


Pfizer Breast Cancer Data Updates

San Antonio Breast Cancer
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**Palbociclib:
RWE and RCT**



**CDK4/6i RWE:
P-VERIFY**



**Additional
Information**

Palbociclib in Women Aged ≥ 70 Years as First-Line Treatment for Endocrine-Sensitive Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Locally Advanced or Metastatic Breast Cancer: Final Results of **PalomAGE**

Carola E, et al. SABCS 2024. Poster P2-07-17.

PalomAGE: Study Design¹⁻⁵

G8 Screening Tool →

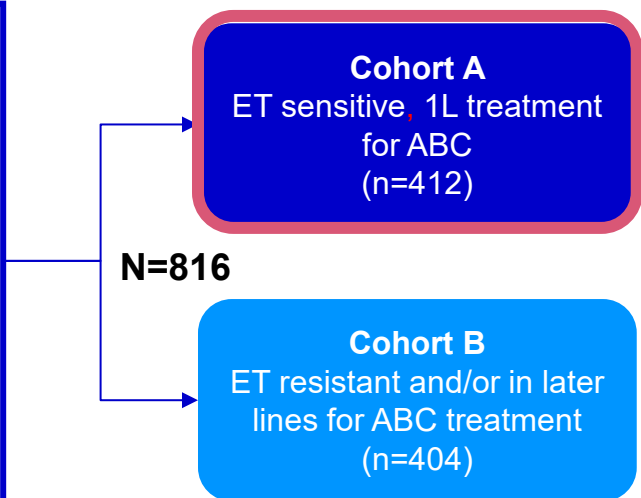
DIALOG G-CODE →

Real-world, noninterventional, prospective, French multicentered study

Objective: To present the final results from **cohort A** on primary and selected secondary outcomes from PalomAGE, a RWD study designed to evaluate the safety, effectiveness, and tolerability/QoL outcomes of PAL plus ET in women ≥70 years with HR+/HER2- ABC

KEY ELIGIBILITY CRITERIA

- Women aged ≥70 years with HR+/HER2- ABC
- Patients who initiated PAL without prior CDK4/6i exposure between October 2018 to December 2020



Primary Outcome

- Cohort A: 18-month PAL discontinuation rate*

Secondary Outcomes

- TTF[†]
- AEs, per NCI-CTCAE v5.0
- rwPFS[‡]
- Geriatric Assessment per G8-screening tool^{2,3,§}
- QoL per EORTC QLQ-C30 and QLQ-ELD14^{4,5,||}

Statistical Analyses

- Factors associated with TTF will be investigated by uni- and multivariate analyses, performed using Cox PH models (significance level was set at 5%)
- TTF and rwPFS were estimated using the KM method

*PAL discontinuation rate was defined by the proportion of patients who permanently discontinued PAL (±ET) for toxicities (NCI-CTCAE v5.0), patient's decision, disease progression, or death. [†]TTF was defined as the time from PAL initiation to its discontinuation. [‡]rwPFS was defined as time from PAL initiation to the first progression or death from any cause. [§]The G8 screening tool was used to identify patients with G8 score ≤14/17 who should benefit from a GA and Geriatric Core Dataset (DIALOG G-CODE), a validated GA standardized tool of 7 geriatric domains: social environment, functional status, nutritional status, cognitive status, mobility, depressive mood, and comorbidities.^{2,3} ^{||}QoL was assessed using the EORTC QLQ-C30 and QLQ-ELD14 (specifically designed to assess QoL in patients with cancer ≥70 years) questionnaires.^{4,5} 1L=first-line; ABC=advanced breast cancer; AE=adverse event; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EORTC QLQ=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; KM=Kaplan-Meier; NCI-CTCAE v5.0=National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.1); PAL=palbociclib; QoL=quality of life; RWD=real-world data; rwPFS=real-world progression-free survival; TTF=time to treatment failure.

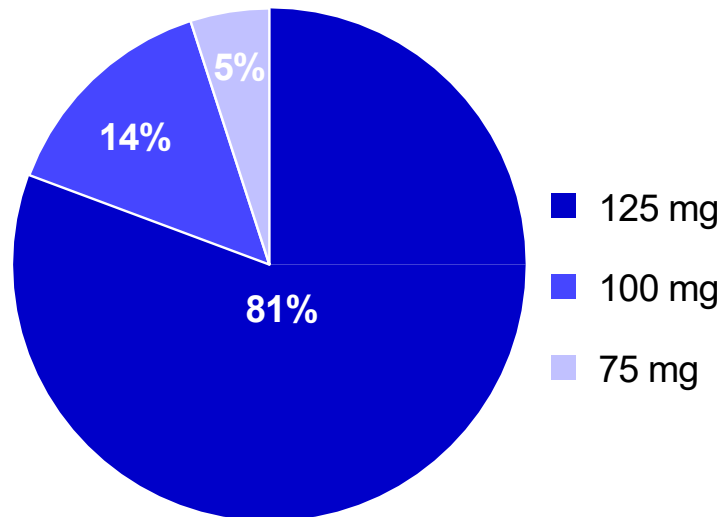
1. Carola E, et al. SABCS 2024. Poster P2-07-17.
2. Soubeyran P, et al. *PLoS One*. 2014;9(12):e115060.
3. Paillaud E, et al. *Eur J Cancer*. 2018;103:61-68.
4. Groenvold M, et al. *J Clin Epidemiol*. 1997;50(4):441-450.
5. Wheelwright S, et al. *Br J Cancer*. 2013;109(4):852-858.

PalomAGE: Cohort A—Study Population

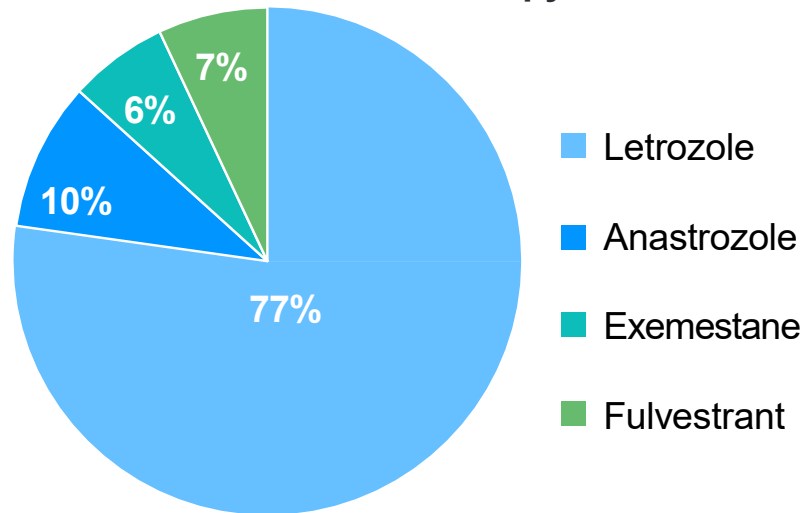
Among 816 patients included, 412 initiated PAL in **cohort A** (safety analysis set), with 382 (93%) receiving ≥1 cycle of PAL (full analysis set) evaluable for effectiveness outcomes.

Safety Analysis Set (N=412)

Palbociclib Initiation Dose



Concurrent Endocrine Therapy



- Patients initiating PAL at reduced dose (100 or 75 mg) were older, presented more often with ECOG PS ≥2, and had poorer geriatric scores (data not shown)

ECOG PS=Eastern Cooperative Oncology Group performance status; ET=endocrine therapy; PAL=palbociclib.

Carola E, et al. SABCS 2024. Poster P2-07-17.

PalomAGE: Cohort A—Baseline Characteristics (1 of 2)

Safety Analysis Set (N=412)*

Characteristics	Cohort A (N=412)
Age	
Median age, years (min-max)	78 (70–94)
Mean, years (SD)	79 (6)
≥80 years old, n (%)	183 (44)
ECOG PS, n (%)	
0-1	295 (72)
≥2	72 (17)
Not done/missing	45 (11)
Disease characteristics, n (%)	
<i>De novo</i> mBC	207 (50)
Location of metastasis, n (%)	
Visceral	172 (42)
Bone only	133 (32)
≥3 metastatic sites	38 (9)
G8 scores ≤14 (potentially frail), n (%) Available N=405†	280 (69)

*Main baseline characteristics are presented here, with a focus on factors associated with decreased TTF in uni- and multivariate analyses. †Available N is the number of patients with completed questionnaires.

ECOG PS=Eastern Cooperative Oncology Group performance status; G8=geriatric assessment score; mBC=metastatic breast cancer; SD=standard deviation; TTF=time to treatment failure.

PalomAGE: Cohort A—Baseline Characteristics (2 of 2)

Safety Analysis Set (N=412)*

Characteristics	Cohort A (N=412)
DIALOG G—CODE, n (%)	
Do you live alone? Yes, <i>Available N[†]=340</i>	154 (45)
Do you have a person able to provide you care and support? Yes, <i>Available N[†]=328</i>	273 (83)
ADLs alteration (≤ 5), <i>Available N[†]=363</i>	53 (15)
IADLs alteration (≤ 3), <i>Available N[†]=363</i>	104 (29)
Mobility, inability to perform the test (time ≥ 20 sec), <i>Available N[†]=279</i>	66 (24)
Nutritional status (Unintentional weight loss $>10\%$ in 6 months), <i>Available N[†]=320</i>	244 (76)
Cognitive status, <i>Available N[†]</i>	337
Threshold dementia (score <3)	66 (20)
Threshold deeper evaluation (score <4)	143 (42)
Depressive mood (mini GDS score $\geq 1/4$), <i>Available N[†]=352</i>	167 (47)
Charlson comorbidities score ≥ 4 , <i>Available N[†]=346</i>	296 (86)

*Main baseline characteristics are presented here, with a focus on factors associated with decreased TTF in uni- and multivariate analyses. [†]Available N is the number of patients with completed questionnaires.

ADL=activity of daily living; GDS=geriatric depression scale; IADL=instrumental activities of daily living; SD=standard deviation; TTF=time to treatment failure.

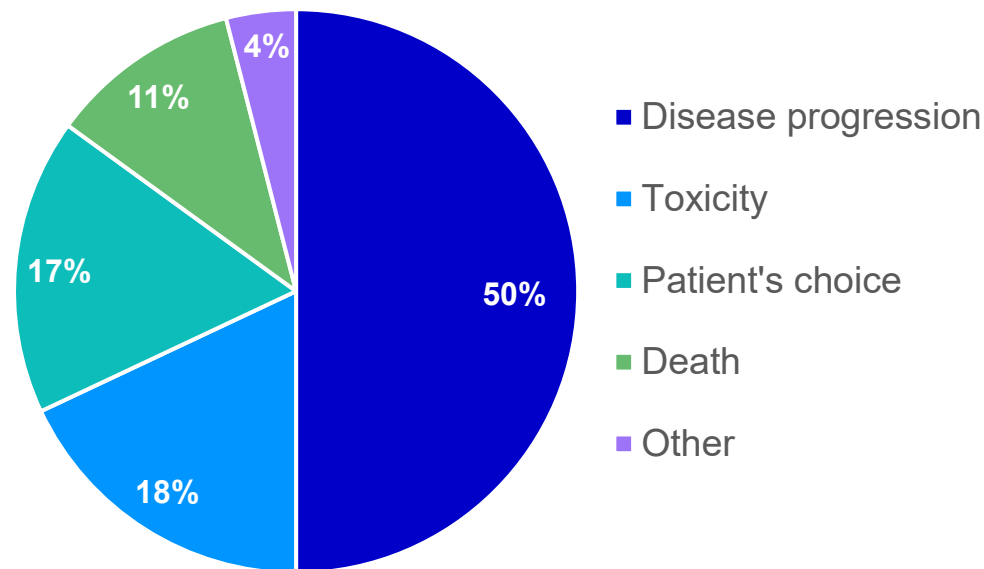
Carola E, et al. SABCS 2024. Poster P2-07-17.

PalomAGE: Cohort A—Discontinuation Rate

Primary Outcome (FAS, N=382)*

- The 18-month PAL discontinuation rate was 41% (n=158; 95% CI, 36-46)
- Median follow-up was 25.2 months (95% CI, 21.7-28.4)

Reasons for Treatment Discontinuation Observed Among 158 Patients



*The FAS included patients who received at least 1 cycle of PAL.
CI=confidence interval; FAS=full analysis set; PAL=palbociclib.

