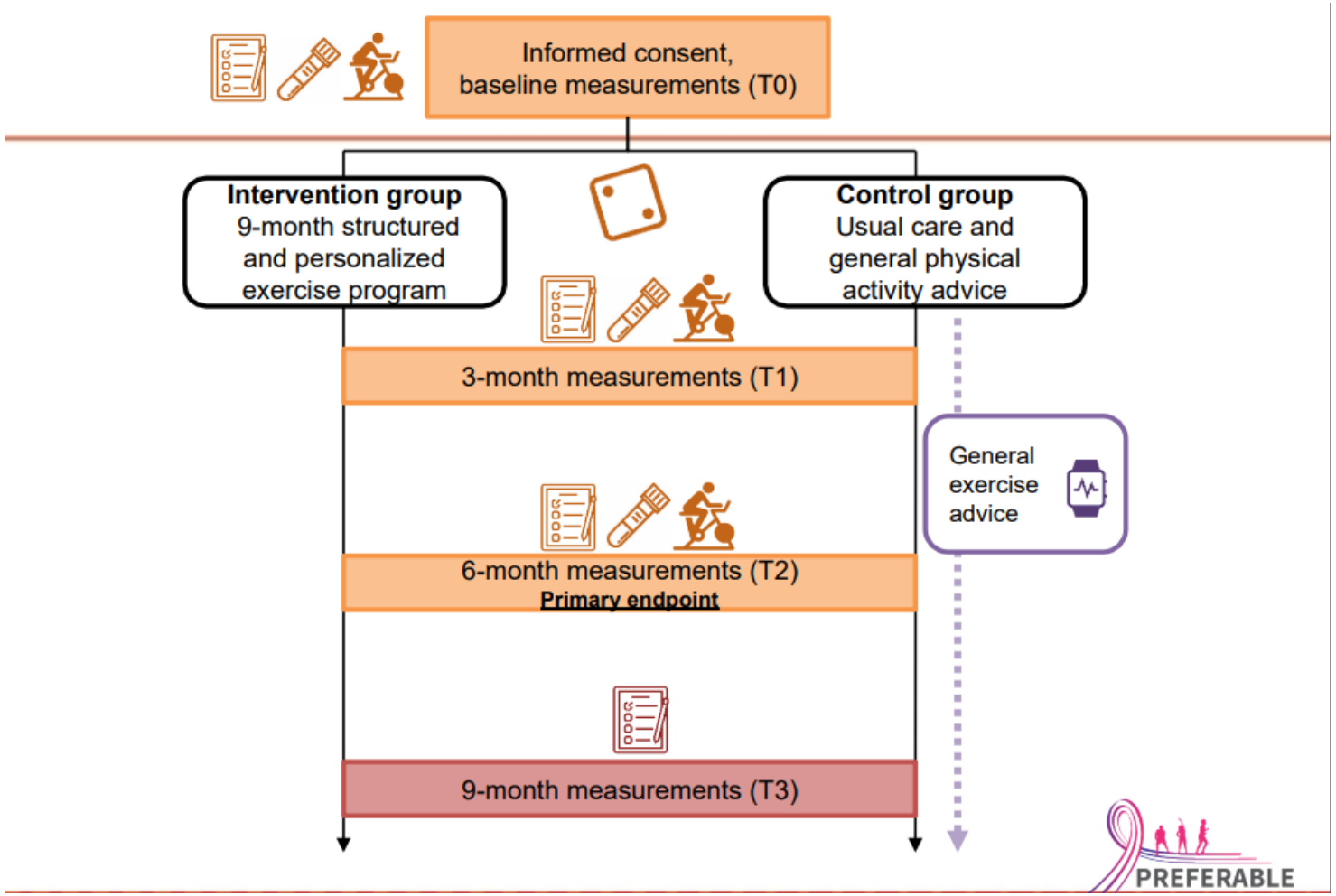
Inclusion criteria:

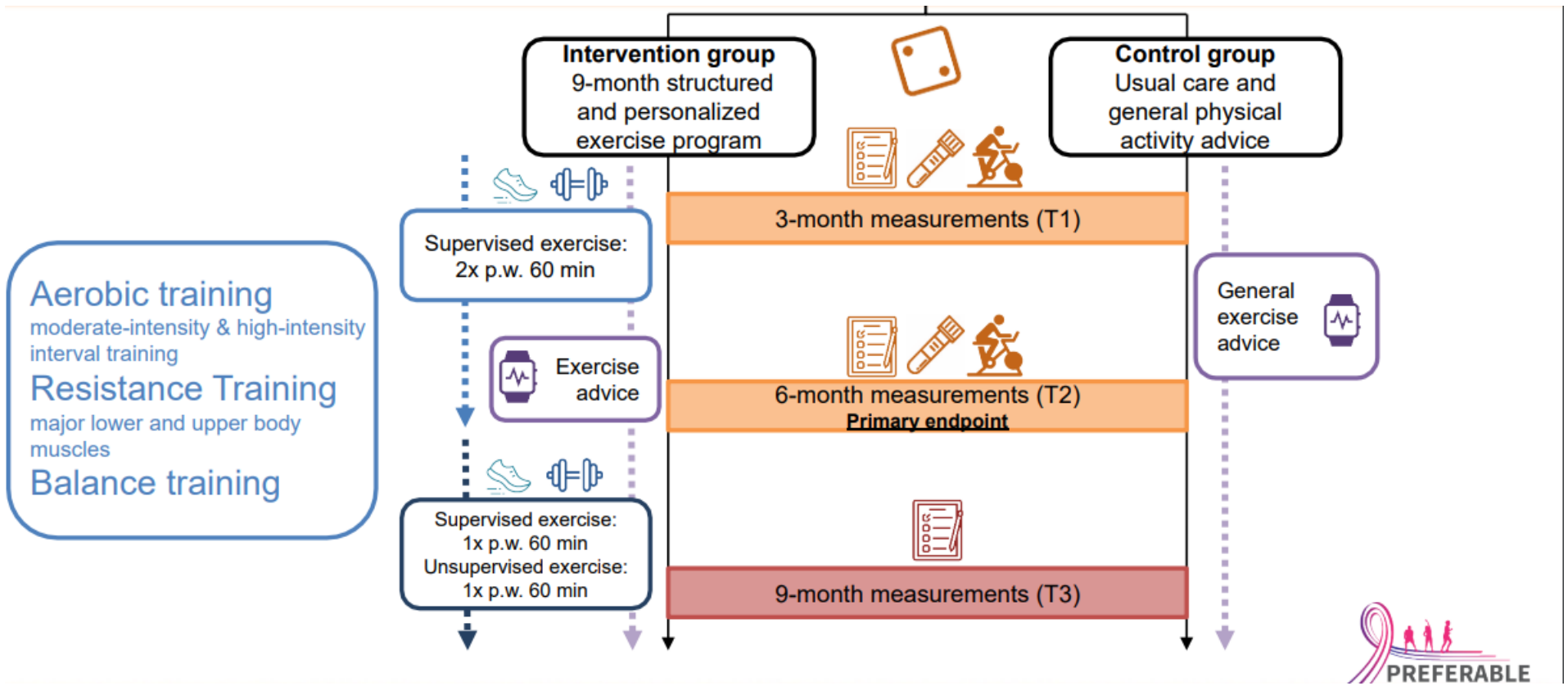
- *Age ≥ 18 years*
- *Diagnosis of breast cancer stage IV*
- *ECOG performance status ≤ 2*
- *Life expectancy of ≥6 months*

Exclusion criteria:

- *Contraindication for exercise*
- *Unstable bone metastases*
- *Too physically active (>210 min/wk)*

PREFERABLE


Informed consent,
baseline measurements (T0)
Intervention group
9-month structured
and personalized
exercise program
Control group
Usual care and
general physical
activity advice
3-month measurements (T1)
General
exercise
advice
6-month measurements (T2)
Primary endpoint
9-month measurements (T3)
PREFERABLE


Intervention group
9-month structured and personalized exercise program
Control group
Usual care and general physical activity advice
Aerobic training
moderate-intensity & high-intensity interval training
Resistance Training
major lower and upper body muscles
Balance training
Supervised exercise: 2x p.w. 60 min
Exercise advice
Supervised exercise: 1x p.w. 60 min
Unsupervised exercise: 1x p.w. 60 min
3-month measurements (T1)
6-month measurements (T2)
Primary endpoint
9-month measurements (T3)
General exercise advice
PREFERABLE

Methods: objectives

Primary endpoints:
- Cancer-related **physical fatigue**
- Health-related **QoL**

Secondary endpoints include:
- Pain, breast cancer specific symptoms, anxiety, depression
- Polyneuropathy, sleep
- Treatment related toxicities
- **Physical fitness**/performance, body composition
- Biomarkers
- Physical activity
- QALYs and direct and indirect costs

- EORTC-FA-12
- EORTC-QLQ-30 summary score

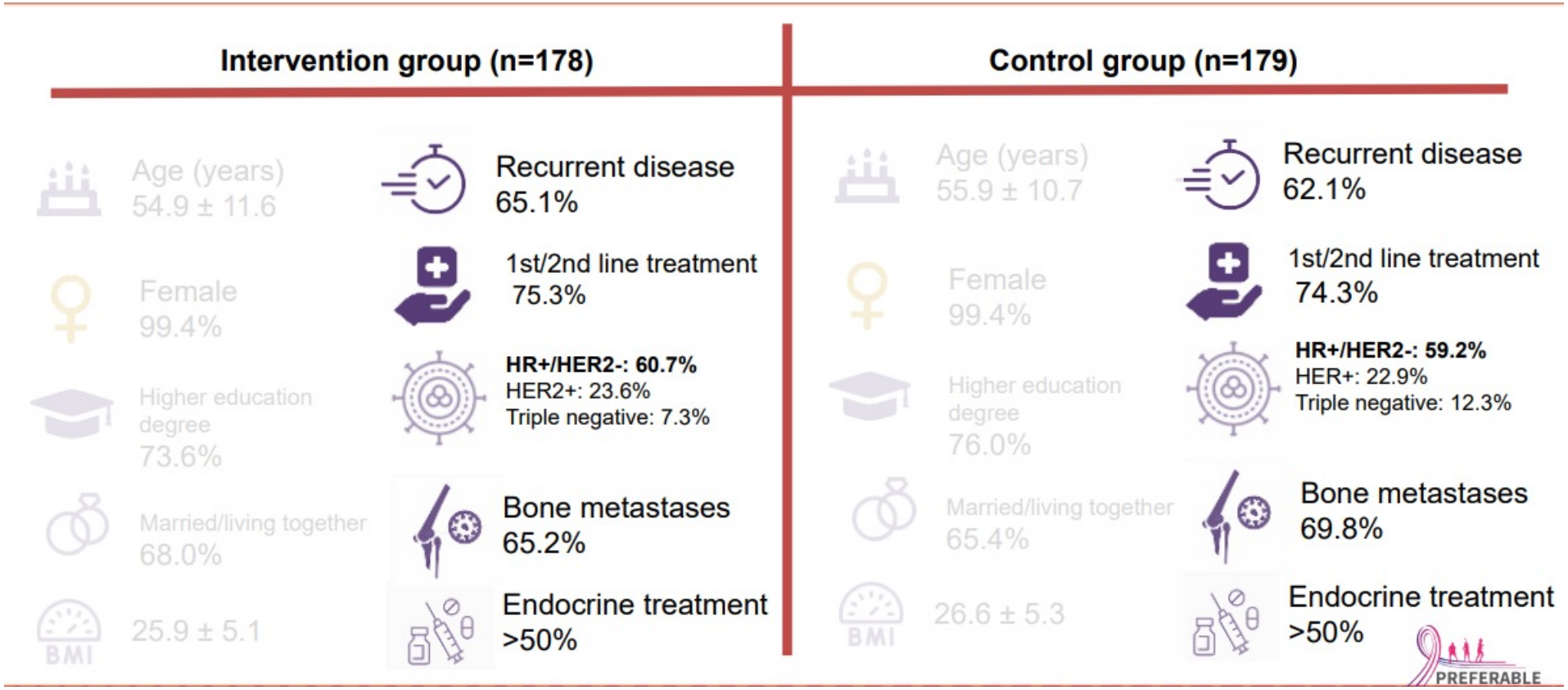
Trial successful if either or both are statistically significant.*

- Steep ramp test (maximal short exercise capacity (MSEC))

*At 6-month post baseline, using mixed effect models adjusted for baseline and stratification factors (Bonferroni correction).

