SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Gedatolisib, a multitarget PI3K/AKT/mTOR inhibitor, plus fulvestrant with or without palbociclib for second-line treatment of patients with HR+/HER2-/*PIK3CA*-WT advanced breast cancer: updated results from the randomized, phase 3 VIKTORIA-1 trial

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December 11, 2025

GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS

Disclosure Information

Barbara Pistilli, MD

I have the following relevant financial relationships to disclose:

- **Consulting fees**: AstraZeneca (institutional), Seagen (institutional), Gilead (institutional), Novartis (institutional), Lilly (institutional), MSD (institutional), Pierre Fabre (personal), Daiichi Sankyo (institutional/personal), Olema (institutional)
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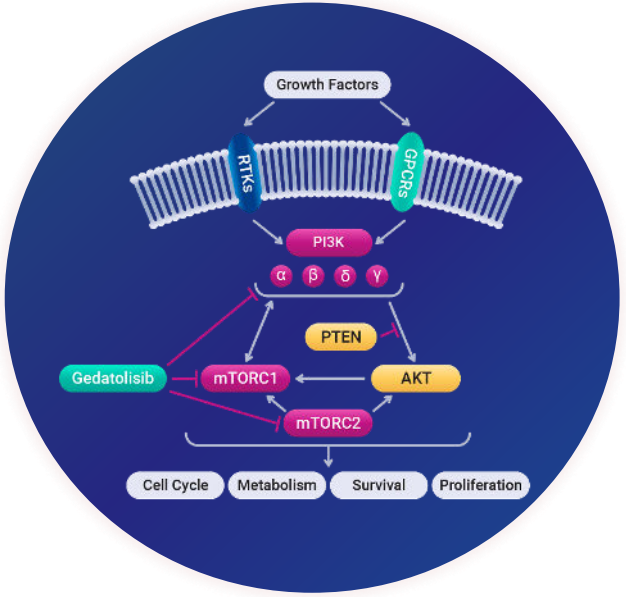
Background

- The PI3K/AKT/mTOR (PAM) pathway drives breast cancer growth and contributes to ET and CDK4/6i resistance
  - Most available therapies are indicated only for patients with PI3K-pathway activation[1,2]
  - **There remains a need for safe, effective therapies for *PIK3CA*-WT disease**
- In **VIKTORIA-1 trial,** gedatolisib, a highly potent multitarget PAM inhibitor, demonstrated statistically significant and clinically meaningful efficacy in patients with HR+, HER2-negative, *PIK3CA*-WT ABC, who received prior CDK4/6i[3]
  - **Gedatolisib + palbo + fulvestrant, mPFS 9.3 mo. (HR, 0.24; 95% CI, 0.17-0.35; *P* < 0.0001)**
  - **Gedatolisib + fulvestrant, mPFS 7.4 mo. (HR, 0.33; 95% CI, 0.24-0.48; *P* < 0.0001)**
- Treatment-related adverse events associated with gedatolisib were mainly grade 1-2[3]
  - Hyperglycemia and diarrhea were relatively uncommon
  - Grade 3 stomatitis: triplet, 19.2%; doublet,12.3%



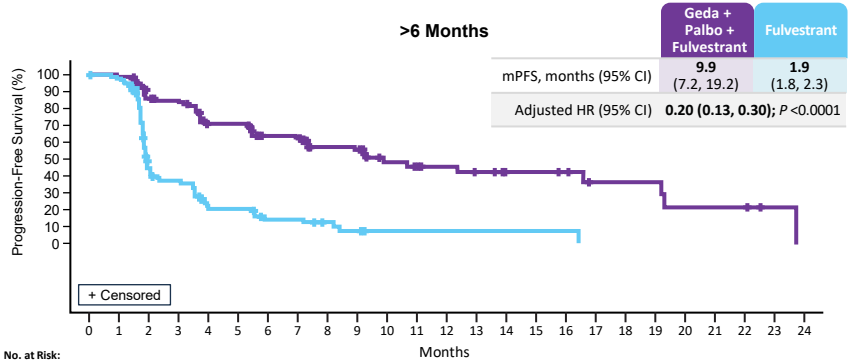
Here we examine additional subgroups, expanded safety, and initial patient-reported outcomes

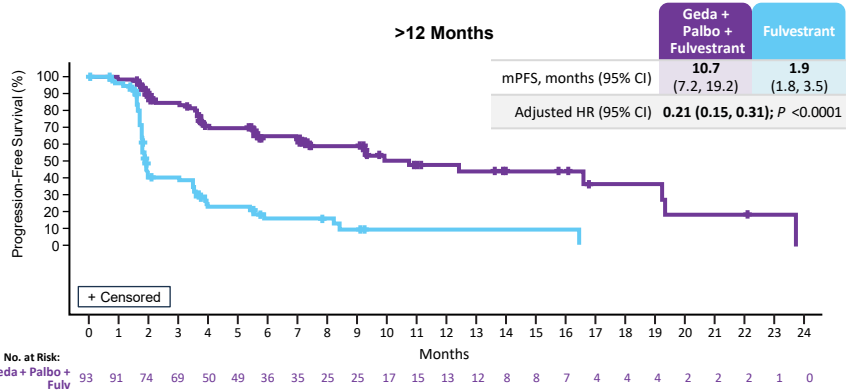
Abbreviations: ABC, advanced breast cancer; AKT, protein kinase B; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; ET, endocrine therapy; GPCRs, G protein-coupled receptors; HER2-negative, human epidermal growth factor receptor 2-negative; HR, hazard ratio; HR+, hormone receptor-positive; mo., months; mPFS, median progression-free survival; mTORC, mechanistic target of rapamycin complex; PAM, PI3K/AKT/mTOR; PI3K, phosphatidylinositol 3-kinase; PTEN, phosphatase and tensin entity; RTKs, receptor tyrosine kinases; TRAE, treatment-related adverse event; WT, wild-type

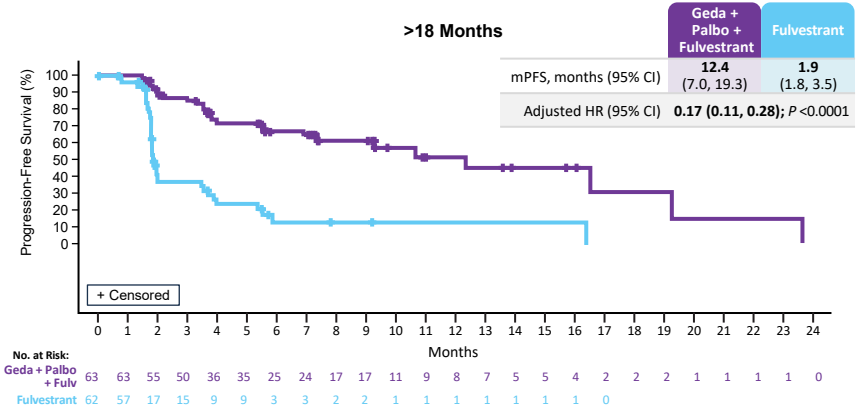
1. Andre F. *N Engl J Med.* 2019;380:1929-40; 2. Turner NC. *N Engl J Med*. 2023;388:2058-70; 3. Hurvitz SA, et al. ESMO 2025. LBA17.

