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Gedatolisib Plus Fulvestrant, With & Without Palbociclib, vs Fulvestrant in Patients With HR+/HER2-/*PIK3CA* Wild-Type Advanced Breast Cancer: First Results from VIKTORIA-1

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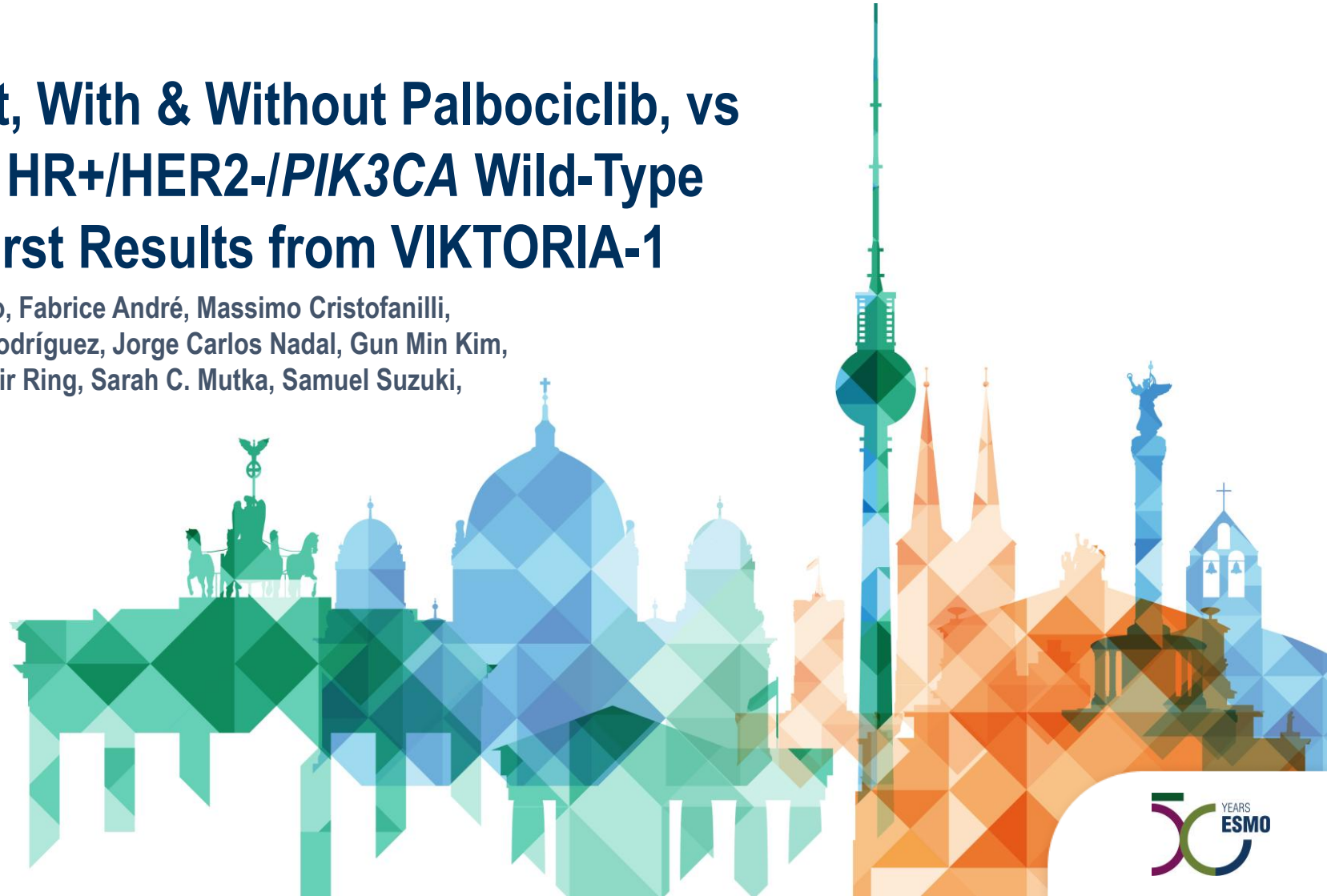

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50 YEARS ESMO

Declaration of Interests Sara A. Hurvitz, MD, FACP

Advisory/Consulting (paid to institution): BeOne, BriaCell, BridgeBio Oncology Therapeutics, Bristol Myers Squibb, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Luminate, Mersana Therapeutics Inc, Novartis, Prelude Therapeutics, ALX Oncology, Bayer HealthCare Pharmaceuticals, BeOne, Blueprint Medicines, EMBioSys

Contracted Research as PI (paid to institution): Arvinas (steering committee member), AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Celcuity (steering committee member), Daiichi Sankyo Inc (steering committee member), Dantari, F Hoffmann-La Roche Ltd (steering committee member), G1 Therapeutics Inc, Genentech, a member of the Roche Group (steering committee member), Gilead Sciences Inc, GSK, Greenwich LifeSciences Inc, Jazz Pharmaceuticals Inc (steering committee member), Eli Lilly (steering committee member), MacroGenics Inc, Menarini Group (steering committee member), Novartis (steering committee member), Orum Therapeutics, Pfizer Inc, Radius Health Inc, Sanofi (steering committee member), Seagen Inc (steering committee member), Stemline Therapeutics Inc, Zymeworks Inc

Data and Safety Monitoring Boards/Committees: Atossa Therapeutics, Roche**,** InClin, Quantum Leap Healthcare Collaborative

Royalties: Elseiver, McGraw Hill, Sage, Springer, Wiley, Wolters-Kluwer

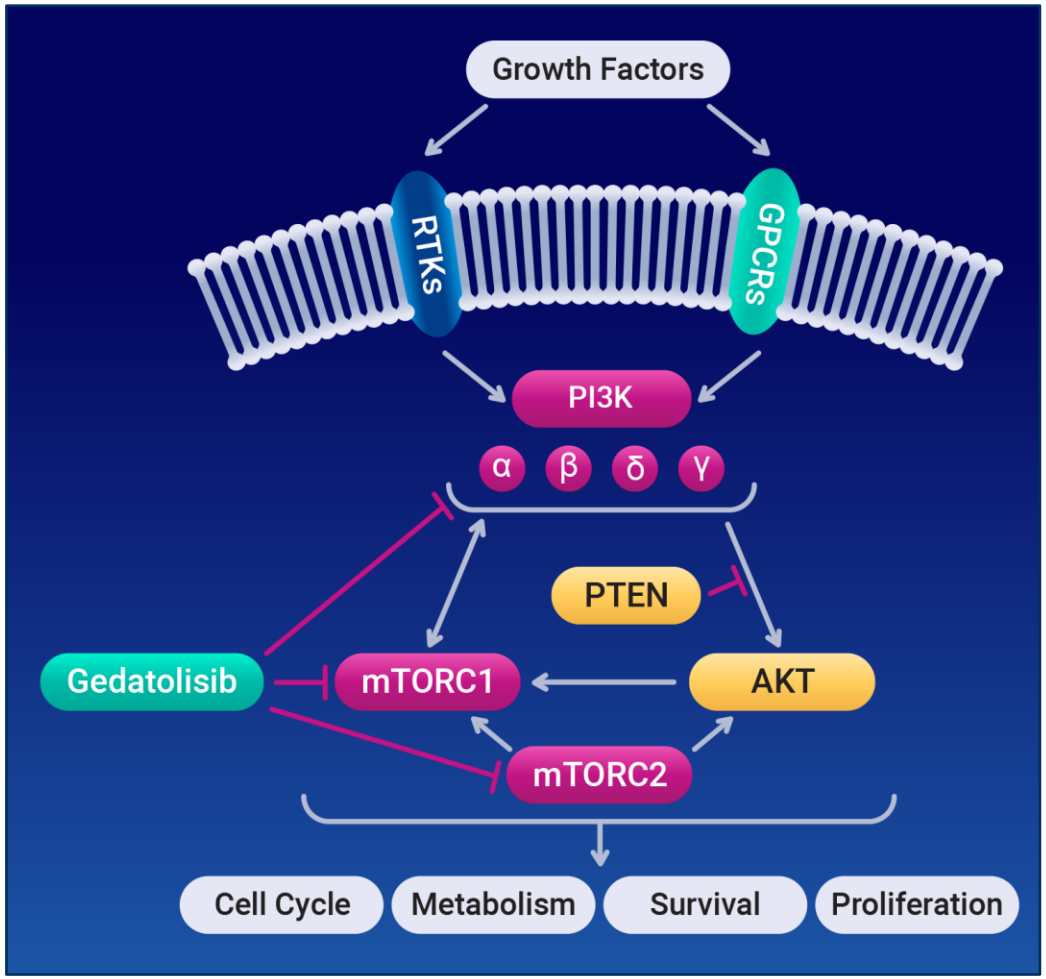
Integration Panel Member: US Department of Defense Congressionally Directed Medical Research Program, Breast Cancer Research Program

Stocks: ROMTech (spouse)

Study sponsored by Celcuity Inc.

