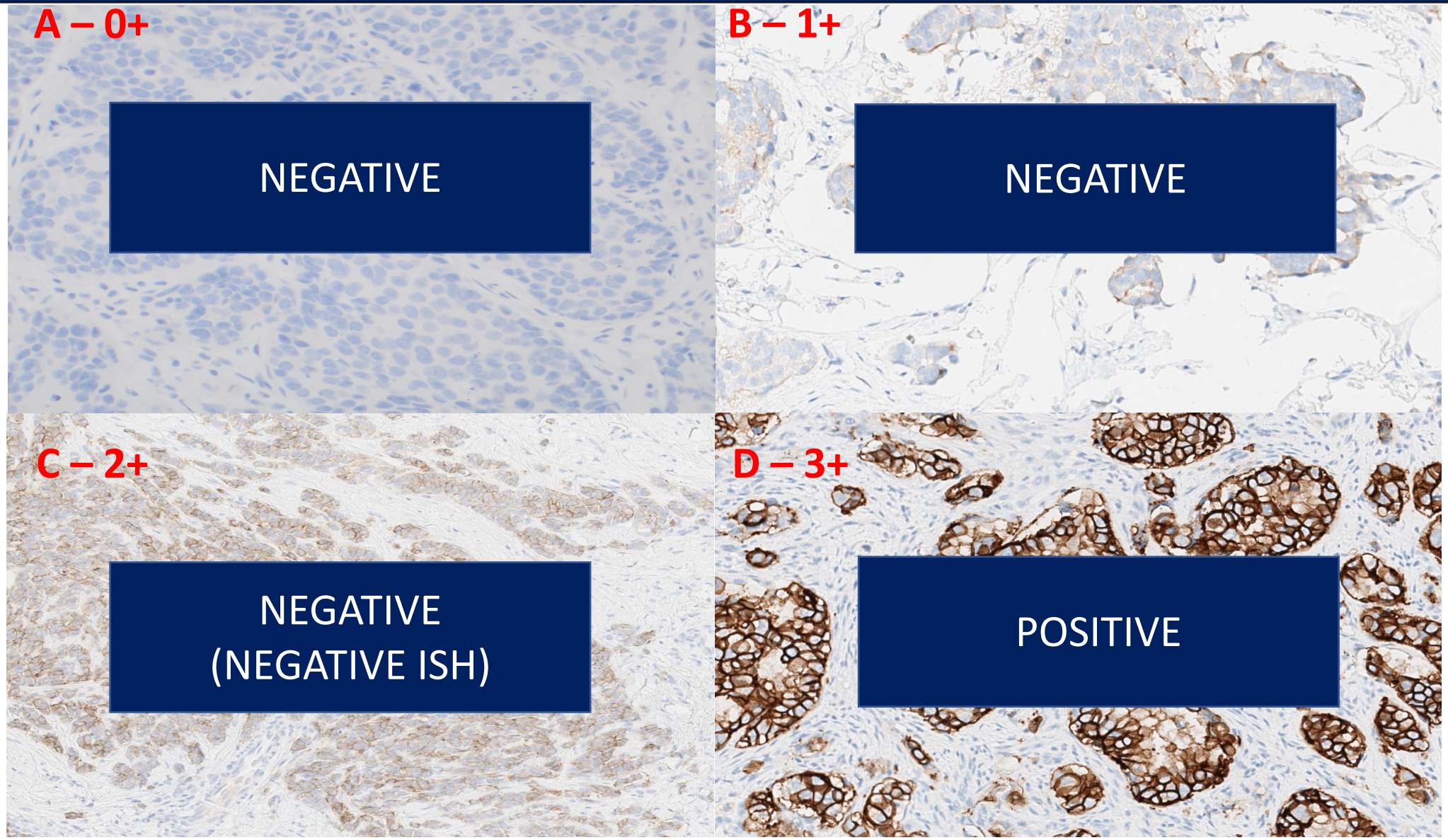
Updates in Breast Cancer Management: Targeted Therapies

Melissa Yacur, MD
Inova Schar Cancer Institute
August 5, 2023

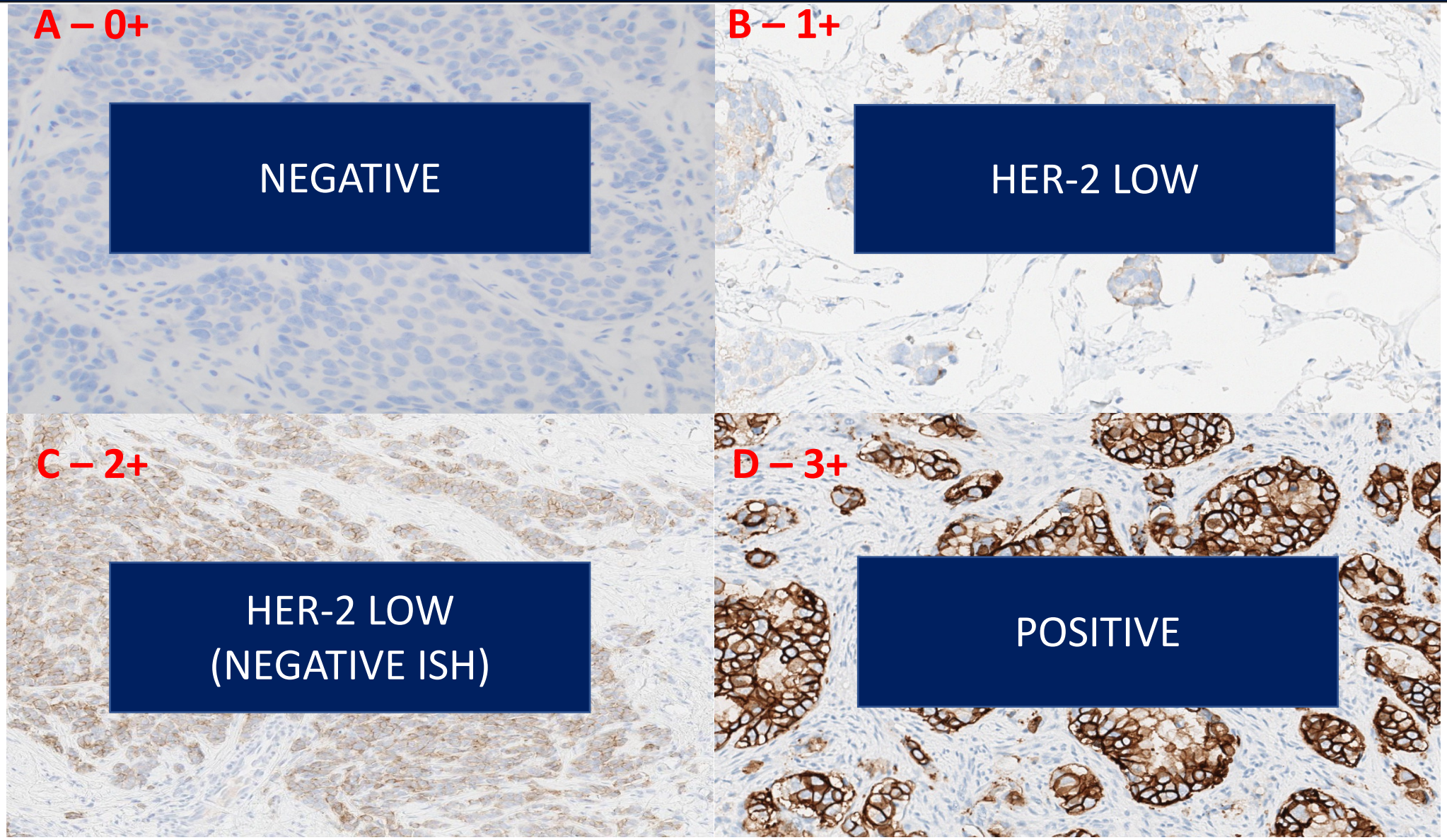
Objectives

- Trastuzumab-deruxtecan for Her-2 Low Breast cancer
- Adjuvant CDK 4/6 inhibitors for hormone-positive (HR+)/Her-2 negative tumors
- Targeting ESR1 mutations in metastatic HR+ breast cancer

