COR2ED

THE HEART OF MEDICAL EDUCATION

DEVELOPED BY BREAST CANCER CONNECT

This programme is developed by BREAST CANCER CONNECT, an international group of experts in the field of breast cancer.

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BREAST CANCER CONNECT ANIMATED VIDEO

ER+ METASTATIC BREAST CANCER: THE PATIENT JOURNEY ON ELACESTRANT TREATMENT

Prof. Maria Vittoria Dieci

November 2023

ER+, estrogen receptor positive

CLINICAL TAKEAWAYS

- PROs results demonstrating no difference between treatment arms in the EMERALD trial, support elacestrant as a clinically meaningful option in this setting
- Elacestrant has a manageable safety profile
- If a patient progresses on elacestrant, the choice of subsequent therapy line should be based on multiple factors including sensitivity to prior treatments, disease burden, tumour biology. In this context, ADCs represent a new option

ADC, antibody-drug conjugate; PRO, patient-reported outcome

CLINICAL SCENARIO

THE ROAD AFTER SELECTING ELACESTRANT

PATIENT CASE OVERVIEW

MONICA D.

AGE
- 54 y.o. postmenopausal woman

MEDICAL HISTORY
- Well controlled hypertension, osteopenic, BMI=29
- +FH of prostate cancer in father, 80 y.o

DIAGNOSIS (2021)	1L TREATMENT (2021)	PROGRESSION (2023)	MUTATION TEST RESULTS	2L TREATMENT (2023)
ER+/HER2- *de novo* mBC (bone mets)	Letrozole + ribociclib	New Bone & Liver mets	*ESR1* mutation	Elacestrant

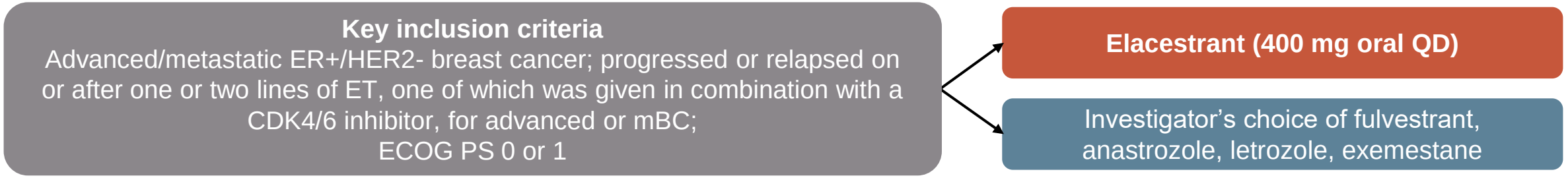
1L, first-line; 2L, second-line; BMI, body mass index; ER, estrogen receptor; ESR1, estrogen receptor 1 (gene); FH, family history; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mets, metastases; y.o, years old

EMERALD TRIAL PFS RESULTS: LANDMARK ANALYSIS & PFS BY DURATION OF PRIOR CDK4/6i

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; PFS, progression-free survival

PHASE 3 EMERALD: STUDY DESIGN

- A multicentre, international, randomised, open-label, active-controlled phase 3 trial for postmenopausal patients with ER+/HER2- mBC



- Primary end point: assess PFS in all patients and those with m*ESR1*
- Secondary end point: assess OS in all patients and those with m*ESR1*
- Study design considerations:
  - planned sample size: 466 patients (randomised 1:1)
  - planned number of countries/study sites: ~17/215
  - planned study duration: ~30–33 months
  - stratification factors: m*ESR1* status (detected by ctDNA), prior fulvestrant and presence of visceral disease

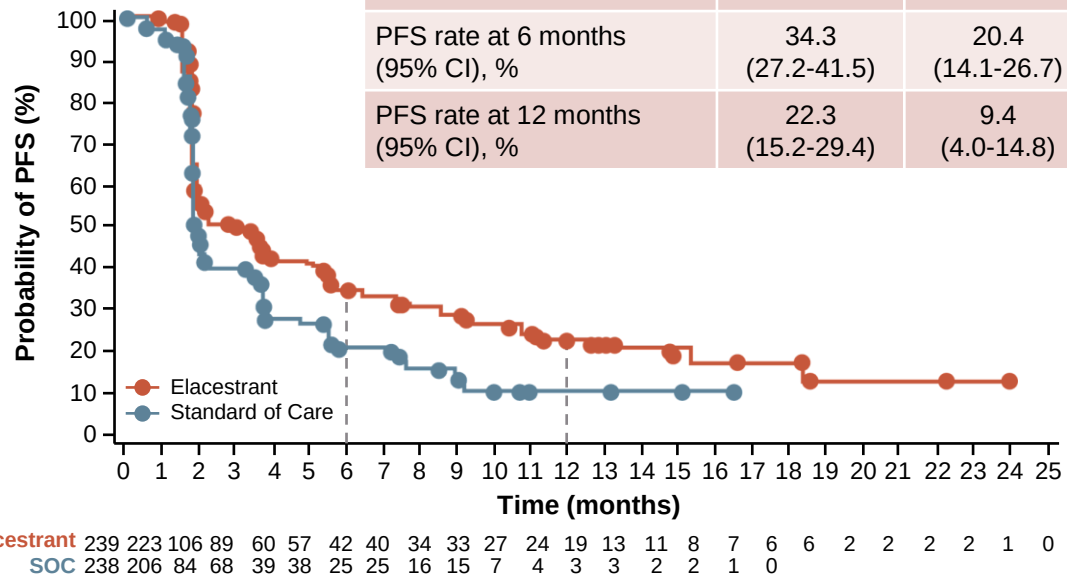
CDK4/6, cyclin-dependent kinase 4/6; ctDNA, circulating tumour DNA; ECOG PS; Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; ET, endocrine therapy; HER2, hormone epidermal growth factor receptor 2; mBC, metastatic breast cancer; mESR1, estrogen receptor 1 (gene) mutation; OS, overall survival; PFS, progression-free survival; QD, use "every day"

Bardia A, et al. Cancer Res 2022;82(4 Suppl):Abstract nr GS2-02 (SABCS 2021. Oral presentation); Bidard F-C, et al. J Clin Oncol. 2022;40:3246-3256

EMERALD: PFS RATE AT 6 & 12 MONTHS ALL PATIENTS AND m*ESR1* GROUP

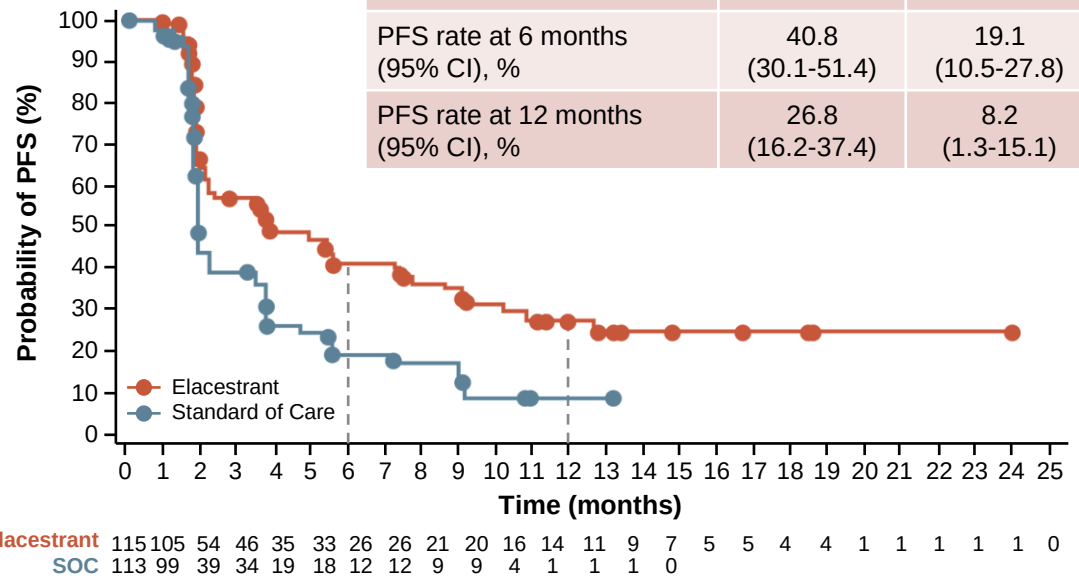
All patients

	Elacestrant	SoC
N	**239**	**238**
PFS rate at 6 months (95% CI), %	34.3 (27.2-41.5)	20.4 (14.1-26.7)
PFS rate at 12 months (95% CI), %	22.3 (15.2-29.4)	9.4 (4.0-14.8)