PalomAGE: Cohort A—Safety

Secondary Outcome

Incidence of AEs Related to Treatment (Preferred Term, SAF, N=412)*					
	Grade 1 n (%)	Grade 2 n (%)	Grade 3-4 n (%)	Grade 5 n (%)	All n (%)
Neutropenia	47 (11)	100 (24)	199 (48)	—	261 (63)
Asthenia	52 (13)	34 (8)	6 (2)	—	86 (21)
Anaemia	53 (13)	29 (7)	17 (4)	—	81 (20)
Thrombocytopenia	35 (9)	18 (4)	5 (1)	—	55 (13)
Alopecia	41 (10)	8 (2)	1 (0)	—	48 (12)
Interstitial lung disease	—	2 (1)	1 (0)	1 (0)	4 (1)
Cerebrovascular accident	—	—	1 (0)	1 (0)	1 (0)

- 81% of patients presented ≥1 AE related to treatment
 - 63% experienced any-grade neutropenia; febrile neutropenia was reported in 1% of patients
- **AEs led to palbociclib dose reduction in 35% of patients and permanent discontinuations in 11% of patients without any new safety signals**

*A patient is counted more than once in the grading analysis when experiencing different grades of the same event. “—” denotes no patients experienced the indicated AE.
AE=adverse event; SAF=safety analysis set.

PalomAGE: Cohort A—TTF and rwPFS

Secondary Outcomes

TTF and rwPFS

- **Median TTF was 23.0 months (95% CI, 19.8-26.0)**
- **Median rwPFS was 30.4 months (95% CI, 25.7-NR):** 164 patients (43% of FAS) experienced disease progression or death
- At the end of the study, 94% of patients were still alive, and 39% continued PAL treatment

Factors Associated With TTF

- Per univariate analysis, the following baseline factors were associated with decreased TTF:
 - Higher age
 - Poorer ECOG PS score
 - ≥3 metastatic sites
 - G8 ≤14
 - IADLs ≤3
 - Absence of a person able to provide care and support (caregiver)
- According to the multivariate analysis, the risk of treatment failure was **significantly higher in patients with an impaired G8 score and those lacking a caregiver or support**

Results of Multivariate Analysis (FAS, N=303*)				
Variables	N	HR	95% CI	P value
Under geriatric evaluation threshold (G8 score ≤14)				<0.001
No	94	1.00	Reference	
Yes	209	1.76	1.24-2.49	
Have a person able to provide care and support				0.004
Yes	255	1.00	Reference	
No	48	1.77	1.23-2.56	

Results should be interpreted with caution as analysis was not adjusted for potential differences in baseline patient characteristics (eg, starting dose, disease severity, etc)

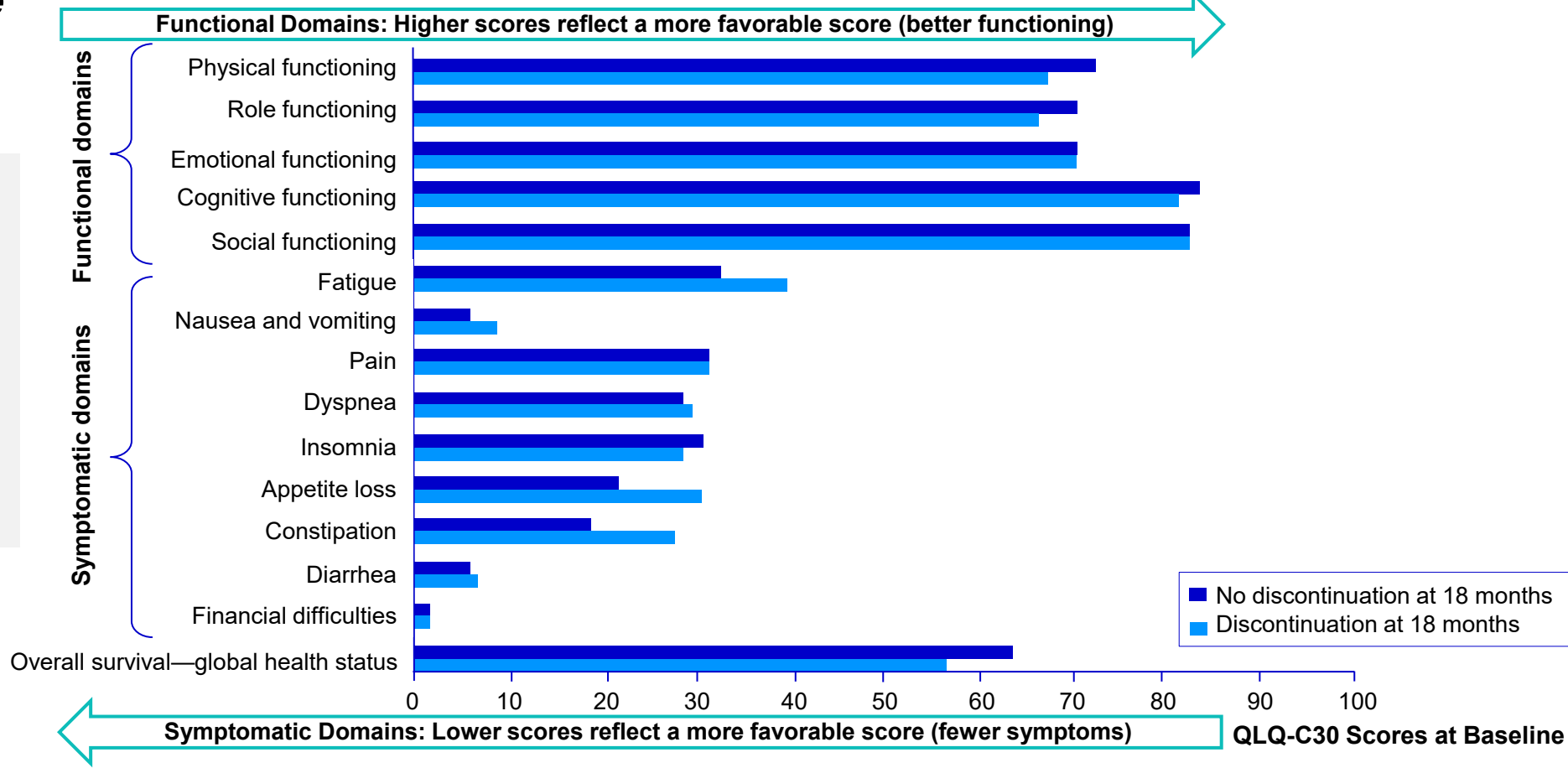
*Among the FAS, 79 patients have missing values for at least one variable included in the model and were excluded from the analysis. The model was adjusted for age, and variables significant at the 10% level were considered as candidate variables for the multivariable analysis. A step-by-step manual process was used to construct the final model with a significance level set at 5%.
 CI=confidence interval; ECOG PS=Eastern Cooperative Oncology Group performance status; FAS=full analysis set; G8=geriatric assessment score; HR=hazard ratio; IADL=instrumental activity of daily living; NR=not reached; PAL=palbociclib; rwPFS=real-world progression-free survival; TTF=time to treatment failure.

PalomAGE: Cohort A—QoL EORTC QLQ-C30

Secondary Outcome

QLQ-C30 Scores at Baseline According to the 18-Month PAL Discontinuation (FAS, N=338*)

Among patients who fully completed all the items of the questionnaire at baseline and at 18 months (n=118), **all scores appeared to remain stable over time** (data not shown).



Results should be interpreted with caution as analysis was not adjusted for potential differences in baseline patient characteristics (eg, starting dose, disease severity).

*Due to missing data on the questionnaire, none of the QoL scores could be calculated for 41 patients, and 3 patients were not evaluable for discontinuation at 18 months (lost to follow-up). EORTC QLQ=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; FAS=final analysis set; PAL=palbociclib; QoL=quality of life.

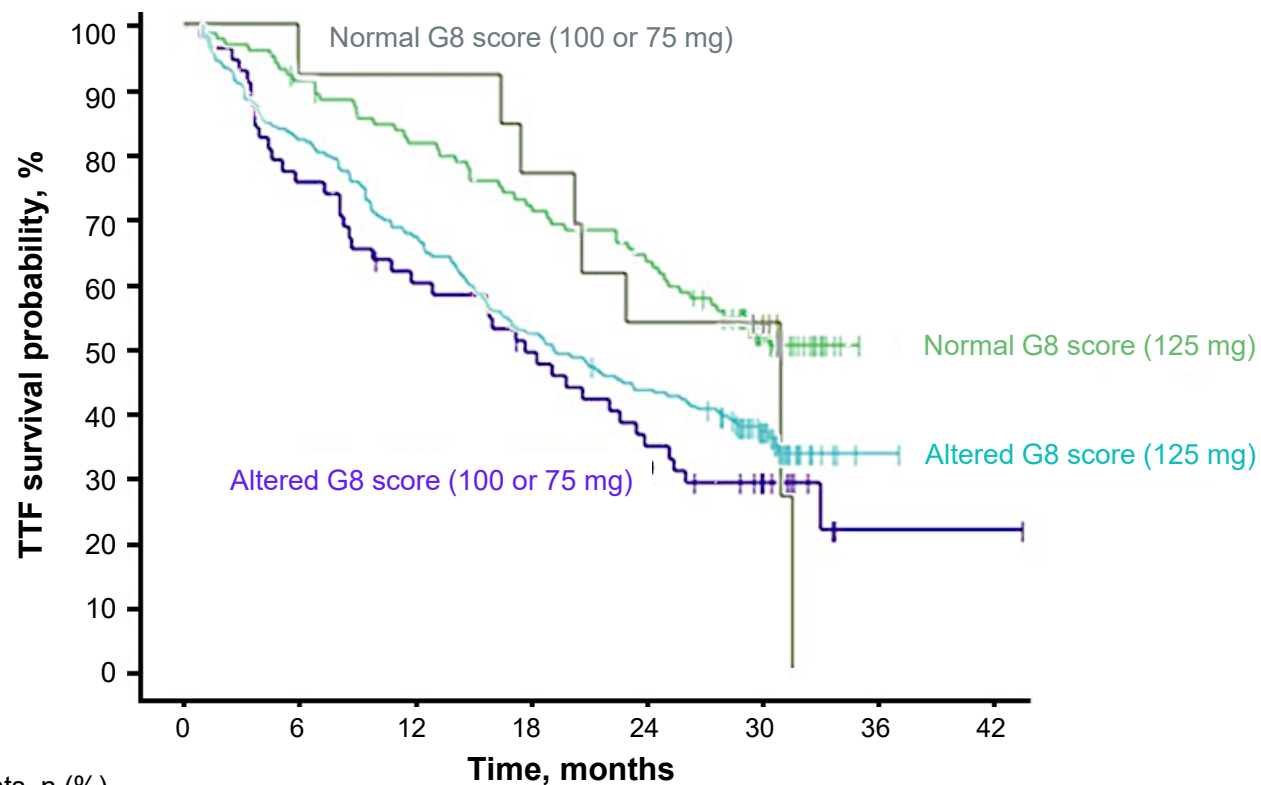
Carola E, et al. SABCS 2024. Poster P2-07-17.

PalomAGE: Cohort A—TTF by Geriatric Status and Initiation Dose

Exploratory Analyses

TTF Curve by Starting Dose Among Patients With Normal or Altered G8 Score (FAS, N=375*)†

- Higher 18-month PAL discontinuation rate, shorter median TTF, and shorter median rwPFS were observed with a reduced dose of PAL at initiation without reaching statistical significance
- When examining patient subgroups based on geriatric status and the rate of permanent discontinuation, minimal variations were observed across the different initiation doses
- At a fixed initiation dose, patients with an impaired G8 score exhibited a **higher discontinuation rate (data not shown) at 18 months and a shorter TTF**



	Patients, n (%)								
Normal G8 score (125 mg)	106 (0)	96 (9)	85 (19)	75 (29)	67 (38)	34 (49)	0 (50)	0 (50)	
Altered G8 score (125 mg)	198 (0)	163 (35)	133 (65)	103 (95)	85 (112)	47 (124)	1 (127)	0 (127)	
Normal G8 score (100 or 75 mg)	13 (0)	13 (1)	12 (1)	10 (3)	7 (6)	5 (6)	0 (8)	0 (8)	
Altered G8 score (100 or 75 mg)	58 (0)	44 (14)	34 (23)	27 (29)	19 (37)	12 (40)	1 (41)	1 (41)	

Results should be interpreted with caution as analysis was not adjusted for potential differences in baseline patient characteristics (eg, starting dose, disease severity).

*In the effectiveness analysis, 7 patients have no information about G8 score at inclusion. †Normal G8 score defined as scores >14; altered scores defined as those ≤14. FAS=full analysis set; G8=geriatric assessment score; TTF=time to treatment failure.