Background

- The PI3K/AKT/mTOR (PAM) pathway drives breast cancer growth and contributes to endocrine and CDK4/6i resistance
  - Most available therapies are indicated only for patients with PI3K-pathway activation[1,2]
  - There remains a need for safe and effective therapies for those with *PIK3CA*-WT disease
- Gedatolisib, a highly potent multitarget PAM inhibitor of all class I PI3K isoforms, mTORC1, and mTORC2, has shown compelling preliminary clinical activity in combination with palbociclib & fulvestrant as 2L+ therapy in HR+/HER2- ABC
  - Median PFS of 12.9 months in all CDK4/6i-pretreated disease (n=27)[3]
  - Median PFS of 9.0 months in *PIK3CA*-WT disease (n=60)[4]
  - Median PFS of 14.6 months in *PIK3CA*-mutated disease (n=30)[4]
- We aimed to evaluate gedatolisib in patients with HR+/HER2- ABC after progression on a CDK4/6i and NSAI



Abbreviations: ABC, advanced breast cancer; AKT, protein kinase B; 2L, second-line; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; GPCRs, G protein-coupled receptors; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; mTORC, mechanistic target of rapamycin complex; NSAI, non-steroidal aromatase inhibitor; PAM, PI3K/AKT/mTOR; PFS, progression-free survival; PI3K, phosphatidylinositol 3-kinase; PTEN, phosphatase and tensin entity; RTKs, receptor tyrosine kinases; WT, wild-type

1. Andre F. *N Engl J Med.* 2019;380:1929-40; 2. Turner NC. *N Engl J Med*. 2023;388:2058-70; 3. Layman R. *Lancet Oncol.* 2024;25:474-8; 4. Data on file, Celcuity Inc.: 65 of 90 patients (72%) had received prior treatment with a CDK4/6i inhibitor

Presenter: Sara A. Hurvitz, MD, FACP

VIKTORIA-1 Study Design

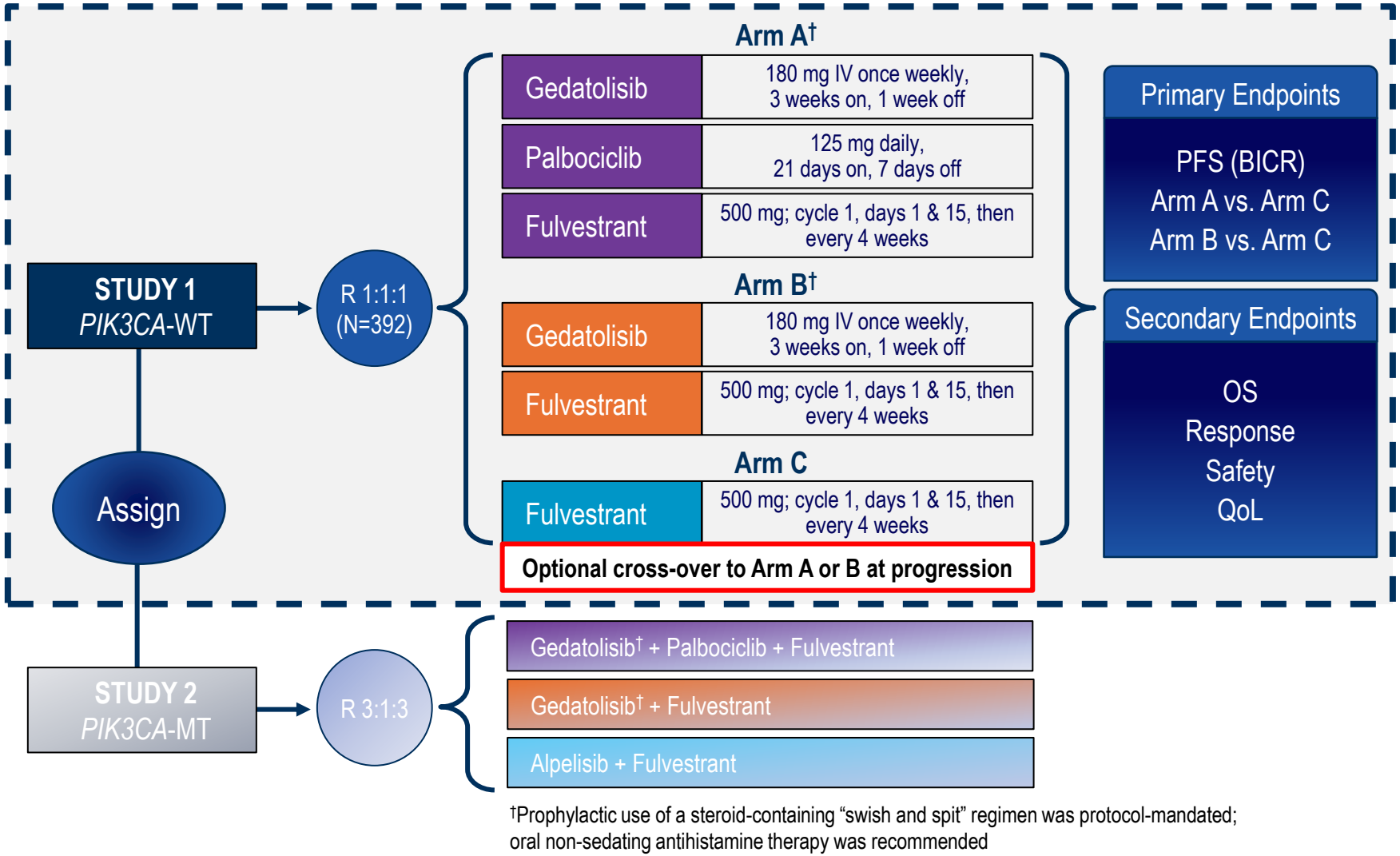
HR+/HER2-
Advanced Breast Cancer

Eligibility Criteria

- Pre- & postmenopausal women & men
- **Progression on/after CDK4/6i + NSAI**
- ≤2 lines of prior ET for ABC
- Measurable disease, RECIST v1.1
- Screening result for *PIK3CA* status
- No T2DM with HbA1c >6.4% or T1DM
- No prior mTORi, PI3Ki, or AKTi
- No prior chemotherapy for ABC

Stratification Factors

- Lung/liver metastases (yes/no)
- TTP on immediate prior therapy (≤ or >6 months)
- Region (US/Canada or ROW)



†Prophylactic use of a steroid-containing "swish and spit" regimen was protocol-mandated; oral non-sedating antihistamine therapy was recommended

Abbreviations: ABC, advanced breast cancer; AKTi, protein kinase B inhibitor; BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; ET, endocrine therapy; HbA1c, hemoglobin A1c; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; IV, intravenous; MT, mutated; mTORi, mechanistic target of rapamycin inhibitor; NSAI, non-steroidal aromatase inhibitor; OS, overall survival; PFS, progression-free survival; PI3Ki, phosphatidylinositol 3-kinase inhibitor; QoL, quality of life; R, randomization; ROW, rest of world; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TTP, time to progression; WT, wild-type