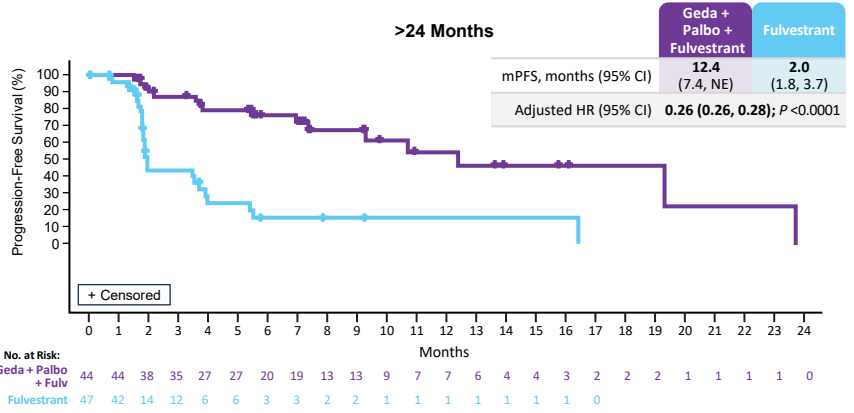
PFS by TTP on Immediate Prior Therapy:

Gedatolisib Triplet vs. Fulvestrant









PFS by TTP on Immediate Prior Therapy:

Gedatolisib Doublet vs. Fulvestrant

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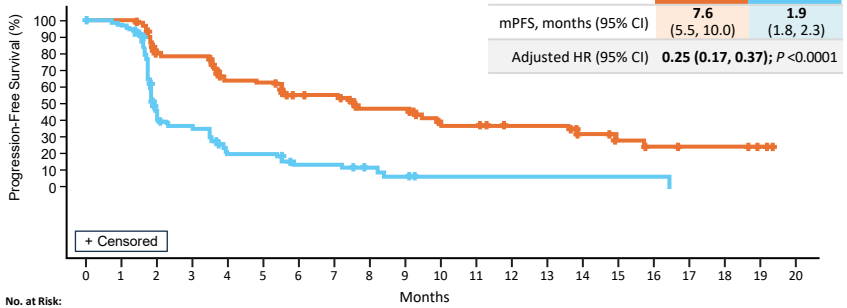
>6 Months

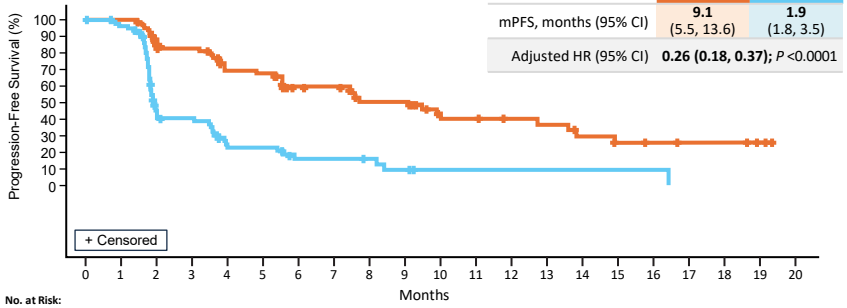
	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**7.6** (5.5, 10.0)	**1.9** (1.8, 2.3)
Adjusted HR (95% CI)	**0.25 (0.17, 0.37);** *P* <0.0001	



No. at Risk:																				
Geda + Fulv	104	102	78	74	54	53	38	37	28	28	18	18	15	15	10	7	5	4	4	2	0
Fulvestrant	106	95	35	28	14	14	8	8	5	3	1	1	1	1	1	1	1	0			

>12 Months

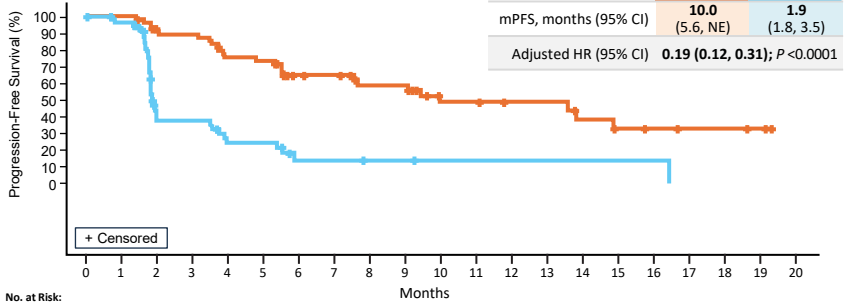
	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**9.1** (5.5, 13.6)	**1.9** (1.8, 3.5)
Adjusted HR (95% CI)	**0.26 (0.18, 0.37);** *P* <0.0001	



No. at Risk:																				
Geda + Fulv	80	77	63	59	44	43	31	30	23	23	14	14	12	11	8	6	5	4	4	2	0
Fulvestrant	85	77	27	24	12	12	6	6	5	3	1	1	1	1	1	1	1	0			

>18 Months

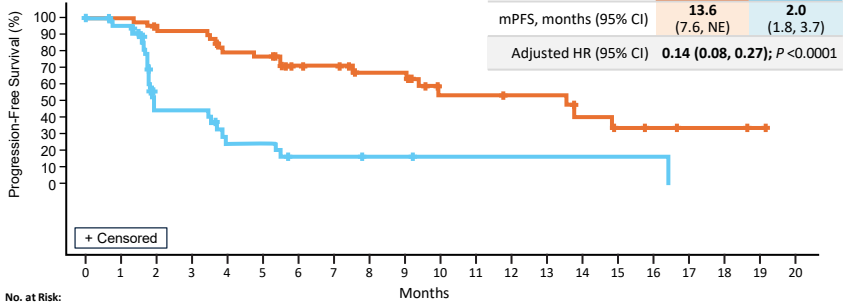
	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**10.0** (5.6, NE)	**1.9** (1.8, 3.5)
Adjusted HR (95% CI)	**0.19 (0.12, 0.31);** *P* <0.0001	



No. at Risk:																				
Geda + Fulv	59	56	49	47	37	36	26	25	20	20	12	12	10	10	7	5	4	3	3	2	0
Fulvestrant	62	57	17	15	9	9	3	3	2	2	1	1	1	1	1	1	1	0			