PalomAGE: Authors' Conclusions and Study Limitations

Authors' Conclusions—Discussion

- PalomAGE shows that PAL plus ET is well tolerated when used as a 1L treatment for women ≥ 70 years with HR+ /HER2- ABC without additional risk of AEs and with similar effectiveness to younger patients
- Importantly, this study highlights the necessity of tailoring treatment approaches according to geriatric assessments (G8 and DIALOG G-CODE) rather than relying solely on chronological age
- Frailty and social support may influence treatment continuation and patient outcomes
- As the landscape of cancer care evolves, integrating comprehensive geriatric assessments and support systems will be essential in optimizing treatment strategies for older and frail patients, enhancing their QoL and overall satisfaction with care

Limitations

- There is the potential for missing, inaccurate, or incomplete data
- Patient selection and the diagnostic or monitoring procedures used are those applied per the usual treatment paradigm of the treating physician rather than being dictated by a protocol
- Adverse events may be underreported in real-world studies
- No control arm, which limits contextualization to other treatments
- The findings from the PalomAGE study may not be generalized to other patients

*Observational analyses are not intended for direct comparisons with clinical trials.
Observational analyses are designed to evaluate associations among variables and cannot establish causality.*

1L=first-line; ABC=advanced/metastatic breast cancer; AE=adverse event; ET=endocrine therapy; G8=geriatric assessment; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; QoL=quality of life; PAL=palbociclib.

Carola E, et al. SABCS 2024. Poster P2-07-17.

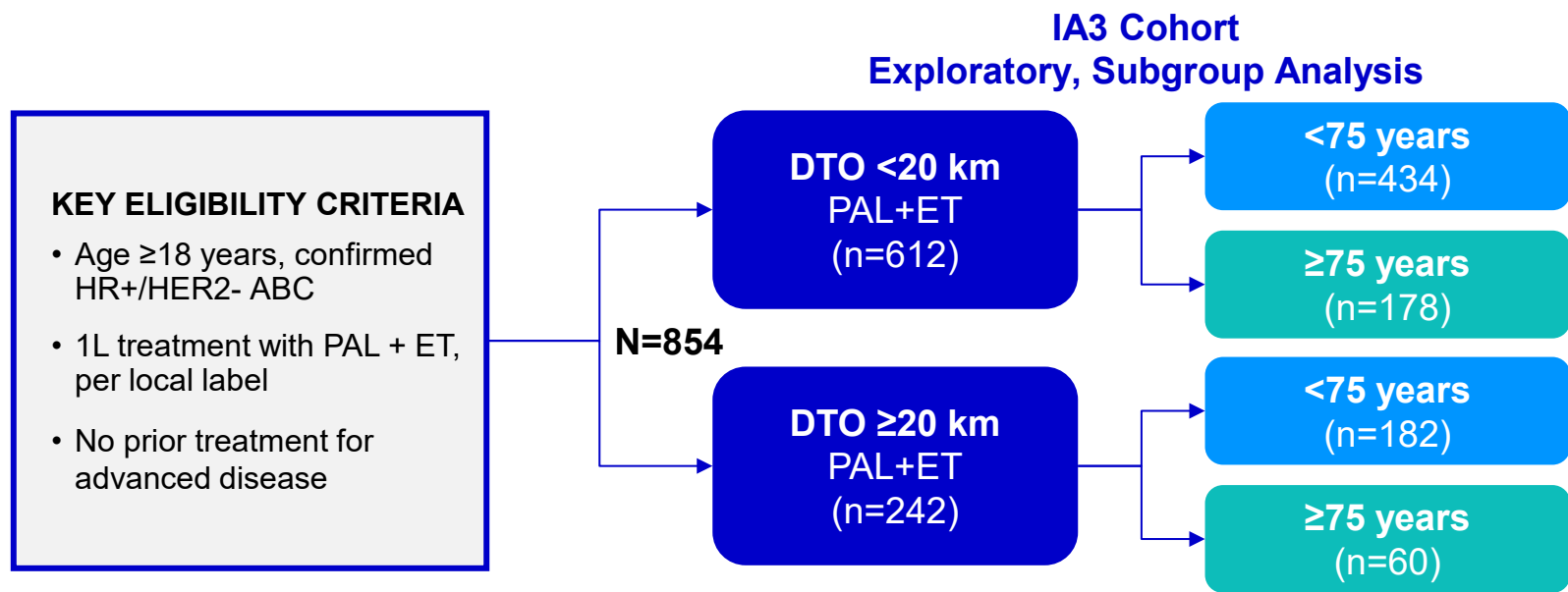
Distance to Treating Oncologist as Potential Prognostic Real-World-Factor for Patients With HR+/HER2- Advanced Breast Cancer—Results From the Non-Interventional Study **PERFORM**

Lux MP, et al. SABCS 2024. Poster P4-07-20.

PERFORM: Study Design (IA3 Cohort)

Real-world, prospective, noninterventional study conducted in ≈240 urban and rural study sites across Germany and Austria

Objective: To explore whether distance to treating oncologist (DTO) in patients with HR+/HER2- ABC influences toxicity, therapy management, and disease progression in the PERFORM study third interim analysis (IA3)*



Primary Outcomes

- 1L rwPFS[†]

Secondary Outcomes

- Treatment patterns
- Effectiveness (including outcomes in second- and third-line treatment)
- Treatment expectation/satisfaction
- Potential impact of socioeconomic status on outcomes
- QoL
- Patterns of biomarker analyses and genetic testing²

Statistical Analyses

- rwPFS analyses are based on KM estimation
- Multivariable or other types of analyses controlling for potential confounders have not been done

*More than 1400 patients with HR+/HER2- ABC treated with palbociclib plus ET in the 1L setting are currently enrolled. Three years after the first patient enrollment, the IA3 was conducted with a data cutoff in September 2023. Demographics, disease characteristics, and socioeconomic information, including DTO, are documented at baseline. [†]rwPFS is defined as the start of 1L treatment to first progression or death, whichever comes first. Patients without tumor progression or death at the time of analysis are censored at their last date of last contact or at the start date of a 2L therapy, whichever comes first.
1L=first-line; 2L=second-line; ABC=advanced breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; KM=Kaplan-Meier; PAL=palbociclib; QoL=quality of life; rwPFS=real-world progression-free survival.

1. Lux MP, et al. SABCS 2024. Poster P4-07-20.
2. Lux MP, et al. *Future Oncol.* 2022;18(36):3971-3982.

PERFORM: IA3—Patient and Socioeconomic Characteristics* (1 of 2)

Characteristics	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
Age at start of 1L treatment, years						
Median (Q1-Q3)	68.60 (59.04-76.83)	63.00 (55.78-69.34)	79.41 (77.56-81.97)	66.53 (58.18-74.70)	62.06 (55.81-68.09)	79.50 (77.74-82.32)
Sex, n (%)						
Female	607 (99.2)	431 (99.3)	176 (98.9)	240 (99.2)	181 (99.5)	59 (98.3)
Male	5 (0.8)	3 (0.7)	2 (1.1)	2 (0.8)	1 (0.5)	1 (1.7)
Menopausal status, n (%)						
Pre-/perimenopausal	45 (7.3)	45 (10.3)	0 (0.0)	19 (7.8)	19 (10.4)	0 (0.0)
Postmenopausal	562 (91.8)	386 (88.9)	176 (98.9)	221 (91.3)	162 (89.0)	59 (98.3)
ECOG PS, n (%)						
0	285 (46.6)	228 (52.5)	57 (32.0)	122 (50.4)	98 (53.8)	24 (40.0)
1	249 (40.7)	167 (38.5)	82 (46.1)	90 (37.2)	61 (33.5)	29 (48.3)
≥2	61 (10.0)	29 (6.7)	32 (18.0)	26 (10.7)	19 (10.4)	7 (11.7)
No assessment done/missing	17 (2.8)	10 (2.3)	7 (4.0)	4 (1.7)	4 (2.2)	0 (0.0)

*At inclusion by distance to treating oncologist and age.

1L=first-line; DTO=distance to treating oncologist; ECOG PS=Eastern Cooperative Oncology Group performance status; IA3=third interim analysis; Q=quartile.

Lux MP, et al. SABCS 2024. Poster P4-07-20.

PERFORM: IA3—Patient and Socioeconomic Characteristics* (2 of 2)

Characteristics	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
Occupation, n (%)						
Employed full-time	94 (15.4)	93 (21.4)	1 (0.6)	41 (16.9)	41 (22.5)	0 (0.0)
Employed part-time†	74 (12.1)	72 (16.6)	2 (1.1)	31 (12.8)	30 (16.5)	1 (1.7)
Not gainfully employed/retired	383 (62.6)	227 (52.3)	156 (87.6)	152 (62.8)	99 (54.4)	53 (88.3)
Missing/not derivable	61 (10.0)	42 (9.7)	19 (10.7)	18 (7.4)	12 (6.6)	6 (10.0)
No. of additional persons in household, n (%)						
0	250 (40.8)	148 (34.1)	102 (57.3)	72 (29.8)	47 (25.8)	25 (41.7)
≤3 other persons	314 (51.3)	248 (57.1)	66 (37.1)	147 (60.7)	116 (63.7)	31 (51.7)
>3 other persons	17 (2.8)	15 (3.5)	2 (1.1)	7 (2.9)	7 (3.8)	0 (0.0)
Missing/not derivable	31 (5.1)	23 (5.3)	8 (4.5)	16 (6.6)	12 (6.6)	4 (6.7)
No. of children, n (%)						
0	92 (15.0)	79 (18.2)	13 (7.3)	35 (14.5)	30 (16.5)	5 (8.3)
1 or 2	383 (62.6)	272 (62.7)	111 (62.4)	145 (59.9)	110 (60.4)	35 (58.3)
≥3	101 (16.5)	62 (14.3)	39 (21.9)	50 (20.7)	32 (17.6)	18 (30.0)
Missing	36 (5.9)	21 (4.8)	15 (8.4)	12 (5.0)	10 (5.5)	2 (3.3)

*At inclusion by distance to treating oncologist and age. †Including primary/secondary occupation. DTO=distance to treating oncologist; IA3=third interim analysis.

PERFORM: IA3—Tumor Characteristics (1 of 2)*

Characteristics	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
Time since initial diagnosis, years						
Median (Q1-Q3)	3.46 (0.13-10.89)	3.28 (0.13-10.07)	4.00 (0.11-13.05)	2.36 (0.10-9.18)	2.97 (0.13-8.78)	0.16 (0.09-9.68)
Tumor stage, n (%)						
Locoregionally advanced	31 (5.1)	15 (3.5)	16 (9.0)	16 (6.6)	11 (6.0)	5 (8.3)
Metastatic	580 (94.8)	418 (96.3)	173 (91.0)	225 (93.0)	171 (94.0)	54 (90.0)
Missing	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.4)	0 (0.0)	1 (1.7)
De novo ABC, n (%)						
Yes	223 (36.4)	153 (35.3)	70 (39.3)	102 (42.1)	67 (36.8)	35 (58.3)
No	389 (63.6)	281 (64.7)	108 (60.7)	140 (57.9)	115 (63.2)	25 (41.7)

- Tumor stages seem largely comparable among the subgroups, irrespective of age
- Patients with a DTO ≥20 km appear to be slightly more likely to present with de novo ABC than patients with a DTO <20 km (42.1% vs 36.4%)

*At inclusion by distance to treating oncologist and age.
ABC=advanced breast cancer; DTO=distance to treating oncologist; IA3=third interim analysis; Q=quartile.

PERFORM: IA3—Tumor Characteristics (2 of 2)*

Characteristics	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
No. of metastatic sites present, n (%)						
0†	46 (7.5)	27 (6.2)	19 (10.7)	26 (10.7)	18 (9.9)	8 (13.3)
1	378 (61.8)	269 (62.0)	109 (61.2)	139 (57.4)	104 (57.1)	35 (58.3)
2	114 (18.6)	78 (18.0)	36 (20.2)	54 (22.3)	42 (23.1)	12 (20.0)
3	57 (9.3)	46 (10.6)	11 (6.2)	15 (6.2)	12 (6.6)	3 (5.0)
≥4	17 (2.8)	14 (3.2)	3 (1.7)	8 (3.3)	6 (3.3)	2 (3.3)
Disease site, n (%)						
Visceral‡	286 (46.7)	209 (48.2)	77 (43.3)	106 (43.8)	78 (42.9)	28 (46.7)
Nonvisceral only§ (excl. bone only)	69 (11.3)	41 (9.4)	28 (15.7)	29 (12.0)	23 (12.6)	6 (10.0)
Bone only	211 (34.5)	157 (36.2)	54 (30.3)	81 (33.5)	63 (34.6)	18 (30.0)
No. metastases present at inclusion†	46 (7.5)	27 (6.2)	19 (10.7)	26 (10.7)	18 (9.9)	8 (13.3)

- Number of metastatic sites seem largely comparable among the subgroups, irrespective of age

*At inclusion by distance to treating oncologist and age. †Patients with locoregionally advanced disease or metastases, that were removed before inclusion (eg, radiation, surgery). ‡Visceral sites: all metastatic sites excluding nonvisceral sites and bone only (eg, lung, liver, pleura, peritoneum, brain). §Nonvisceral sites (excluding bone only): lymph nodes (distant, regional), skin, soft tissue. DTO=distance to treating oncologist; IA3=third interim analysis.