Her-2 Low



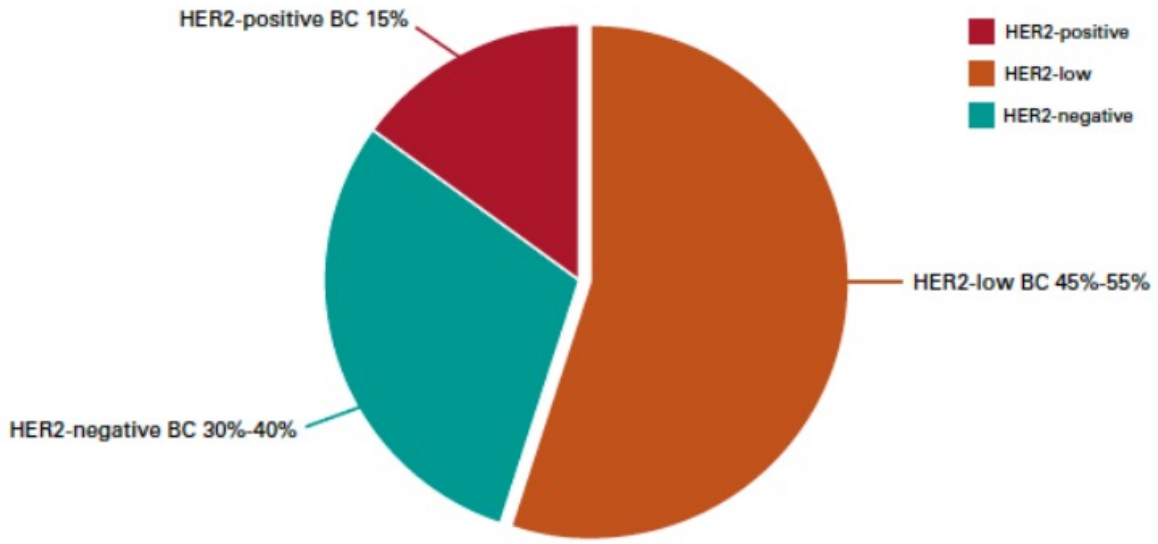
Images A and C courtesy of Her2Know. Images B and D courtesy of Dr. Michael Stamatakos



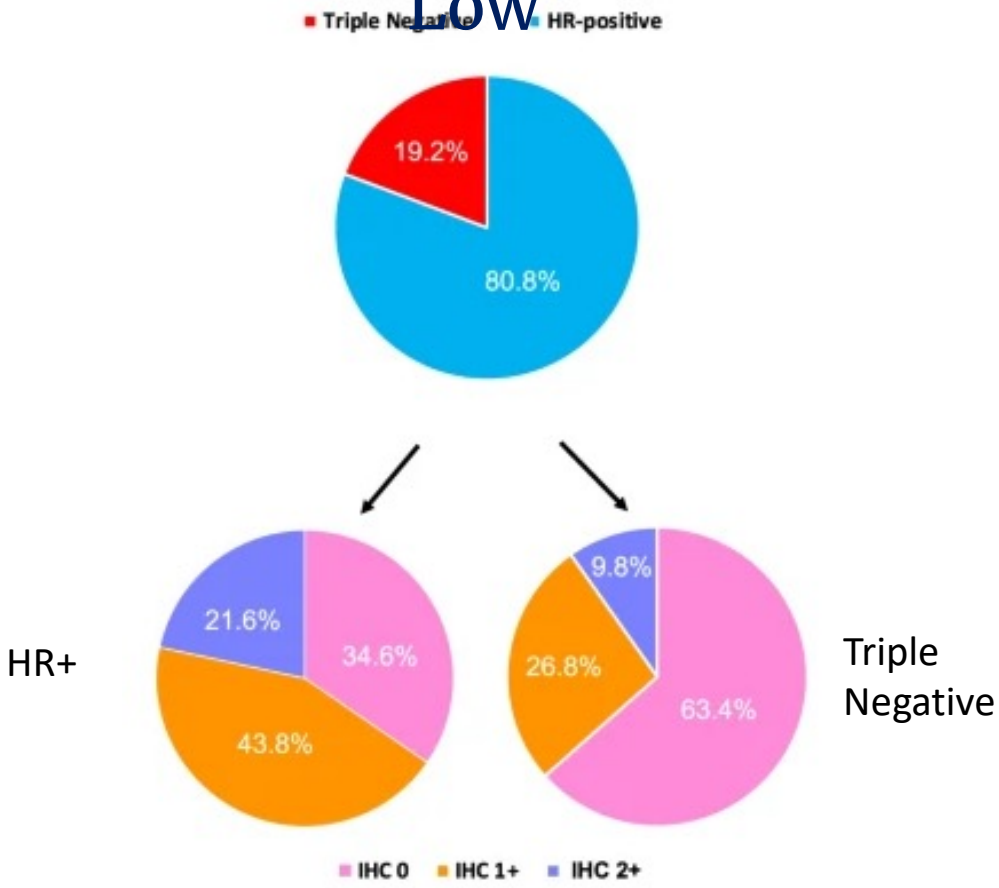
Images A and C courtesy of Her2Know. Images B and D courtesy of Dr. Michael Stamatakos

Prevalence of Her-2 Low

All Breast Cancers



Her-2 Zero and Low



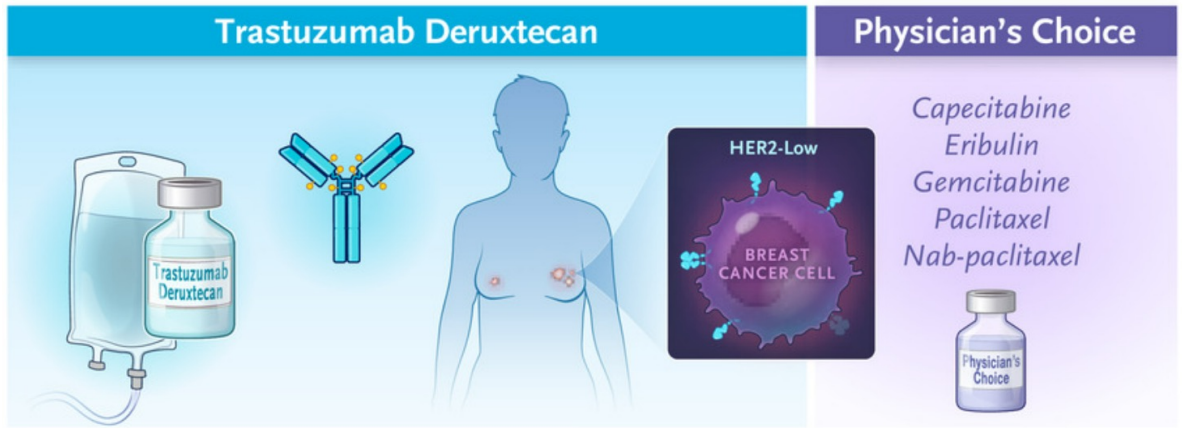
Tarantino P, et al. J Clin Oncol. 2020;38(17):1951-1962.
Schettini F, et al. NPJ Breast Cancer. 2021;7(1):1.

What Does This Mean For Patients?

- Her-2 low tumors are emerging as a distinct subgroup in terms of tumor biology, response to therapy, and prognosis
- No standard of care currently to incorporate Her-2 directed therapy in the local/locally advanced setting for Her-2 low
- With recent data, advanced disease can be targeted

Denkert, et al, Clinical and molecular characteristics of HER2-low-positive breast cancer: pooled analysis of individual patient data from four prospective, neoadjuvant clinical trials. Lancet Onc 2021 Aug;22(8):1151-1161

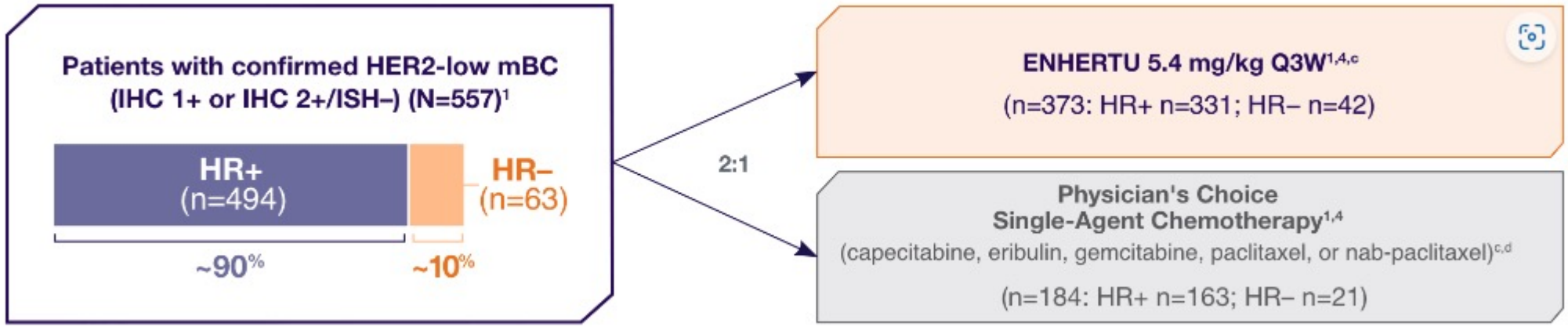
Destiny-Breast04



Eligibility Criteria:
-Her-2 low (IHC 1+ or IHC 2+/ISH -)
-At least one prior line of chemo for metastatic disease or disease recurrence 6 months or less after adjuvant therapy
-At least one line of endocrine therapy if metastatic HR+
- Could be HR+ or HR -

Modi S, et al. Presented at: ASCO; June 3-June 7, 2022; Chicago. Abstract LBA3. Modi S, et al. N Engl J Med. 2022;387(1