>24 Months

	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**13.6** (7.6, NE)	**2.0** (1.8, 3.7)
Adjusted HR (95% CI)	**0.14 (0.08, 0.27);** *P* <0.0001	



No. at Risk:																				
Geda + Fulv	43	40	37	36	30	29	22	21	17	17	10	10	9	9	6	4	3	2	2	1	0
Fulvestrant	47	42	14	12	6	6	3	3	2	2	1	1	1	1	1	1	1	0			

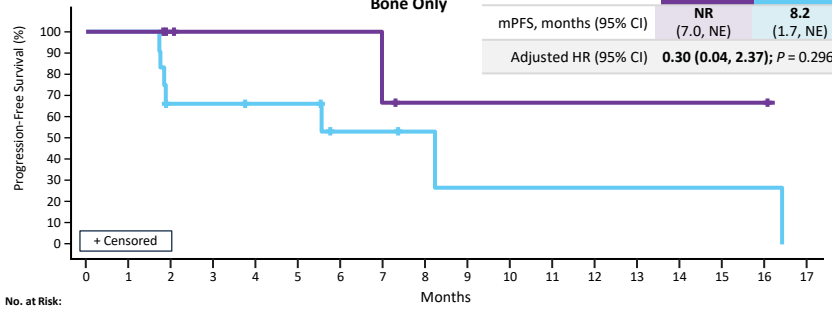
PFS by Bone Metastases Status:

Bone Only vs. Non-Bone Only

Gedatolisib Triplet

Bone Only

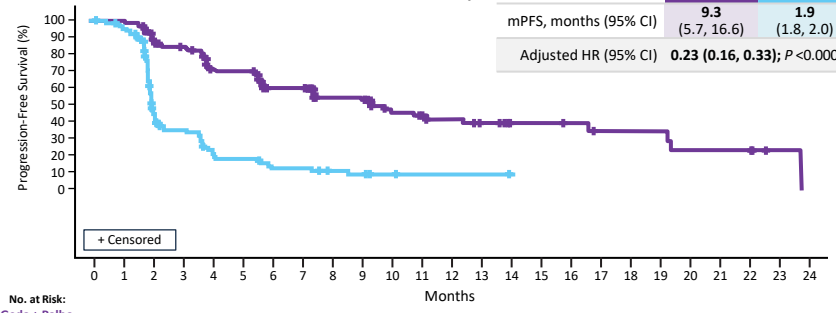
	Geda + Palbo + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	NR (7.0, NE)	8.2 (1.7, NE)
Adjusted HR (95% CI)	**0.30 (0.04, 2.37)**; *P* = 0.2969	



No. at Risk:																	
Geda + Palbo + Fulv	6	6	4	3	3	3	3	2	1	1	1	1	1	1	1	1	0
Fulvestrant	12	12	7	7	6	6	3	3	2	1	1	1	1	1	1	1	0

Non-Bone Only

	Geda + Palbo + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	9.3 (5.7, 16.6)	1.9 (1.8, 2.0)
Adjusted HR (95% CI)	**0.23 (0.16, 0.33)**; *P* <0.0001	

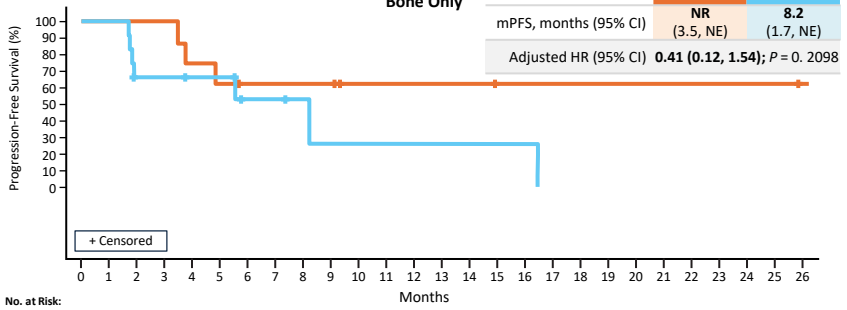


No. at Risk:																								
Geda + Palbo + Fulv	125	121	99	91	66	65	47	47	34	33	23	21	18	15	9	9	8	6	6	6	4	4	4	1	0
Fulvestrant	119	102	38	28	14	14	8	8	5	4	2	1	1	1	0										

Gedatolisib Doublet

Bone Only

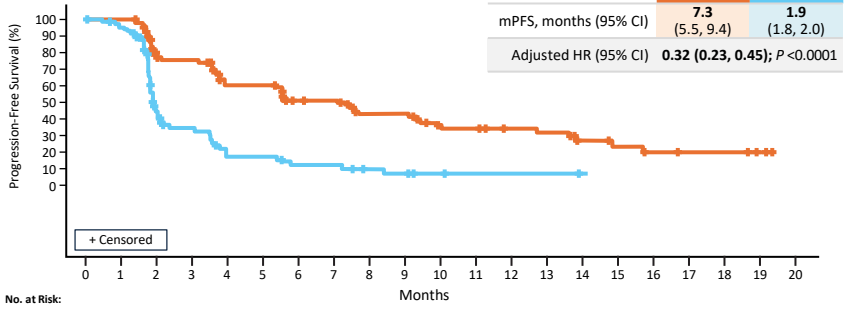
	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	NR (3.5, NE)	8.2 (1.7, NE)
Adjusted HR (95% CI)	**0.41 (0.12, 1.54)**; *P* = 0. 2098	



No. at Risk:																									
Geda + Fulv	8	8	8	8	6	5	4	4	4	4	2	2	2	2	1	1	1	1	1	1	1	1	1	1	0
Fulvestrant	12	12	7	7	6	6	3	3	2	1	1	1	1	1	1	1	1	0							

Non-Bone Only

	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	7.3 (5.5, 9.4)	1.9 (1.8, 2.0)
Adjusted HR (95% CI)	**0.32 (0.23, 0.45)**; *P* <0.0001	



No. at Risk:																				
Geda + Fulv	122	118	85	81	58	58	41	40	29	29	20	20	15	14	9	7	5	4	4	2	0
Fulvestrant	119	102	38	28	14	14	8	8	5	4	2	1	1	1	0						

Stomatitis: Time to First Onset

Event	Gedatolisib + Palbo + Fulvestrant (n=130)		Gedatolisib + Fulvestrant (n=130)	
Pts with treatment-related stomatitis*†, n (%)	90 (69.2%)		74 (56.9%)	
Median time to onset (first instance), days (range)	7.5 (1-259)		4.0 (1-524)	
Grade 1	n=57	**8.0** (1-259)	n=48	**4.5** (1-524)
Grade 2	n=24	**7.5** (1-146)	n=16	**3.5** (1-158)
Grade 3	n=9	**4.0** (1-20)	n=10	**3.5** (2-87)