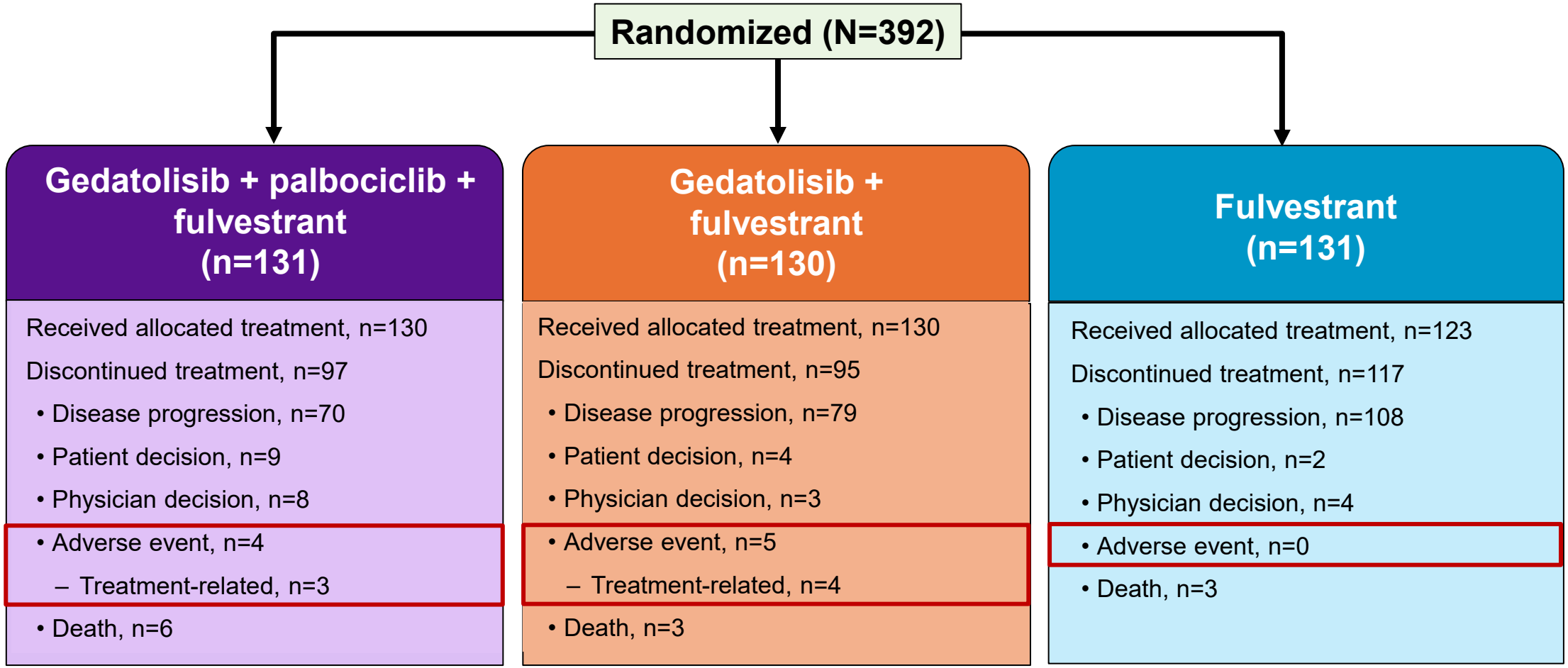
Presenter: Sara A. Hurvitz, MD, FACP

Statistical Considerations

- **Co-primary endpoints (PFS by blinded independent central review [BICR]), tested hierarchically**
  - One-sided overall alpha of 0.025
  - PFS for Arm A vs. Arm C per BICR, with 98% power to detect HR ≤0.50
  - PFS for Arm B vs. Arm C per BICR, with 75% power to detect HR ≤0.65
- **Key secondary endpoint (OS)**
  - OS is hierarchically tested if PFS for each co-primary endpoint is significant
  - Interim analysis for OS was planned to coincide with the primary PFS analysis
  - Interim boundary, one-sided alpha of 0.00017 for each comparison to maintain overall type I error rate ≤0.025 in the primary OS analysis

Abbreviations: BICR, blinded independent central review; HR, hazard ratio; PFS, progression-free survival; OS, overall survival

Patient Disposition



Data cut-off: 30 May 2025; median follow-up: 10.1 months (interquartile range, 6.6-15.1)

Baseline Demographics and Disease Characteristics

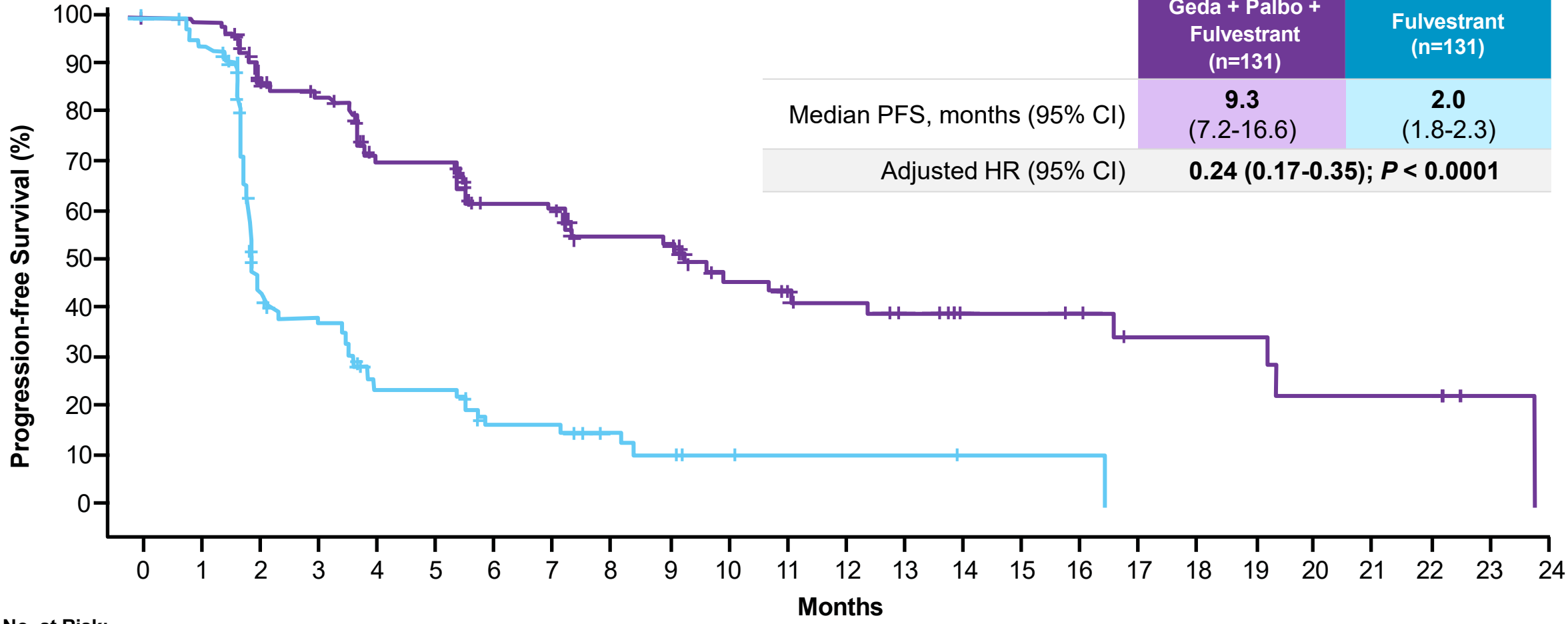
Characteristic	Gedatolisib + Palbo + Fulvestrant (n=131)	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=131)
Age, yr, median (range)	57 (33-83)	57 (32-81)	54 (28-83)
Female sex, n (%)	129 (98.5)	130 (100)	128 (97.7)
Postmenopausal, n (%)	101 (77.1)	93 (71.5)	92 (70.2)
Race/ethnic group, n (%)			
White	85 (64.9)	95 (73.1)	95 (72.5)
Asian	18 (13.7)	19 (14.6)	25 (19.1)
Black/African American	5 (3.8)	3 (2.3)	1 (0.8)
Other/Unknown	23 (17.6)	13 (10.0)	10 (7.6)
Geographic region, n (%)			
United States/Canada	21 (16.0)	21 (16.2)	22 (16.8)
Asia Pacific	18 (13.7)	18 (13.8)	26 (19.8)
Latin America	35 (26.7)	36 (27.7)	35 (26.7)
Europe	57 (43.5)	55 (42.3)	48 (36.6)
ABC at diagnosis, n (%)	63 (48.1)	51 (39.2)	45 (34.4)
ECOG PS score, n (%)			
0	70 (53.4)	85 (65.4)	77 (58.8)
1	61 (46.6)	45 (34.6)	54 (41.2)