PREFERABLE

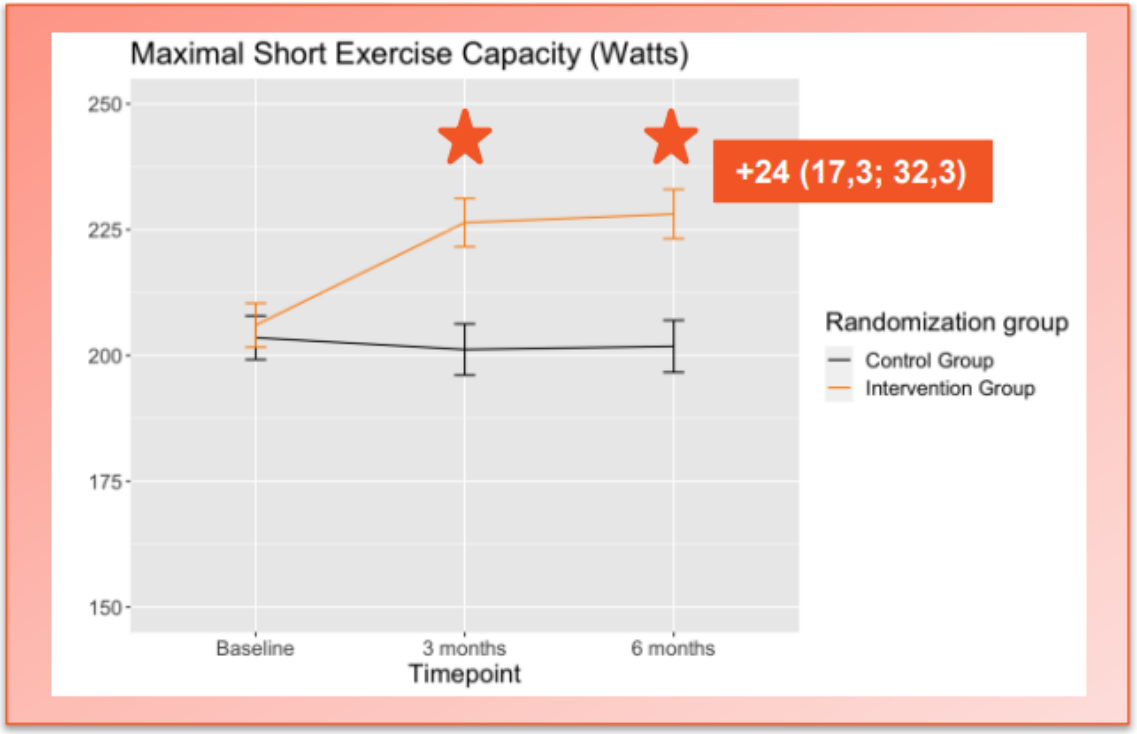
Baseline characteristics



Results: attendance, SAE & fitness outcome

Median attendance
[IQR] = 77% [48-92]

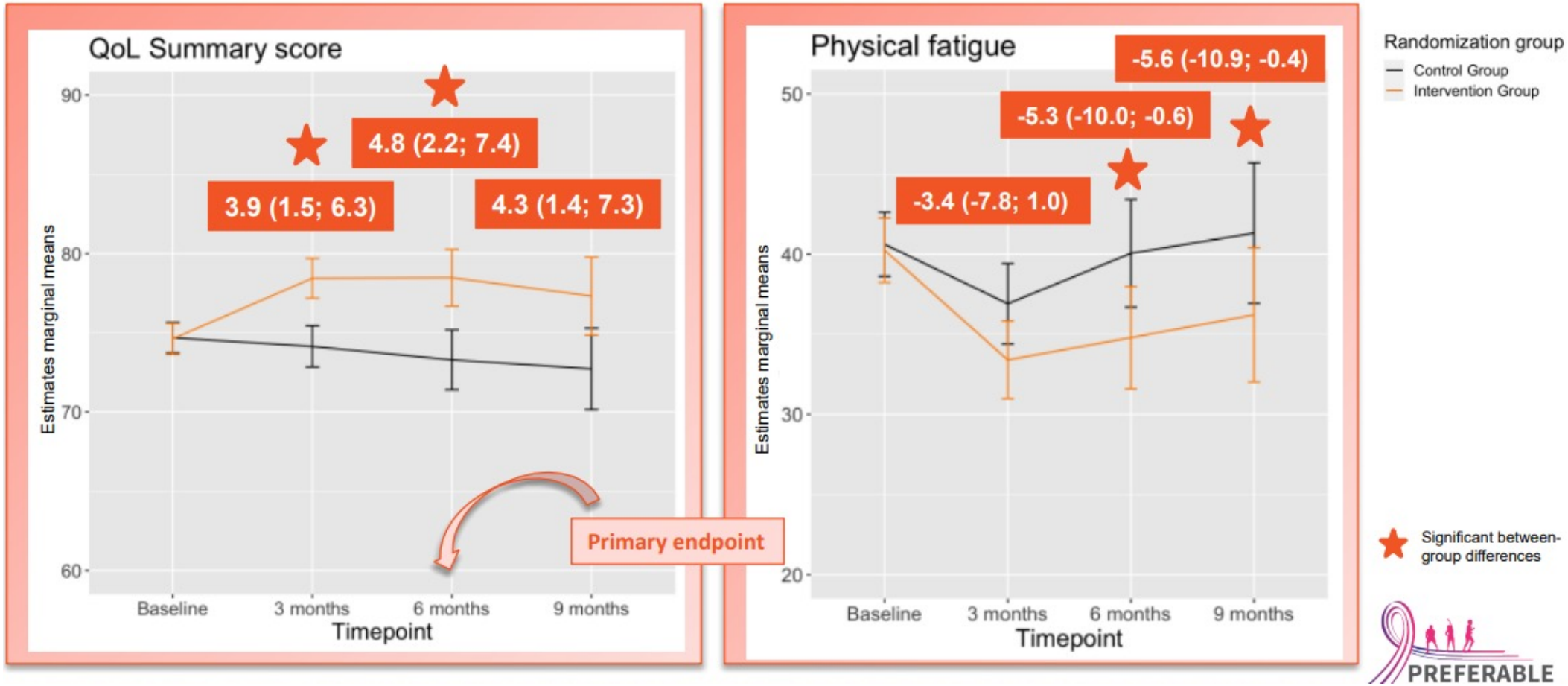
6-month post-BL:
18% discontinuation
- 44% due to death



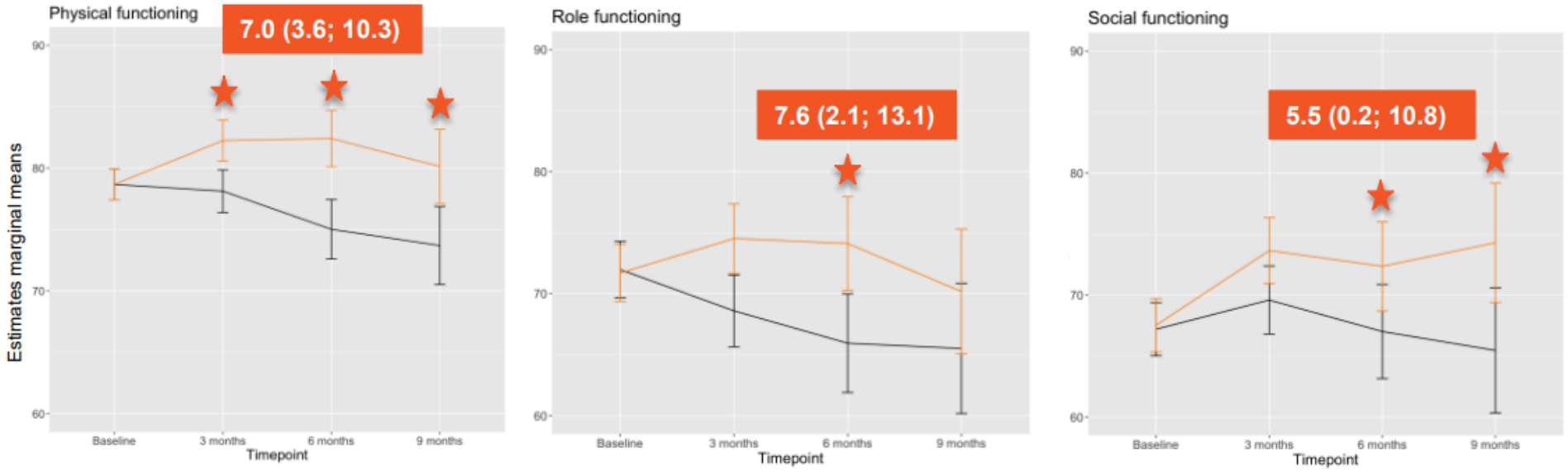
Two SAEs: 1 wrist fracture and 1 sacral stress fracture, none related to bone metastases.