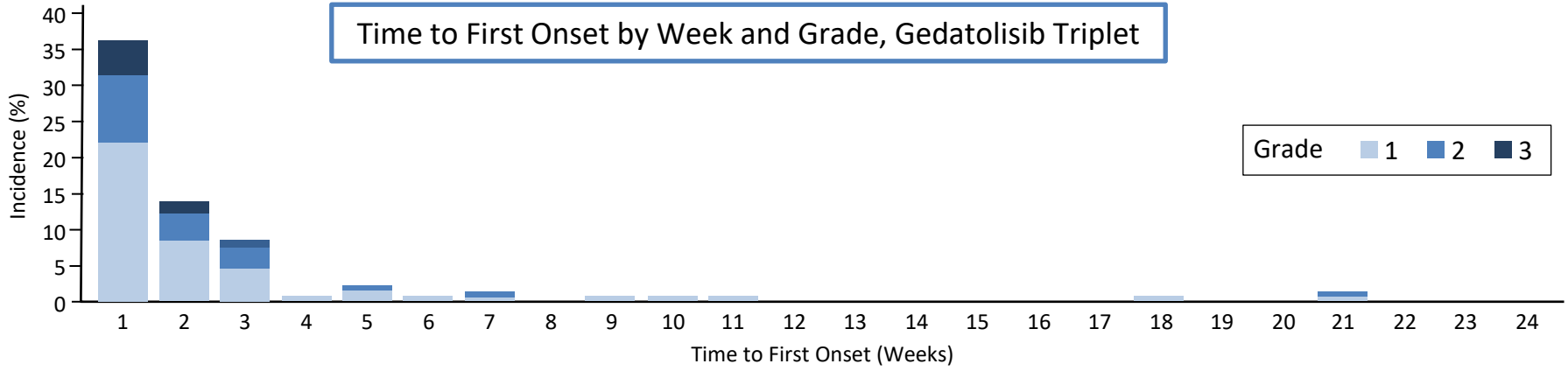
*Stomatitis is a combination of the following terms: aphthous ulcer; gingival pain; gingivitis; lip ulceration; oral mucosal inflammation; mouth ulceration; stomatitis
†Dexamethasone "swish-and-spit" mouthwash, provided by the sponsor, was required prophylactic treatment for gedatolisib, starting prior to first infusion and continued daily for 8 weeks, and as clinically indicated thereafter

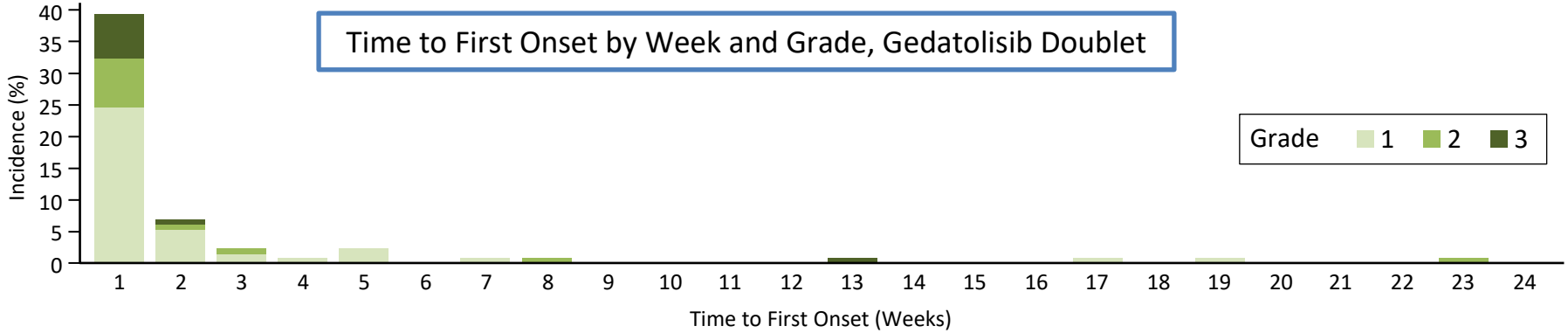
The majority of patients experienced Grade 1 stomatitis as the first event

Abbreviations: Palbo, palbociclib, Pts, patients

Stomatitis: Time to First Onset

Safety Analysis Set, Weeks 1-24





Stomatitis: Time to Improvement

Event		Gedatolisib + Palbo + Fulvestrant (n=130)		Gedatolisib + Fulvestrant (n=130)	
Pts with treatment-related stomatitis*†, n (%)		90 (69.2%)		74 (56.9%)	
Median time to improvement (from worst grade), days (range)					
	Grade 3 to lower	n=25	**12.0** (3-103)	n=16	**7.5** (2-112)
	Grade 2 to lower	n=25	**14.0** (4-229)	n=18	**9.0** (3-41)
	Grade 1 to lower	n=40	**27.5** (1-402)	n=40	**17.5** (1-317)

*Stomatitis is a combination of the following terms: aphthous ulcer; gingival pain; gingivitis; lip ulceration; oral mucosal inflammation; mouth ulceration; stomatitis
†Dexamethasone "swish-and-spit" mouthwash, provided by the sponsor, was required prophylactic treatment for gedatolisib, starting prior to first infusion and continued daily for 8 weeks, and as clinically indicated thereafter

Grade 2/3 events generally improved to a lower grade within 1-2 weeks

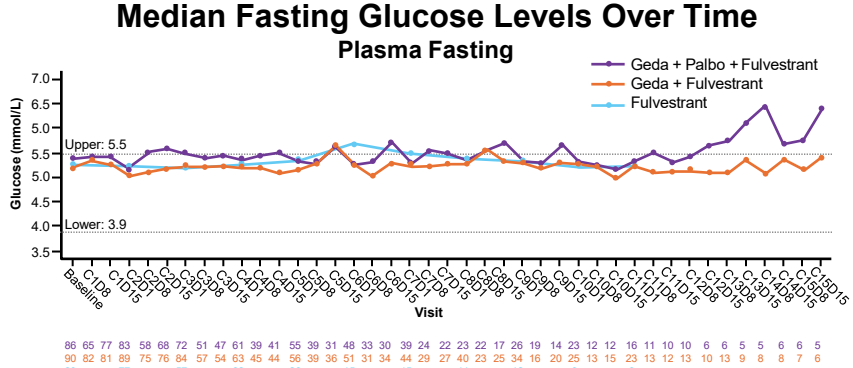
Abbreviations: Palbo, palbociclib, Pts, patients