Characteristic	Gedatolisib + Palbo + Fulvestrant (n=131)	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=131)
Liver or lung mets, n (%)	102 (77.9)	104 (80.0)	109 (83.2)
Prior (neo)adjuvant tx, n (%)			
Chemotherapy	33 (25.2)	39 (30.0)	38 (29.0)
Endocrine therapy	46 (35.1)	57 (43.8)	64 (48.9)
Prior lines, ET for ABC, n (%)			
0	3 (2.3)	2 (1.5)	4 (3.1)
1	113 (86.3)	113 (86.9)	115 (87.8)
2	15 (11.5)	15 (11.5)	12 (9.2)
TTP on immediate prior tx, n (%)			
≤6 months	21 (16.0)	19 (14.6)	20 (15.3)
>6 months	109 (83.2)	111 (85.4)	111 (84.7)
Prior adjuvant CDK4/6i, n (%)	3 (2.3)	6 (4.6)	4 (3.1)
Prior CDK4/6i for ABC, n (%)			
Palbociclib	56 (42.7)	47 (36.2)	52 (39.7)
Ribociclib	59 (45.0)	62 (47.7)	70 (53.4)
Abemaciclib	23 (17.6)	26 (20.0)	16 (12.2)
Prior CDK4/6i for ABC, mo., median duration (IQR)	21.7 (13.7-35.0)	18.1 (10.8-30.0)	20.0 (12.0-34.2)

Abbreviations: ABC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ET, endocrine therapy; IQR, interquartile range; mets, metastases; mo., months; Palbo, palbociclib; TTP, time to disease progression; tx, therapy; yr, years

1st Co-Primary Endpoint: Progression-Free Survival

Gedatolisib Triplet vs. Fulvestrant, BICR Assessment



	Geda + Palbo + Fulvestrant (n=131)	Fulvestrant (n=131)
Median PFS, months (95% CI)	**9.3** (7.2-16.6)	**2.0** (1.8-2.3)
Adjusted HR (95% CI)	**0.24 (0.17-0.35); *P* < 0.0001**	

No. at Risk:

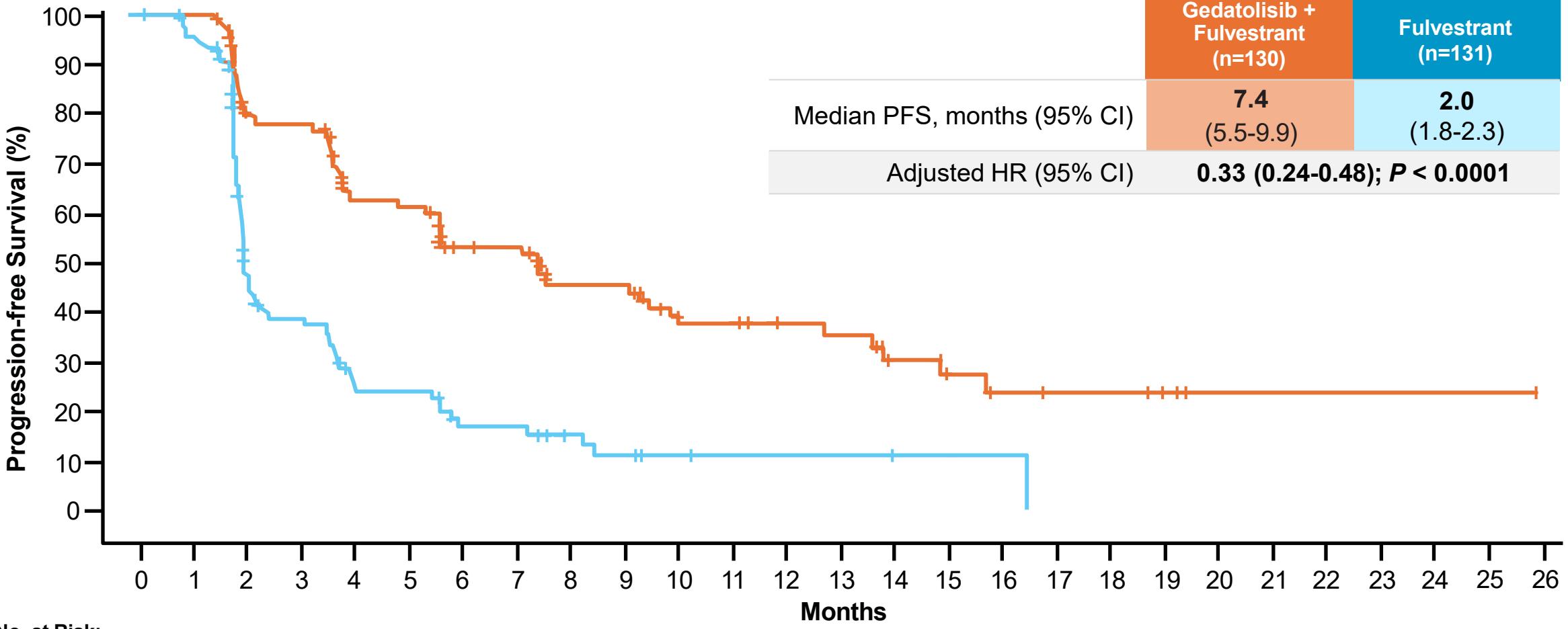
Geda + Palbo + Fulv	131	127	103	94	69	68	50	49	35	34	24	22	19	16	10	10	9	6	6	6	4	4	4	1	0
Fulv	131	114	45	35	20	20	11	11	7	5	3	2	2	2	1	1	1	0							

Presenter: Sara A. Hurvitz, MD, FACP

2nd Co-Primary Endpoint: Progression-Free Survival

Gedatolisib Doublet vs. Fulvestrant, BICR Assessment

	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=131)
Median PFS, months (95% CI)	**7.4** (5.5-9.9)	**2.0** (1.8-2.3)
Adjusted HR (95% CI)	**0.33 (0.24-0.48); *P* < 0.0001**	



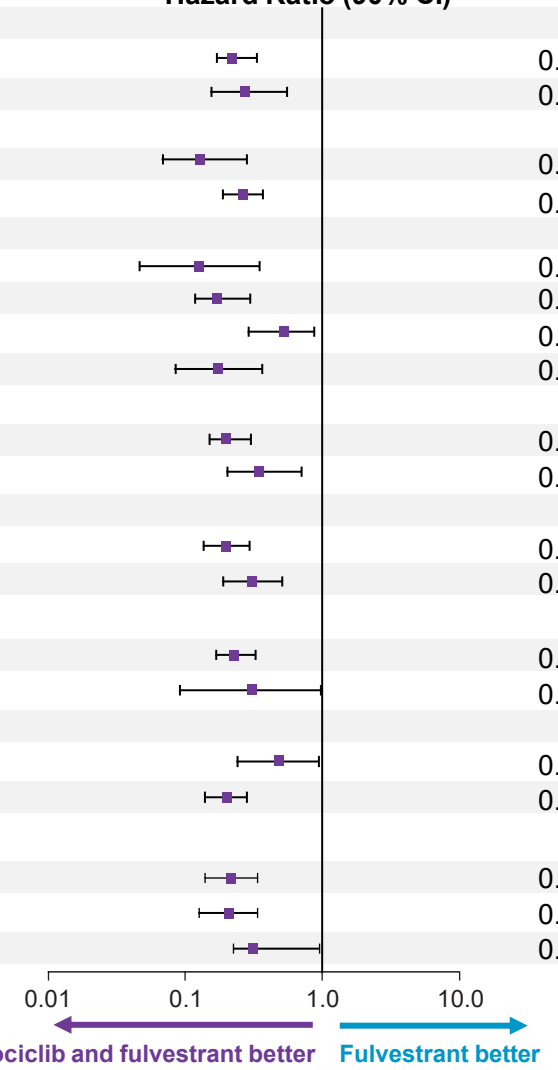
No. at Risk:

Geda + Fulv	130	126	93	89	64	63	45	44	33	33	22	22	17	16	11	8	6	5	5	3	1	1	1	1	1	1	0
Fulv	131	114	45	35	20	20	11	11	7	5	3	2	2	2	1	1	1	0									