PERFORM: IA3—Effectiveness¹

rwPFS Rates

	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
1L rwPFS						
Events, n (%)	208 (34.0)	154 (35.5)	54 (30.3)	92 (38.0)	74 (40.7)	18 (30.0)
6-month rate, % (95% CI)	85.9 (82.8-88.4)	85.5 (81.8-88.6)	86.7 (80.6-90.9)	82.7 (77.2-86.9)	81.9 (75.4-86.9)	84.8 (72.8-91.8)
12-month rate, % (95% CI)	73.2 (69.2-76.7)	72.3 (67.6-76.5)	75.2 (67.7-81.2)	71.0 (64.4-76.6)	69.9 (62.2-76.3)	74.3 (60.2-84.0)
18-month rate, % (95% CI)	64.2 (59.8-68.3)	61.9 (56.5-66.8)	70.1 (61.9-76.8)	59.8 (52.2-66.6)	58.3 (49.5-66.1)	65.1 (48.7-77.4)
24-month rate, % (95% CI)	55.1 (49.7-60.1)	52.5 (45.9-58.7)	61.5 (52.0-69.7)	46.7 (37.1-55.7)	45.7 (35.6-55.2)	32.5 (2.0-72.5)

- The lowest 24-month PFS rate of 32.5% was observed in patients ≥75 years with DTO ≥20 km, while the overall 24-month PFS rate in the DTO subgroups <20 km and ≥20 km, amounted to 55.1% and 46.7%, respectively*
- Median follow-up time was 18.6 months²

*Observational analyses are not intended for direct comparisons with clinical trials.
Observational analyses are designed to evaluate associations among variables and cannot establish causality.*

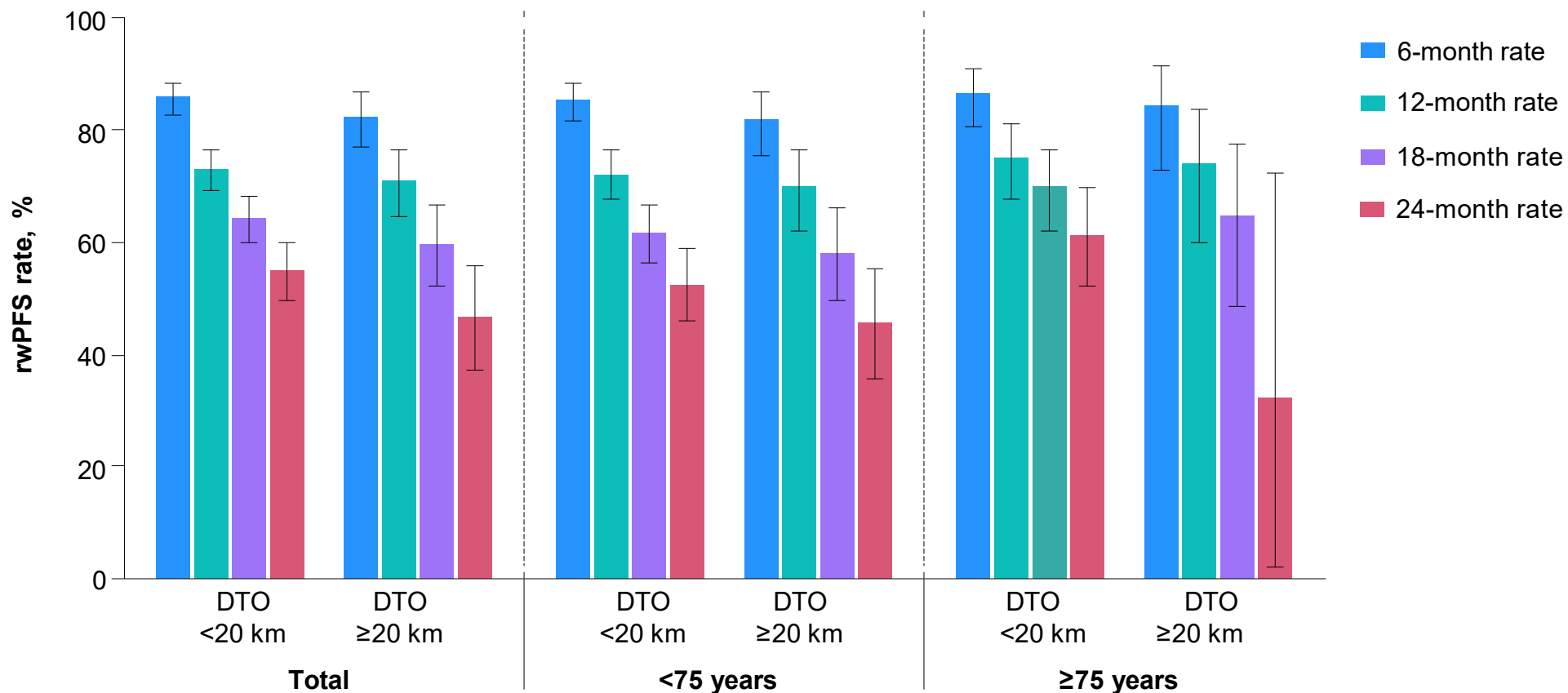
***This observation might be especially influenced by low sample size, limited follow-up time, and potential confounders and, therefore, requires further investigation.**

1L=first-line; DTO=distance to treating oncologist; IA3=third interim analysis; rwPFS=real-world progression-free survival.

1. Lux MP, et al. SABCS 2024. Poster P4-07-20.
2. Pfeiler G, et al. ESMO 2024. Poster 356.

PERFORM: IA3—Effectiveness

rwPFS Rates of Age-Stratified Subgroups DTO <20 km and DTO ≥20 km



*Observational analyses are not intended for direct comparisons with clinical trials.
Observational analyses are designed to evaluate associations among variables and cannot establish causality.*

DTO=distance to treating oncologist; IA3=third interim analysis; rwPFS=real-world progression-free survival.

Lux MP, et al. SABCS 2024. Poster P4-07-20.

PERFORM: IA3—Reasons for End of 1L Treatment

	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
Reasons for end of 1L treatment, n (%)						
PD	172 (28.1)	133 (30.6)	39 (21.9)	75 (31.0)	61 (33.5)	14 (23.3)
SAE	36 (5.9)	21 (4.8)	15 (8.4)	14 (5.8)	8 (4.4)	6 (10.0)
Lost to follow-up	21 (3.4)	16 (3.7)	5 (2.8)	9 (3.7)	6 (3.3)	3 (5.0)
Withdrawal of informed consent	8 (1.3)	5 (1.2)	3 (1.7)	7 (2.9)	7 (3.8)	0 (0.0)
Other	23 (3.8)	17 (3.9)	6 (3.4)	10 (4.1)	7 (3.8)	3 (5.0)
Still under treatment	352 (57.5)	242 (55.8)	110 (61.8)	127 (52.5)	93 (51.1)	34 (56.7)

- 34.0% of patients in the DTO <20 km and 38.0% in the DTO ≥20 km subgroups experienced disease progression or death

1L=first-line; DTO=distance to treating oncologist; IA3=third interim analysis; PD=progressive disease; SAE=serious adverse event.

Lux MP, et al. SABCS 2024. Poster P4-07-20.

PERFORM: IA3—Safety (1 of 2)

Adverse Events and Therapy Modifications

	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
AEs, n (%)						
TEAE	519 (84.8)	361 (83.2)	158 (88.8)	209 (86.4)	158 (86.8)	51 (85)
Serious TEAE	168 (27.5)	112 (25.8)	56 (31.5)	65 (26.9)	46 (25.3)	19 (31.7)
Grade 1/2 TEAE	456 (74.5)	316 (72.8)	140 (78.7)	182 (75.2)	138 (75.8)	44 (73.3)
Grade 3/4 TEAE	303 (49.5)	206 (47.5)	97 (54.5)	121 (50)	86 (47.3)	35 (58.3)
TEAE leading to discontinuation of PAL	59 (9.6)	41 (9.4)	18 (10.1)	25 (10.3)	17 (9.3)	8 (13.3)
PAL-related AE	386 (63.1)	259 (59.7)	127 (71.3)	157 (64.9)	115 (63.2)	42 (70)
PAL-related SAE	20 (3.3)	13 (3.0)	7 (3.9)	7 (2.9)	4 (2.2)	3 (5.0)
PAL-related grade 3/4 AE	200 (32.7)	143 (32.9)	57 (32)	77 (31.8)	52 (28.6)	25 (41.7)
PAL-related AE leading to discontinuation of PAL	24 (3.9)	17 (3.9)	7 (3.9)	7 (2.9)	2 (1.1)	5 (8.3)

- A comparable relative frequency of AEs was observed for PERFORM patients, regardless of DTO

AE=adverse event; DTO=distance to treating oncologist; IA3=third interim analysis; PAL=palbociclib; SAE=serious adverse event; TEAE=treatment-emergent adverse event.

Lux MP, et al. SABCS 2024. Poster P4-07-20

PERFORM: IA3—Safety (2 of 2)

Adverse Events and Therapy Modifications

	DTO <20 km			DTO ≥20 km		
	Total (n=612)	<75 years (n=434)	≥75 years (n=178)	Total (n=242)	<75 years (n=182)	≥75 years (n=60)
Therapy modifications for palbociclib, n (%)*						
Yes	450 (73.5)	312 (71.9)	138 (77.5)	173 (71.5)	127 (69.8)	46 (76.7)
No	162 (26.5)	122 (28.1)	40 (22.5)	69 (28.5)	55 (30.2)	14 (23.3)
Yes, Dose modified	243 (39.7)	165 (38.0)	78 (43.8)	87 (36.0)	57 (31.3)	30 (50.0)

- Therapy modifications for PAL treatment occurred with a comparable frequency among subgroups with a DTO of <20 km or ≥20 km, respectively (73.5% vs 71.5%)
- In both subgroups, ≈10% of patients discontinued PAL-based therapy due to TEAEs
- 3.9% of patients with a DTO of <20 km and 2.9% of patients with a DTO of ≥20 km discontinued therapy due to PAB-related AEs

*Including dose modifications and interruptions within/between cycles or skipped cycles.
 AE=adverse event; DTO=distance to treating oncologist; IA3=third interim analysis; PAL=palbociclib; TEAE=treatment-emergent adverse event.

PERFORM: IA3—Authors' Conclusions and Study Limitations

Conclusions

- These results generally support the use of PAL plus ET as a relevant 1L therapy option regardless of age and DTO in patients with HR+/HER2- ABC
- Moreover, these results indicate that the DTO (travel burden) might be a relevant real-world factor influencing outcome and warrants further analyses including patient-reported outcomes with longer follow-up as well as external validation

Limitations

- Results and conclusions are not necessarily transferable to other countries and healthcare systems
- Socioeconomic/demographic factors, such as DTO, are documented only at one time point (inclusion)
- Generally, further follow-up is needed
- When examining small subgroups of patients without controlling for other variables, it is crucial to acknowledge that factors such as age, a higher percentage of visceral metastases or recurrent disease, and other potentially confounding variables may significantly influence outcome and safety
- Therefore, all provided analyses must be regarded as purely descriptive and exploratory, as they do not allow causal conclusions
- Hypotheses derived from these results warrant further confirmatory investigation

*Observational analyses are not intended for direct comparisons with clinical trials.
Observational analyses are designed to evaluate associations among variables and cannot establish causality.*

1L=first-line; ABC=advanced breast cancer; DTO=distance to treating oncologist; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IA3=third interim analysis; PAL=palbociclib.

Lux MP, et al. SABCS 2024. Poster P4-07-20.

Primary results of the randomised phase IV trial comparing first-line ET plus palbociclib vs standard mono-chemotherapy in women with high risk HER2-/HR+ metastatic breast cancer and indication for chemotherapy – **PADMA study**

Loibl S, et al. SABCS 2024. Oral presentation LB1-03.