Patients with tumours harbouring m*ESR1*

	Elacestrant	SoC
N	**115**	**113**
PFS rate at 6 months (95% CI), %	40.8 (30.1-51.4)	19.1 (10.5-27.8)
PFS rate at 12 months (95% CI), %	26.8 (16.2-37.4)	8.2 (1.3-15.1)



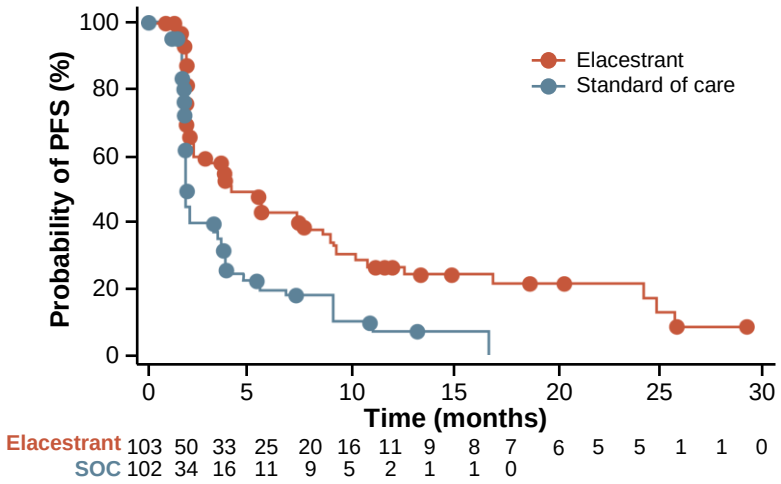
Elacestrant demonstrated a higher PFS rate versus SoC ET at 6 and 12 months in patients with ER+/HER2- advanced/metastatic breast cancer following prior CDK4/6i therapy

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; ER, estrogen receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; mESR1, estrogen receptor 1 (gene) mutation; N, sample size; PFS, progression-free survival; SoC, standard of care

Bidard F-C, et al. J Clin Oncol. 2022;40:3246-3256

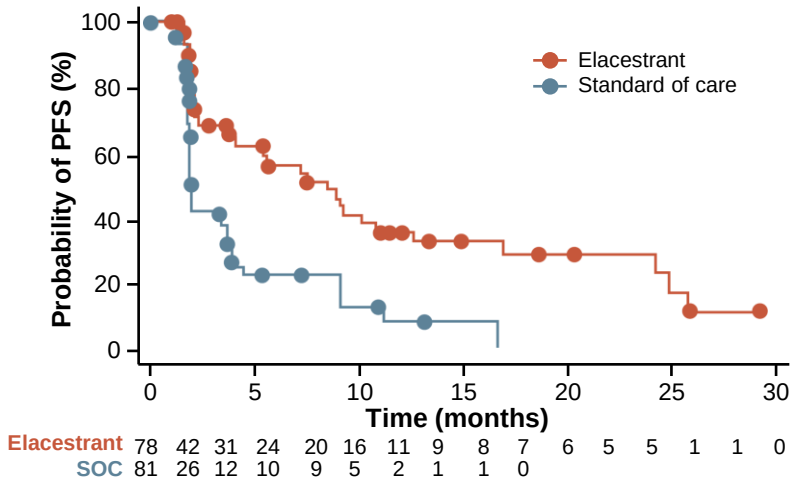
EMERALD: PFS BY DURATION OF CDK4/6i (m*ESR1*)

At least 6 mo CDK4/6i



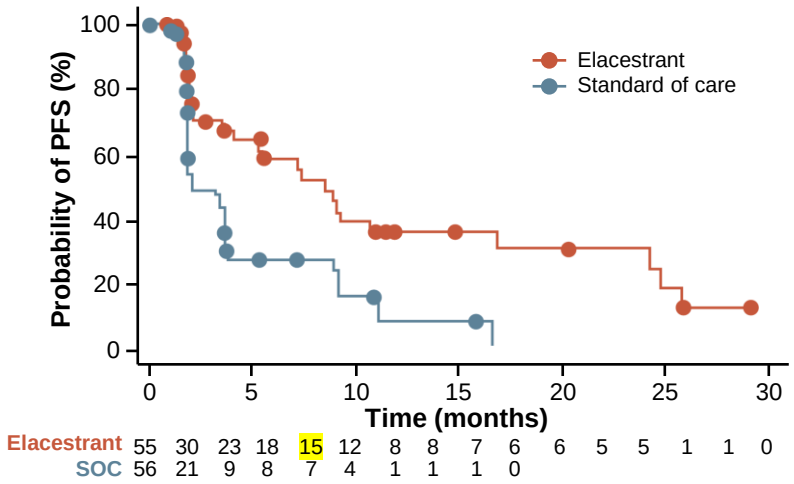
	Elacestrant	SoC Endocrine Therapy
Median PFS (95% CI), months	**4.14** (2.20-7.79)	**1.87** (1.87-3.29)
PFS rate at 12 months (95% CI), %	26.02 (15.12-36.92)	6.45 (0.00-13.65)
Hazard ratio (95% CI)	**0.517** (0.361-0.738)	

At least 12 mo CDK4/6i



	Elacestrant	SoC Endocrine Therapy
Median PFS (95% CI), months	**8.61** (4.14-10.84)	**1.91** (1.87-3.68)
PFS rate at 12 months (95% CI), %	35.81 (21.84-49.78)	8.39 (0.00-17.66)
Hazard ratio (95% CI)	**0.410** (0.262-0.634)	

At least 18 mo CDK4/6i



	Elacestrant	SoC Endocrine Therapy
Median PFS (95% CI), months	**8.61** (5.45-16.89)	**2.10** (1.87-3.75)
PFS rate at 12 months (95% CI), %	35.79 (19.54-52.05)	7.73 (0.00-20.20)
Hazard ratio (95% CI)	**0.466** (0.270-0.791)	

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; mESR1, estrogen receptor 1 (gene) mutation; mo, months; PFS, progression-free survival; SoC, standard of care

Bardia A, et al. Presented at SABCS 2022. December 6-10, 2022. Abstract GS3-01

ELACESTRANT VS SOC: ADVERSE EVENTS

Event		SoC		
	Elacestrant (N=237)	Total (N=229)	Fulvestrant (N=161)	AI (N=68)
Any AE	218 (92.0)	197 (86.0)	144 (89.4)	53 (77.9)
Grade 3 and 4[a]	64 (27.0)	47 (20.5)	33 (20.5)	14 (20.6)
Grade 5[b]	4 (1.7)	6 (2.6)	5 (3.1)	1 (1.5)
Leading to dose reduction	7 (3.0)	0	0	Not applicable
Leading to study drug discontinuation	15 (6.3)	10 (4.4)	6 (3.7)	4 (5.9)

AEs[c] occurring in ≥10% of patients in any arm (n(%))	Elacestrant		Total		Fulvestrant		AI	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Nausea	83 (35.0)[d]	6 (2.5)	43 (18.8)	2 (0.9)	26 (16.1)	0	17 (25.0)	2 (2.9)
Fatigue	45 (19.0)	2 (0.8)	43 (18.8)	2 (0.9)	35 (21.7)	1 (0.6)	8 (11.8)	1 (1.5)
Vomiting	45 (19.0)[e]	2 (0.8)	19 (8.3)	0	12 (7.5)	0	7 (10.3)	0
Decreased appetite	35 (14.8)	2 (0.8)	21 (9.2)	1 (0.4)	12 (7.5)	0	9 (13.2)	1 (1.5)
Arthralgia	34 (14.3)	2 (0.8)	37 (16.2)	0	28 (17.4)	0	9 (13.2)	0
Diarrhoea	33 (13.9)	0	23 (10.0)	2 (0.9)	14 (8.7)	1 (0.6)	9 (13.2)	1 (1.5)
Back pain	33 (13.9)	6 (2.5)	22 (9.6)	1 (0.4)	16 (9.9)	1 (0.6)	6 (8.8)	0
AST increased	31 (13.1)	4 (1.7)	28 (12.2)	2 (0.9)	20 (12.4)	2 (1.2)	8 (11.8)	0
Headache	29 (12.2)	4 (1.7)	26 (11.4)	0	18 (11.2)	0	8 (11.8)	0
Constipation	29 (12.2)	0	15 (6.6)	0	10 (6.2)	0	5 (7.4)	0
Hot flush	27 (11.4)	0	19 (8.3)	0	15 (9.3)	0	4 (5.9)	0
Dyspepsia	24 (10.1)	0	6 (2.6)	0	4 (2.5)	0	2 (2.9)	0
ALT increased	22 (9.3)	5 (2.1)	23 (10.0)	1 (0.4)	17 (10.6)	0	6 (8.8)	1 (1.5)