Presenter: Sara A. Hurvitz, MD, FACP

PFS in Key Subgroups: Gedatolisib Triplet vs. Fulvestrant

Subgroup	Gedatolisib + Palbociclib + Fulvestrant n/N	Gedatolisib + Palbociclib + Fulvestrant mPFS, mo.	Fulvestrant n/N	Fulvestrant mPFS, mo.	Hazard Ratio (90% CI)
Age					
<65 years	39/93	9.3	74/108	1.9	0.23 (0.17-0.35)
≥65 years	20/38	9.7	15/23	2.1	0.28 (0.16-0.55)
Menopause status					
Pre/perimenopause	9/28	11.1	26/36	1.8	0.13 (0.07-0.29)
Postmenopause	50/101	8.9	62/92	2.0	0.27 (0.19-0.38)
Geographic area					
US/Canada	6/21	19.3	14/22	2.0	0.13 (0.05-0.36)
Europe	29/57	9.3	32/48	2.0	0.17 (0.12-0.31)
Latin America	16/35	5.6	20/35	3.7	0.53 (0.29-0.90)
Asia Pacific	8/18	16.6	23/26	1.8	0.18 (0.09-0.37)
Presence of visceral metastasis					
Yes	44/102	10.7	71/100	1.8	0.21 (0.16-0.30)
No	15/29	8.9	18/31	5.6	0.35 (0.20-0.71)
Liver metastasis					
Yes	37/74	9.2	60/72	1.8	0.21 (0.14-0.30)
No	22/57	9.9	29/59	5.4	0.31 (0.19-0.53)
Lines of prior tx for ABC					
<2	52/115	9.7	82/118	2.0	0.23 (0.17-0.33)
≥2	7/16	5.4	7/13	1.8	0.31 (0.09-0.99)
TTP on immediate prior tx					
≤6 months	13/26	7.4	13/25	2.1	0.47 (0.24-0.93)
>6 months	46/105	9.9	76/106	1.9	0.20 (0.14-0.28)
Prior CDK4/6i for ABC					
Ribociclib	29/59	8.9	48/70	1.9	0.22 (0.14-0.34)
Palbociclib	21/56	16.6	37/52	1.9	0.21 (0.13-0.35)
Abemaciclib	13/23	5.4	10/16	3.1	0.31 (0.23-0.97)



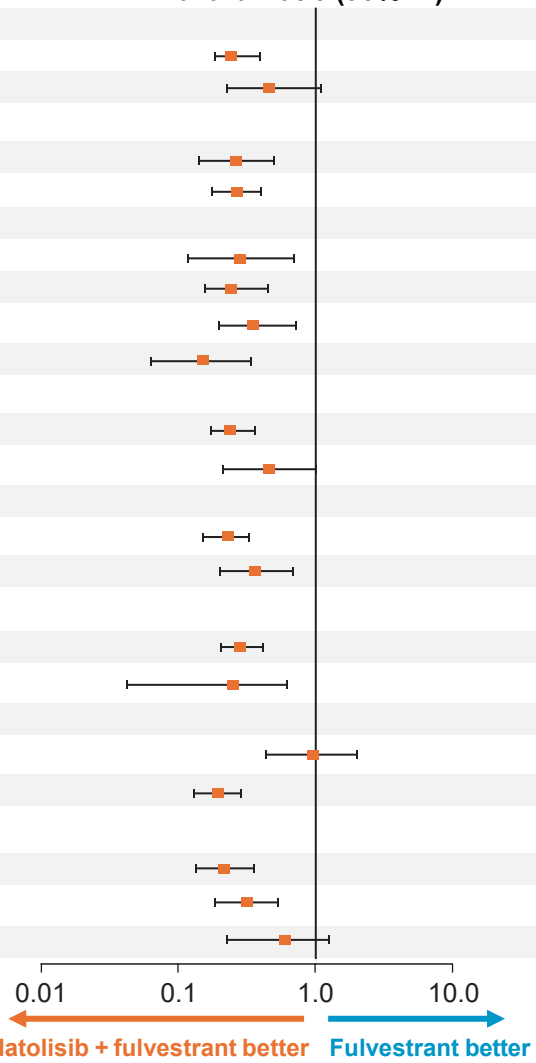
PFS assessed by blinded independent central review

Abbreviations: ABC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; mo., months; mPFS, median progression-free survival; TTP, time to disease progression; tx, therapy

Presenter: Sara A. Hurvitz, MD, FACP

PFS in Key Subgroups: Gedatolisib Doublet vs. Fulvestrant

Subgroup	Gedatolisib + Fulvestrant n/N	Gedatolisib + Fulvestrant mPFS, mo.	Fulvestrant n/N	Fulvestrant mPFS, mo.	Hazard Ratio (90% CI)
Age					
<65 years	52/96	5.6	74/108	1.9	0.31 (0.25-0.46)
≥65 years	17/34	7.7	15/23	2.1	0.53 (0.29-1.10)
Menopause status					
Pre/perimenopause	19/37	5.6	26/36	1.8	0.33 (0.19-0.55)
Postmenopause	50/93	7.6	62/92	2.0	0.33 (0.24-0.47)
Geographic area					
US/Canada	9/21	14.9	14/22	2.0	0.35 (0.17-0.76)
Europe	31/55	7.6	32/48	2.0	0.31 (0.22-0.53)
Latin America	20/36	5.6	20/35	3.7	0.42 (0.26-0.78)
Asia Pacific	9/18	7.3	23/26	1.8	0.21 (0.10-0.42)
Presence of visceral metastasis					
Yes	57/102	7.3	71/100	1.8	0.30 (0.23-0.42)
No	12/28	9.3	18/31	5.6	0.51 (0.27-1.00)
Liver metastasis					
Yes	46/82	7.3	60/72	1.8	0.29 (0.20-0.40)
No	23/48	10.0	29/59	5.4	0.43 (0.26-0.73)
Lines of prior tx for ABC					
<2	62/114	7.3	82/118	2.0	0.35 (0.27-0.48)
≥2	7/16	10.0	7/13	1.8	0.32 (0.07-0.69)
TTP on immediate prior tx					
≤6 months	14/26	5.6	13/25	2.1	0.96 (0.51-1.83)
>6 months	55/104	7.6	76/106	1.9	0.25 (0.18-0.35)
Prior CDK4/6i for ABC					
Ribociclib	31/62	5.6	48/70	1.9	0.27 (0.19-0.42)
Palbociclib	26/47	7.7	37/52	1.9	0.39 (0.24-0.59)
Abemaciclib	15/26	5.6	10/16	3.1	0.66 (0.29-1.21)



PFS assessed by blinded independent central review

Abbreviations: ABC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; mo., months; mPFS, median progression-free survival; TTP, time to disease progression; tx, therapy