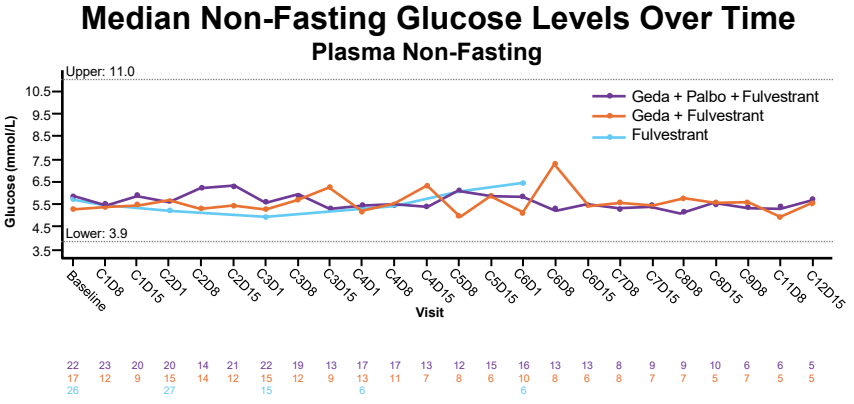
Median Glucose Levels Were Stable

Hyperglycemia, n (%)	Geda + Palbo + Fulvestrant (n=130)	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=123)
All grades	12 (9.2)	15 (11.5)	0
HbA1c (%), median (range)	n=91	n=89	n=72
Baseline (B)	5.4 (4.1-6.4)	5.4 (4.0-6.3)	5.3 (4.0-6.3)
End of treatment (EOT)	5.9 (4.3-8.8)	5.9 (4.5-14.1)	5.5 (4.6-6.8)
Change, B to EOT	0.5 (-1.6 - 2.9)	0.6 (-0.7 - 8.2)	0.2 (-0.6 - 1.3)

Gedatolisib did not produce clinically relevant hyperglycemia and had no dose reductions or withdrawals due to hyperglycemia

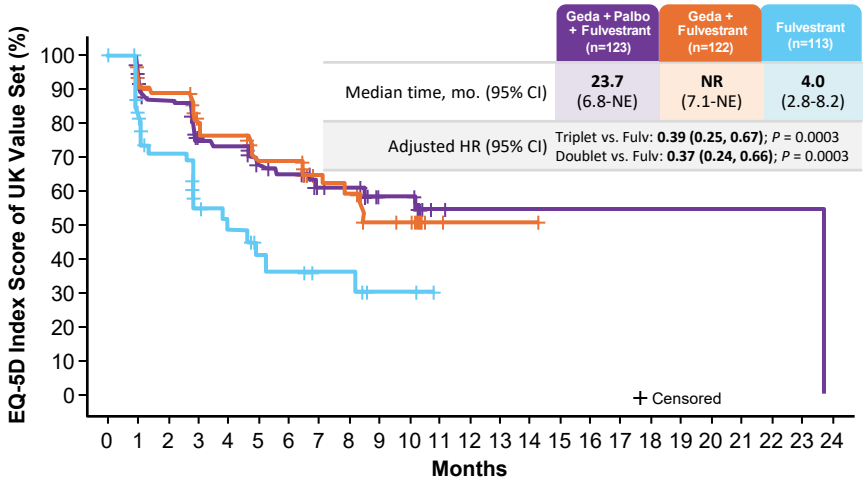
Abbreviations: B, baseline; C, cycle; EOT, end of treatment; Geda, gedatolisib; HbA1c, hemoglobin A1c; Palbo, palbociclib





PRO: Temporal and Mean Change, EQ-5D-5L

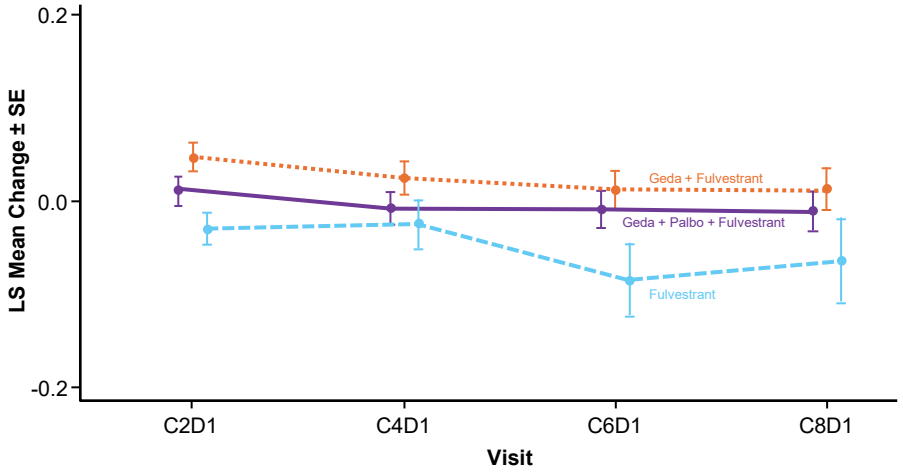
Time to Definitive Deterioration in EQ-5D-5L



No. at Risk:

Geda + Palbo + Fulvestrant	123	102	82	62	60	46	43	29	27	16	16	2	1	1	1	1	1	1	1	1	1	1	0
Geda + Fulvestrant	122	94	78	60	57	41	41	25	23	17	16	2	1	1	1	0							
Fulvestrant	113	55	34	18	15	9	8	6	6	3	3	0											

Mean Changes from BL in EQ-5D-5L



No. at Risk:

	C2D1	C4D1	C6D1	C8D1
Geda + Palbo + Fulvestrant	95	75	63	50
Geda + Fulvestrant	98	75	58	49
Fulvestrant	88	29	15	10

Median time to definitive deterioration was meaningfully delayed in the gedatolisib arms as compared with fulvestrant

Abbreviations: BL, baseline; C, cycle; D, day; EQ-5D-5L, EuroQol 5 Dimension 5 Level; Fulv, fulvestrant; Geda, gedatolisib; LS, least square; mo., months; NE, not estimable; No., number; NR, not reached; Palbo, palbociclib; PRO, patient-reported outcomes; SE, standard error.