[a] AE severity was graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events version 5.0
[b] No fatal events were attributed to study drug by the investigator
[c] Preferred terms were coded using the Medical Dictionary for Regulatory Activities version 23.0.
[d] Grade 1 nausea, n=59 (24.9%); grade 2 nausea, n=18 (7.6%); grade 3 nausea, n= 6 (2.5%); and no patients experienced grade 4 nausea. Percentages reflect maximum grade experienced.
[e] Grade 1 vomiting, n=36 (15.2%); grade 2 vomiting, n=7 (3.0%); grade 3 vomiting, n=2 (0.8%); and no patients experienced grade 4 vomiting. Percentages reflect maximum grade experienced

AE, adverse event; AI, aromatase inhibitor; ALT, alanine transaminase; AST, aspartate transferase; n, number with event; N, number in population; SoC, standard of care

Bidard F-C, et al. J Clin Oncol. 2022;40:3246-3256

EMERALD TRIAL: A CLOSER LOOK AT THE ADVERSE EVENTS

- Most adverse events, including **nausea**, were **grade 1 and 2**, and **no grade 4 TRAEs** were reported[1]
- Only **3.4%** of patients receiving elacestrant and **0.9%** receiving SoC **discontinued therapy** due to any TRAE[1]
- **Dyslipidaemia** was infrequent, mostly **grade 1**, there were **no discontinuations**, and it was similar to SoC[2]
- **No deaths** assessed as treatment-related were reported in either arm[1]
- **No hematologic** safety signal was observed[3]

Nausea summary[2]

Nausea Summary	Elacestrant (n=237)	SoC (n=230)
Grade 3 nausea, n (%)	6 (2.5%)	2 (0.9%)
Dose-reduction rate due to nausea, n (%)	3 (1.3%)	Not applicable
Discontinuation rate due to nausea, n (%)	3 (1.3%)	0 (0%)
Antiemetic use	8%	10.3% (AI) 1.3% (Ful)

AI, aromatase inhibitor; Ful, fulvestrant; SoC, standard of care; TRAE, treatment-related adverse event

1. Bidard F-C, et al. J Clin Oncol. 2022;40:3246-3256

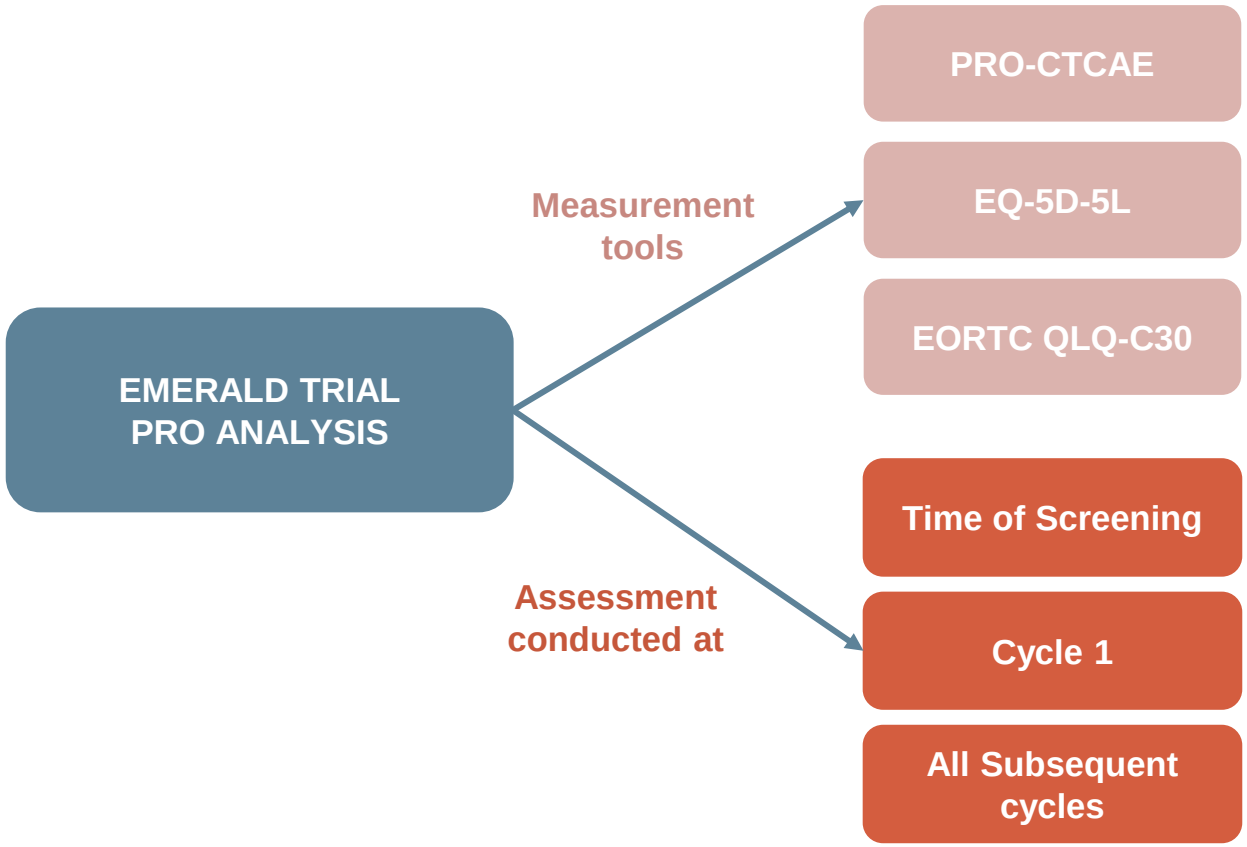
2. Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

3. Bardia A, et al. Presented at SABCS 2022. December 6-10, 2022. Abstract GS3-01

EMERALD TRIAL: PATIENT CENTERED OUTCOME ANALYSIS

PATIENT CENTERED OUTCOME ANALYSIS: EMERALD TRIAL

METHODOLOGY



*All PRO data are for the full ITT population up to cycle 6

Endpoints: Mean score change and change from baseline between treatment groups for EORTC QLQ-C30, PRO-CTCAE and EQ-5D-5L