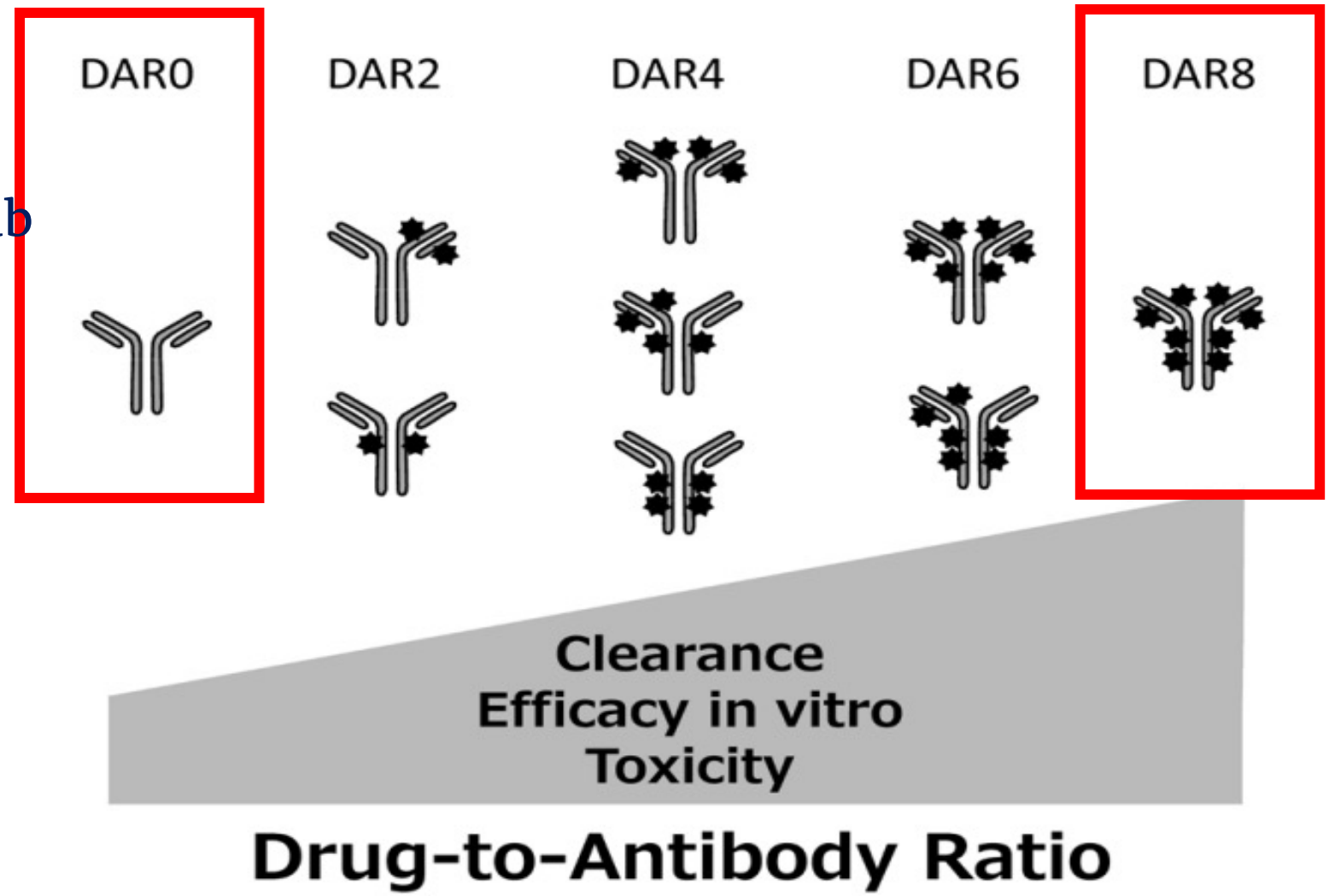
Destiny-04 Trial Design



Enhertuhcp.com

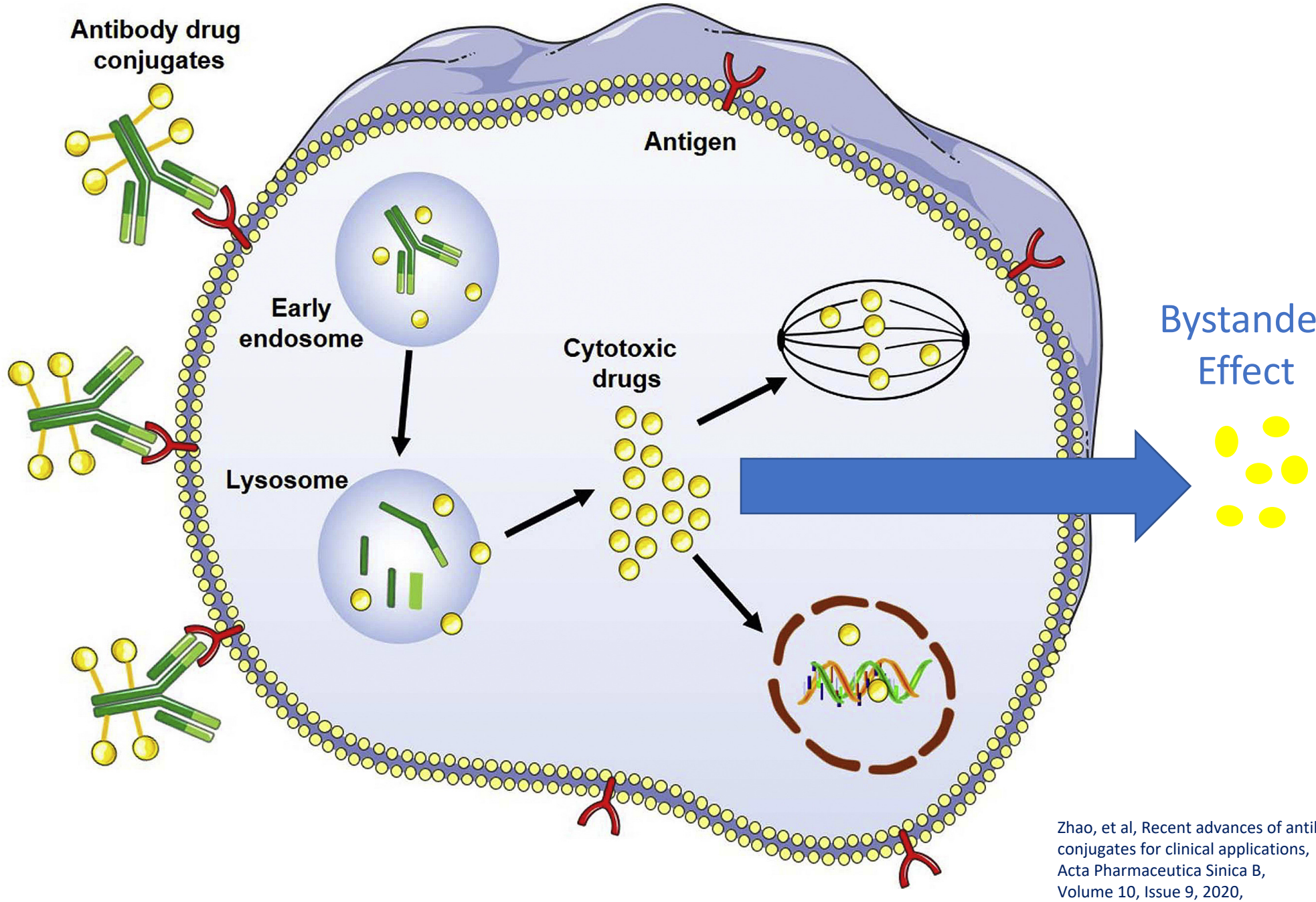
Modi, et al, Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. *N Engl J Med*. 2022;387(1):9-20