Presenter: Sara A. Hurvitz, MD, FACP

PFS in Key Subgroups: Gedatolisib Triplet vs. Doublet

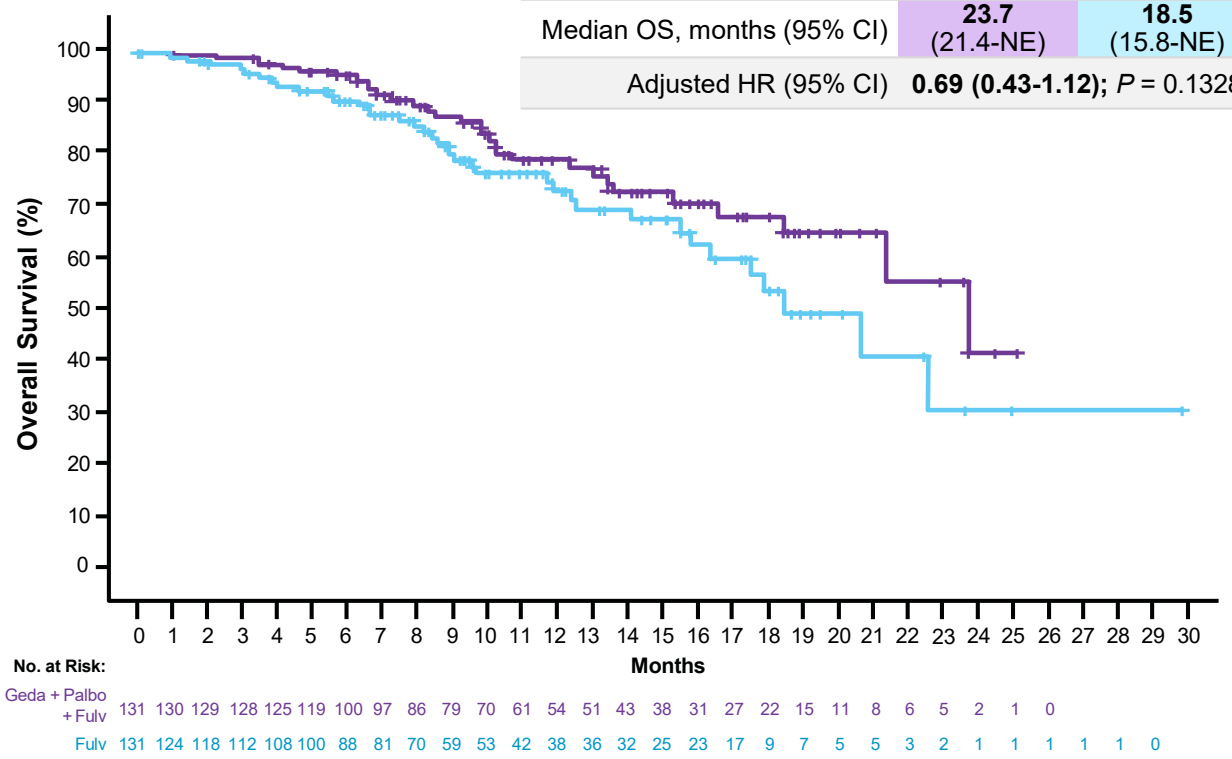
	Gedatolisib + Palbociclib + Fulvestrant		Gedatolisib + Fulvestrant	
Subgroup	**n/N**	**mPFS, mo.**	**n/N**	**mPFS, mo.**
Age				
<65 years	39/93	9.3	52/96	5.6
≥65 years	20/38	9.7	17/34	7.7
Menopause status				
Pre/perimenopause	9/28	11.1	19/37	5.6
Postmenopause	50/101	8.9	50/93	7.6
Geographic area				
US/Canada	6/21	19.3	9/21	14.9
Europe	29/57	9.3	31/55	7.6
Latin America	16/35	5.6	20/36	5.6
Asia Pacific	8/18	16.6	9/18	7.3
Presence of visceral metastasis				
Yes	44/102	10.7	57/102	7.3
No	15/29	8.9	12/28	9.3
Liver metastasis				
Yes	37/74	9.2	46/82	7.3
No	22/57	9.9	23/48	10.0
Lines of prior tx for ABC				
<2	52/115	9.7	62/114	7.3
≥2	7/16	5.4	7/16	10.0
TTP on immediate prior tx				
≤6 months	13/26	7.4	14/26	5.6
>6 months	46/105	9.9	55/104	7.6
Prior CDK4/6i for ABC				
Ribociclib	29/59	8.9	31/62	5.6
Palbociclib	21/56	16.6	26/47	7.7
Abemaciclib	13/23	5.4	15/26	5.6

PFS assessed by blinded independent central review

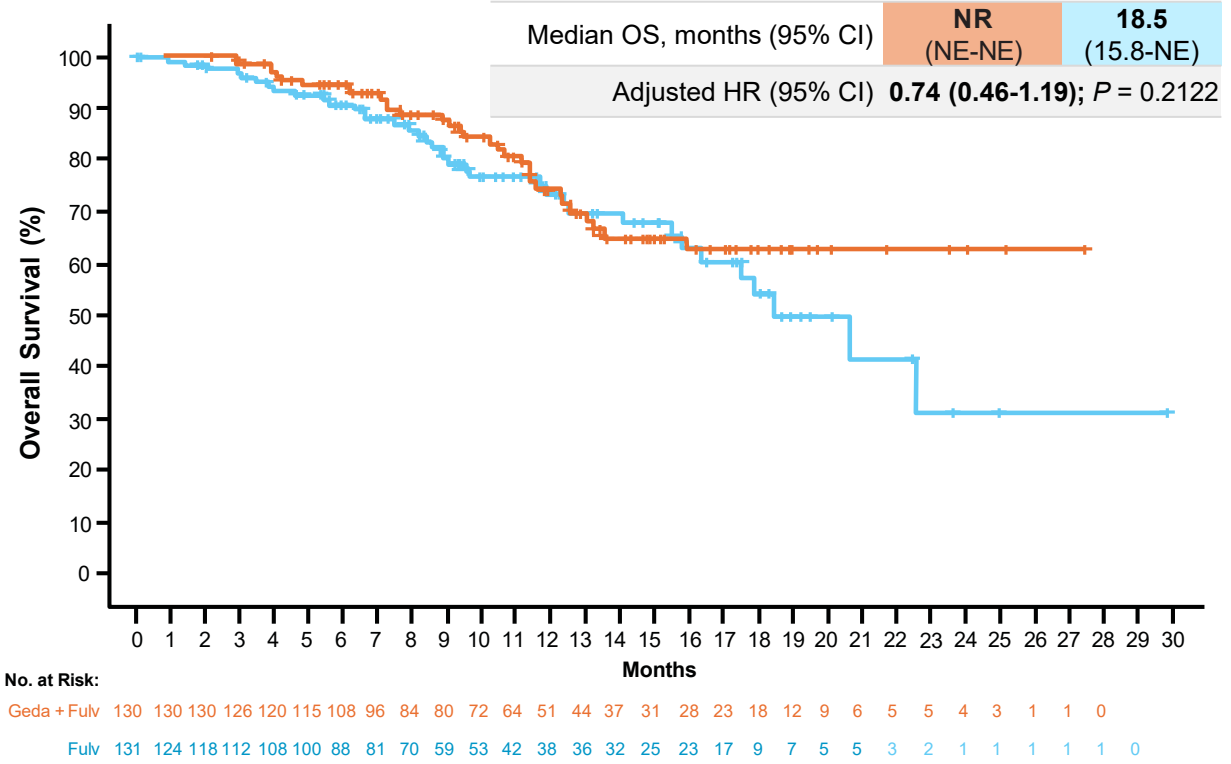
Abbreviations: ABC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; mo., months; mPFS, median progression-free survival; TTP, time to disease progression; tx, therapy

Key Secondary Endpoint: Overall Survival (Interim Analysis)

	Geda + Palbo + Fulvestrant (n=131)	Fulvestrant (n=131)
Median OS, months (95% CI)	**23.7** (21.4-NE)	**18.5** (15.8-NE)
Adjusted HR (95% CI)	**0.69 (0.43-1.12)**; *P* = 0.1328	



	Geda + Fulvestrant (n=130)	Fulvestrant (n=131)
Median OS, months (95% CI)	**NR** (NE-NE)	**18.5** (15.8-NE)
Adjusted HR (95% CI)	**0.74 (0.46-1.19)**; *P* = 0.2122	

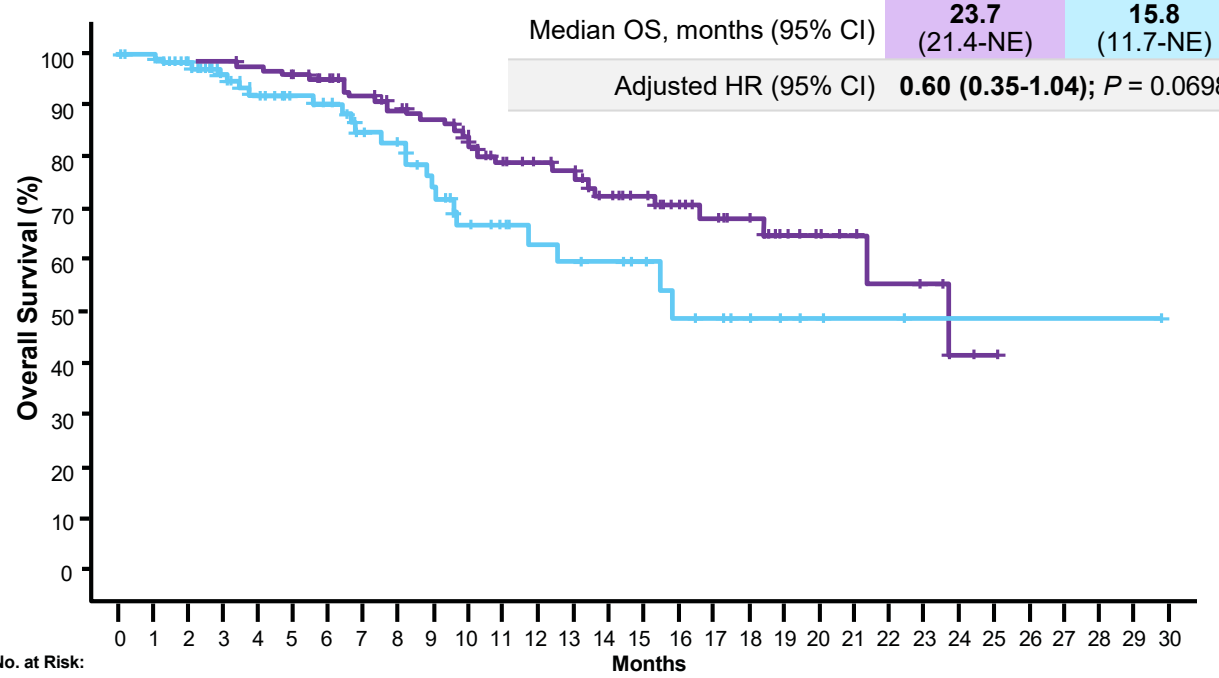


At data cutoff (30 May 2025):