PADMA: Study Design¹

Prospective, randomized, open-label, multicenter, phase IV trial

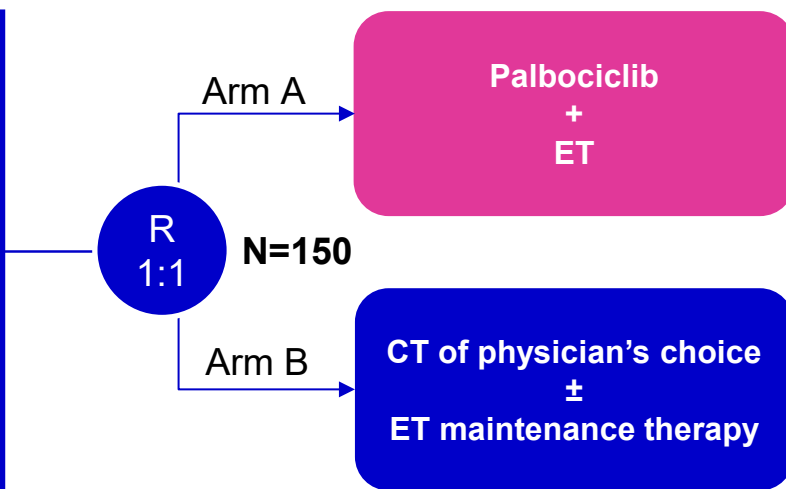
Objective: To compare CDK4/6 inhibitor + ET with standard monochemotherapy ± maintenance ET as first-line therapy in patients with high-risk mBC and a chemotherapy indication.

PATIENT POPULATION

- HR+/HER2- mBC
- Female or male
- Indicated for monochemotherapy
- No prior treatment for metastatic/relapsed disease
- No asymptomatic bone-only, oligometastatic disease
- No uncontrolled/untreated CNS metastases
- Life expectancy >6 months

Stratification

- Endocrine resistant vs endocrine sensitive
- Symptomatic vs asymptomatic metastatic disease



ET with palbociclib: AI or fulvestrant ± GnRHa
ET maintenance: tamoxifen, AI or fulvestrant ± GnRHa
CT: paclitaxel, capecitabine, epirubicin, or vinorelbine

Primary Endpoint

- TTF: defined as time from randomization to discontinuation of treatment due to disease progression, treatment toxicity, patient's preference, or death

Secondary Endpoints

- PFS
- OS
- Safety, tolerability, treatment adherence
- TFST and further time-to-event endpoints
- Patient-reported QoL
- DMTI: call tracking/geofencing with passive collection of information about frequency and duration of phone calls/visits to study site, respectively

Due to slow accrual, the study was stopped in 12/2023 with 130 patients and 100 events without major loss of power with an accrual duration of 70 months and follow-up period of 8 months⁴

Data cutoff: August 1, 2024.

The PALOMA trials did not compare palbociclib+ET with monochemotherapy.^{2,3}

Cross-trial comparisons are unreliable and likely to be confounded due to differences in study design and patient populations.

AI=aromatase inhibitor; CDK4/6=cyclin-dependent kinase 4/6; CNS=central nervous system; CT=chemotherapy; DMTI=Daily Monitoring of Treatment Impact; ET=endocrine therapy; FACT-B=Functional Assessment of Cancer Therapy—Breast; GnRHa=gonadotropin-releasing hormone agonists; HER=human epidermal growth factor receptor; HR=hormone receptor; mBC=metastatic breast cancer; OS=overall survival; PFS=progression-free survival; QoL=quality of life; R=randomization; TFST=time to first subsequent treatment; TTF=time to treatment failure.

1. Loibl S, et al. SABCS 2024. Oral presentation LB1-03
 2. Finn RS, et al. *N Engl J Med.* 2016;375:1925-1936
 3. Turner NC, et al. *N Engl J Med.* 2015;373:209-219 4. Data on file

PADMA: Baseline Characteristics

	Palbociclib+ET N=61	CT-based N=59	Overall N=120
Median age (range), years	63 (42.0-85.0)	62 (31.0-80.0)	62 (31.0-85.0)
Postmenopausal status, n (%)	54 (88.5)	52 (88.1)	106 (88.3)
Liver metastases, n (%)	28 (45.9)	22 (37.3)	50 (41.7)
Endocrine resistant, n (%)*	17 (27.9)	21 (35.6)	38 (31.7)
Metastasis at initial diagnosis, n (%)	20 (33.3)	24 (40.7)	44 (37.0)
Prior (neo)adjuvant CT, n (%)	29 (47.5)	25 (42.4)	54 (45.0)
HER2-low (IHC 1-2), n (%)†	41 (73.2)	30 (58.8)	71 (66.4)
Pathogenic variants (tissue), n (%)‡			
- <i>PIK3CA</i>	11 (18.0)	16 (27.1)	27 (22.5)
- <i>BRCA1/2</i>	3 (4.9)	4 (6.8)	7 (5.8)
- <i>ESR1</i>	1 (1.6)	1 (1.7)	2 (1.7)

*According to clean data; endocrine resistant=relapse on or within 12 months of end of adjuvant ET.

†From metastasis (N=47), otherwise if available from initial diagnosis (N=24).

‡Tested in 81 patients.

BRCA=breast cancer gene; CT=chemotherapy; ESR1=estrogen receptor 1; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry; PIK3CA=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

PADMA: Study Treatment

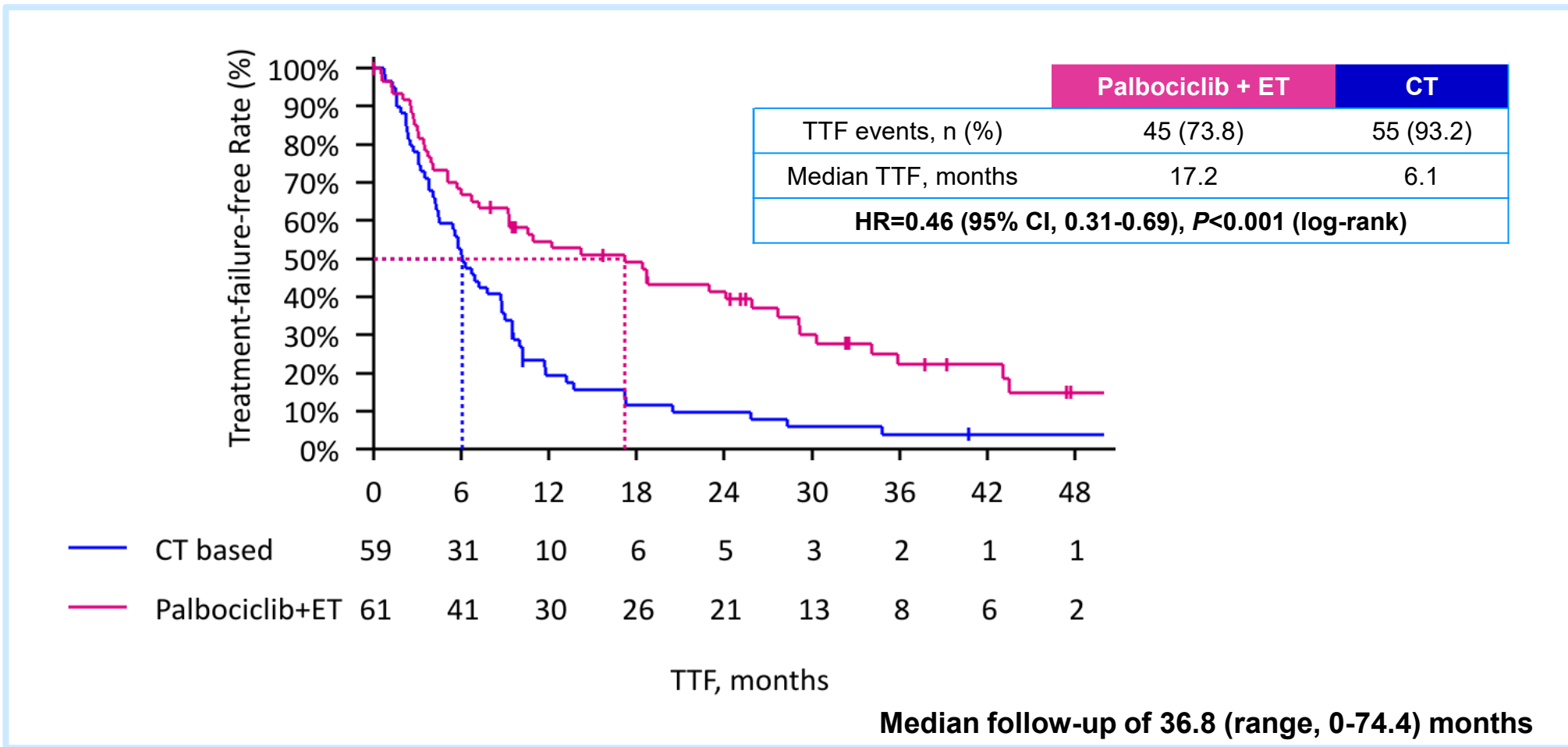
	Palbociclib + ET (n=62)*	CT based (n=58)
Type of treatment of physician's choice CT, n (%)		
Capecitabine	—	40 (69.0)
Paclitaxel	—	17 (29.3)
Vinorelbine	—	1 (1.7)
Received ET maintenance after CT, n (%)	—	13 (22.4)
Type of ET, n (%)†		
Aromatase inhibitor	48 (77.4)	9 (15.5)
Tamoxifen	—	3 (5.2)
Fulvestrant	14 (22.6)	1 (1.7)
Median duration palbociclib or CT (range), weeks	51.0 (1.0-322.0)	19.5 (2.0-122.0)

*One patient who was randomized to the CT-based arm received palbociclib + ET.

†Pre- or perimenopausal women receiving AI or fulvestrant required GnRH analogue or ovarian ablation.

AI=aromatase inhibitor; CT=chemotherapy; ET=endocrine therapy; GnRH=gonadotropin-releasing hormone.

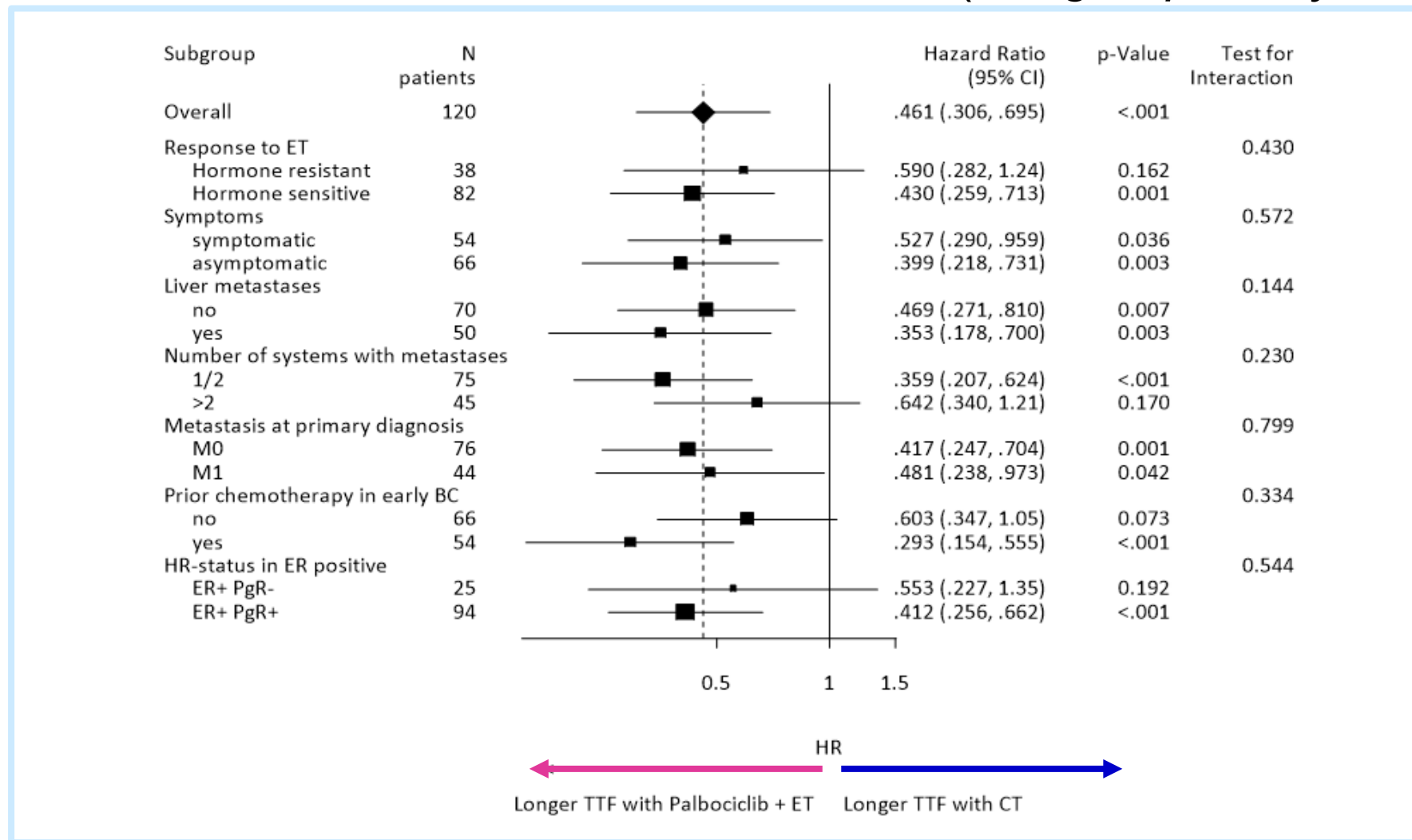
PADMA: Effectiveness—Time to Treatment Failure (*Primary Endpoint*)



CI=confidence interval; CT=chemotherapy; ET=endocrine therapy; HR=hazard ratio; TTF=time to treatment failure.