Trastuzumab



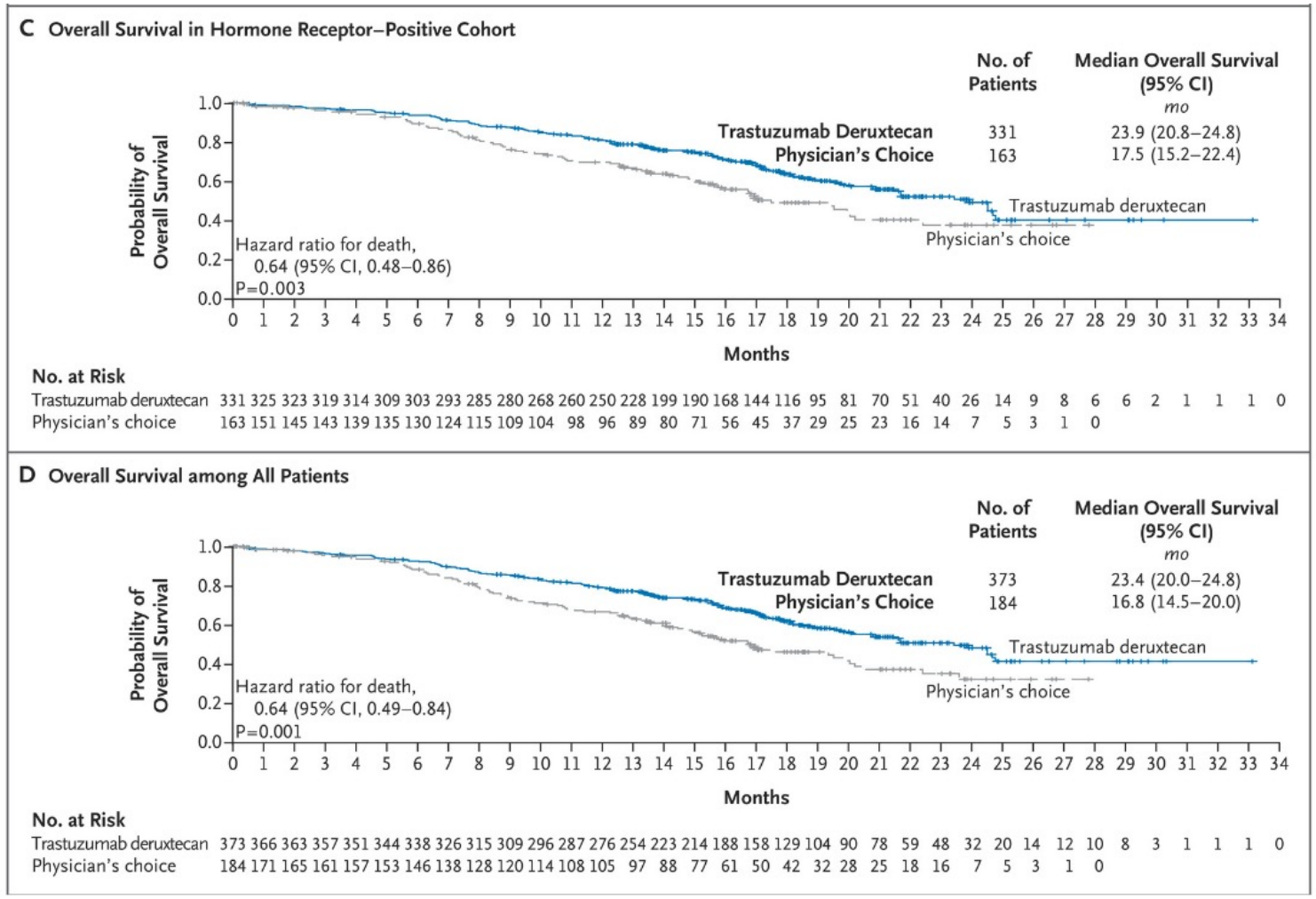
Trastuzumab deruxtecan

Nakada T, et al. Chem Pharm Bull. 2019;67:173-185



Zhao, et al, Recent advances of antibody drug conjugates for clinical applications, Acta Pharmaceutica Sinica B, Volume 10, Issue 9, 2020,

Destiny-Breast04



P=0.003

P=0.001

Modi S, et al. Presented at: ASCO; June 3-June 7, 2022; Chicago. Abstract LBA3. Modi S, et al. N Engl J Med. 2022;387

Summary

- Her-2 low (IHC 1+ or 2+) is an exciting new target in breast cancer
- Current data supports use of trastuzumab-deruxtecan in the advanced setting after at least one line of prior therapy or rapid recurrence
- Bystander effect of this drug likely plays a role in its effectiveness

Adjuvant CDK 4/6 inhibitors

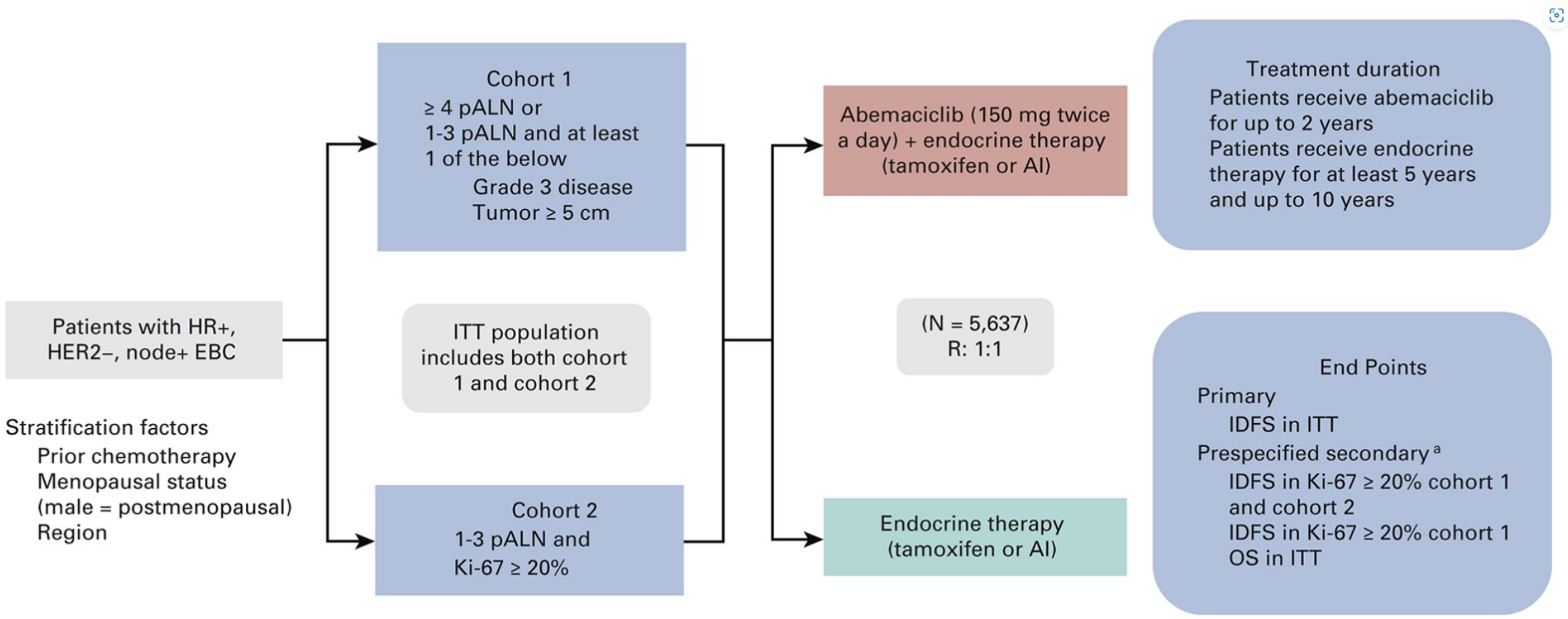
Breast carcinoma TNM anatomic stage group AJCC UICC 8th edition

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

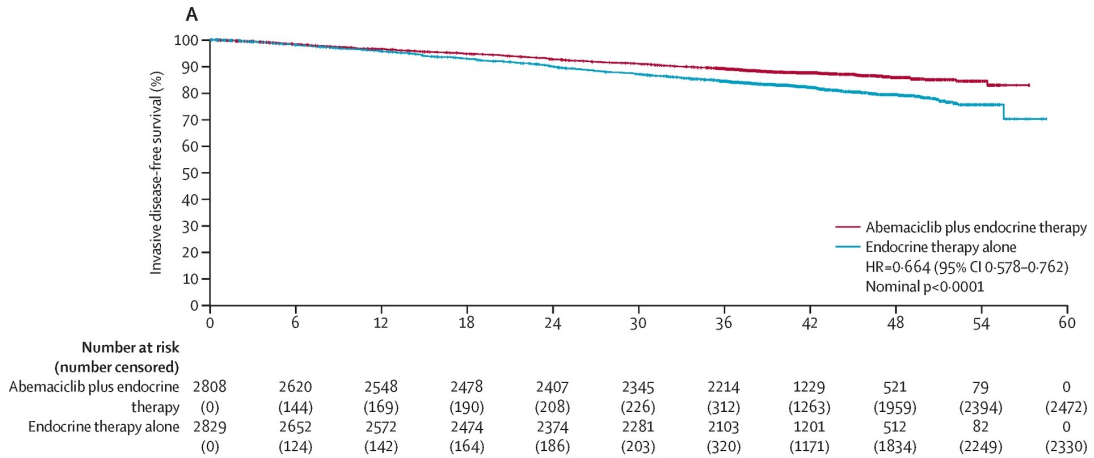
- The anatomic stage group table should only be used in global regions where biomarker tests are not routinely available.
- Cancer registries in the US must use the prognostic stage group table for case reporting.