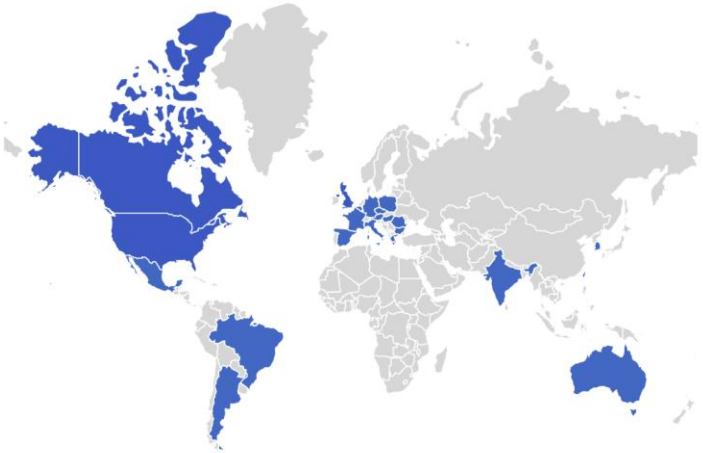
Conclusions

- 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
- Significant efficacy was observed irrespective of the duration of prior treatment.
- Measures to mitigate stomatitis were effective; most patients experienced resolution to a lower grade of stomatitis in about 2 weeks
- Notably, hyperglycemia was low in both gedatolisib arms, and HbA1c levels were stable over time
- Both gedatolisib regimens delayed time to definitive deterioration of well-being (EQ-5D-5L) vs fulvestrant

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

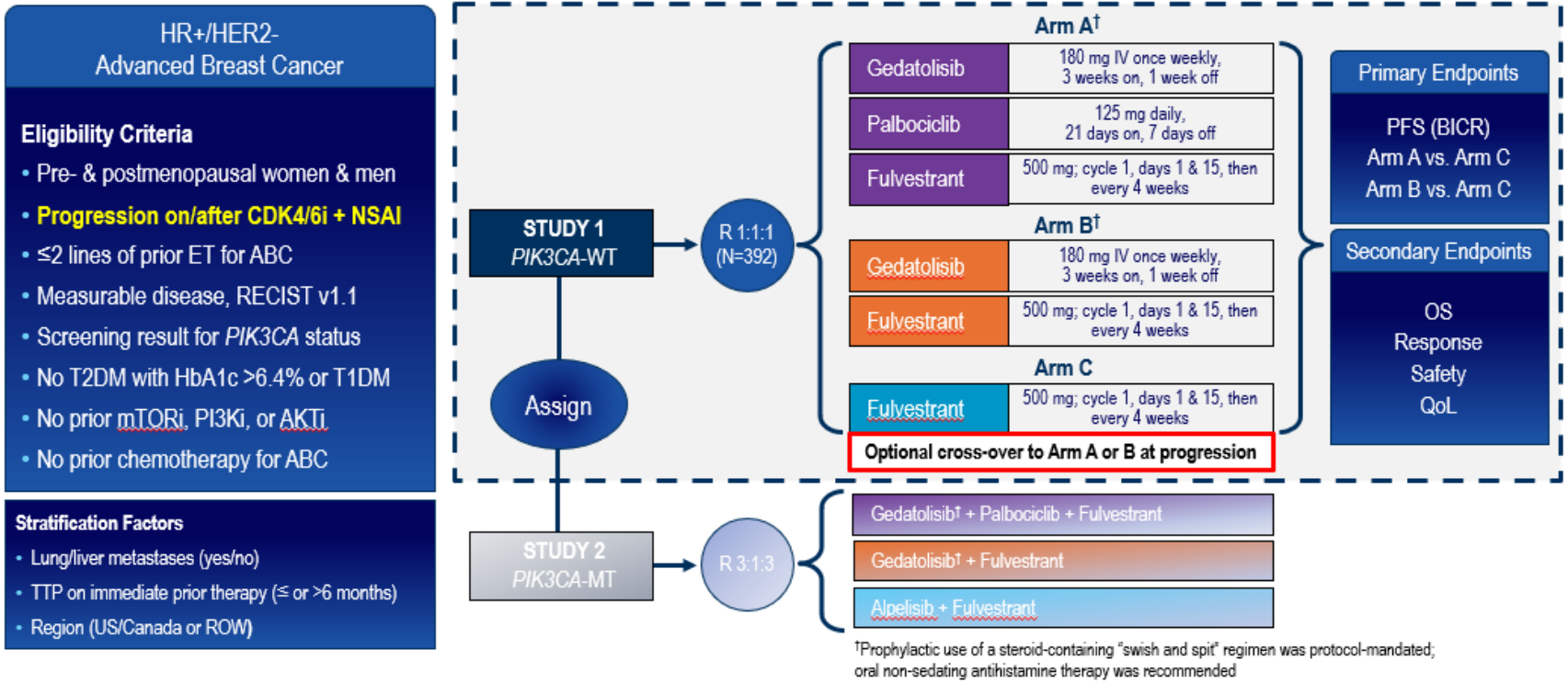
Acknowledgments

- We thank the 392 clinical trial participants and their families/caregivers from the 147 sites in 23 countries for participating in this trial
- We thank the VIKTORIA-1 investigators and their staff who participated in this work
- We are grateful for the participation and insights of the VIKTORIA-1 Steering Committee
- This study was sponsored by Celcuity Inc.



Supplementary Material

VIKTORIA-1 Study Design



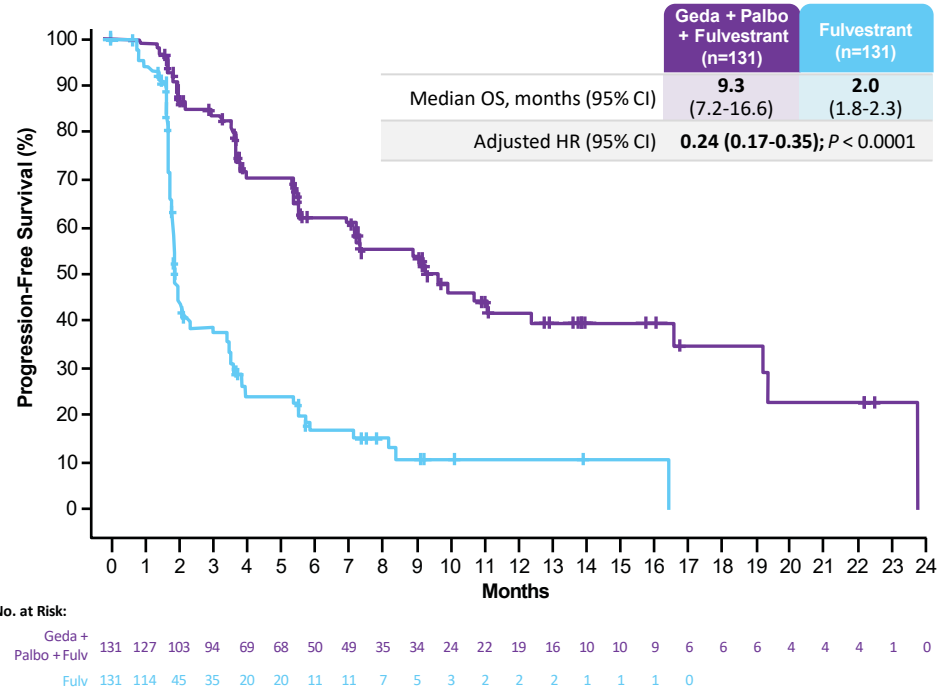
†Prophylactic use of a steroid-containing "swish and spit" regimen was protocol-mandated; oral non-sedating antihistamine therapy was recommended