- 99 patients (25.3%) across arms died: gedatolisib triplet, n=30 (22.9%); gedatolisib doublet, n=32 (24.6%); fulvestrant, n=37 (28.2%)
- Represents 48% of the protocol-specified events for OS analysis
- Of 108 patients with disease progression on fulvestrant, 63 (58.3%) crossed over: geda triplet, n=52 (48.1%); geda doublet, n=11 (10.2%)

Sensitivity Analysis: Interim OS Censored at Cross-Over

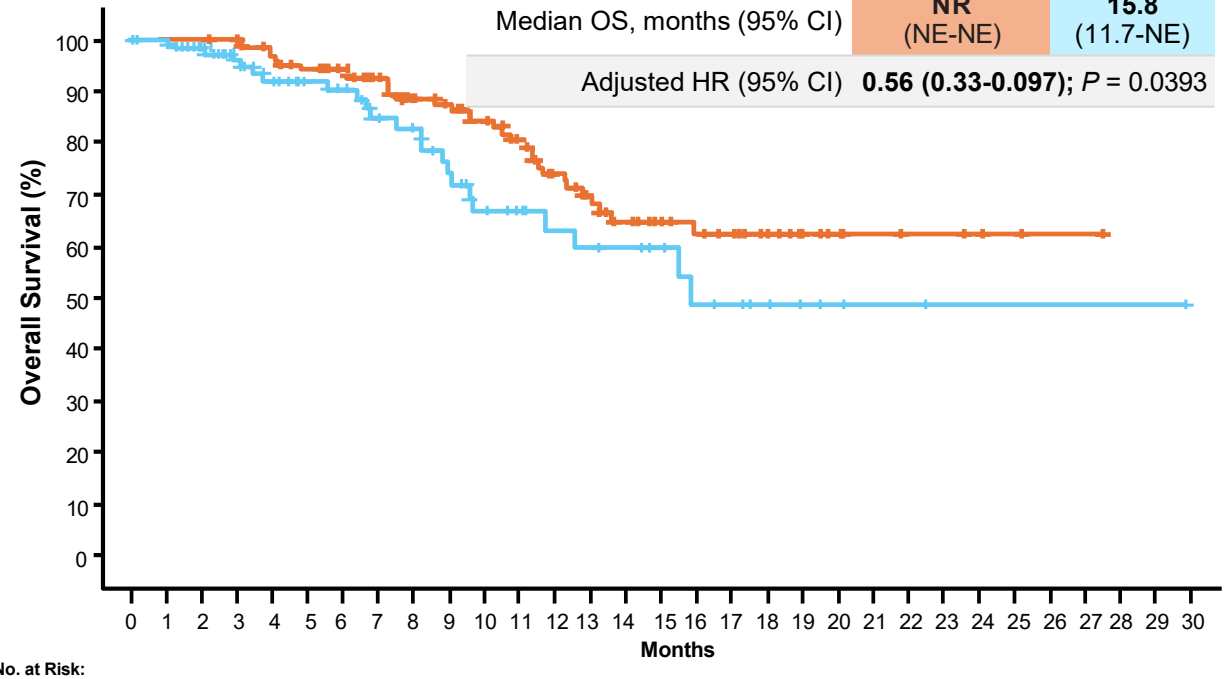
	Geda + Palbo + Fulvestrant (n=131)	Fulvestrant (n=131)
Median OS, months (95% CI)	**23.7** (21.4-NE)	**15.8** (11.7-NE)
Adjusted HR (95% CI)	**0.60 (0.35-1.04)**; *P* = 0.0698	



No. at Risk:

Geda + Palbo + Fulv	131	130	129	128	125	119	111	97	86	79	70	61	54	51	43	38	31	27	22	15	11	8	6	5	2	1	0		
Fulvestrant	131	124	103	75	64	57	52	43	40	33	26	22	18	17	16	13	9	8	6	4	3	2	2	1	1	1	1	1	1	1	0

	Geda + Fulvestrant (n=130)	Fulvestrant (n=131)
Median OS, months (95% CI)	**NR** (NE-NE)	**15.8** (11.7-NE)
Adjusted HR (95% CI)	**0.56 (0.33-0.097)**; *P* = 0.0393	



No. at Risk:

Geda + Fulv	130	130	130	126	120	115	108	96	84	80	72	64	51	44	37	31	28	23	18	12	9	6	5	5	4	3	1	1	0
Fulvestrant	131	124	103	75	64	57	52	43	40	33	26	22	18	17	16	13	9	8	6	4	3	2	2	1	1	1	1	1	1	1	0

63 patients in the fulvestrant arm who crossed over to one of the gedatolisib regimens were censored in this sensitivity analysis

Presenter: Sara A. Hurvitz, MD, FACP

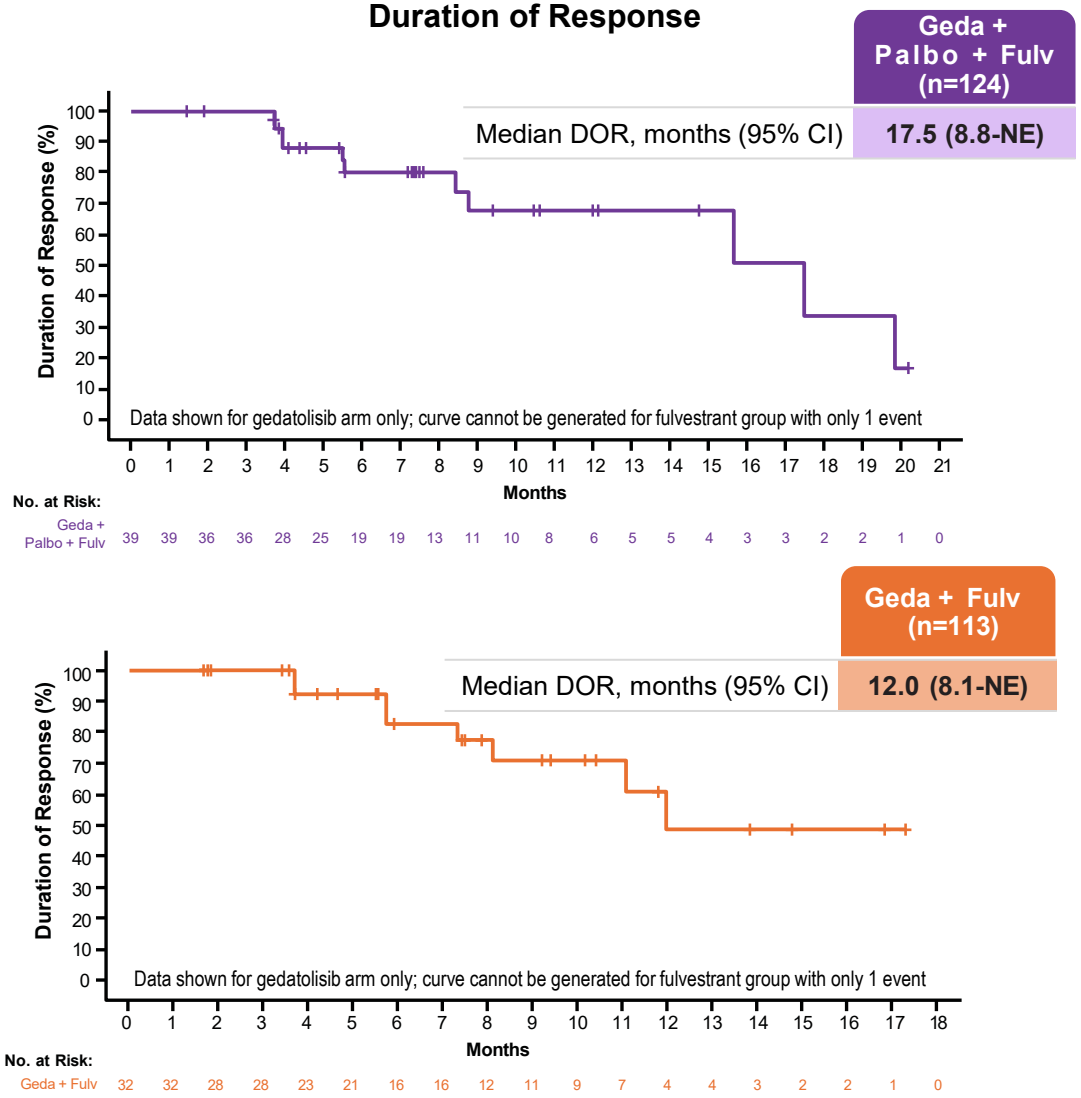
Secondary Endpoint: Tumor Response (BICR Assessment)