Loibl S, et al. SABCS 2024. Oral presentation LB1-03.

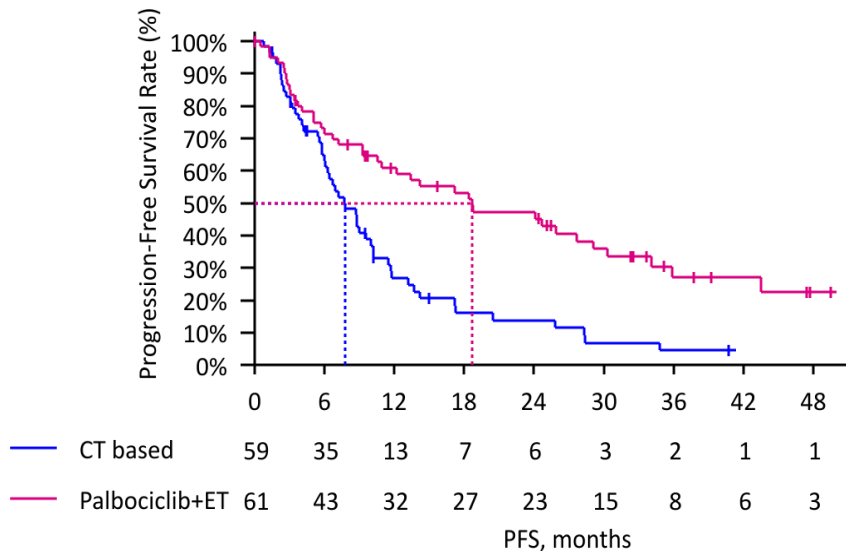
PADMA: Effectiveness—Time to Treatment Failure (*Subgroup Analyses*)



Small patient numbers can be a limitation of subgroup analyses. These analyses may not be powered to detect significant differences and were not designed to compare across subgroups. Any comparison between groups should be approached with caution.
 BC=breast cancer; CI=confidence interval; CT=chemotherapy; ER=estrogen receptor; ET=endocrine therapy; HR=hormone receptor; PgR=progesterone receptor; TTF=time to treatment failure.

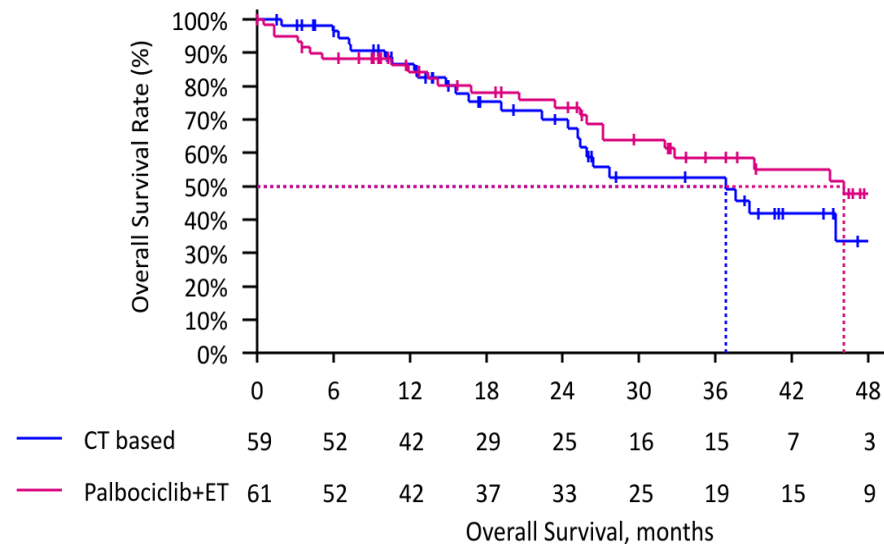
PADMA: Effectiveness—PFS and OS (Secondary Endpoints)

Progression-Free Survival



	Palbociclib + ET	CT
PFS events, n (%)	40 (65.6)	50 (84.7)
Median PFS, months	18.7	7.8
HR=0.45, (95% CI: 0.29-0.70), P<0.001 (log-rank)		

Overall Survival



	Palbociclib + ET	CT
OS events, n (%)	25 (41.0)	24 (40.7)
Median OS, months	46.1	36.8
Proportional hazard cannot be assumed		

CI=confidence interval; CT=chemotherapy; ET=endocrine therapy; HR=hazard ratio; OS=overall survival; PFS=progression-free survival.

Loibl S, et al. SABCS 2024. Oral presentation LB1-03.

PADMA: Safety—Treatment-Related Adverse Events (*Secondary Endpoint*)

	Palbociclib+ET (n=62)		CT based (n=58)	
	Any grade	Grades 3-4	Any grade	Grades 3-4
Any TRAE, n (%)	60 (96.8)	37 (59.7)	55 (94.8)	16 (27.6)
Any hematological TRAE, n (%)	60 (96.8)	34 (54.8)	34 (58.6)	4 (6.9)
Any nonhematological TRAE, n (%)	51 (82.3)	12 (19.4)	54 (93.1)	13 (22.4)
Treatment-related SAE, n (%)	7 (11.3)	5 (8.1)	6 (10.3)	6 (10.3)
Treatment-related death, n (%)	1 (1.6)	—	0 (0.0)	—

- Hematological toxicity significantly higher in the palbociclib + ET arm than the CT-based arm (96.8% vs 58.6%; $P < 0.001$); comparable nonhematological toxicity
- One treatment-related death (septic shock; palbociclib + ET arm)

CT=chemotherapy; ET=endocrine therapy; SAE=serious adverse event; TRAE=treatment-related adverse event.

Loibl S, et al. SABCS 2024. Oral presentation LB1-03.

PADMA: Authors' Conclusions¹

- The PADMA trial in high-risk* HR+/HER2- mBC met its primary endpoint (TTF) and showed a statistically significant and clinically meaningful improvement in TTF and PFS for palbociclib + ET over mono-CT (± ET maintenance) as first-line therapy
 - Median TTF: 17.2 vs 6.1 months; hazard ratio=0.46 (95% CI, 0.31-0.69), $P<0.001$
 - Median PFS: 18.7 vs 7.8 months; hazard ratio=0.45 (95% CI, 0.29-0.70), $P<0.001$
- After a median follow-up of 36.8 months, there was a numerical trend for an improved OS for palbociclib + ET: 46.1 vs 36.8 months
- No new safety signals were observed
- These results support existing international guidelines advocating the use of ET + CDK4/6i as standard first-line treatment for patients with HR+/HER2- mBC

The PALOMA trials did not compare palbociclib + ET with monochemotherapy.^{2,3} Cross-trial comparisons are unreliable, as they are likely to be confounded due to differences in study design and patient populations.

*Patients were considered high risk if they were candidates suitable for randomization for monochemotherapy treatment.

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; CI=confidence interval; CT=chemotherapy; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; mBC=metastatic breast cancer; OS=overall survival; PFS=progression-free survival; TTF=time to treatment failure.

1. Loibl S, et al. SABCS 2024. Oral presentation LB1-03
2. Finn RS, et al. *N Engl J Med.* 2016;375:1925-1936
3. Turner NC, et al. *N Engl J Med.* 2015;373:209-219

Comparative Overall Survival of CDK4/6 Inhibitors Plus an Aromatase Inhibitor in HR+/HER2- Metastatic Breast Cancer in the US Real-World Setting (**P-VERIFY**)*

Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03.

*Presented at an SABCS Poster Spotlight Session.

P-VERIFY: Study Background and Rationale

- The combination of a CDK4/6 inhibitor with endocrine therapy is a standard-of-care, 1L treatment for patients with HR+/HER2- mBC¹
- Palbociclib was the first CDK4/6 inhibitor approved in the US in 2015, followed by ribociclib and abemaciclib in 2017²⁻⁴
 - OS was a secondary endpoint in all 3 pivotal 1L CDK4/6 inhibitor RCTs: **palbociclib + LET did not show a statistically significant OS difference in PALOMA-2⁵**; abemaciclib + NSAI did not show a statistically significant OS difference in MONARCH-3⁶; ribociclib + LET demonstrated a statistically significant OS difference in MONALEESA-2⁷
- There are no CDK4/6 head-to-head RCTs. However, several RW studies have attempted to evaluate comparative effectiveness between the 3 CDK4/6 inhibitors⁸⁻¹⁷
 - Findings were inconsistent across these studies, limited by small sample sizes and short follow-up
 - Most did not show significant differences in rwPFS and/or OS among the CDK4/6 inhibitors
- Large-scale RW comparative studies with longer follow-up are needed to further elucidate the relative effectiveness of the 3 approved CDK4/6 inhibitors

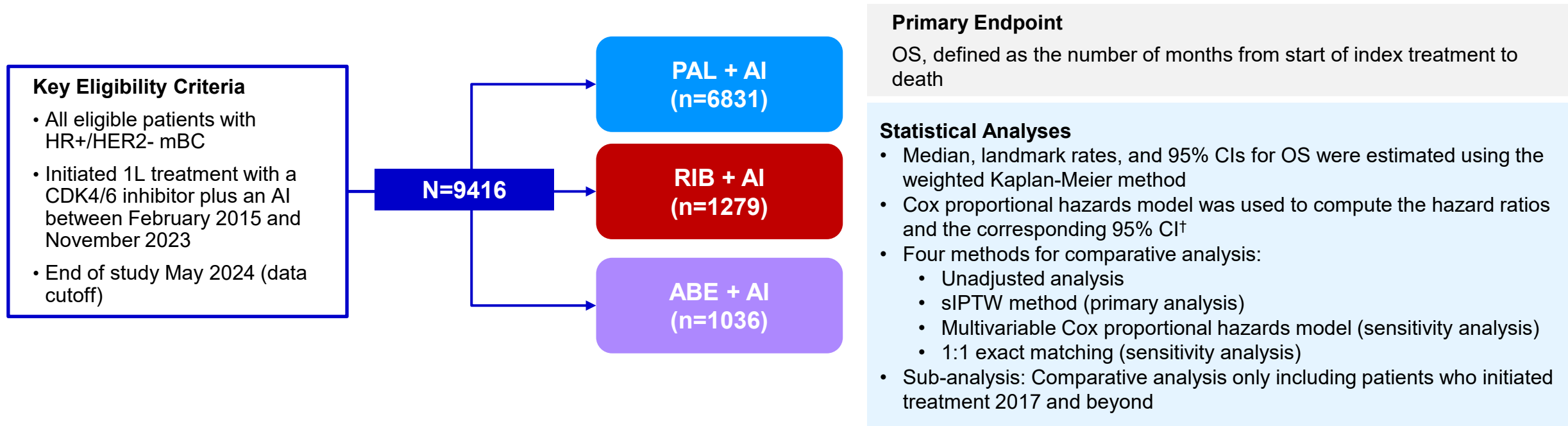
1L=first-line; CDK4/6=cyclin-dependent kinase 4/6; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; LET=letrozole; mBC=metastatic breast cancer; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; RCT=randomized controlled trial; RW=real-world; rwPFS=real world progression-free survival.

1. Gradishar WJ, et al. *J Natl Compr Canc Netw*. 2023;21(6):594-608. 2. Kisqali (ribociclib). Prescribing information. Novartis; 2024. Accessed November 22, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/209092s019lbl.pdf. 3. Ibrance (palbociclib). Prescribing information. Pfizer; 2023. Accessed November 22, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/212436s005s006lbl.pdf. 4. Verzenio (abemaciclib). Prescribing information. Lilly; 2023. Accessed November 22, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208716s010s011lbl.pdf. 5. Slamon DJ, et al. *J Clin Oncol*. 2024;42(9):994-1000. 6. Goetz MP, et al. *Ann Oncol*. 2024;35(8):718-727. 7. Hortobagyi GN, et al. *N Engl J Med*. 2022;386(10):942-950. 8. Cejuela M, et al. *Int J Mol Sci*. 2023;24(10):8448. 9. Kahraman S, et al. *Future Oncol*. 2023;19(10):727-736. 10. Buller W, et al. *J Oncol Pharm Pract*. 2023;29(8):1825-1835. 11. Vernieri C, et al. *J Clin Oncol*. 2024;42:1014. 12. Gehrchen ML, et al. *BJC Reports*. 2024;2(1):44. 13. Abdallah HMA, et al. *Ann Oncol*. 2023;34:S369-S370. 14. Thill M, et al. *Cancer Res*. 2024;84(suppl 9):PO1-04-12. 15. Al-Ziftawi NH, et al. *Front Oncol*. 2023;13:1203684. 16. Miron AI, et al. *Diagnostics (Basel)*. 2023;13(11):1938. 17. Tang H, et al. *Cancers (Basel)*. 2023;15(21):5164.