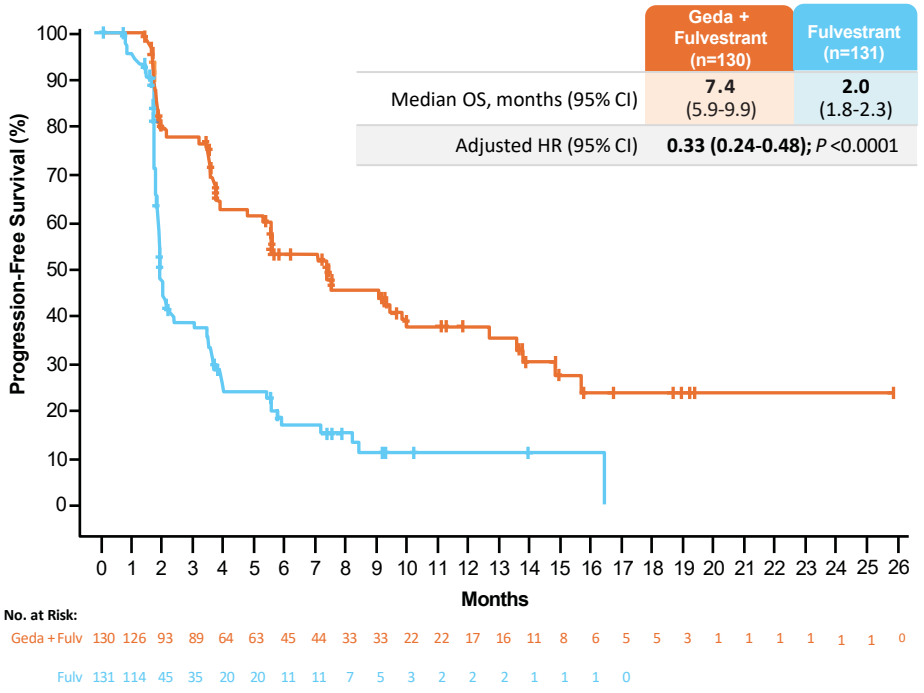
Abbreviations: ABC, advanced breast cancer; AKTi, protein kinase B inhibitor; BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; ET, endocrine therapy; HbA1c, hemoglobin A1c; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; 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

Hurvitz SA, et al. ESMO 2025. LBA17.

Co-Primary Endpoints: Progression-Free Survival (BICR)

Gedatolisib triplet and gedatolisib doublet vs. fulvestrant





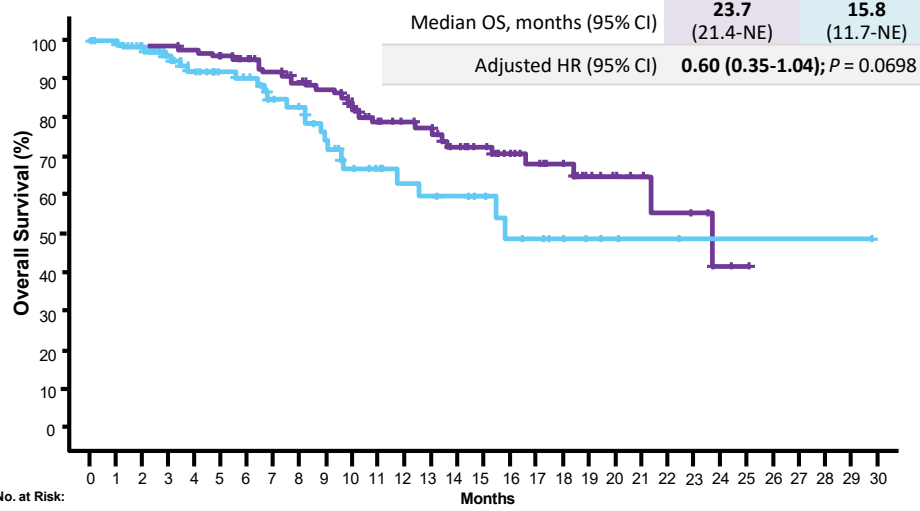
Abbreviations: BICR, blinded independent central review; CI, confidence interval; Fulv, fulvestrant; Geda, gedatolisib; HR, hazard ratio; mPFS, median progression-free survival; No., number; OS, overall survival; Palbo, palbociclib.

Hurvitz SA, et al. ESMO 2025. LBA17.

Interim OS, Censored at Cross-Over

Gedatolisib triplet and gedatolisib doublet vs. fulvestrant

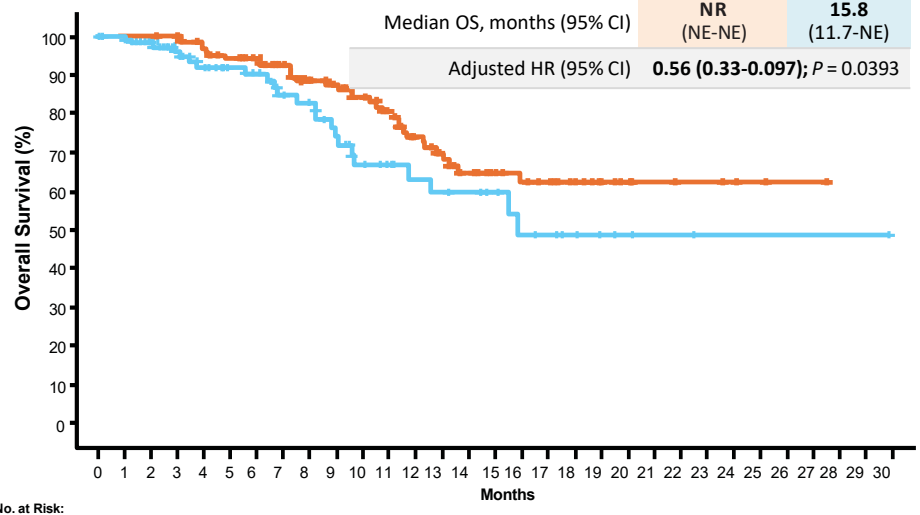
	Geda + Palbo + Fulvestrant (n=131)	Fulvestrant (n=131)
Median OS, months (95% CI)	**23.7** (21.4-NE)	**15.8** (11.7-NE)
Adjusted HR (95% CI)	**0.60 (0.35-1.04);** *P* = 0.0698	



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

Abbreviations: CI, confidence interval; Fulv, fulvestrant; Geda, gedatolisib; HR, hazard ratio; NE, not estimable; no., number; NR, not reached; OS, overall survival; Palbo, palbociclib.

Hurvitz SA, et al. ESMO 2025. LBA17.