PRO tools were assessed for all patient & patient with *ESR1*m

PRO completions rate

- 80% and 90% until cycle 4
- ~70% by cycle 6

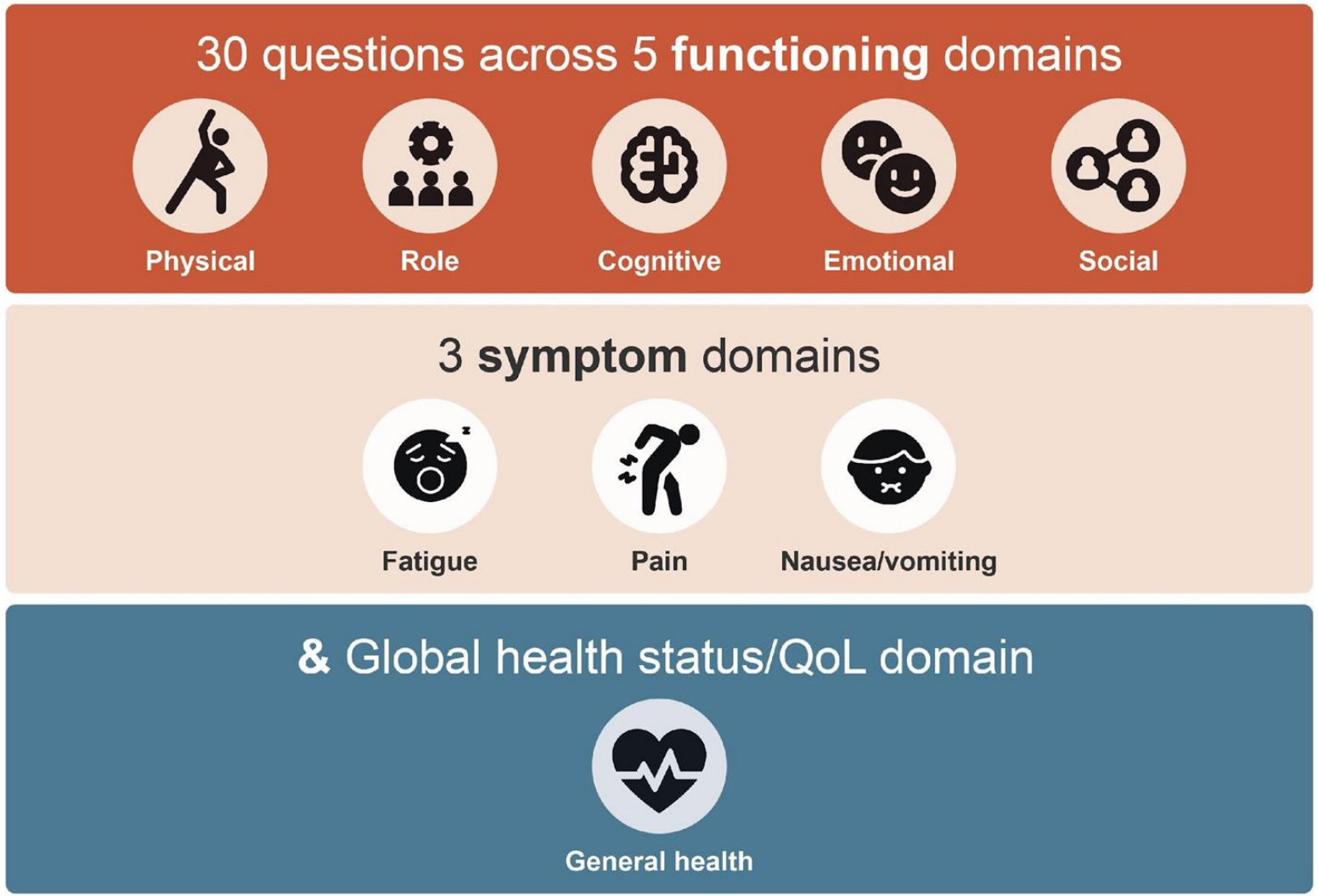
Incomplete PRO assessments where primarily due to:

- Patient language
- Patient refusal
- Technical problems
- COVID-19-related issues (study overlap with pandemic)

COVID-19, coronavirus disease 2019; EQ-5D-5L, EuroQol 5-Dimensions 5-Levels; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ESR1m, estrogen receptor 1 (gene) mutation; ITT, intent-to-treat; PRO, patient-reported outcome; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

EORTC QLQ-C30: Methods

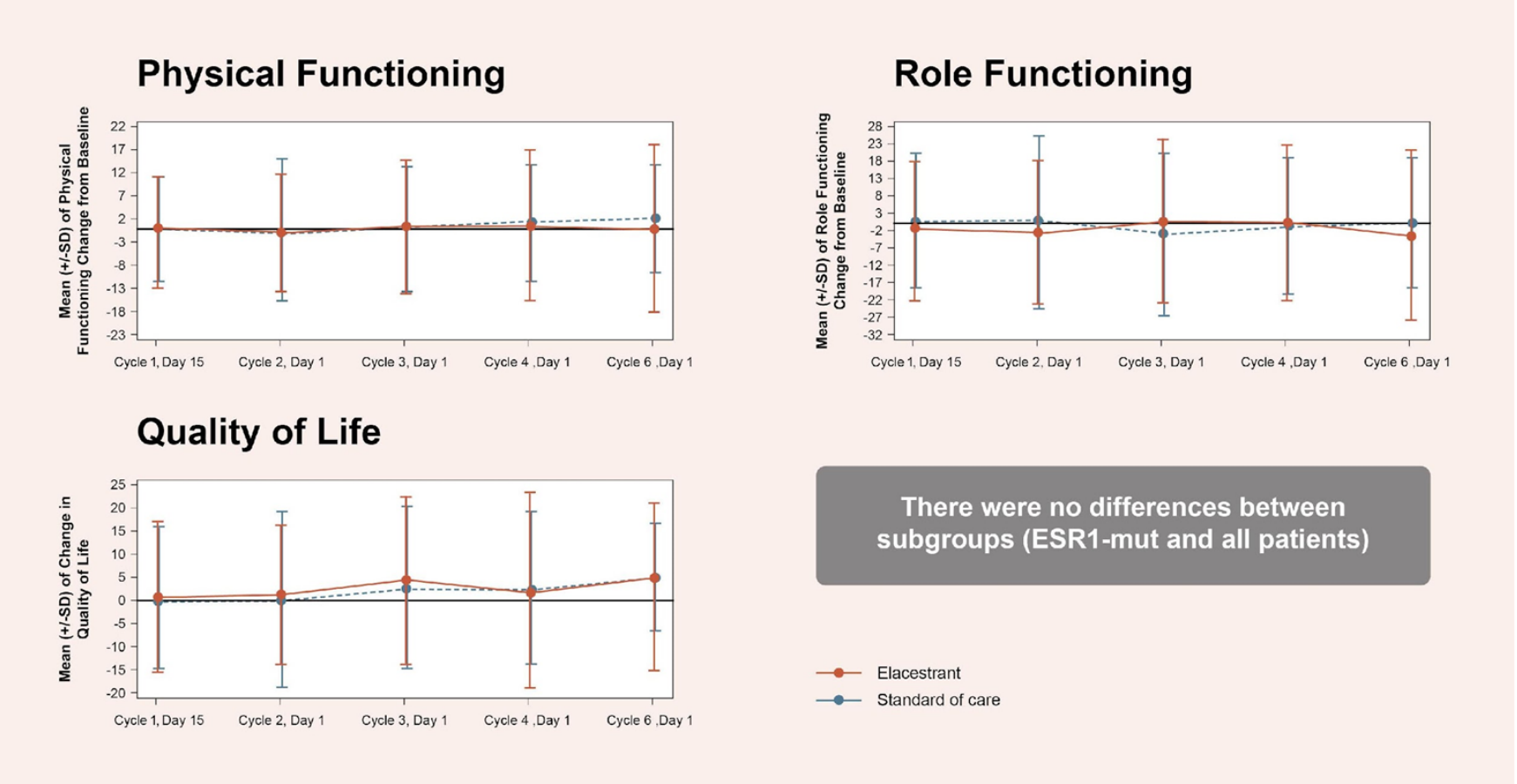


EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; QoL, quality of life

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

EORTC QLQ-C30: RESULTS

- EORTC QLQ-C30 scores were similar for elacestrant and SoC, with no differences across all time points for functional, symptom, and global health status/QoL domains

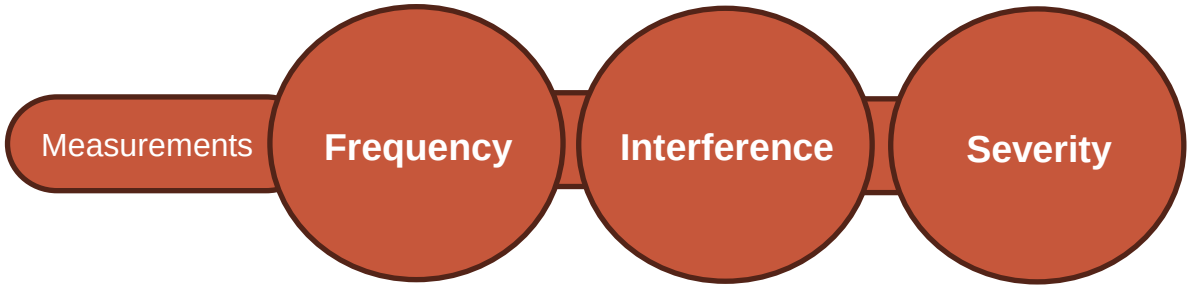


EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ESR1, estrogen receptor 1 (gene); mut, mutant; QoL, quality of life; SD, standard deviation; SoC, standard of care