PREFERABLE

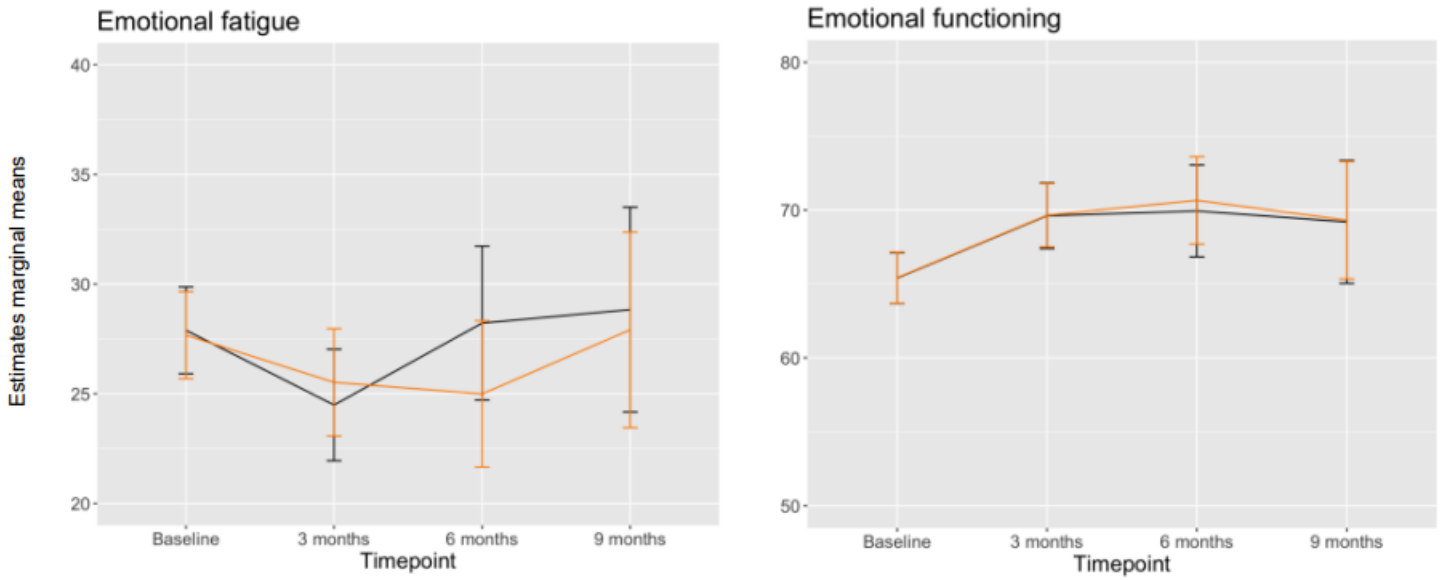
Results: primary outcomes



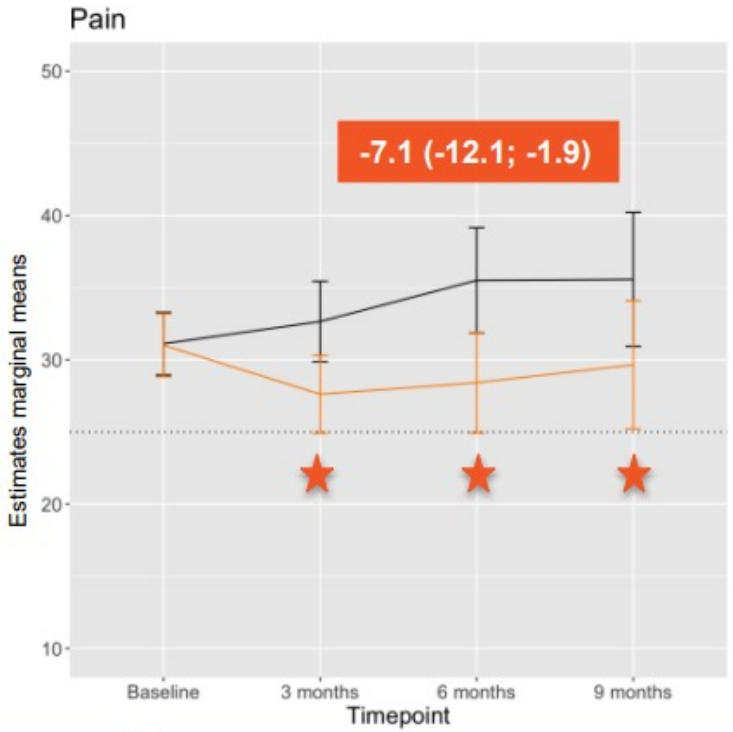
Results: QoL: functional scales

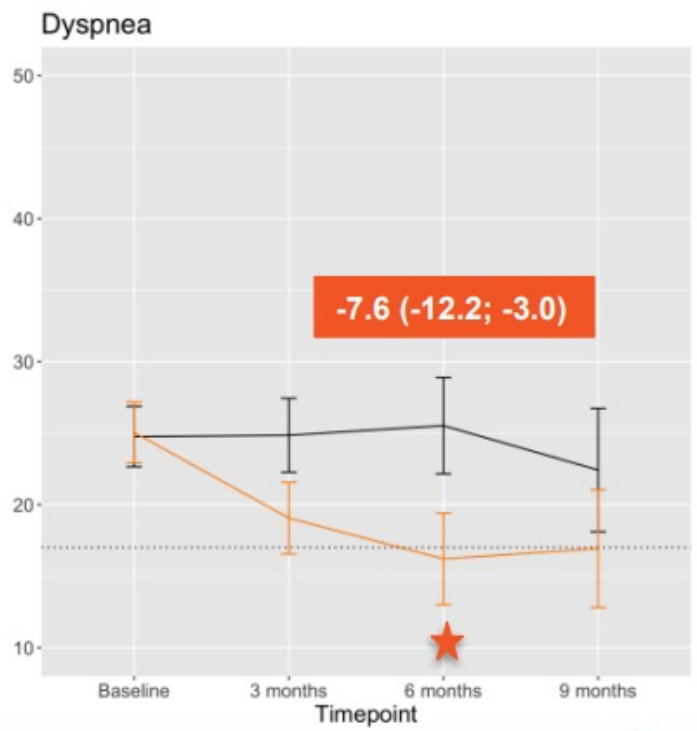


Results: emotional fatigue and functioning



Results: pain and dyspnea





PREFERABLE-PERSPECTIVE
(questionnaire n=420):

Concerns that **pain** and **fatigue** worsens while exercising

(Sweegers et al. Sup. Care Can. 2023)

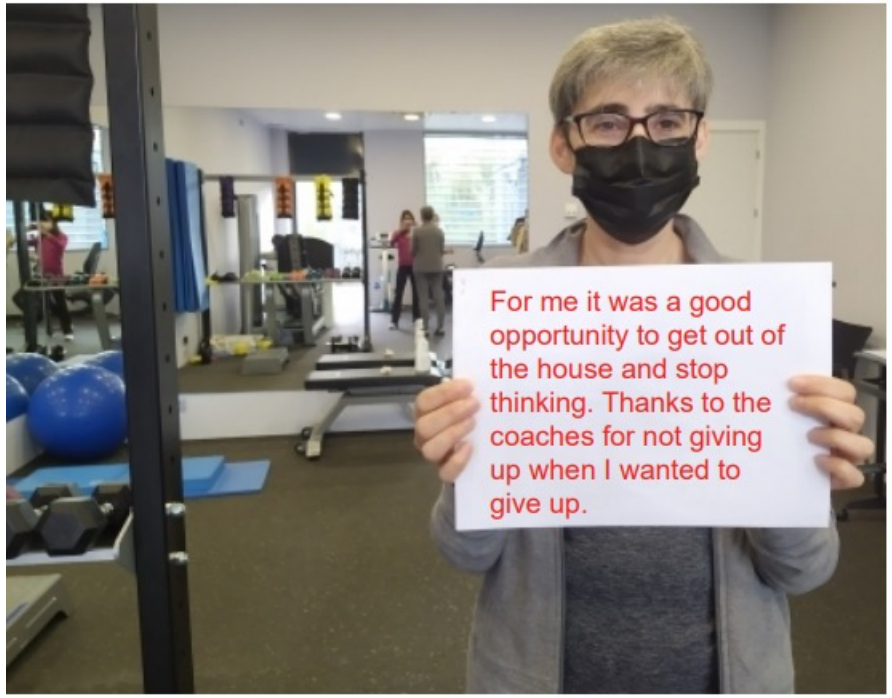
58%
Pain

% Scoring above clinical important threshold at baseline*

57%
Dyspnea

PREFERABLE

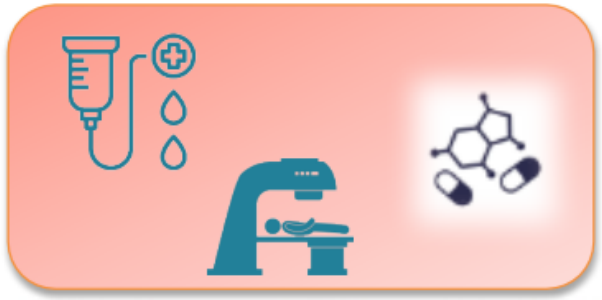
Patients get the last word



PREFERABLE

Conclusion

- A supervised resistance and aerobic exercise intervention resulted in beneficial effects on fatigue, HRQoL, and other clinically relevant outcomes of patients with mBC.
- We recommend supervised exercise as part of supportive care regimens during palliative treatment.



PREFERABLE

Weight reduction and exercise

Practice changing? ***Yes***

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients
- Health education after breast cancer
- Safety and toxicity according to age, race and realworld data
- PRO outcome: utility?
- New anti emetic regimen

Toxicity related to age, race and real world data

Immune Related Adverse Events in Patients ≥ 65 years vs. < 65 years with Breast Cancer Treated with Immunotherapy

Neelima Vidula, MD

Massachusetts General Hospital, Harvard Medical School

Complete author list:

Neelima Vidula, Jennifer Hutchinson, Abigail McLaren, Lianne Ryan, Andrzej Niemierko, and Aditya Bardia

SABCS

DECEMBER 5–9, 2023

Background and methods

- Pembrolizumab is approved for early and advanced triple-negative breast cancer (TNBC)[1,2].
- Atezolizumab was previously approved for advanced TNBC[3].
- Toxicity of immunotherapy (IO) and immune related adverse events (irAEs) in patients ≥ 65 years with breast cancer are not described in detail in results from registration trials.
- Understanding real-world IO toxicity and irAEs in patients with breast cancer ≥ 65 years may inform clinical decision making.
- Retrospective review of patients ≥ 65 years vs. < 65 years with breast cancer who received IO at an academic institution was conducted.
- IO toxicity and irAEs (classified by NCI CTCAE v. 5.0) after IO start were determined, and compared between cohorts.
- Cohorts compared with Pearson's chi-squared test (categorical variables) and Wilcoxon-rank sum test (continuous variables), with $p < 0.05$ for statistical significance.

[1]Schmid, NEJM, 2020. [2]Cortes, NEJM, 2022. [3]Schmid, NEJM, 2018.

Table 1: Demographic characteristics of patients receiving IO.