Patients With Evaluable Disease

Endpoint, n (%)	Geda + Palbo + Fulvestrant (n=124)	Gedatolisib + Fulvestrant (n=113)	Fulvestrant (n=105)
Best Overall Response			
Complete response	1 (0.8)	0	0
Partial response	38 (30.6)	32 (28.3)	1 (1.0)
Stable disease	67 (54.0)	55 (48.7)	40 (38.1)
Progressive disease	17 (13.7)	26 (23.0)	62 (59.0)
Not evaluable	1 (0.8)	0	2 (1.9)
Objective Response Rate*	39 (31.5)	32 (28.3)	1 (1.0)
Clinical Benefit Rate†	62 (50.0)	55 (48.7)	12 (11.4)
Disease Control Rate‡	106 (85.5)	87 (77.0)	41 (39.0)
Median DOR, months [95% CI]	17.5 [8.8-NE]	12.0 [8.1-NE]	NR [NE]

*Defined as CR+PR
†Defined as CR+PR+SD >24 weeks as assessed by BICR
‡Defined as CR+PR+SD
Abbreviations: BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; Fulv, fulvestrant; Geda, gedatolisib; NE, not estimable; no., number; NR, not reached; Palbo, palbociclib; PR, partial response; SD, stable disease.

Duration of Response



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Safety and Tolerability

Treatment-Related Adverse Events (Safety Population)*

SAE and discontinuation, n (%)	Gedatolisib + palbociclib + fulvestrant (n=130)	Gedatolisib + fulvestrant (n=130)	Fulvestrant (n=123)
Pts with ≥1 SAE	14 (10.8)	12 (9.2)	1 (0.8)
Study treatment D/C due to TRAE	3 (2.3)	4 (3.1)	0
Deaths due to TRAE†	2 (1.5)	0	0

Adverse events, n (%)	Gedatolisib + palbociclib + fulvestrant (n=130)			Gedatolisib + fulvestrant (n=130)			Fulvestrant (n=123)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Stomatitis‡	**90 (69.2)**	**25 (19.2)**	**0**	**74 (56.9)**	**16 (12.3)**	**0**	**0**	**0**	**0**
Neutropenia‡	85 (65.4)	68 (52.3)	13 (10.0)	2 (1.5)	0	1 (0.8)	1 (0.8)	1 (0.8)	0
Nausea	57 (43.8)	5 (3.8)	0	56 (43.1)	1 (0.8)	0	4 (3.3)	0	0
Rash‡	**36 (27.7)**	**6 (4.6)**	**0**	**42 (32.3)**	**7 (5.4)**	**0**	**0**	**0**	**0**
Vomiting	36 (27.7)	2 (1.5)	0	30 (23.1)	0	0	1 (0.8)	0	0
Fatigue	29 (22.3)	2 (1.5)	0	27 (20.8)	1 (0.8)	0	5 (4.1)	0	0
Diarrhea§	**22 (16.9)**	**2 (1.5)**	**0**	**16 (12.3)**	**1 (0.8)**	**0**	**0**	**0**	**0**
Hyperglycemia‡,§	**12 (9.2)**	**3 (2.3)**	**0**	**15 (11.5)**	**3 (2.3)**	**0**	**0**	**0**	**0**

Abbreviations: D/C, discontinued; Pts, patients; SAE, serious adverse event; TRAE, treatment-related adverse event (per investigator)
*Shown are adverse events of any grade that occurred in at least 20% of the patients in any trial group unless otherwise noted
†Grade 5 events include one considered related to palbociclib (pneumonia) and one due to hepatic failure in a patient with multiple liver metastasis considered related to all three drugs (and likely associated with disease)
‡For stomatitis, neutropenia, rash, and hyperglycemia, combined preferred terms shown; if a patient experienced multiple terms, it was counted once for the highest grade.
§Additional events of clinical importance

Conclusions

- **VIKTORIA-1 is the first study to demonstrate a statistically significant and clinically meaningful improvement in PFS with PAM inhibition in patients with *PIK3CA*-WT disease, all of whom received prior CDK4/6i**
  - Gedatolisib triplet, mPFS 9.3 months (HR, 0.24; 95% CI, 0.17-0.35; $P < 0.0001$)
  - Gedatolisib doublet, mPFS 7.4 months (HR, 0.33; 95% CI, 0.24-0.48; $P < 0.0001$)
- **Efficacy of gedatolisib-based therapy was comparable regardless of which prior CDK4/6i was used**
- Adverse events associated with gedatolisib in VIKTORIA-1 were mainly Grade 1 or 2 in severity
  - **Hyperglycemia was low** (9.2% for triplet, 11.5% for doublet), **as was diarrhea** (16.9% and 12.3%, respectively), which is unexpected for a drug targeting the PAM pathway
  - Study treatment discontinuation due to TRAEs was reported in 2.3% (triplet) and 3.1% (doublet) of patients
- **These results validate the PAM pathway as a molecular driver in *PIK3CA*-WT disease**

Gedatolisib plus fulvestrant, with or without palbociclib, represents a potential new standard of care for patients with HR+, HER2-negative, *PIK3CA*-WT ABC whose disease progressed on or after treatment with a CDK4/6 inhibitor

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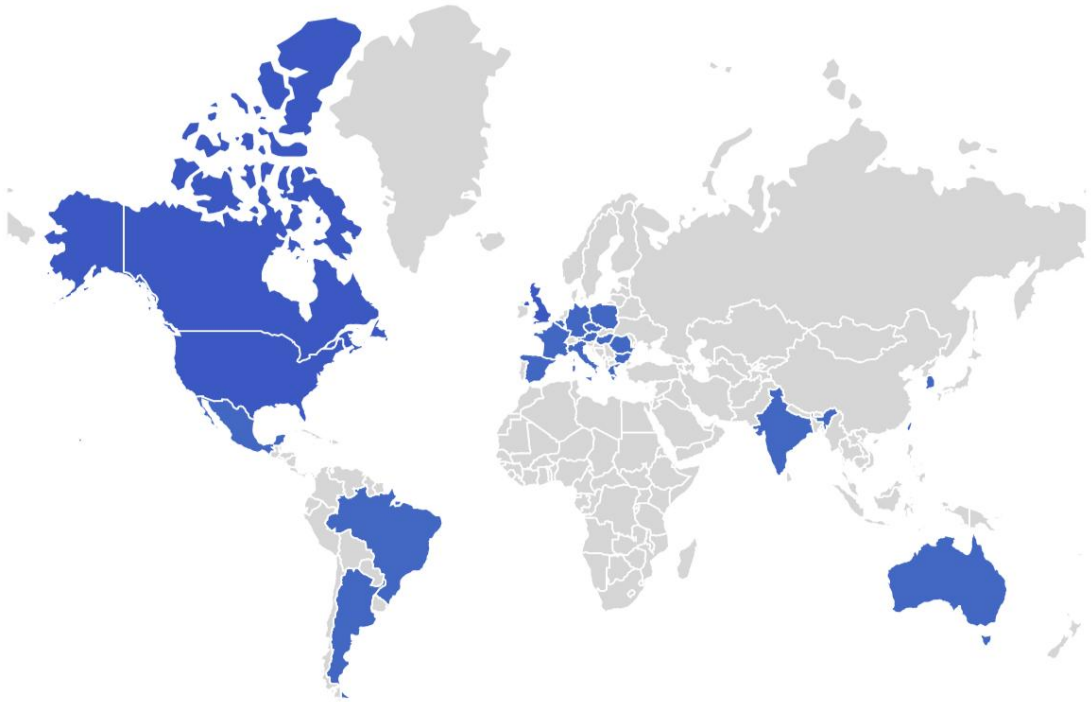

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