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

PRO-CTCAE: METHODS

Questionnaire measuring subject-reported frequency, severity & interference of AEs of interest including **nausea, vomiting, joint & muscle pain, & hot flashes** occurring during cancer clinical trials



AE, adverse event; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events

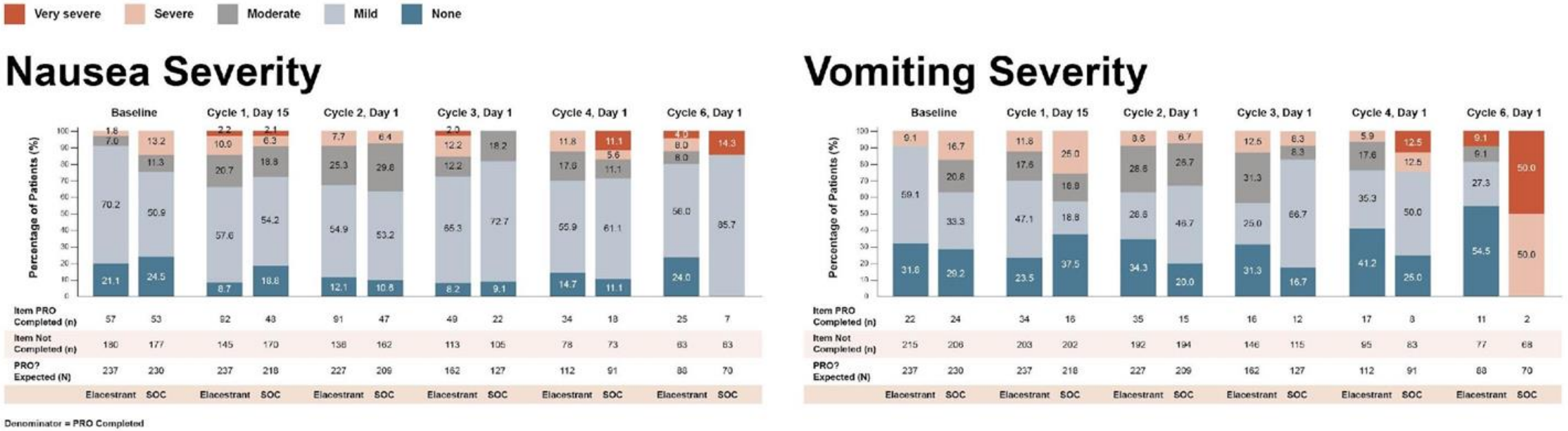
Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

PRO-CTCAE: ADVERSE EVENTS RESULTS

There were no differences between subgroups (ESR1-mut and all patients)

Fewer patients reported severe nausea with elacestrant vs. SoC by cycle 6 (4.0% vs 14.3%)

Fewer patients reported severe vomiting with elacestrant vs. SoC by cycle 6 (9.1% vs 50%)



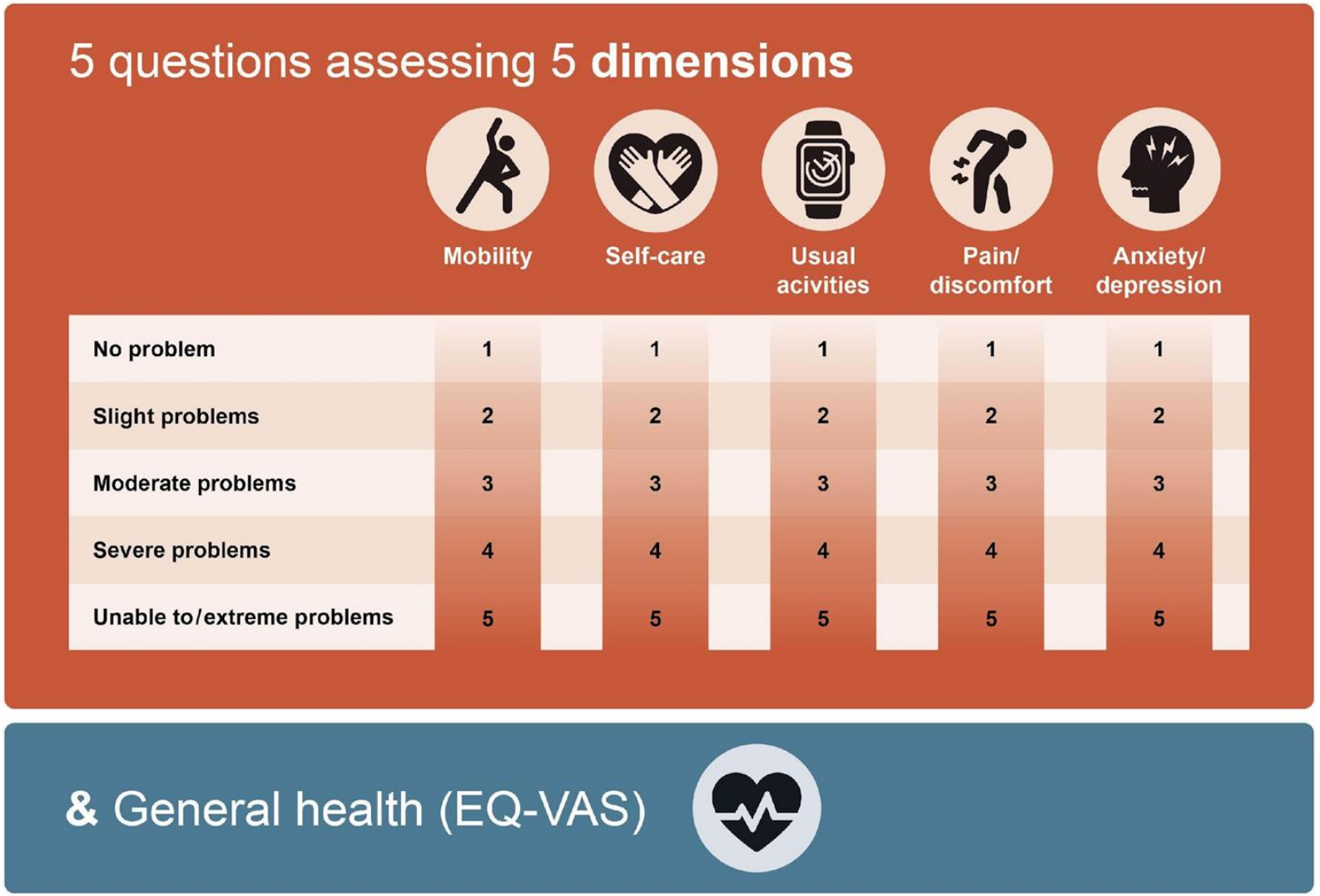
Denominator = PRO Completed

There were no clinically meaningful differences across all time points in other adverse events typically observed with patients with cancer on ET, such as fatigue, joint pain, muscle pain, and hot flashes

ESR1, estrogen receptor 1 (gene); ET, Endocrine Therapy; mut, mutation; n, number with event; N, number in population; PRO, patient-reported outcome; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; SoC, standard of care