Characteristic	≥ 65 years (N=25)	< 65 years (N=104)	p value
Median age at IO start (years) (Interquartile range, IQR)	73 (69-74)	48 (39-56)	< 0.001
Stage			0.008
I	1 (4.0%)	7 (6.7%)	
II	8 (32.0%)	39 (37.5%)	
III	0 (0%)	25 (24%)	
IV	16 (64%)	33 (31.7%)	
Baseline ECOG Performance Status			0.009
0	14 (56%)	85 (81.7%)	
1	11 (44%)	17 (16.3%)	
2	0 (0%)	2 (1.9%)	
Subtype			0.92
TNBC	19 (76%)	81 (78%)	
HER2+	2 (8%)	6 (5.8%)	
HR+/HER2-	4 (16%)	17 (16%)	
First IO Regimen			0.092
Atezolizumab	1 (4%)	18 (17%)	
Pembrolizumab	24 (96%)	86 (83%)	
Autoimmune comorbidity			0.25
No	14 (56%)	71 (68%)	
Yes	11 (44%)	33 (32%)	

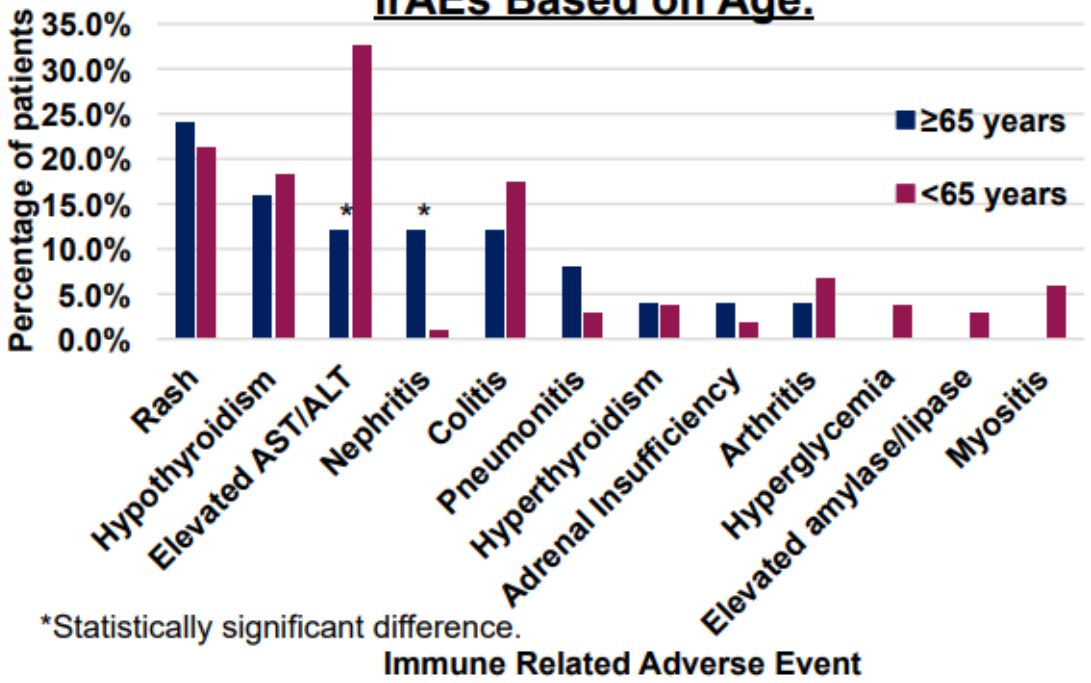
Results

Characteristics of IO* Toxicity.

Variable (median, Interquartile range [IQR] OR #, %)	≥ 65 years [Median 73, IQR (69-74)], (N=25)	< 65 years [Median 48, IQR (39-56)], (N=104)	p value
IO duration (months)	2.3 (1.6-4.4)	5.4 (2.1-10.7)	0.006
IO interruption for toxicity	4 (16%)	7 (7%)	0.14
IO dose # at toxicity interruption	2 (2-4)	5 (2-6)	0.31
IO discontinuation for toxicity	4 (16%)	7 (7%)	0.14

*Majority pembrolizumab in both cohorts.

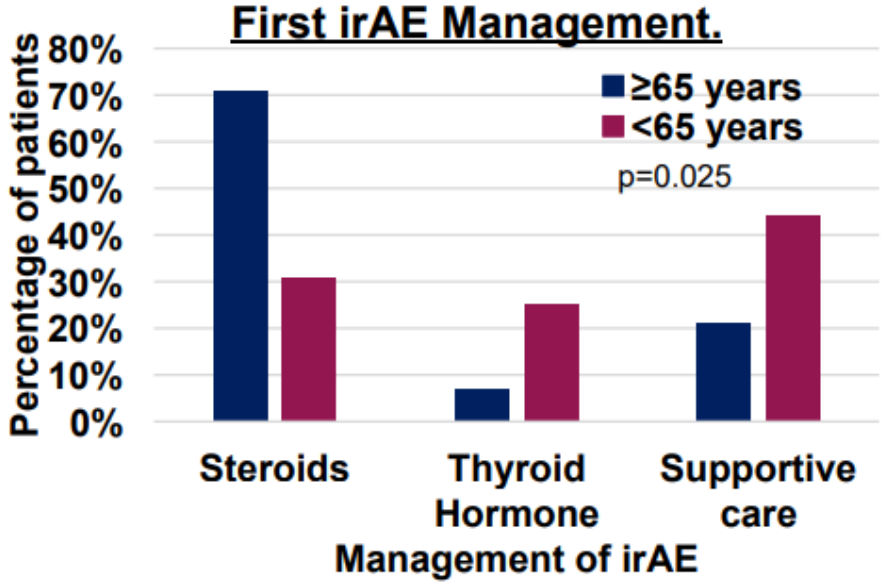
IrAEs Based on Age.



*Statistically significant difference.

- Similar overall rates of irAEs between cohorts (≥ 65 years: 72%, < 65 years: 64%, p=0.47). Similar # irAE/patient in both cohorts (p=0.42).
- Significantly higher rate of immune related nephritis in patients ≥ 65 years (≥ 65 years: 12% vs. < 65 years: 1%, p=0.004).
- Significantly higher rate of transaminitis in patients < 65 years (≥ 65 years: 12%, < 65 years: 33%, p=0.04).
- Similar rates of hypothyroidism in patients ≥ 65 years and < 65 years, but significantly higher rates of grade 2-3 vs. grade 1 hypothyroidism in patients < 65 years (p=0.017).

Results and conclusions

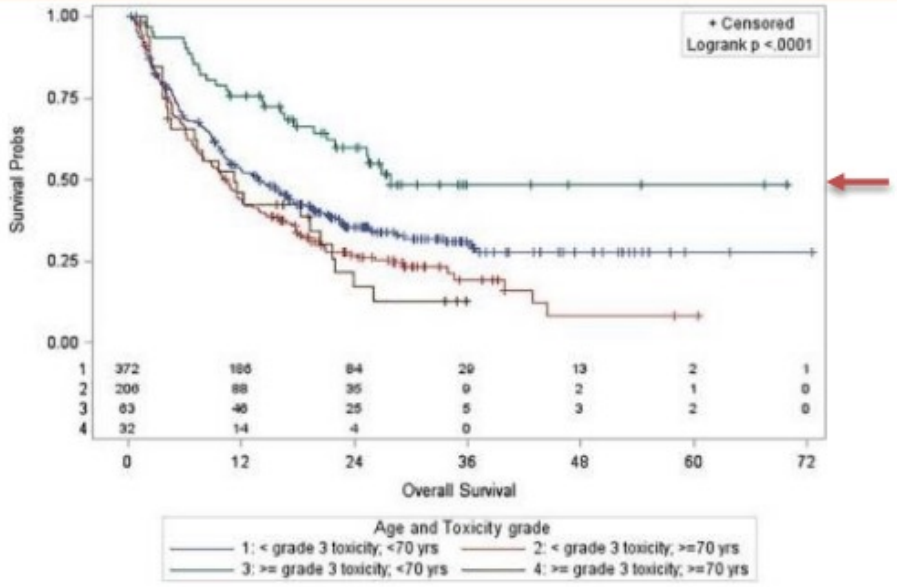


- Toxicity management differed by age (p=0.025). Significantly more steroid use for irAE management in patients ≥ 65 years (≥ 65 years: 71% vs. < 65 years: 31%, p=0.004).
- Rates of full resolution of irAEs were similar (≥ 65 years: 67%, < 65 years: 57%, p=0.47).
- Late onset irAEs (≥ 65 years: 8%, < 65 years: 6%, p=0.77) and deaths from irAEs (≥ 65 years: 4%, < 65 years: 0%, p=0.055) were rare in both cohorts.

Conclusions:

- In this real-world cohort, similar overall rates of irAEs were observed in patients ≥ 65 years and < 65 years.
- However, the spectrum of irAEs and management differed based on age.
  - More immune related nephritis and steroid use for irAEs were observed in patients ≥ 65 years.
  - More transaminitis and higher grade hypothyroidism were seen in patients < 65 years.
- Validation in a larger cohort is merited, and a multi-center analysis is underway.

Discussant: other studies



		N (%) of Under 70 Cohort (N=435)		N (%) of 70 and Older Cohort (N=238)		P-value (X^2)
		n	%	n	%	
Any Grade Toxicity	Total Patients	125	28.7	86	36.1	0.05
≥ Grade 3 Toxicity	Total Patients	63	14.5	32	13.5	0.71
	Grade 3	58	13.3	30	12.6	0.79
	Grade 4	4	0.92	1	0.4	0.66
	Grade 5	2	0.46	1	0.4	0.66
≥ Grade 3 Toxicity Types	Dermatitis	8	1.8	7	2.9	0.35
	Colitis	23	5.3	10	4.2	0.53
	Hypothyroid	6	1.4	0	0	0.10
	Hyperthyroid	2	0.5	0	0	0.54
	Hepatitis	9	2.1	8	3.4	0.31
	Pneumonitis	9	2.1	7	2.9	0.48
	Other	13	3.0	2	0.8	0.10

- irAEs in a cohort of 673 pts, 35% ≥ 70y, 40% had melanoma, 46% received nivolumab
  - ≥ G3 IrAEs did not differ by age (age cut off 70y, p= 0.71)
  - Median OS significantly longer for pts <70y with ≥ G3 IrAEs.
- Current study showed significant irAE difference with age despite small sample size; Sample size in current study is limited for OS association.