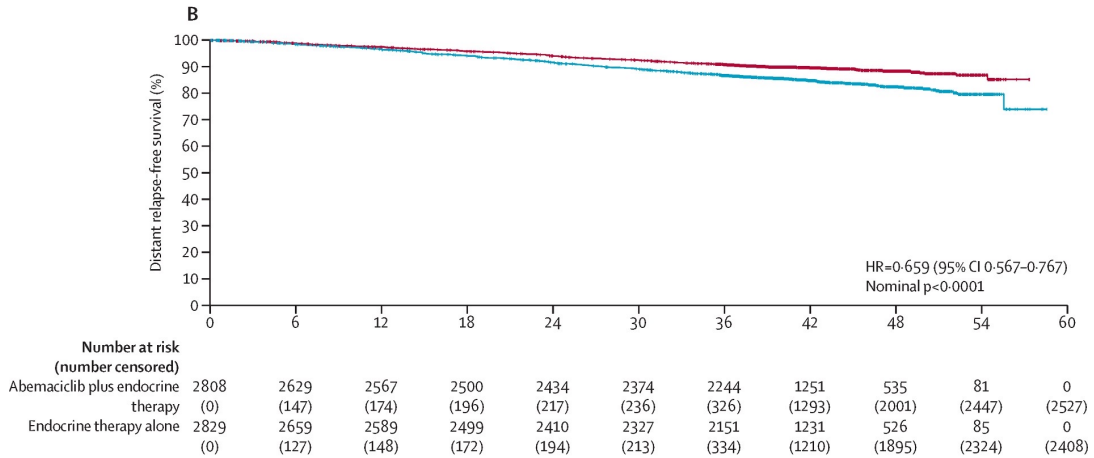
TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

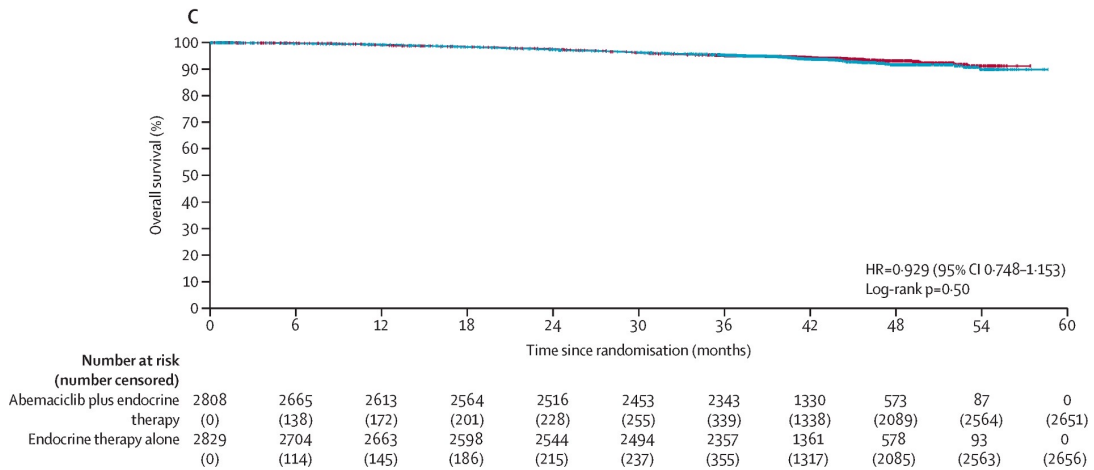
MonarchE -- abemaciclib



Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). *J Clin Oncol*. 2020;38(34):3987-3998.







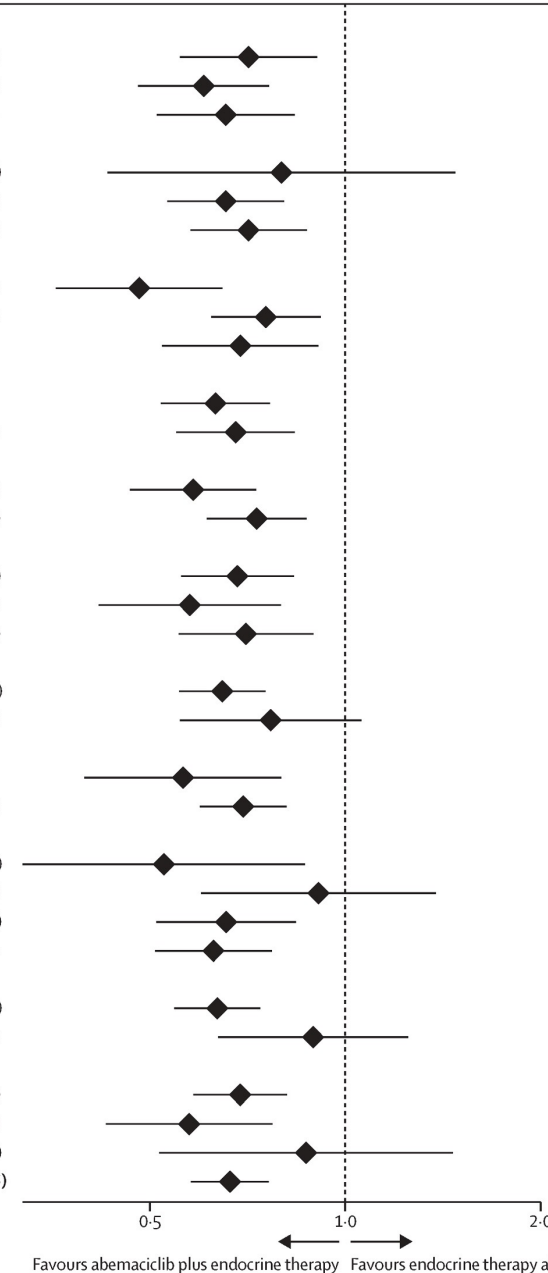
iDFS in ITT
HR 0.66
p=<0.0001

Distant relapse-free survival in ITT
HR 0.66
p=<0.0001

OS
HR 0.93

A

	Abemaciclib plus endocrine therapy		Endocrine therapy alone		Hazard ratio (95% CI)	$p_{interaction}$
	Events/N	3-year invasive disease-free survival	Events/N	3-year invasive disease-free survival		
Number of positive lymph nodes						0·66
1–3	111/1118	91·0 (89·0–92·5)	158/1142	87·3 (85·2–89·2)	0·709 (0·556–0·904)	
4–9	113/1107	90·8 (88·8–92·4)	188/1126	85·4 (83·2–87·4)	0·605 (0·479–0·763)	
10 or more	110/575	83·0 (79·6–85·9)	153/554	76·2 (72·2–79·6)	0·654 (0·512–0·835)	
Histological grade						0·75
Grade 1	18/209	92·9 (88·3–95·7)	23/216	91·6 (86·8–94·7)	0·797 (0·430–1·478)	
Grade 2	148/1377	90·2 (88·4–91·7)	226/1395	85·9 (83·9–87·7)	0·654 (0·532–0·805)	
Grade 3	157/1086	87·0 (84·8–89·0)	213/1064	82·0 (79·5–84·3)	0·709 (0·577–0·872)	
Primary tumour size, cm						0·044
<2	66/781	93·1 (91·0–94·7)	131/767	85·0 (82·2–87·5)	0·481 (0·358–0·646)	
2–5	177/1371	88·2 (86·3–89·8)	242/1419	85·5 (83·5–87·3)	0·754 (0·621–0·916)	
≥5	86/607	86·8 (83·7–89·3)	121/610	81·2 (77·7–84·2)	0·689 (0·522–0·908)	
Previous chemotherapy						0·61
Neoadjuvant	170/1039	84·8 (82·3–86·9)	261/1048	77·4 (74·7–79·9)	0·631 (0·520–0·765)	
Adjuvant	147/1642	92·1 (90·6–93·3)	215/1647	88·7 (87·1–90·2)	0·678 (0·549–0·836)	
Menopausal status						0·12
Premenopausal	125/1221	91·1 (89·3–92·6)	205/1232	85·0 (82·8–87·0)	0·583 (0·466–0·728)	
Postmenopausal	211/1587	87·7 (85·9–89·3)	294/1597	84·0 (82·1–85·8)	0·730 (0·612–0·871)	
Region						0·60
North America or Europe	162/1470	90·2 (88·4–91·6)	238/1479	85·8 (83·8–87·6)	0·682 (0·559–0·833)	
Asia	59/574	90·9 (88·2–93·0)	98/582	85·2 (81·9–87·9)	0·576 (0·417–0·795)	
Other	115/764	86·1 (83·3–88·4)	163/768	81·4 (78·4–84·0)	0·703 (0·554–0·893)	
Age, years						0·35
<65	270/2371	89·6 (88·3–90·8)	414/2416	84·6 (83·0–86·0)	0·646 (0·554–0·753)	
≥65	66/437	86·8 (83·0–89·8)	85/413	83·5 (79·5–86·9)	0·767 (0·556–1·059)	
Progesterone receptor status						0·26
Negative	50/298	83·2 (78·3–87·1)	86/295	73·0 (67·4–77·8)	0·562 (0·396–0·796)	
Positive	280/2426	89·8 (88·5–91·0)	400/2456	85·6 (84·1–87·0)	0·696 (0·597–0·811)	
Tumour stage						0·35
Stage IIA	23/324	93·4 (90·0–95·7)	46/353	88·4 (84·4–91·4)	0·525 (0·318–0·866)	
Stage IIB	42/392	89·8 (86·2–92·5)	47/387	88·2 (84·4–91·1)	0·909 (0·599–1·378)	
Stage IIIA	104/1029	90·4 (88·3–92·1)	157/1026	86·3 (84·0–88·3)	0·655 (0·511–0·839)	
Stage IIIC	148/950	86·8 (84·4–88·8)	227/963	79·3 (76·5–81·8)	0·626 (0·509–0·770)	
Baseline ECOG PS						0·088
0	277/2405	89·4 (88·1–90·6)	418/2369	84·4 (82·8–85·9)	0·635 (0·545–0·739)	
1	59/401	88·0 (84·2–90·9)	80/455	84·7 (81·0–87·8)	0·892 (0·637–1·250)	
Race						0·34
White	236/1947	89·0 (87·4–90·3)	334/1978	84·7 (83·0–86·2)	0·688 (0·583–0·812)	
Asian	71/675	91·1 (88·6–93·1)	116/669	84·6 (81·5–87·2)	0·574 (0·427–0·771)	
All others	26/146	81·6 (73·8–87·3)	31/140	80·6 (72·8–86·4)	0·869 (0·516–1·463)	
Overall	**336/2808**	**89·2 (87·9–90·3)**	**499/2829**	**84·4 (83·0–85·8)**	**0·664 (0·578–0·762)**	