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

EQ-5D-5L: METHODS

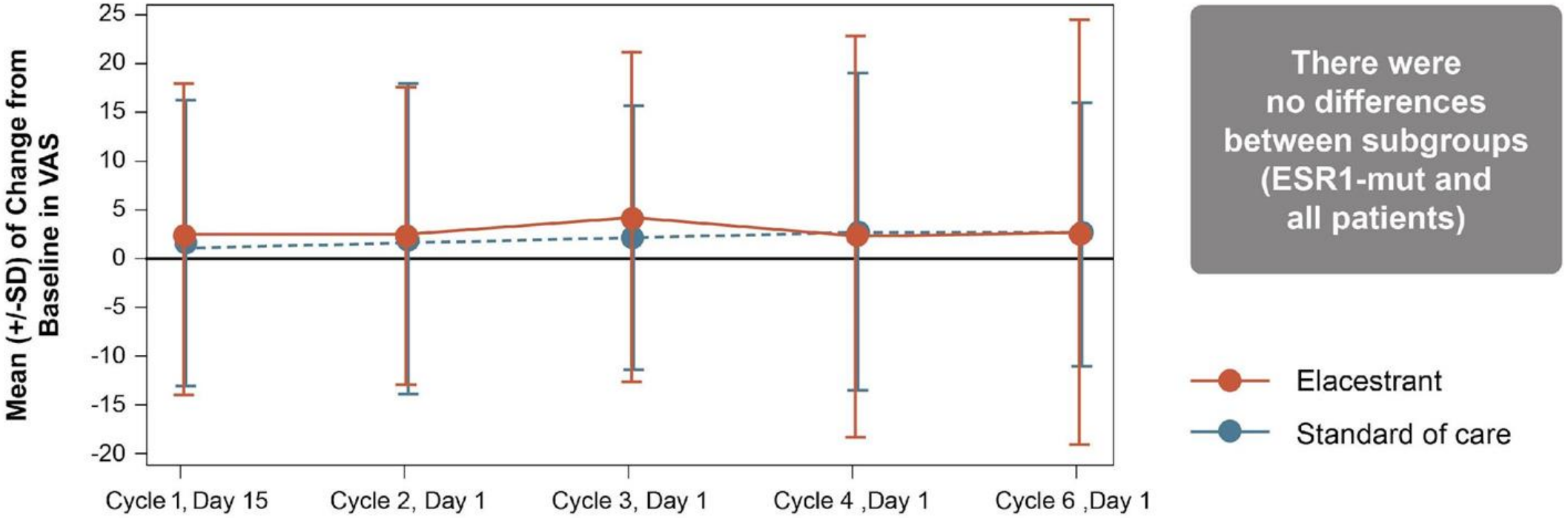


EQ-5D-5L, EuroQol 5-Dimensions 5-Levels; EQ-VAS, EuroQol visual analogue scale

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

EQ-5D-5L: RESULTS

- EQ-5D-5L scores were generally comparable in all patients (elacestrant vs SoC) for mobility, self-care, and usual activities



EQ-5D-5L, EuroQol 5-Dimensions 5-Levels; ESR1, estrogen receptor 1 (gene); SD, standard deviation; SoC, standard of care; VAS, visual analogue scale

Cortes J. et al. ESMO Op. 2023;8(suppl 4):101377. Available at: https://doi.org/10.1016/j.esmoop.2023.101377 (accessed November 2023). Presented at ESMO Breast Cancer Annual Congress (2023). Abstract 188O

ELACESTRANT AND MANAGING TREATMENT RELATED ADVERSE EVENTS

ELACESTRANT AND TREATMENT RELATED ADVERSE EVENTS

PATIENT CASE DEVELOPMENT

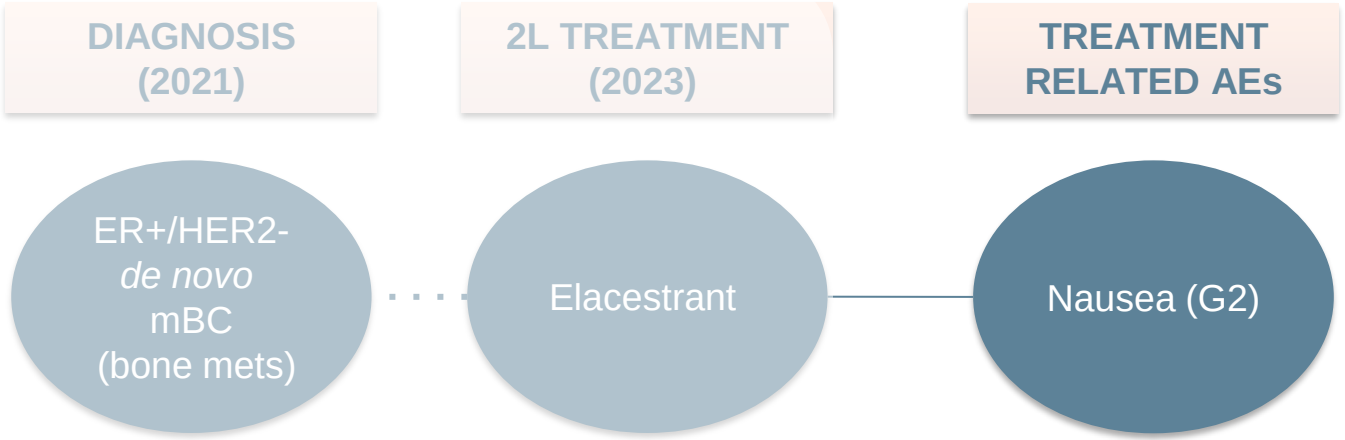
MONICA D.

AGE

- 54 y.o. postmenopausal woman

MEDICAL HISTORY

- Well controlled hypertension, osteopenic, BMI=29
- +FH of prostate cancer in father, 80 y.o



2L, second-line; AE, adverse event; BMI, body mass index; ER, estrogen receptor; FH, family history; G2, grade 2; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mets, metastases; y.o, years old

ELACESTRANT AND TREATMENT RELATED ADVERSE EVENTS
DOSING RECOMMENDATIONS

Initial dose recommendations

- 345 mg/day (PO)

Dose reduction recommendations for adverse reactions

- First dose reduction: 258 mg/day
- Second dose reduction: 172 mg/day
- Permanently discontinue if dose reduction <172 mg/day required

Modifications for adverse reactions

- Grade 1: Continue at current dose level
- Grade 2: Consider dose interruption until recovery to Grade ≤1 or baseline, then resume at same dose
- Grade 3:
  - Interrupt dose until recovery to Grade ≤1 or baseline, then resume at next lower dose
  - If Grade 3 toxicity recurs, interrupt until recovery to Grade ≤1 or baseline, then resume elacestrant reduced by another dose level
- Grade 4:
  - Interrupt dose until recovery to Grade ≤1 or baseline, then resume at next lower dose
  - Permanently discontinue if Grade 4 or intolerable adverse reaction recurs

PO, orally

Medscape. Elacestrant Dosage & Usage. 2023. Available at: https://reference.medscape.com/drug/orserdu-elacestrant-4000317 (accessed November 2023)

ELACESTRANT AND TREATMENT RELATED ADVERSE EVENTS

PATIENT CASE DEVELOPMENT

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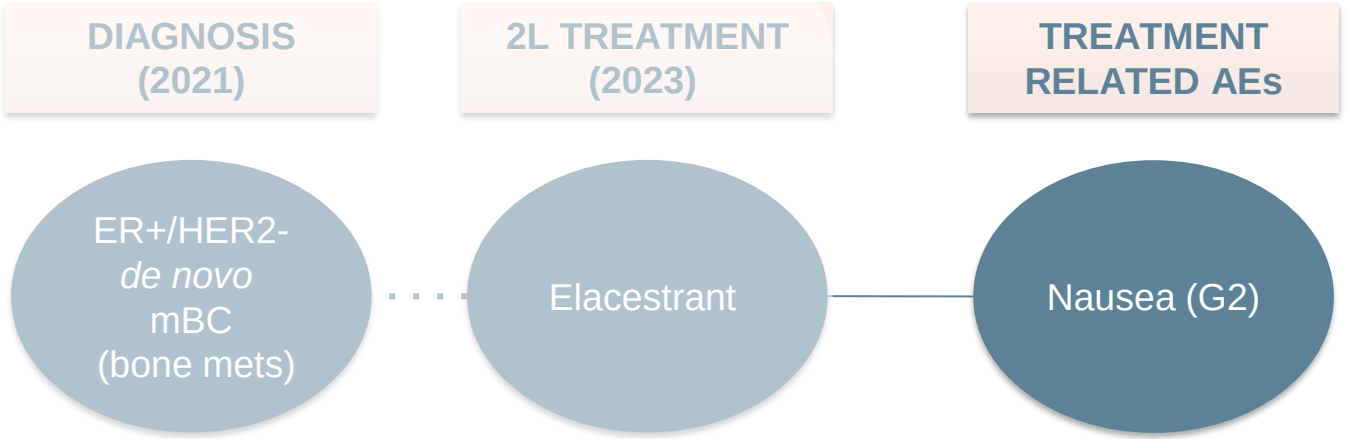


Adverse event management recommendations for Monica:

- Drug was suspended for 1 week, then restarted at the same dose no Grade ≥2 AEs occurred thereafter
- Drug to be taken with food to reduce nausea

2L, second-line; AE, adverse event; BMI, body mass index; ER, estrogen receptor; FH, family history; G2, grade 2; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mets, metastases; y.o, years old

DISEASE PROGRESSION: BEYOND ELACESTRANT

DISEASE PROGRESSION: BEYOND ELACESTRANT

PATIENT CASE DEVELOPMENT

MONICA D.