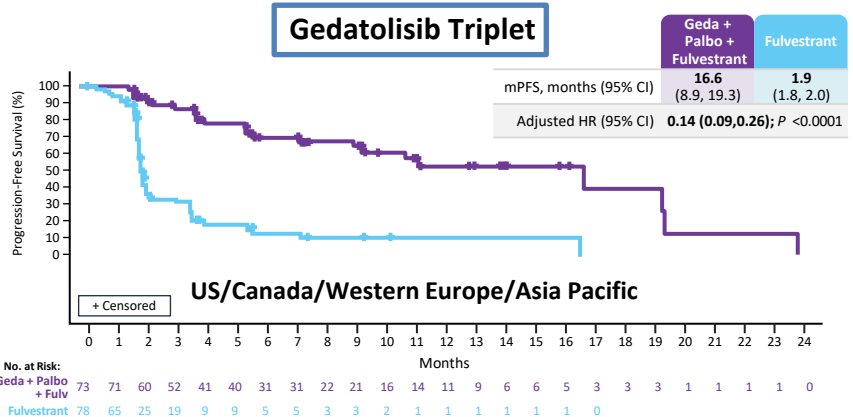
PFS by Region

US/Canada/Western Europe/Asia Pacific vs. Rest of World

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

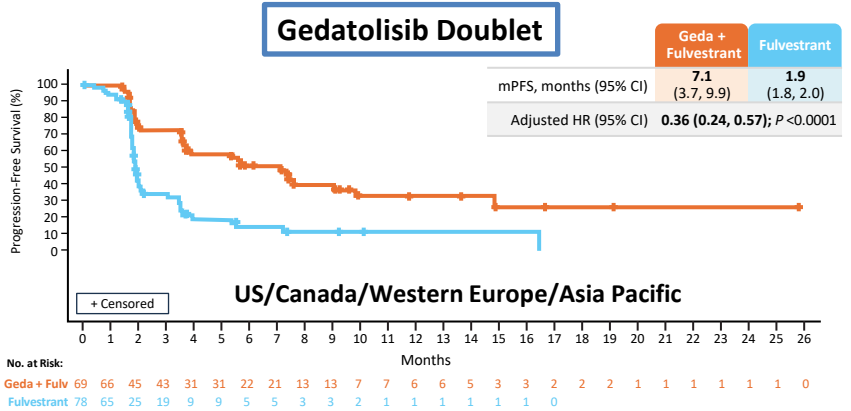
Gedatolisib Triplet



	Geda + Palbo + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**16.6** (8.9, 19.3)	**1.9** (1.8, 2.0)
Adjusted HR (95% CI)	**0.14 (0.09,0.26)**; *P* <0.0001	

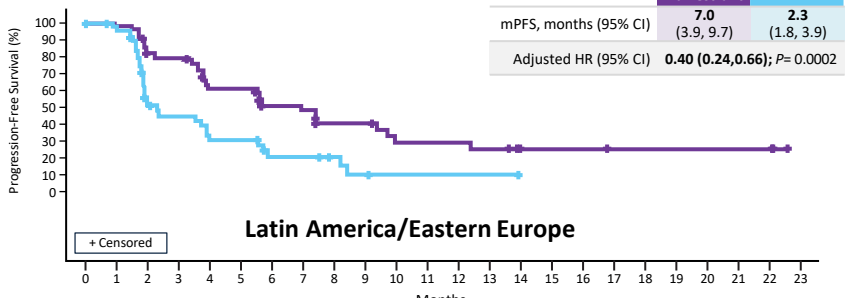
No. at Risk:																								
Geda + Palbo + Fulv	73	71	60	52	41	40	31	31	22	21	16	14	11	9	6	6	5	3	3	3	1	1	1	1	0
Fulvestrant	78	65	25	19	9	9	5	5	3	3	2	1	1	1	1	1	1	0							

Gedatolisib Doublet



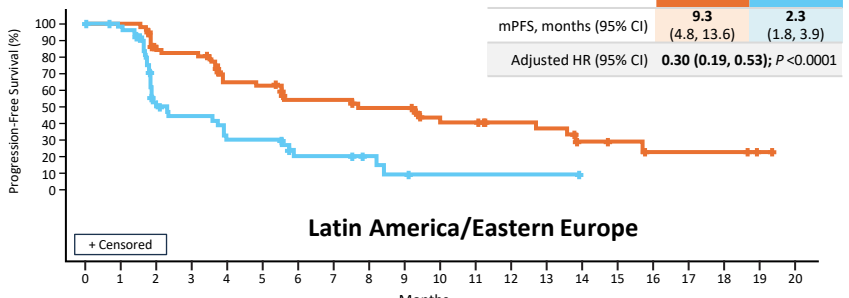
	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**7.1** (3.7, 9.9)	**1.9** (1.8, 2.0)
Adjusted HR (95% CI)	**0.36 (0.24, 0.57)**; *P* <0.0001	

No. at Risk:																									
Geda + Fulv	69	66	45	43	31	31	22	21	13	13	7	7	6	6	5	3	3	2	2	2	1	1	1	1	1	1	0
Fulvestrant	78	65	25	19	9	9	5	5	3	3	2	1	1	1	1	1	1	0									



	Geda + Palbo + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**7.0** (3.9, 9.7)	**2.3** (1.8, 3.9)
Adjusted HR (95% CI)	**0.40 (0.24,0.66)**; *P*= 0.0002	

No. at Risk:																								
Geda + Palbo + Fulv	58	56	43	42	28	28	19	18	13	13	8	8	8	7	4	4	4	3	3	3	3	3	3	0
Fulvestrant	53	49	20	16	11	11	6	6	4	2	1	1	1	1	0									



	Geda + Fulvestrant	Fulvestrant
mPFS, months (95% CI)	**9.3** (4.8, 13.6)	**2.3** (1.8, 3.9)
Adjusted HR (95% CI)	**0.30 (0.19, 0.53)**; *P* <0.0001	

No. at Risk:																				
Geda + Fulv	61	60	48	46	33	32	23	23	20	20	15	15	11	10	6	5	3	3	3	1	0
Fulvestrant	53	49	20	16	11	11	6	6	4	2	1	1	1	1	0						

Ad hoc analysis; Asia Pacific includes Australia, India, Singapore, South Korea, Taiwan; Eastern Europe includes Bulgaria, Czechia, Hungary, Poland, Romania; Latin America includes Argentina, Brazil, Mexico; Western Europe includes Austria, Belgium, France, Germany, Greece, Italy, Spain, United Kingdom

Abbreviations: CI, confidence interval; Fulv, fulvestrant; Geda, gedatolisib; HR, hazard ratio; mPFS, median progression-free survival; no., number; Palbo, palbociclib; PFS, progression-free survival.