Adjuvant Ribociclib -- NATALEE

Key Inclusion Criteria

- Pre- or post-menopausal HR+/Her-2 neg
- Anatomic Stage IIA (N0 + high risk features or 1-3 LN+)
- High risk features defined as G2 with Ki-67 >20%/high genomic risk or G3
- Stage IIB or III

Key Exclusion Criteria:

- Prior CDK 4/6 inhibitor
- Uncontrolled heart disease or cardiac repolarization abnormality

Primary End-Point:

- Invasive disease-free survival

Secondary End-Points:

- Distant disease-free survival
- Overall survival

Randomized 1:1 ribociclib (400 mg/day, 21 days on, 7 days off) + ET v ET alone for 3 years

Slamon, et al, ASCO 2023 abstract session

NATALEE Patient Characteristics

	Ribo + ET	ET
Age, median	52	52
Menopausal Status		
Men/Pre	1126 (44%)	1132 (44%)
Post	1423 (56%)	1420 (56%)
Anatomic Stage		
IIA	479 (19%)	521 (20%)
IIB	532 (21%)	513 (20%)
III	1528 (60%)	1512 (59%)
Prior ET		
Yes	72%	71%
Prior Chemotherapy		
Yes	88%	88%

Slamon, et al, ASCO 2023 abstract session

NATALEE Results

	Ribo + ET	ET
3-year iDFS %	90.4	87.1

Median follow-up: 27.7 months
HR: 0.75
p=0.0014

Absolute iDFS benefit is 3.3%

	Ribo + ET	ET
3-year Distant DFS %	90.8	88.6

HR: 0.74
p=0.0017

Absolute DDFS benefit is 2.2%

Survival/subgroup analysis data still immature

Slamon, et al, ASCO 2023 abstract session

Adjuvant Palbociclib -- PALLAS

Key Inclusion Criteria
- Pre- or post-menopausal HR+/Her-2 neg
- Stage II-III

- Stage IIA capped at N=1000

Key Exclusion Criteria:
- Prior CDK 4/6 inhibitor

Primary End-Point:
- Invasive disease-free survival

Secondary End-Points:
- Distant disease-free survival
- Locoregional recurrence-free survival
- Overall survival

Randomized 1:1 palbociclib (125 mg/day, 21 days on, 7 days off) + ET v ET alone for 2 years

DeMichele, et al, ASCO 2023, Rapid Abstract Updates

PALLAS Patient Characteristics – Stage IIA group

	Palbo + ET	ET
Age, median	55	53
Menopausal Status		
Pre	194 (45%	216 (46)
Post	306 (54%)	288 (53)
Prior Chemotherapy		
Yes	56%	55%

DeMichele, et al, ASCO 2023, Rapid Abstract Updates

PALLAS Results

Median follow-up: 43 months

Stage IIA	Palbo + ET	ET
4-year iDFS %	92.9	92.1

HR: 0.75
p=0.23

Stage IIB/III	Palbo + ET	ET
4-year iDFS %	85.3	83.6

HR: 0.91
p=0.24

No benefit to adding adjuvant Palbociclib for 2 years was seen, regardless of stage

DeMichele, et al, ASCO 2023, Rapid Abstract Updates

Comparison between Adjuvant CDK 4/6i Trials

	MonarchE	NATALEE	PALLAS
Drug	Abemaciclib	Ribociclib	Palbociclib
Duration	2 years	3 years	2 years
Eligibility			
Lower Risk	1-3 +LNs with: ->5 cm -G3 -Ki-67 >=20%	Stage IIA: -N1 -N0 with: • G2 + high Ki-67, high risk genomics, • G3	Stage IIA
Higher Risk	>=4 LN+	Stage IIB/IIIA	Stage IIB/IIIA

Comparison between Adjuvant CDK 4/6 Trials – Results

	MonarchE	NATALEE	PALLAS
iDFS – Intervention	85.8%	90.4%	IIA: 92.9% IIB/IIIa: 85.3%
iDFS – Control	79.4%	87.1%	IIA: 92.1% IIB/IIIA: 83.6%
iDFS HR	0.67%	0.75%	0.96

Summary

- Adjuvant CDK 4/6 inhibitors can provide an iDFS benefit for certain patients
- Currently, only abemaciclib is approved by the FDA for high-risk patients
- Overall survival data remains immature

ESR1

EMERALD

- Phase III trial of elacestrant v. standard of care therapy
- HR+/Her-2 advanced/metastatic, post-menopausal women or men
- Standard of care therapy included anastrozole, letrozole, exemestane, or fulvestrant monotherapy
- Progression after first- or second-line endocrine therapy (must include CDK4/6 + ET)
- Allowed one chemotherapy regimen in advanced/metastatic setting
- With or without ESR1 mutation

Bidard, et al, *Journal of Clinical Onology*, 40, No. 28, 2022

EMERALD – Patient Characteristics

Parameter	Elacestrant		SOC					
			Total		Fulvestrant		AI	
	All (n = 239)	*ESR1* Mutation (n = 115)	All (n = 238)	*ESR1* Mutation (n = 113)	All (n = 165)	*ESR1* Mutation (n = 83)	All (n = 73)	*ESR1* Mutation (n = 30)
Median age, years (range)	63 (24-89)	64 (28-89)	64 (32-83)	63 (32-83)	63 (32-83)	62 (32-83)	67 (44-83)	68 (44-83)
Female, n (%)	233 (97.5)	115 (100)	237 (99.6)	113 (100)	164 (99.4)	83 (100)	73 (100)	30 (100)
Race or ethnicity, n (%)								
White	168 (88.4)	84 (89.4)	170 (87.6)	80 (87.0)	113 (86.9)	56 (84.8)	57 (89.1)	24 (92.3)
Asian	16 (8.4)	5 (5.3)	16 (8.2)	8 (8.7)	14 (10.8)	8 (12.1)	2 (3.1)	0
Black or African American	5 (2.6)	4 (4.3)	7 (3.6)	4 (4.3)	3 (2.3)	2 (3.0)	4 (6.3)	2 (7.7)
Other race	1 (0.5)	1 (1.1)	1 (0.5)	0	0	0	1 (1.6)	0
Hispanic	19 (7.9)	10 (8.7)	18 (7.6)	10 (8.8)	10 (6.1)	7 (8.4)	8 (11.0)	3 (10.0)
ECOG performance status 0, n (%)	143 (59.8)	67 (58.3)	135 (56.7)	62 (54.9)	91 (55.2)	46 (55.4)	44 (60.3)	16 (53.3)
Visceral metastasis[a], n (%)	163 (68.2)	81 (70.4)	169 (71)	84 (74.3)	117 (70.9)	60 (72.3)	52 (71.2)	24 (80.0)
Prior adjuvant therapy, n (%)	158 (66.1)	62 (53.9)	141 (59.2)	65 (57.5)	90 (54.5)	43 (51.8)	51 (69.9)	22 (73.3)
Prior CDK4/6 inhibitor, n (%)	239 (100)	115 (100)	238 (100)	113 (100)	165 (100)	83 (100)	73 (100)	30 (100)
No. of prior lines of endocrine therapy in the advanced or metastatic setting, n (%)								
1	129 (54.0)	73 (63.5)	141 (59.2)	69 (61.1)	120 (72.7)	64 (77.1)	21 (28.8)	5 (16.7)
2	110 (46.0)	42 (36.5)	97 (40.8)	44 (38.9)	45 (27.3)	19 (22.9)	52 (71.2)	25 (83.3)