AGE

- 57 y.o. postmenopausal woman

MEDICAL HISTORY

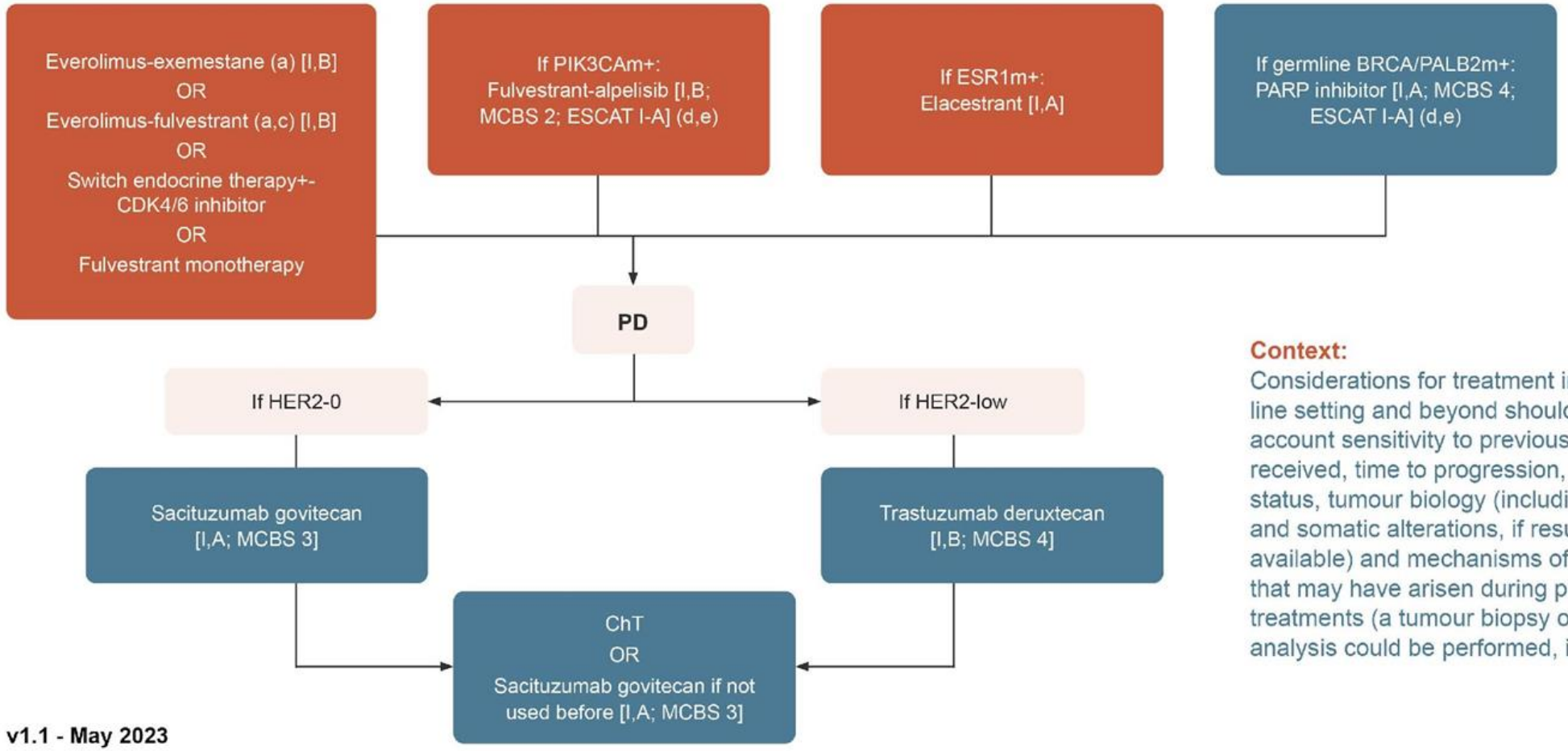
- Well controlled hypertension, osteopenic, BMI=29
- +FH of prostate cancer in father, 80 y.o

DIAGNOSIS (2021)	2L TREATMENT (2023)	TREATMENT RELATED AEs	PROGRESSION (20??)
ER+/HER2- *de novo* mBC (bone mets)	Elacestrant	Nausea (G3)	?

2L, second-line; AE, adverse event; BMI, body mass index; ER, estrogen receptor; FH, family history; G3, grade 3; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mets, metastases; y.o, years old

DISEASE PROGRESSION: BEYOND ELACESTRANT

ESMO 2023 RECOMMENDATIONS



Context:
Considerations for treatment in the third-line setting and beyond should take into account sensitivity to previous treatments received, time to progression, *gBRCAm* status, tumour biology (including germline and somatic alterations, if results are available) and mechanisms of resistance that may have arisen during previous treatments (a tumour biopsy or ctDNA analysis could be performed, if feasible).

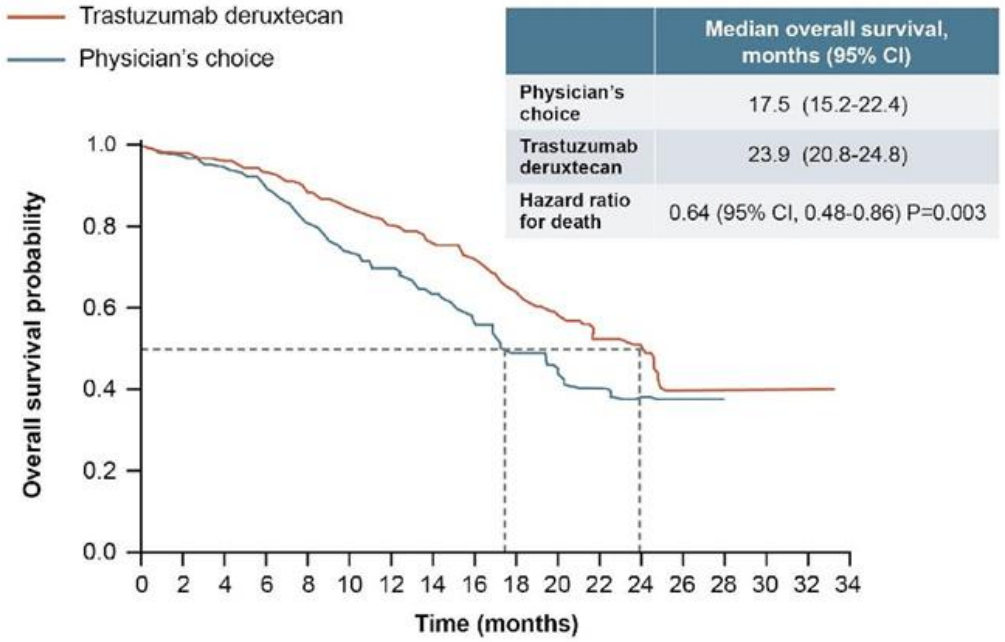
BRCA, breast cancer susceptibility gene; CDK4/6, cyclin-dependent kinase 4/6; ChT, chemotherapy; ctDNA, circulating tumour DNA; ESR1m, estrogen receptor 1 (gene) mutation; ESCAT I-A, ESMO Scale for Clinical Actionability of Molecular Targets; gBRCAm, germline BRCA mutations; HER2, human epidermal growth factor receptor 2; MCBS, magnitude of clinical benefit scale (ESMO); PALB2m, partner and localizer of BRCA2 (gene) mutation; PARP, poly(ADP-ribose) polymerase; PD, progression disease; PIK3CAm, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (gene) mutation

Gennari A, et al. Ann Oncol. 2021 Dec;32(12):1475-1495; Curigliano G, et al. ESMO Metastatic Breast Cancer Living Guidelines, v1.1 May 2023 (ER-positive HER2-negative Breast Cancer). Available at: https://www.esmo.org/living-guidelines/esmo-metastatic-breast-cancer-living-guideline/er-positive-her2-negative-breast-cancer (accessed November 2023)