Real-world analysis comparing Black and White patients with triple-negative breast cancer receiving therapy per KEYNOTE-522

Mara L. Hofherr, Katherine Clifton, Spenser January, Farah Raheem, Lauren Lyons, Jerline Hsin, Shawna Kraft, Allison J. Schepers, Jodi Taraba, Colleen Bohnenkamp, Shelly Hummert, Lisa Grate, Sidney V. Keisner, Jacob Hobbs, Todd Davis, Kristin Bastian, Dawn Minikel, Traci White, Avneek Sandu, Fouad Boulbol, Kelsey Finch, Olivia Fahey, Yontan Resnick, Alison Svoboda, Kayla Harwood, Emily Armgardt, Doug Mazewski, Amiee Keegan, Wai Yu, Meredith Watson-Rose, Katherine Madden, Suganya Arunachalam Karikalan, Lida Mina, Emily J. Owens, Andrew A. Davis

SABCS
DECEMBER 5–9, 2023

Objectives and methods

- Despite the significant improvement in pathological complete response (pCR) and event-free survival rates across all patients, the landmark trial included only 4.5% Black patients.
- Lack of inclusion of a representative and diverse population of patients is a consistent issue in registrational clinical trials.
- We assessed real-world toxicity and treatment outcomes across Black and White patients who received standard-of-care treatment per KEYNOTE-522 in a multicenter retrospective cohort study including 577 patients from 17 sites.
- Our patient population included 18.2% Black patients (n = 105) and 74.2% White patients (n = 428)

1. Schmid et al, 2020
2. Schmid et al, 2022

Results

Response (n=444)	Black (n = 86)	White (n = 358)	P value
Pathologic Complete Response	52.3% (n = 45)	55.9% (n = 200)	P = 0.6

Adverse Drug Reactions (n = 534)	Black (n = 105)	White (n = 429)	P value
Grade 3+ Immune Related ADR	20.9% (n = 22)	33.8% (n = 145)	**P = 0.011**
Hospitalization Rate	39% (n = 41)	36% (n = 154)	P = 0.5
Acute Care Utilization	38% (n = 30)	38% (n =163)	P = 0.9

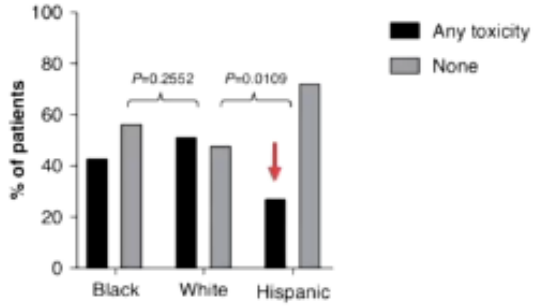
Conclusions

- To our knowledge, this is the largest real-world study to report data on safety and efficacy across Black and White women in patients who received treatment per KEYNOTE-522.
- Black patients had similar pCR rates and similarly high rates of treatment-related hospitalizations compared to White patients.
- Notably, White patients had a significantly higher frequency of grade 3+ irAEs. Further research is needed to validate this finding and to explore the biological rationale for this.

Discussant: other studies

- Peravali et al reported irAEs in stage IV solid malignancies (N = 293), **41.6% of patients were AA**.
  - irAE was **significantly higher in Caucasians vs AA (** 60.4% vs 30.8% P = 0.01).
  - Higher median OS in Caucasian vs AA in patients with irAE (20.6 vs 12.9 mo, P = 0.02) and in those with endocrine irAEs (21.8 vs 15.8 mo, P = 0.03).

- Florez et al reported irAEs in patients with lung or Head & Neck cancer (N=207)
  - ORR for Hispanic/Black trended lower compared with non-Hispanic White
    - 27.0% of Hispanic
    - **32.5% of Black**
    - 38.7% non-Hispanic White
  - irAEs higher non-Hispanic White:
    - 30% of Hispanic
    - **40% of Black**
    - **50% non-Hispanic White**



Toxicity related to age, race and Safety in the real world data compared with the studies

Safety Evaluation From the KEYNOTE-522 Study of Neoadjuvant Pembrolizumab (or Placebo) Plus Chemotherapy Followed by Adjuvant Pembrolizumab (or Placebo) in Patients With Early Triple-Negative Breast Cancer

Javier Cortés[1]; Rebecca Dent; Lajos Pusztai; Heather McArthur; Sherko Kümmel; Carsten Denkert; Yeon Hee Park; Rina Hui; Masato Takahashi; Carlos Henrique Barrios; Yalin Zhu; Xiaoli Zhang; Wilbur Pan; Vassiliki Karantza; Joyce O'Shaughnessy; Peter Schmid

[1]International Breast Cancer Center (IBCC) & Faculty of Biomedical and Health Sciences, Department of Medicine, Universidad Europea de Madrid, Madrid, Spain

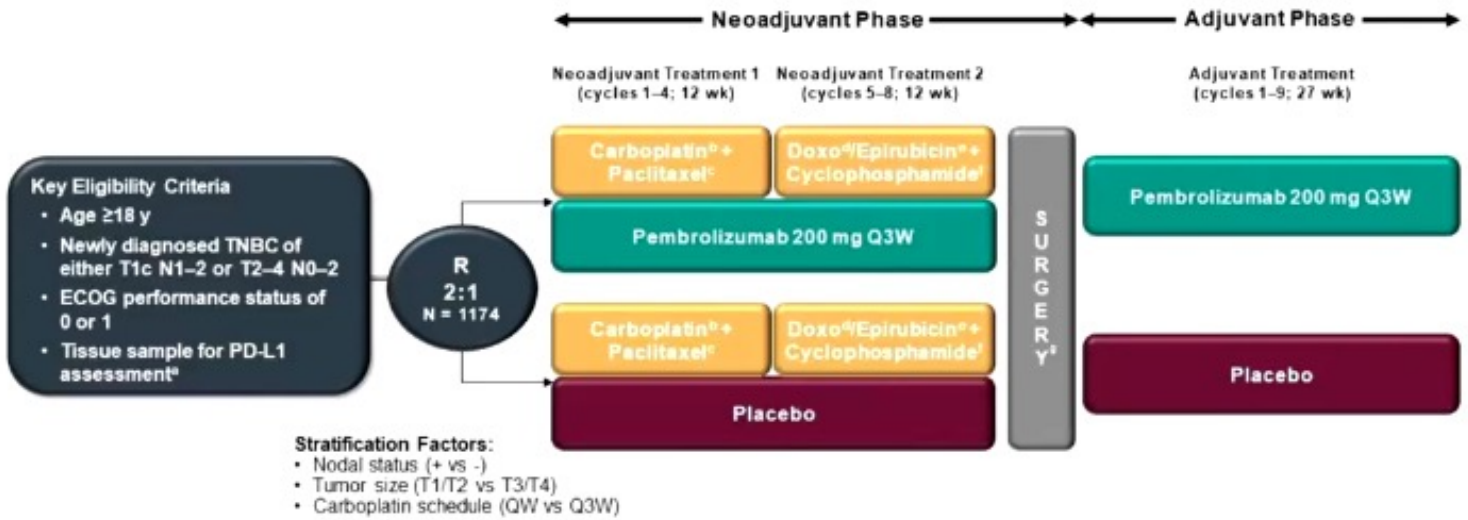
Disclosures for Javier Cortés: Consultant for AstraZeneca, Athenex, Bioasis, BioInvent, Boehringer Ingelheim, Celgene, Cellestia, Clovis Oncology, Daiichi Sankyo, Ellipses, Erytech, Gemoab, Gilead, GSK, Hibercell, Leuko, Lilly, Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD), Polyphor, Roche, and Seattle Genetics; Grant/Research support from Ariad Pharmaceuticals, AstraZeneca, Baxalta GMBH/Servier Affaires, Bayer Healthcare, Eisai, F. Hoffman-La Roche, Guardant Health, MSD, Pfizer, Piqur Therapeutics, Puma C, Queen Mary University of London, and Roche; Stockholder in MedSIR; Fees for non-CME services received directly from commercial interest or their agents from Celgene, Daiichi Sankyo, Eisai, Lilly, MSD, Novartis, Pfizer, Roche, and Samsung Bioepis; Travel/Accommodation from Daiichi Sankyo, Eisai, Novartis, Pfizer, and Roche; Patent for HER2 as a predictor of response to dual HER2 blockade in the absence of cytotoxic therapy

This study was sponsored by MSD. Medical writing assistance was provided by Christabel Wilson, MSc, of ICON plc (Blue Bell, PA, USA). This assistance was funded by MSD

SABCS
DECEMBER 5–9, 2023

Objective and methods

- Objective: to report additional safety findings, beyond the already published safety results, on immune-mediated AEs and management in the combined phases from IA4 of KEYNOTE-522



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)

[a]Must consist of ≥2 separate tumor cores from the primary tumor. [b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW. [c]Paclitaxel dose was 80 mg/m^2 QW. [d]Doxorubicin dose was 60 mg/m^2 Q3W. [e]Epirubicin dose was 90 mg/m^2 Q3W. [f]Cyclophosphamide dose was 600 mg/m^2 Q3W. [g]Definitive surgery occurred approximately 3–6 wk after completion of neoadjuvant therapy. The type of breast-conserving surgery or mastectomy with or without axillary lymph node dissection was at the discretion of the treating physician.

Results in both phases

Results in Combined Phases (Neoadjuvant and Adjuvant)

Summary of Immune-Mediated AEs and Infusion Reactions

	Pembro + Chemo/Pembro n = 783	Pbo + Chemo/Pbo n = 389
Any	341 (43.6)	85 (21.9)
Grade 1/2	224 (28.6)	77 (19.8)
Grade 3/4	115 (14.7)	8 (2.1)[a]
Grade 5	2 (0.3)[b]	0
Led to dose reduction[c]		
Chemotherapy[d]	1 (0.1)[e]	0
Led to treatment interruption		
Pembrolizumab/placebo	43 (5.5)	9 (2.3)
Chemotherapy[d]	88 (11.2)	25 (6.4)
Led to discontinuation of any drug		
Pembrolizumab/placebo	61 (7.8)	4 (1.0)
Chemotherapy[d]	45 (5.7)	7 (1.8)

Data are n (%) of patients. [a]There were no grade 4 immune-mediated AEs or infusion reactions. [b]n = 1 with pneumonitis (neoadjuvant phase), n = 1 with autoimmune encephalitis (adjuvant phase). [c]Dose reduction was not allowed for pembrolizumab or placebo. [d]Chemotherapy was administered during the neoadjuvant phase only. [e]Due to severe skin reaction.

Time to Onset and Management of the Most Common (≥20 Patients) Immune-Mediated AEs and Infusion Reactions

	Pembro + Chemo/Pembro n = 783	Pbo + Chemo/Pbo n = 389
Infusion reactions, n (%)	141 (18.0)	45 (11.6)
Median time to onset (range), d	16 (1–458)	22 (1–325)
Treated with corticosteroids, n	85	28
Hypothyroidism, n (%)	118 (15.1)	22 (5.7)
Median time to onset (range), d	105 (7–510)	255 (7–527)
Treated with thyroid replacement, n	106	13
Severe skin reactions, n (%)	45 (5.7)	4 (1.0)
Median time to onset (range), d	64 (4–479)	50.5 (32–186)
Treated with corticosteroids, n	28	0
Hyperthyroidism, n (%)	41 (5.2)	7 (1.8)
Median time to onset (range), d	107 (20–470)	184 (1–284)
Adrenal insufficiency, n (%)	20 (2.6)	0
Median time to onset (range), d	175.5 (100–383)	–
Treated with hormone replacement, n	20	–

d, days; n, number of patients.

Conclusions

- Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab had a manageable safety profile that was generally consistent with the known safety profiles of pembrolizumab and the chemotherapy regimens in patients with newly diagnosed, high-risk, early TNBC
- No new immune-mediated AEs were identified
- Most immune-mediated AEs and infusion reactions were grade 1/2, were manageable with treatment interruption, corticosteroids, and/or hormone replacement, and did not result in discontinuation of study treatment
- Together with the clinical benefits previously reported,[1,2] our safety results support neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab as a standard of care regimen in this setting

Schmid P, et al. N Engl J Med. 2020;382(9):810-821. 2. Schmid P, et al. N Engl J Med. 2022;386(6):556-567.