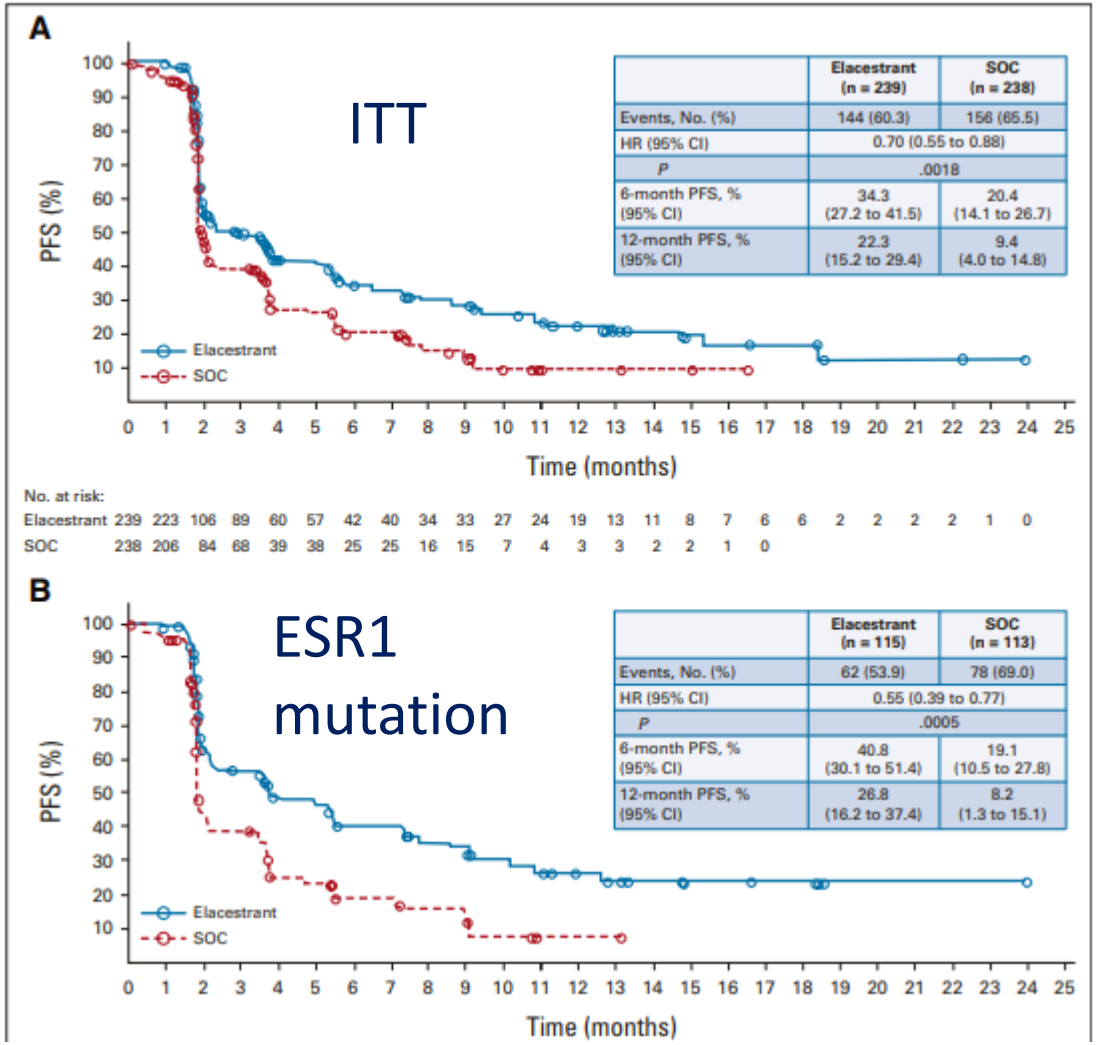
Bidard, et al, *Journal of Clinical Onology*, 40, No. 28, 2022

EMERALD – Patient Characteristics

No. of prior lines of endocrine therapy in the advanced or metastatic setting, n (%)								
1	129 (54.0)	73 (63.5)	141 (59.2)	69 (61.1)	120 (72.7)	64 (77.1)	21 (28.8)	5 (16.7)
2	110 (46.0)	42 (36.5)	97 (40.8)	44 (38.9)	45 (27.3)	19 (22.9)	52 (71.2)	25 (83.3)
No. of prior lines of chemotherapy in the advanced or metastatic setting, n (%)								
0	191 (79.9)	89 (77.4)	180 (75.6)	81 (71.7)	132 (80.0)	64 (77.1)	48 (65.8)	17 (56.7)
1	48 (20.1)	26 (22.6)	58 (24.4)	32 (28.3)	33 (20.0)	19 (22.9)	25 (34.2)	13 (43.3)
Prior therapies for advanced or metastatic disease, n (%)								
Any prior endocrine therapy[b]	232 (97.1)	112 (97.4)	233 (97.9)	109 (96.5)	161 (97.6)	79 (95.2)	72 (98.6)	30 (100.0)
Fulvestrant	70 (29.3)	27 (23.5)	75 (31.5)	28 (24.8)	6 (3.6)	1 (1.2)	69 (94.5)	27 (90.0)
AI	193 (80.8)	101 (87.8)	193 (81.1)	96 (85.0)	159 (96.4)	78 (94.0)	34 (46.6)	18 (60.0)
Tamoxifen	19 (7.9)	9 (7.8)	15 (6.3)	9 (8.0)	10 (6.1)	6 (7.2)	5 (6.8)	3 (10.0)
mTOR inhibitor	10 (4.2)	6 (5.2)	6 (2.5)	3 (2.7)	5 (3.0)	2 (2.4)	1 (1.4)	1 (3.3)
PI3K inhibitor	3 (1.3)	1 (0.9)	1 (0.4)	0	1 (0.6)	0	0	0

Bidard, et al, *Journal of Clinical Onology*, 40, No. 28, 2022

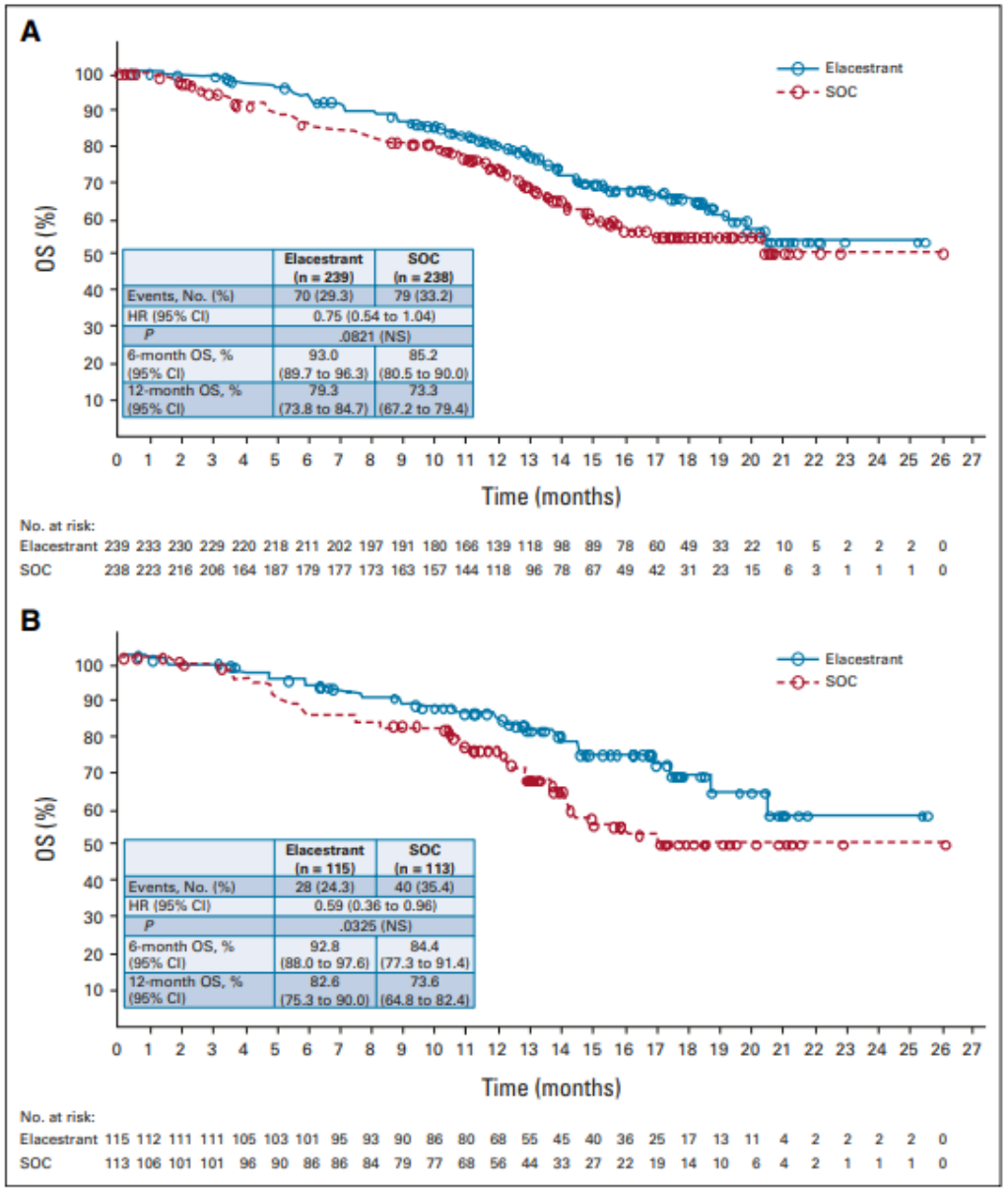
PFS



	Elacestrant (n = 239)	SOC (n = 238)
Events, No. (%)	144 (60.3)	156 (65.5)
HR (95% CI)	0.70 (0.55 to 0.88)	
P	.0018	
6-month PFS, % (95% CI)	34.3 (27.2 to 41.5)	20.4 (14.1 to 26.7)
12-month PFS, % (95% CI)	22.3 (15.2 to 29.4)	9.4 (4.0 to 14.8)