OPTIMAL TREATMENT SEQUENCE IN ER+/HER2- mBC IN 2023

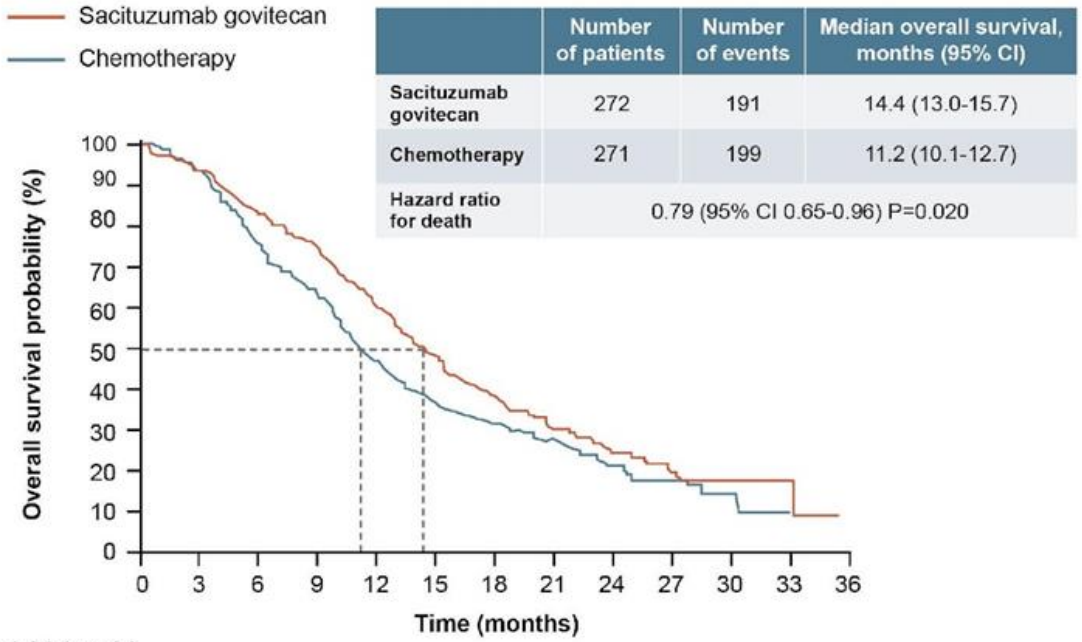
ADCs IN 2L & 3L SETTING

DESTINY-Breast04: Trastuzumab deruxtecan vs SoC 2L +, HER2-low only[1]



	Median overall survival, months (95% CI)
Physician's choice	17.5 (15.2-22.4)
Trastuzumab deruxtecan	23.9 (20.8-24.8)
Hazard ratio for death	0.64 (95% CI, 0.48-0.86) P=0.003

TROPiCS-02: Sacituzumab govitecan vs SoC 3L +, all comers[2]



	Number of patients	Number of events	Median overall survival, months (95% CI)
Sacituzumab govitecan	272	191	14.4 (13.0-15.7)
Chemotherapy	271	199	11.2 (10.1-12.7)
Hazard ratio for death	0.79 (95% CI 0.65-0.96) P=0.020		

Number at risk (events)

Sacituzumab govitecan	272 (0)	252 (16)	221 (44)	197 (67)	160 (104)	129 (137)	80 (158)	53 (173)	31 (183)	20 (188)	4 (190)	2 (190)	0 (191)
Chemotherapy	271 (0)	246 (16)	196 (64)	164 (95)	122 (137)	92 (163)	70 (174)	49 (183)	23 (193)	13 (196)	5 (198)	1 (199)	0 (199)

2L, second-line; 3L, third-line; ADC, antibody-drug conjugate; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; SoC, standard of care

1. Modi S, et al. N Eng J Med. 2022;387:9-20; 2. Rugo HS, et al. Lancet. 2023;402:1423-1433

ORAL SERDS FUTURE PERSPECTIVES & CONCLUSION

SERD, selective estrogen receptor degrader

ONGOING ORAL SERDS PHASE 3 TRIALS IN ER+/HER2- mBC

Trial ID	Drug	Patient cohort(s)	Sample size	Primary Endpoint	Setting
NCT04964934 (SERENA-6)	Camizestrant	**E:** camizestrant + palbociclib or abemaciclib or ribociclib; **C:** anastrozole or letrozole + palbociclib or abemaciclib or ribociclib	300	mPFS	ER+/HER2-, ESR1 mutated
NCT04711252 (SERENA-4)	Camizestrant	**E:** camizestrant + palbociclib **C:** anastrozole + palbociclib	1342	mPFS	ER+/HER2- mBC, ≥ 1L (AI or TAM pre-treated)
NCT04975308 (EMBER-3)	Imlunestrant	**E:** imlunestrant **E:** imlunestrant + abemaciclib **C:** exemestane or fulvestrant	860	mPFS	ER+/HER2- mBC, ≥ 1L
NCT05306340 (evERA)	Giredestrant	**E:** giredestrant + everolimus **C:** exemestant or fulvestrant or tamoxifen + everolimus	320	mPFS	ER+/HER2- mBC, ≥ 1L (after CDK4-6i)
NCT04546009 (persevERA)	Giredestrant	**E:** giredestrant + letrozole - matching placebo + palbociclib **C:** letrozole + giredestrant - matching placebo + palbociclib	992	mPFS	ER+/HER2- mBC, without therapeutic options

1L, first-line; AI, aromatase inhibitor; C, comparator; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; E, experimental; ER, estrogen receptor; ESR1, estrogen receptor 1 (gene); HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mPFS, median progression-free survival; TAM, tamoxifen

1. https://www.clinicaltrials.gov/study/NCT04964934 (accessed November 2023)
2. https://www.clinicaltrials.gov/study/NCT04711252 (accessed November 2023)
3. https://clinicaltrials.gov/study/NCT04975308 (accessed November 2023)
4. https://clinicaltrials.gov/study/NCT05306340 (accessed November 2023)
5. https://clinicaltrials.gov/study/NCT04546009 (accessed November 2023)

ONGOING PHASE 3 TRIALS IN ER+/HER2- eBC

Trial ID	Drug	Phase	Patient cohort(s)	Sample size	Primary Endpoint	Setting
NCT05512364 (TREAT ctDNA)	Elacestrant	3	**E:** elacestrant monotherapy **C:** standard ET (the same PTS were receiving at the time of ctDNA detection)	220	DMFS	High-risk (either stage IIB-III or ≥ypT1c and/or ypN+)
NCT04436744 (lidERA)	Giredestrant	3	**E:** giredestrant **C:** ET of physician's choice	4100	iDFS	Stage I-III
NCT05774951 (CAMBRIA1)	Camizestrant	3	**E:** camizestrant **C:** continue standard ET of investigator's choice	4300	iBCFS	High-risk eBC after at least 2 years (no more than 5 years) of ET

C, comparator; ctDNA, circulating tumour DNA; DMFS, distant metastasis-free survival; E, experimental; eBC, early breast cancer; ER, estrogen receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; iBCFS, invasive breast cancer-free survival; iDFS, invasive disease-free survival; pts, patients; ypT1c, residual tumour at surgery of ≥1 cm; ypN+, pathological lymph node involvement

1. https://www.clinicaltrials.gov/study/NCT05512364 (accessed November 2023)
2. https://www.clinicaltrials.gov/study/NCT04961996?cond=BREAST%20CANCER&intr=GIREDESTRANT&term=EARLY%20BREAST%20CANCER%20&rank=3 (accessed November 2023)
3. https://clinicaltrials.gov/study/NCT05774951 (accessed November 2023)

CLINICAL TAKEAWAYS

- PRO results demonstrate no difference between treatment arms in the EMERALD trial, support elacestrant as a clinically meaningful option in this setting
- Elacestrant has a manageable safety profile
- If a patient progresses on elacestrant, the choice of subsequent therapy line should be based on multiple factors including sensitivity to prior treatments, disease burden, tumour biology. In this context, ADCs represent a new option

ADC, antibody-drug conjugate; PRO, patient-reported outcome

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