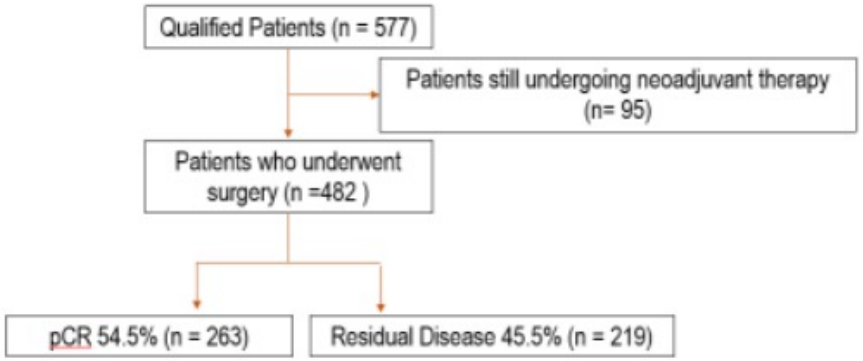
Real-world analysis of adverse events in patients with triple-negative breast cancer receiving therapy per KEYNOTE-522

Mara L. Hofherr, Andrew A. Davis, Spenser January, Farah Raheem, Lauren Lyons, Jerline Hsin, Shawna Kraft, Allison J. Schepers, Jodi Taraba, Colleen Bohnenkamp, Shelly Hummert, Lisa Grate, Sidney V. Keisner, Jacob Hobbs, Todd Davis, Kristin Bastian, Dawn Minikel, Traci White, Avneek Sandu, Fouad Boulbol, Kelsey Finch, Olivia Fahey, Yontan Resnick, Alison Svoboda, Kayla Harwood, Emily Armgardt, Doug Mazewski, Amiee Keegan, Wai Yu, Meredith Watson-Rose, Katherine Madden, Suganya Arunachalam Karikalan, Lida Mina, Emily J. Owens, Katherine Clifton

SABCS
DECEMBER 5–9, 2023

Background and methods

- KEYNOTE-522 provided significant improvement in pathologic complete response (pCR) and event-free survival; however, real word outcome and toxicity data are limited.
- 17 sites were included in this retrospective cohort study. All sites had IRB approval. Washington University was the central site to collate and analyze the data.
- Data regarding immune-related (irAEs) and non immune-related toxicities and unplanned interactions with the healthcare system (ER visits, hospitalizations) were collected.



1. Schmid et al, 2020
2. Schmid et al, 2022

Results

Safety	Any Grade (n=577)	Grade 3+	KN522, Any Grade (n= 783)	KN522 Grade 3+
Adverse Drug Event (ADE) Causing Dose Reductions	217 (37.6%)		No equivalent reported	
ADE Causing Early Discontinuation	228 (39.5%)		216 (27.7%)	
Patients who experienced an immune-related adverse effect (irAE)?	412 (71.4%)	184 (31.9%)	262 (33.5%)	101 (12.9%)

- If patients had an ADE that caused a dose reduction, they were significantly more likely to have residual disease (P = 0.039).
- There was no difference in pCR for patients who discontinued treatment early vs. those who did not.
- For example, high rates of all grade hepatitis/transaminitis (19.9%), hypothyroidism (18%) and adrenal insufficiency (7.8%) were observed. See our poster for a complete list of all grade and G3+ irAEs.

Conclusions

- The treatment-related toxicity and dose reductions may account for a lower pCR rate compared to the registrational trial.
- More grade 3+ irAEs occurred in our real-world analysis including rash, adrenal insufficiency, colitis, AKI, pneumonitis, inflammatory arthritis, type I diabetes, and myocarditis.
- Limitations of this study include the retrospective design without formal CTCAE criteria and lack of data on neoadjuvant vs. adjuvant toxicity.
- Providers should carefully monitor for short and long-term irAEs to ensure optimal patient outcomes.

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients
- Health education after breast cancer
- Safety and toxicity according to age, race and realworld data
- PRO outcome: utility?
- New anti emetic regimen

Importance of (e)PRO? Pro or contra?

Practice changing?

Could MyHealth study be practice changing?

Nurse-led individualized follow-up versus regular physician-led visits after early breast cancer (MyHealth) – a randomized controlled trial

Lena Saltbæk, MD, PhD
Cancer Survivorship, Danish Cancer Institute, Denmark &
Department of Clinical Oncology and Palliative Care, Zealand University Hospital, Denmark

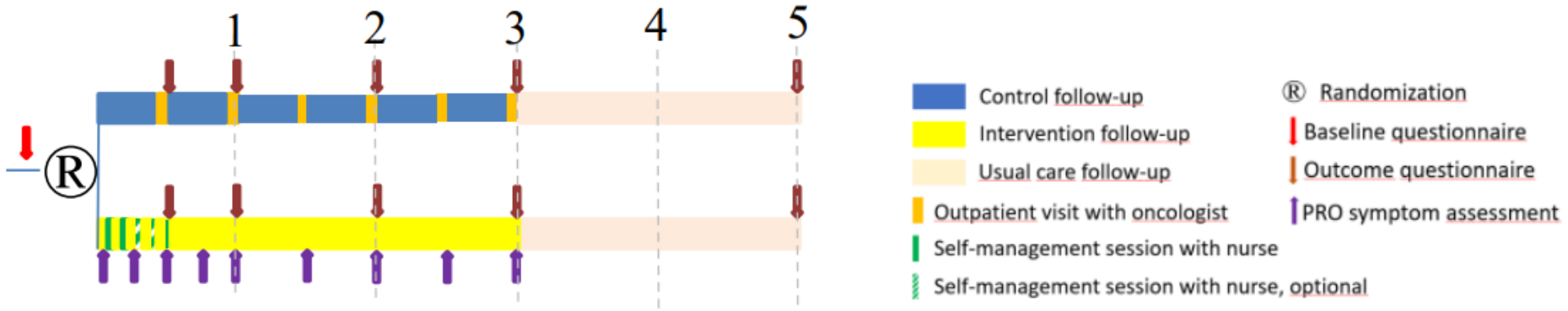
Acknowledgements The Danish Cancer Society; Region Zealand; Copenhagen University Hospital
Financial disclosures I have no financial relationships to disclose

Objectives and methods

- To investigate if a nurse-led follow-up program with self-management and symptom assessment using PRO was superior to physician-led follow-up.
- Endpoints:

Primary: **Breast cancer-specific HRQoL** (TOI-PFB summary score of FACT-B)

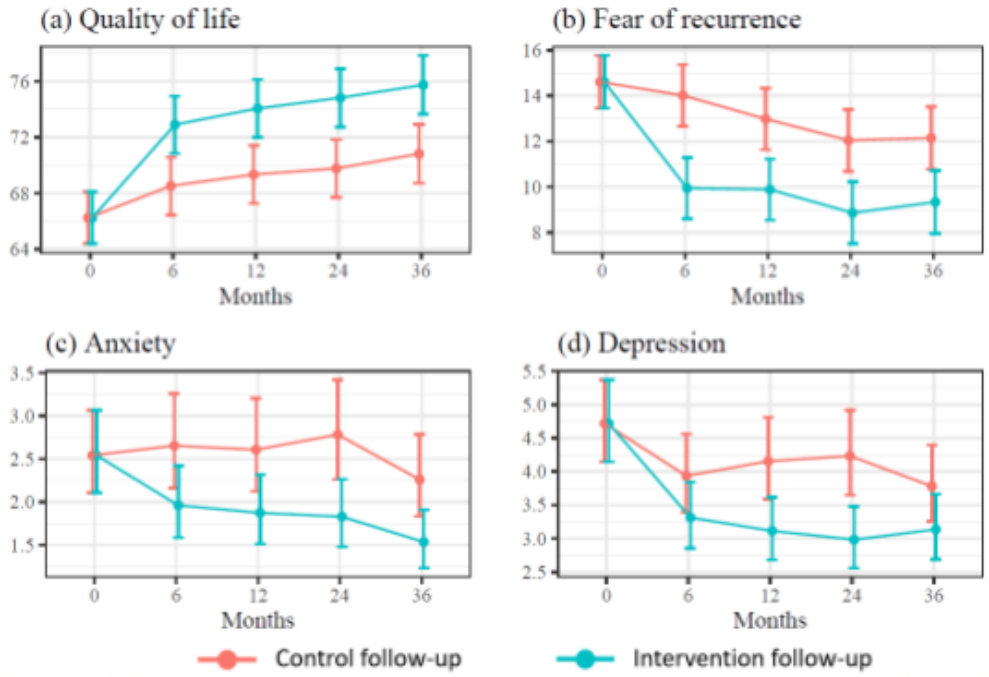
Secondary: **Fear of recurrence** (CARQ4), **anxiety** (GAD7) and **depression** (PHQ9)



Results

503 patients with stage I-II breast cancer were randomized to intervention (n=251) or control (n=252) follow-up

Effects of intervention follow-up 0-36 months after randomization



	Intervention Mean (SD)	Control Mean (SD)	P-value
Physician visit	1.47 (1.81)	5.26 (2.32)	<0.001
Physician telephone	1.00 (1.34)	1.17 (1.12)	0.140
Nurse visit	0.40 (0.65)	0.05 (0.23)	<0.001
Nurse telephone	3.60 (2.71)	0.50 (1.14)	<0.001
Mammograms	1.99 (1.09)	2.07 (0.95)	0.384
Other diagnostic imaging	1.43 (1.68)	1.53 (2.13)	0.554

Conclusions

The MyHealth study suggests a new strategy for follow-up after early breast cancer providing:

- Significant improvement in breast cancer-specific HRQoL
- Significant reduction in fear of recurrence, anxiety and depression
- Effective utilization of healthcare resources
- No increase in the number of diagnostic imaging examinations

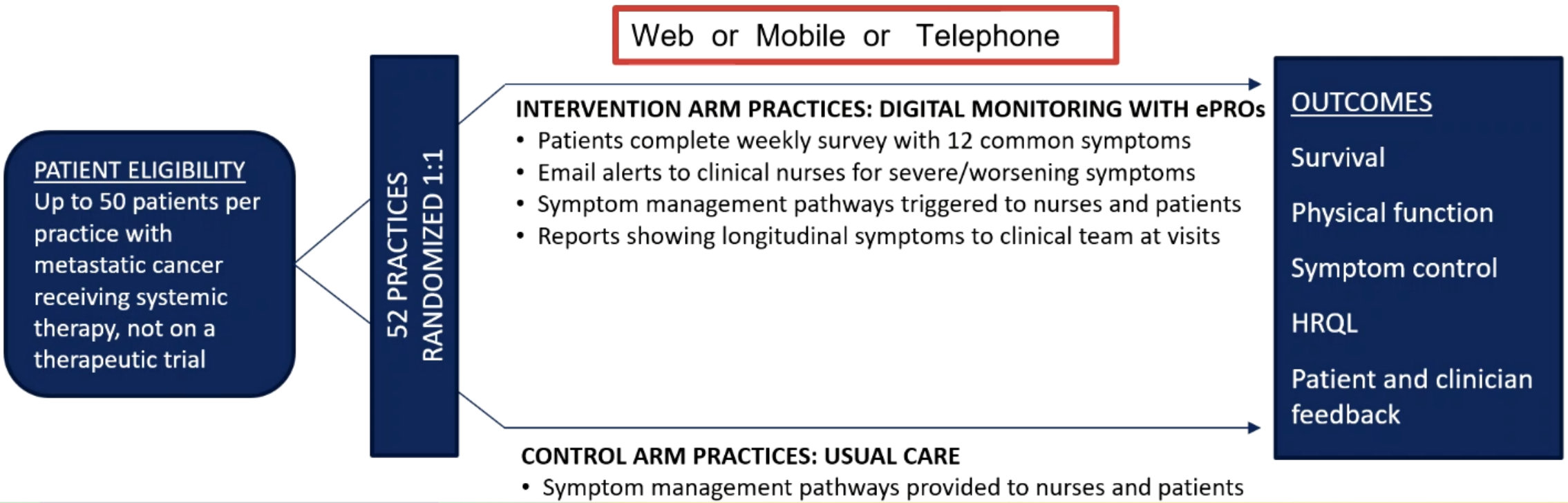
MADRID 2023 ESMO congress

Remote symptom monitoring with electronic patient-reported outcomes (ePROs) during treatment for metastatic cancer: Results from the PRO-TECT trial (Alliance AFT-39)