	Elacestrant (n = 115)	SOC (n = 113)
Events, No. (%)	62 (53.9)	78 (69.0)
HR (95% CI)	0.55 (0.39 to 0.77)	
P	.0005	
6-month PFS, % (95% CI)	40.8 (30.1 to 51.4)	19.1 (10.5 to 27.8)
12-month PFS, % (95% CI)	26.8 (16.2 to 37.4)	8.2 (1.3 to 15.1)

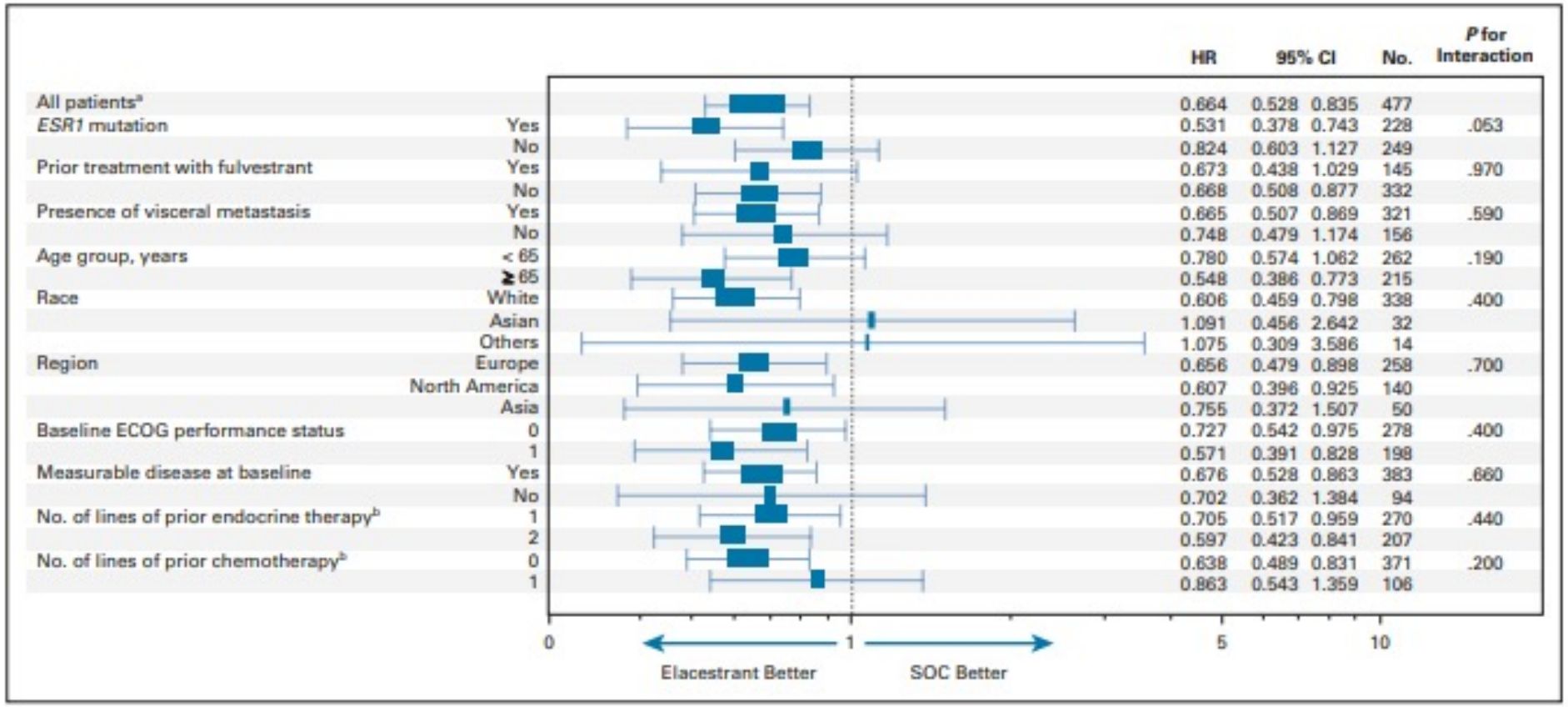
OS



	Elacestrant (n = 239)	SOC (n = 238)
Events, No. (%)	70 (29.3)	79 (33.2)
HR (95% CI)	0.75 (0.54 to 1.04)	
P	.0821 (NS)	
6-month OS, % (95% CI)	93.0 (89.7 to 96.3)	85.2 (80.5 to 90.0)
12-month OS, % (95% CI)	79.3 (73.8 to 84.7)	73.3 (67.2 to 79.4)

	Elacestrant (n = 115)	SOC (n = 113)
Events, No. (%)	28 (24.3)	40 (35.4)
HR (95% CI)	0.59 (0.36 to 0.96)	
P	.0325 (NS)	
6-month OS, % (95% CI)	92.8 (88.0 to 97.6)	84.4 (77.3 to 91.4)
12-month OS, % (95% CI)	82.6 (75.3 to 90.0)	73.6 (64.8 to 82.4)

Bidard,et al, JCO 40:3246-3256, 2022



Bidard, et al, *Journal of Clinical Onology*, 40, No. 28, 2022

AEs[c] Occurring in ≥ 10% of Patients in Any Arm	Elacestrant		Total		Fulvestrant		AI	
	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4
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
Diarrhea	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)

Bidard, et al, *Journal of Clinical Onology*, 40, No. 28, 2022

Duration on CDK4/6i in the metastatic setting						
	At least 6 months (92.3%)		**At least 12 months (71.6%)**		**At least 18 months (50.0%)**	
	Elacestrant (n=103)	SOC Hormonal Therapy (n=102)	Elacestrant (n=78)	SOC Hormonal Therapy (n=81)	Elacestrant (n=55)	SOC Hormonal Therapy (n=56)
Median PFS, months (95% CI)	**4.14** (2.20-7.79)	**1.87** (1.87-3.29)	**8.61** (4.14-10.84)	**1.91** (1.87-3.68)	**8.61** (5.45-16.89)	**2.10** (1.87-3.75)
PFS rate at 6 months, % (95% CI)	42.43 (31.15-53.71)	19.15 (9.95-28.35)	55.81 (42.69-68.94)	22.66 (11.63-33.69)	58.57 (43.02-74.12)	27.06 (13.05-41.07)
PFS rate at 12 months, % (95% CI)	26.02 (15.12-36.92)	6.45 (0.00-13.65)	35.81 (21.84-49.78)	8.39 (0.00-17.66)	35.79 (19.54-52.05)	7.73 (0.00-20.20)
PFS rate at 18 months, % (95% CI)	20.70 (9.77-31.63)	0.00	28.49 (14.08-42.89)	0.00	30.68 (13.94-47.42)	0.00
Hazard ratio (95% CI)	**0.517** (0.361-0.738)		**0.410** (0.262-0.634)		**0.466** (0.270-0.791)	

CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; PFS, progression-free survival; SOC, standard of care (investigator's choice).
Presented at the 2022 San Antonio Breast Cancer Symposium, December 6-10, 2022, San Antonio, Texas.[3]

EMERALD Phase 3 Trial of Elacestrant Versus standard of Care Endocrine Therapy In Patients With ER+/Her2- Metastatic Breast Cancer: Updated Results by Duration of Prior CDK4/6i in Metastatic Setting, Clinical Advances in Hematology & Oncology, Volume 21, Issue 2, Supplement 3, Feb 2023

Summary

- Elacestrant can be used in advanced HR+ disease as second- or third-line therapy after ET + CDK 4/6 inhibitor for patients with an ESR1 mutation
- PFS was modest, OS did not accrue enough events
- Benefit was seen across subgroups regardless of duration of prior exposure to CDK 4/6 inhibitor

Take Home Points

- Targeted therapies are improving outcomes for breast cancer patients
- Her-2 1+ and 2+ by IHC is now a target for trastuzumab deruxtecan in the advanced setting
- Adjuvant abemaciclib for high-risk patients is currently the only FDA-approved CDK 4/6 inhibitor, but more likely to come
- ESR1 mutations can extend endocrine therapy options in the metastatic setting for HR+ patients