Ethan Basch, MD
Professor and Chief of Oncology
University of North Carolina, USA

PRO-TECT
Cancer Symptom Study

- Cluster randomized trial at 52 US community oncology practices, across 25 states
- Funded by PCORI, sponsored by Alliance Foundation Trials

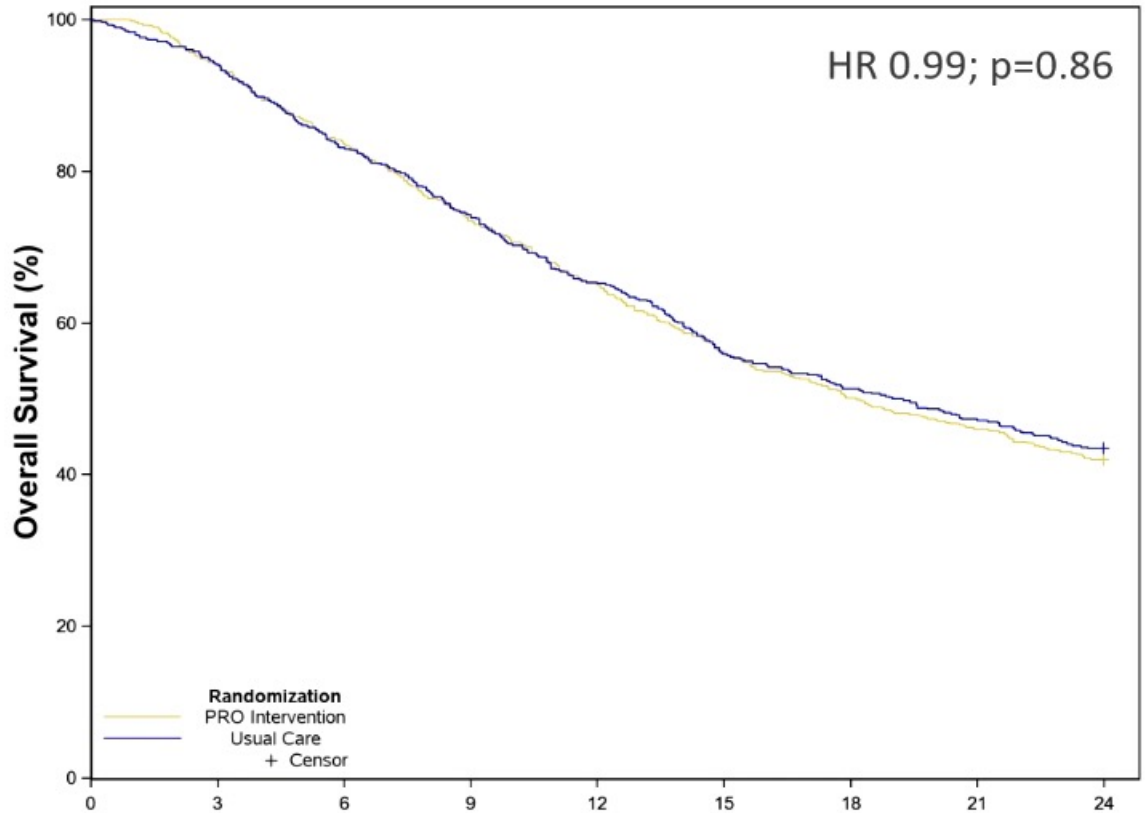


Statistics

- Primary outcome: Overall survival (all cause)
  - Included all deaths with censoring on last date known alive
  - Based on medical chart abstraction and linkage to US National Death Index data
  - All patients followed for 2 years after date of enrollment
  - 90% power to detect hazard ratio of 0.76 using a 2-sided alpha = 0.05 log rank test with 576 observed deaths, with an intracluster correlation coefficient of 0.001
- Secondary outcomes:
  - Emergency visits/hospitalizations within 1 year of enrollment
  - Health-related quality of life, symptoms, physical function by EORTC QLQ-C30 (previously reported: *JAMA* 2022;327:2413-2422)
- Exploratory outcomes:
  - Compliance with weekly ePRO surveys; patient & clinician feedback on using ePROs

BASELINE CHARACTERISTICS		ePRO Arm (N=593)	Standard Care Arm (N=598)
Age - median (range)		**64** (29-89)	**62** (28-93)
Female sex – no. (%)		359 (**60.5%**)	335 (**56.1%**)
Race – no. (%)	White	473 (**80.4%**)	452 (**78.5%**)
	Black	99 (**16.8%**)	94 (**16.3%**)
	Other	13 (**2.1%**)	29 (**5.1%**)
Cancer type – no. (%)	Thoracic	118 (**19.9%**)	110 (**18.4%**)
	Breast	97 (**16.4%**)	80 (**13.4%**)
	Gastrointestinal	173 (**29.2%**)	219 (**36.6%**)
	Genitourinary	69 (**11.6%**)	44 (**7.4%**)
	Gynecologic	64 (**10.8%**)	53 (**8.9%**)
	Hematologic	31 (**5.2%**)	31 (**5.2%**)
	Other	41 (**6.9%**)	61 (**10.2%**)
Education – no. (%)	≤High School	218 (**36.8%**)	250 (**41.8%**)
Rural		154 (**26.0%**)	163 (**27.3%**)

Results: Overall Survival



Patients-at-Risk

PRO Intervention	593	557	496	436	385	333	297	273	18
Usual Care	598	563	497	444	390	334	307	282	22

- No significant difference in overall survival between groups
- Unadjusted estimated survival at two years was:

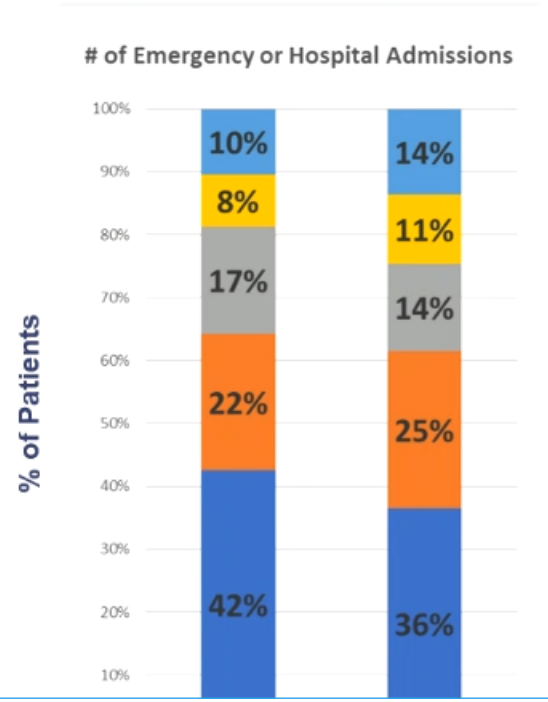
  42.0% (95% CI 38.2-46.2%) for the ePRO group

  43.5% (95% CI 39.7-47.6%) for the usual care control

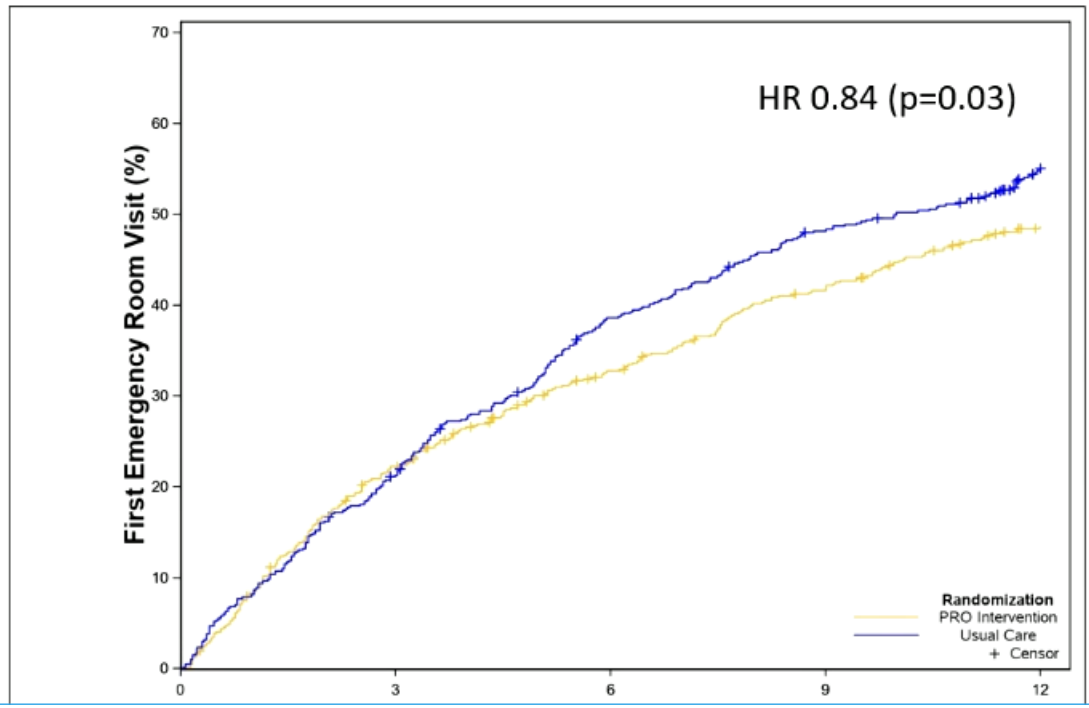
Results: Emergency or Hospital Admissions

Decreased mean # of admissions per patient over one year with ePROs vs Usual Care: 1.48 vs. 1.81 (p=0.006).

6% reduction in emergency or hospital admissions with ePROs



Improved (lengthened) time to first emergency admission with ePROs (HR 0.84; p=0.03)



Results: Emergency or Hospital Admissions

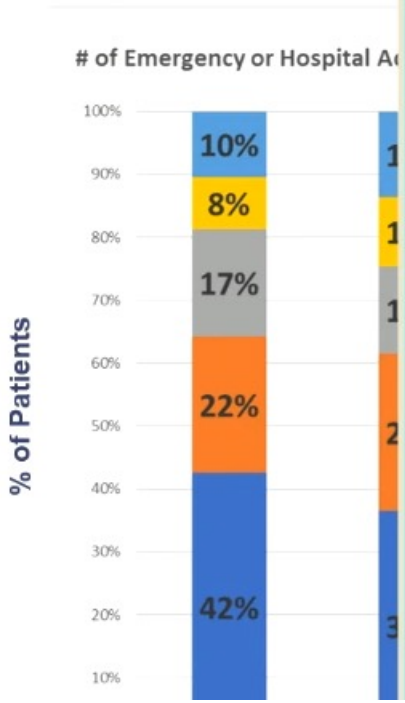
Decreased mean # of a .48 vs. 1.81 (p=0.006).

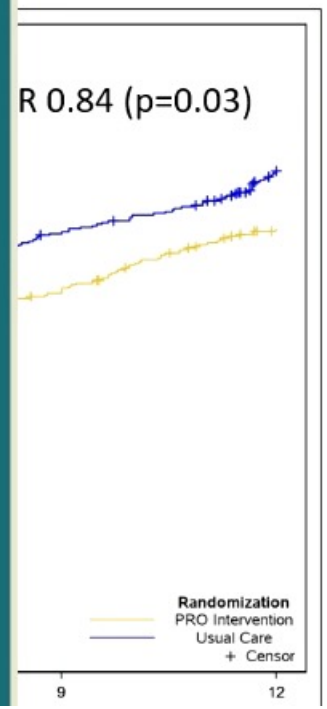
6% reduction in emerg / admission hospital admissions wi

Improved
- Physical functioning
- Symptom control
- HRQoL

In addition,
- Patients' satisfactory overall was high

However,
- ~1/4 of nurses were reluctant to





Importance of (e)PRO? Pro or contra?

Practice changing?

Yes in early disease, No in MBC

Highlights of supportive care

- Chemoprevention, fertility techniques and breast cancer outcome, pregnancy in BRCA patients
- Health education after breast cancer
- Safety and toxicity according to age, race and realworld data
- PRO outcome: utility?
- New anti emetic regimen?

Rapid fire session: low dose vs standard dose olanzapine?

Pratice changing?

A randomized, open-label phase III trial **E**valuating **L**ow-Dose Vs. standard-dose **O**lanzapine with triple **A**ntiemetic therapy for **P**revention of highly emetogenic chemotherapy-induced **N**ausea and vomiting in solid tumors (**OLA**nza**PiNE**).

Jyoti Bajpai*, Kapu V, Rath S, Kumar S, Sekar A, Srikant A , Pawar A , Srinivas S , Bhargava P ,Gulia S, Noronha V , Joshi A, Prabhash K, Banavali S, Dr. Rajiv Sarin, Badwe R, Gupta S

Tata Memorial Centre,Homi Bhabha National Institute (HBNI), Mumbai, India

SABCS
DECEMBER 5–9, 2023

Study design and Participants:

- **Prospective, randomized, open-label, Phase III study** evaluating LD-OLZ (2.5 mg) Vs SD olanzapine (10 mg) with standard TAE therapy for the prevention of CINV in subjects receiving HEC
- Patients of either sex aged between 13 and 75years, with the diagnosis of a solid tumour(breast cancer or other solid tumours who had not received chemotherapy earlier) who were planned to receive **doxorubicin60 mg/m^{2}plus cyclophosphamide 600 mg/m^{2}or cisplatin ≥70 mg/m^2,** per cycle, with or without other chemotherapeutic agents, were included in the study.

Study outcome and endpoints

The Primary endpoint (PEP) : to evaluate the proportion of patients with:

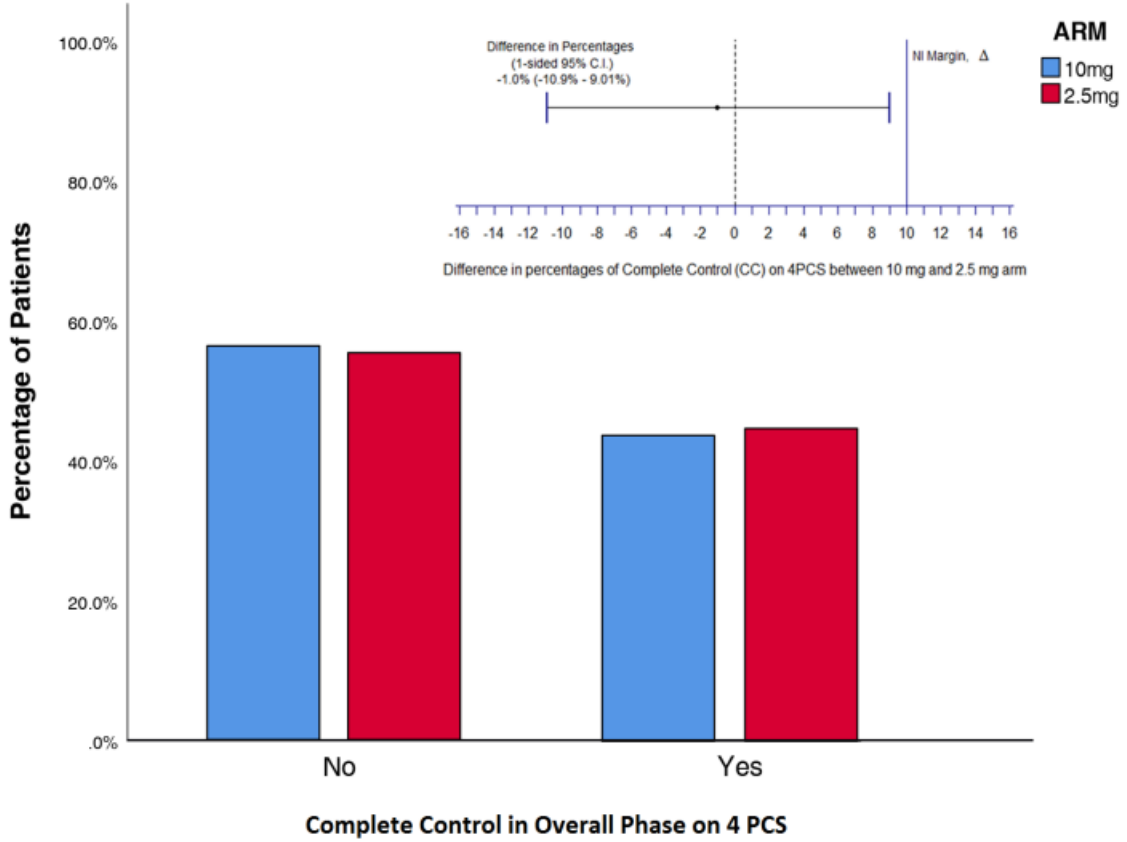
- **Complete control** defined as **no emetic episode (EE), no use of rescue medications (RM), and no or mild nausea assessed in the overall phase (OP) =0-120 hours (h)**.

Secondary endpoints (SEP) : to compare the two study groups for the proportion of patients with:

- Complete response **(CR)** defined as no EE, no use of RM in acute (AP)(0- 24h), delayed(DP) (25-120h) and OP (0-120h).
- Complete control **(CC):**defined as no EE, no use of RM, no or mild nausea in AP, DP, acute, delayed, and overall phases.
- Total control **(TC):**defined as no EE, no use of RM, and no nausea in the acute, delayed, and OP.
- Time to treatment failure (TTF):defined as the time from HEC administration to an episode of vomiting, or the use of RM.
- Incidence of daytime somnolence

The pre-specified tertiary (exploratory) endpoint was the effect on appetite

Primary outcome: complete control



The complete control in the overall phase was 59 (44.7%) of 132 Vs 59 (43.7%) of 135 in 2.5mg Vs 10 mg olanzapine arms, respectively, with a difference of ***-1% (1-sided 95% CI,-1.00 to 9.01%)***, which excludes the non-inferiority margin of 10%.

Results: outcome

OUTCOMES (4-point categorical Scale)	Experimental 2.5mg arm (N=132)	Standard 10mg arm (N=135)	Difference in proportions (95% C.I.)	P value†
Primary Endpoint				
Complete Control (Overall phase ,0-120 hours)	**59 (44.7%)**	**59 (43.7%)**	**-1.00% to 9.01%**	**0.870**
Secondary Endpoints				
Complete Control				
Acute (0-24 hours)	66 (50%)	66 (48.9%)	-11% (-13.11% - 0.88%)	0.856
Delayed (25-120 hours)	67 (50.8%)	79 (58.5%)	7.7% (-4.15% - 19.67%)	0.163
Complete Response				
Overall phase (0-120 hours)	67 (50.8%)	69 (51.1%)	0.3% (-11.64% - 12.35%)	0.954
Acute phase (0-24 hours)	74 (56.1%)	77 (57%)	0.9% (-10.92% - 12.87%)	0.872
Delayed phase (25-120 hours)	73 (55.3%)	85 (63%)	7.7% (-4.1% - 19.42%)	0.203
Total Control				
Overall phase (0-120 hours)	21 (13.6%)	18 (15.6%)	2% (-6.55% - 10.38%)	0.657
Acute phase (0-24 hours)	33 (25%)	31 (23%)	-2% (-12.28% - 8.21%)	0.697
Delayed phase (25-120 hours)	27 (20.5%)	30 (22%)	1.5% (-8.06% - 11.59%)	0.725

Results: outcome

OUTCOMES(4-point categorical Scale)	Experimental 2.5mg arm (N=132)	Standard 10mg arm (N=135)	P value†
Daytime somnolence (DTS)- any grade in overall phase)	86(65.2%)	121(89.6%)	<0.001
Severe grade Day 1	6(4.5%)	54(40%)	<0.001
Severe grade Day 2	4(3.0%)	41(30.4%)	0.004
Severe grade Day 3	1(0.8%)	31(23%)	<0.001
Severe grade Day 4	0(0%)	18(13.3%)	<0.001
Severe grade Day 5	1(0.8%)	11(8.1%)	0.004
Time to treatment failure-hours) Median (IQR)	120 (24, 120)	120 (24, 120)	0.866
Failure in Counts (%)	65 (49.2%)	66 (48.9%)	0.954
Alteration in Appetite (Decreased)			
Day 1	23 (17.4%)	33 (24.4%)	0.159
Day 2	21 (15.9%)	37 (27.4%)	0.023
Day 3	16 (12.1%)	32 (23.7%)	0.014
Day 4	11 (8.3%)	28 (20.7%)	0.004
Day 5	8 (6.1%)	27 (20%)	0.001

In 2.5 mg Vs10 mg olanzapine arms, there was significantly less DTS of any grade in the overall phase, and severe-grade DTS on day 1

Conclusions

Daily low-dose (2.5mg) olanzapine is non-inferior to its 10mg dose, in combination with standard triple anti-emetics, in controlling CINV without the requirement of delayed steroids and is superior with respect to daytime somnolence in patients receiving HEC.

This merits its consideration as an antiemetic regimen of choice for highly emetogenic chemotherapy.

Take care and support each other