P-VERIFY: Study Design

Retrospective comparative effectiveness study¹

Objective: To compare OS in patients receiving palbociclib, ribociclib, or abemaciclib in combination with an AI as 1L treatment for HR+/HER2-mBC in routine clinical practice in the US by use of the US nationwide Flatiron Health EHR deidentified longitudinal database*



- Patients were followed from the start of index treatment (palbociclib + AI, ribociclib + AI, or abemaciclib + AI) to the end of May 2024 (data cutoff), death, or last medical activity, whichever came first
- Date of death was a consensus mortality endpoint based on EHR, Social Security Death Index, and obituary data, validated against the National Death Index
- Patients still alive were censored at the end of the study

*The study included patient-level data originating from ≈280 US cancer clinics (≈800 sites of care) and curated via technology-enabled abstraction.

[†]Variables in the propensity score model included sex, age, race, practice type, ECOG performance status, disease stage at initial diagnosis, visceral metastasis, bone-only metastasis, number of disease sites, disease-free interval (from initial breast cancer diagnosis to mBC diagnosis).²

1L=first-line; ABE=abemaciclib; AI=aromatase inhibitor; CDK4/6=cyclin-dependent kinase 4/6; CI=confidence interval; EHR=electronic health record; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; mBC=metastatic breast cancer; OS=overall survival; PAL=palbociclib; RIB=ribociclib; sIPTW=stabilized inverse probability of treatment weighting.

1. Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03. 2. Pfizer. Data on file.

P-VERIFY: Patient Characteristics After sIPTW (1 of 4)

- After sIPTW, baseline demographics and clinical characteristics were generally balanced between the 3 groups (standardized difference <0.1)

Characteristic	Cohort			Standardized difference		
	PAL + AI (n=6832)	RIB + AI (n=1274)	ABE + AI (n=1038)	RIB + AI vs PAL + AI	ABE + AI vs PAL + AI	ABE + AI vs RIB + AI
Age at mBC diagnosis, years						
Mean (SD)	65.0 (11.7)	64.6 (12.0)	64.7 (12.1)	-0.0297	-0.0198	0.0097
Median (IQR)	66.0 (17.0)	66.0 (17.0)	66.0 (17.0)			
Sex, n (%)						
Male	70 (1.0)	11 (0.9)	11 (1.1)	-0.0178	0.0068	0.0245
Female	6762 (99.0)	1263 (99.1)	1026 (98.9)			
Race, n (%)						
White	4272 (62.5)	797 (62.6)	654 (63.0)	0.0008	0.0093	0.0086
Black	638 (9.3)	117 (9.2)	94 (9.1)	-0.0063	-0.0081	-0.0018
Other	1922 (28.1)	360 (28.3)	290 (27.9)	0.0032	-0.0048	-0.0081
Practice type, n (%)						
Community	5782 (84.6)	1085 (85.2)	872 (84.0)	0.0154	-0.0169	-0.0323
Academic	1050 (15.4)	189 (14.8)	166 (16.0)			

The balance in these baseline characteristics was assessed using a standardized mean differences approach, with values ≥0.1 indicating a nonnegligible imbalance. ABE=abemaciclib; AI=aromatase inhibitor; IQR=interquartile range; mBC=metastatic breast cancer; PAL=palbociclib; RIB=ribociclib; SD=standard deviation; sIPTW=stabilized inverse probability of treatment weighting.

Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03.

P-VERIFY: Patient Characteristics After sIPTW (2 of 4)

- After sIPTW, baseline demographics and clinical characteristics were generally balanced between the 3 groups (standardized difference <0.1)

Characteristic	Cohort			Standardized difference		
	PAL + AI (n=6832)	RIB + AI (n=1274)	ABE + AI (n=1038)	RIB + AI vs PAL + AI	ABE + AI vs PAL + AI	ABE + AI vs RIB + AI
Disease stage at initial diagnosis, n (%)						
I	720 (10.5)	136 (10.7)	112 (10.8)	0.0052	0.0091	0.0039
II	1538 (22.5)	287 (22.5)	238 (22.9)	0.0005	0.0092	0.0088
III	731 (10.7)	136 (10.7)	110 (10.6)	-0.0003	-0.0044	-0.0041
IV	3473 (50.8)	645 (50.6)	523 (50.4)	-0.0046	-0.0096	-0.0050
Not documented	370 (5.4)	70 (5.5)	56 (5.4)	0.0027	-0.0023	-0.0051
ECOG PS, n (%)						
0	2444 (35.8)	457 (35.9)	369 (35.5)	0.0025	-0.0050	-0.0075
1	1806 (26.4)	329 (25.9)	275 (26.5)	-0.0133	0.0008	0.0141
2, 3, or 4	780 (11.4)	147 (11.5)	119 (11.5)	0.0032	0.0018	-0.0015
Not documented	1801 (26.4)	341 (26.7)	275 (26.5)	0.0082	0.0035	-0.0048
Disease free interval, n (%)*						
De novo mBC	3473 (50.8)	645 (50.6)	523 (50.4)	-0.0046	-0.0096	-0.0050
≤1 year	276 (4.0)	52 (4.1)	42 (4.1)	0.0014	0.0007	-0.0007
>1-5 years	1082 (15.8)	202 (15.8)	162 (15.6)	0.0000	-0.0065	-0.0065
>5 years	2001 (29.3)	376 (29.5)	311 (30.0)	0.0044	0.0154	0.0109

The balance in these baseline characteristics was assessed using a standardized mean differences approach, with values ≥0.1 indicating a nonnegligible imbalance. *Disease-free interval was defined as the interval from initial breast cancer diagnosis to mBC diagnosis. ABE=abemaciclib; AI=aromatase inhibitor; ECOG PS=Eastern Cooperative Oncology Group performance status; mBC=metastatic breast cancer; PAL=palbociclib; RIB=ribociclib; sIPTW=stabilized inverse probability of treatment weighting. Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03.

P-VERIFY: Patient Characteristics After sIPTW (3 of 4)

- After sIPTW, baseline demographics and clinical characteristics were generally balanced between the 3 groups (standardized difference <0.1)

Characteristic	Cohort			Standardized difference		
	PAL + AI (n=6832)	RIB + AI (n=1274)	ABE + AI (n=1038)	RIB + AI vs PAL + AI	ABE + AI vs PAL + AI	ABE + AI vs RIB + AI
Visceral metastases, n (%)*						
No	4458 (65.3)	831 (65.2)	680 (65.5)	-0.0006	0.0060	0.0066
Yes	2374 (34.7)	443 (34.8)	358 (34.5)			
Bone-only metastases, n (%)						
No	3661 (53.6)	683 (53.6)	557 (53.7)	0.0004	0.0020	0.0016
Yes	3171 (46.4)	591 (46.4)	481 (46.3)			
Number of metastatic sites, n (%)†						
1	4010 (58.7)	745 (58.5)	611 (58.8)	-0.0040	0.0029	0.0069
2	1585 (23.2)	304 (23.9)	240 (23.1)	0.0158	-0.0025	-0.0183
≥3	615 (9.0)	111 (8.7)	92 (8.9)	-0.0112	-0.0036	0.0076
Not documented	622 (9.1)	114 (8.9)	95 (9.2)	-0.0055	0.0023	0.0078
Menopausal status at initial diagnosis, n (%)						
Premenopausal	1265 (18.5)	279 (21.9)	204 (19.6)	0.0849	0.0279	-0.0570
Postmenopausal	5138 (75.2)	919 (72.1)	762 (73.4)	-0.0702	-0.0415	0.0286
Not documented	359 (5.2)	65 (5.1)	61 (5.9)	-0.0066	0.0283	0.0349
NA (patient is male)	70 (1.0)	11 (0.9)	11 (1.1)	-0.0178	0.0068	0.0245

The balance in these baseline characteristics was assessed using a standardized mean differences approach, with values ≥0.1 indicating a nonnegligible imbalance. *Visceral metastases were defined as metastatic disease in the lung and/or liver; patients could have had other sites of metastases. No visceral metastasis was defined as no metastatic disease in the lung or liver. †Multiple metastases at the same site were counted as 1 site (eg, 3 bone metastases in a patient's spine were counted as 1 site only). ABE=abemaciclib; AI=aromatase inhibitor; NA=not applicable; PAL=palbociclib; RIB=ribociclib; sIPTW=stabilized inverse probability treatment weighting.

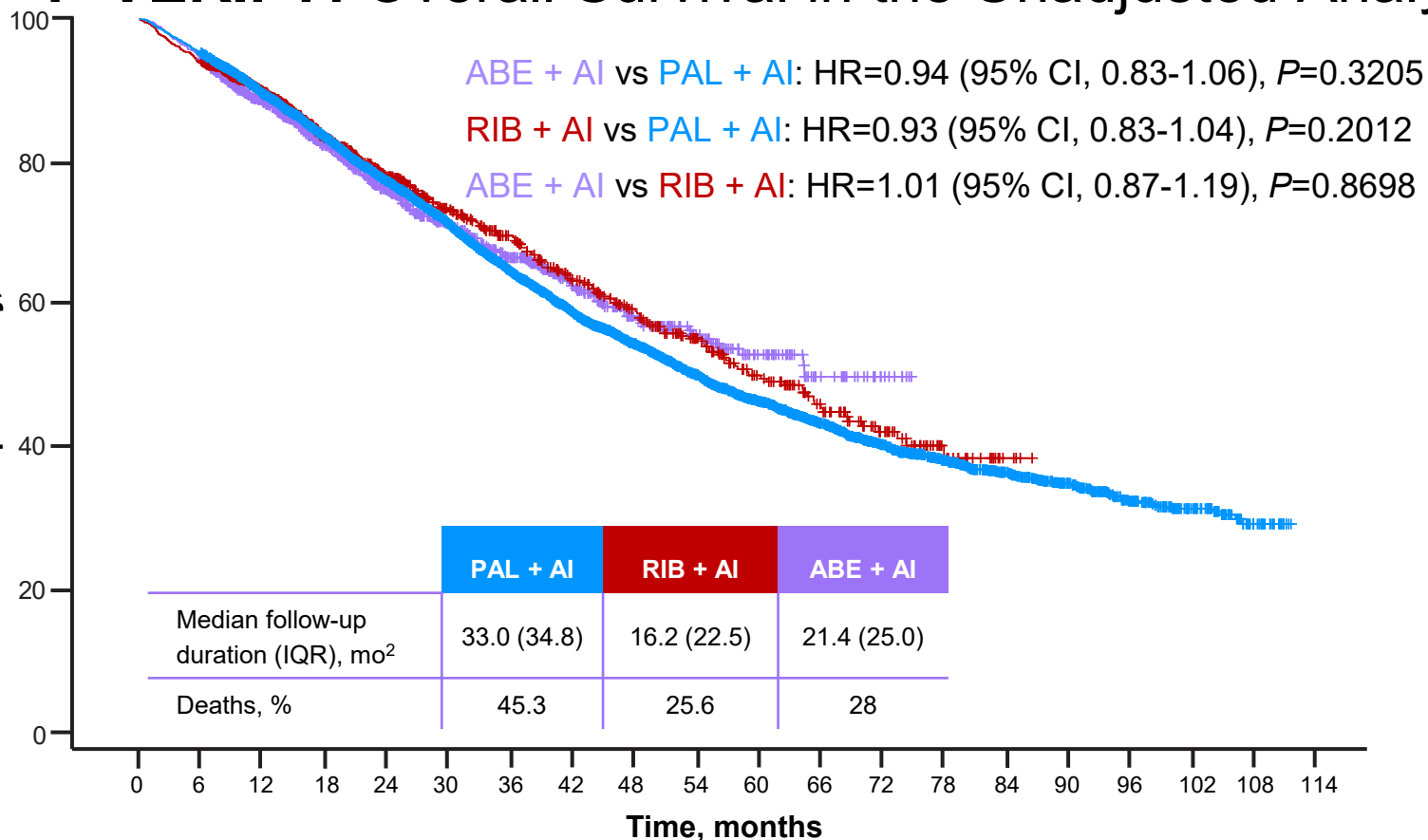
P-VERIFY: Patient Characteristics After sIPTW (4 of 4)

Characteristic	Cohort		
	PAL + AI (n=6832)	RIB + AI (n=1274)	ABE + AI (n=1038)
Year of index date, n (%)			
2015	440 (6.4)	0	0
2016	657 (9.6)	0	0
2017	713 (10.4)	70 (5.5)	0
2018	789 (11.6)	122 (9.6)	58 (5.6)
2019	870 (12.7)	102 (8.0)	125 (12.0)
2020	928 (13.6)	92 (7.2)	146 (14.0)
2021	1026 (15.0)	80 (6.3)	189 (18.2)
2022	870 (12.7)	226 (17.7)	247 (23.8)
2023	539 (7.9)	582 (45.7)	273 (26.3)
Median follow-up duration (IQR), months			
	33.0 (34.7)	15.7 (20.8)	21.5 (25.0)

ABE=abemaciclib; AI=aromatase inhibitor; IQR=interquartile range; PAL=palbociclib; RIB=ribociclib; sIPTW=stabilized inverse probability of treatment weighting.

Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03.

P-VERIFY: Overall Survival in the Unadjusted Analysis



Landmark OS Analysis

Cohort	OS rates, %			Median OS, (95% CI), mo
	12 mo	24 mo	30 mo	
PAL + AI	89.6	77.4	71.4	54.4 (52.4-56.1)
RIB + AI	90.0	78.0	73.3	60.3 (54.7-68.5)
ABE + AI	88.4	76.1	71.5	NR (55.4-NE)

Due to the small numbers of patients at risk after month 30 in the ribociclib and abemaciclib cohorts, point estimates of OS beyond this time point, including the median OS, were not stable^{1,2}

ABE + AI 1036 980 793 607 461 351 281 185 127 92 55 25 8 0
 RIB + AI 1279 1205 851 575 432 342 291 237 197 151 113 84 52 23 4 0
 PAL + AI 6831 6512 5892 5196 4490 3795 3074 2527 2056 1679 1352 1074 827 624 465 325 198 104 32 0

Observational retrospective analyses cannot establish causality between treatments and outcomes. Results are not intended to be compared with clinical trials and should be interpreted in the context of the totality of evidence.

P-VERIFY: Overall Survival in the Unadjusted Analysis

Summary of Events

In the unadjusted analysis, a total of 3714 deaths were observed and a total of 5432 patients were censored at the end of the study (data cutoff)

Cohort	Total (No.)	Died		Censored	
		No.	%	No.	%
PAL + AI	6831	3096	45.3	3735	54.7
RIB + AI	1279	328	25.6	951	74.4
ABE + AI	1036	290	28.0	746	72.0
Total	9146	3714	40.6	5432	59.4

ABE=abemaciclib; AI=aromatase inhibitor; PAL=palbociclib; RIB=ribociclib.

Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03.

P-VERIFY: Overall Survival After sIPTW Analysis (Primary Analysis)

ABE + AI vs PAL + AI: HR=0.95 (95% CI, 0.84-1.08), P=0.4292

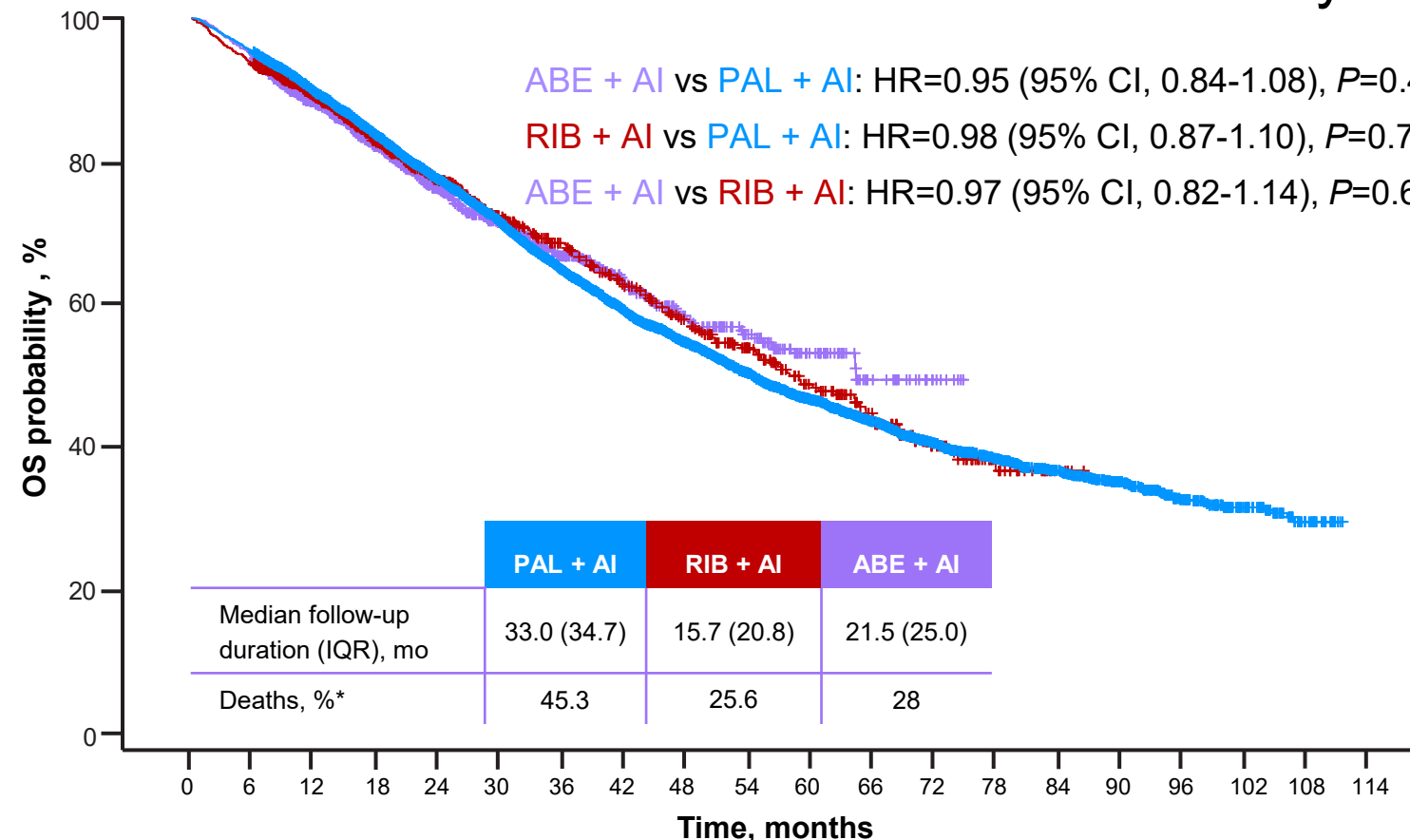
RIB + AI vs PAL + AI: HR=0.98 (95% CI, 0.87-1.10), P=0.7531

ABE + AI vs RIB + AI: HR=0.97 (95% CI, 0.82-1.14), P=0.6956

Landmark OS Analysis

Cohort	OS rates, %			Median OS, (95% CI), mo
	12 mo	24 mo	30 mo	
PAL + AI	89.7	77.5	71.4	54.6 (52.6-56.4)
RIB + AI	89.2	77.3	72.2	59.0 (50.9-66.1)
ABE + AI	88.2	76.1	71.5	64.5 (55.4-NE)

Due to the small numbers of patients at risk after month 30 in the ribociclib and abemaciclib cohorts, point estimates of OS beyond this time point, including the median OS, were not stable^{1,2}



	PAL + AI	RIB + AI	ABE + AI
Median follow-up duration (IQR), mo	33.0 (34.7)	15.7 (20.8)	21.5 (25.0)
Deaths, %*	45.3	25.6	28

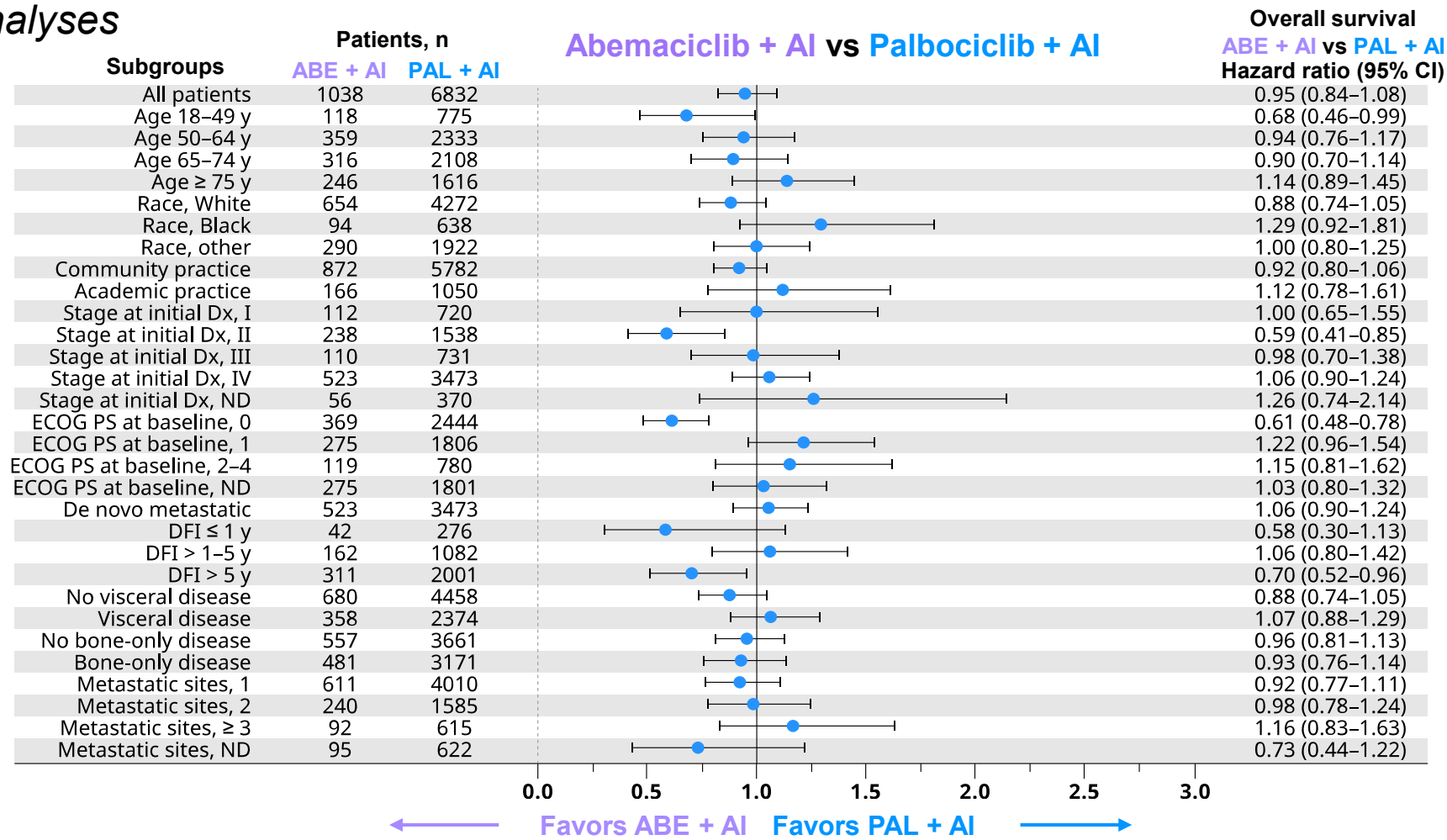
	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102	108	114	
ABE + AI	1038	981	793	610	461	347	278	185	128	91	56	23	8	0							
RIB + AI	1274	1194	826	549	411	326	276	227	188	145	110	82	49	23	3	0					
PAL + AI	6832	6516	5902	5204	4497	3801	3077	2534	2060	1682	1355	1077	829	625	467	328	200	106	33	0	

Observational retrospective analyses cannot establish causality between treatments and outcomes. Results are not intended to be compared with clinical trials and should be interpreted in the context of the totality of evidence.

*Based on unadjusted analysis population. ABE=abemaciclib; AI=aromatase inhibitor; CI=confidence interval; HR=hazard ratio; mo=month; IQR=interquartile range; NE=not estimable; OS=overall survival; PAL=palbociclib; RIB=ribociclib; sIPTW=stabilized inverse probability treatment weighting.
 1. Rugo HS, et al. SABCS 2024. Poster Spotlight PS2-03. 2. Pfizer. Data on file.

P-VERIFY: Overall Survival After sIPTW Analysis by Subgroups (1 of 3)

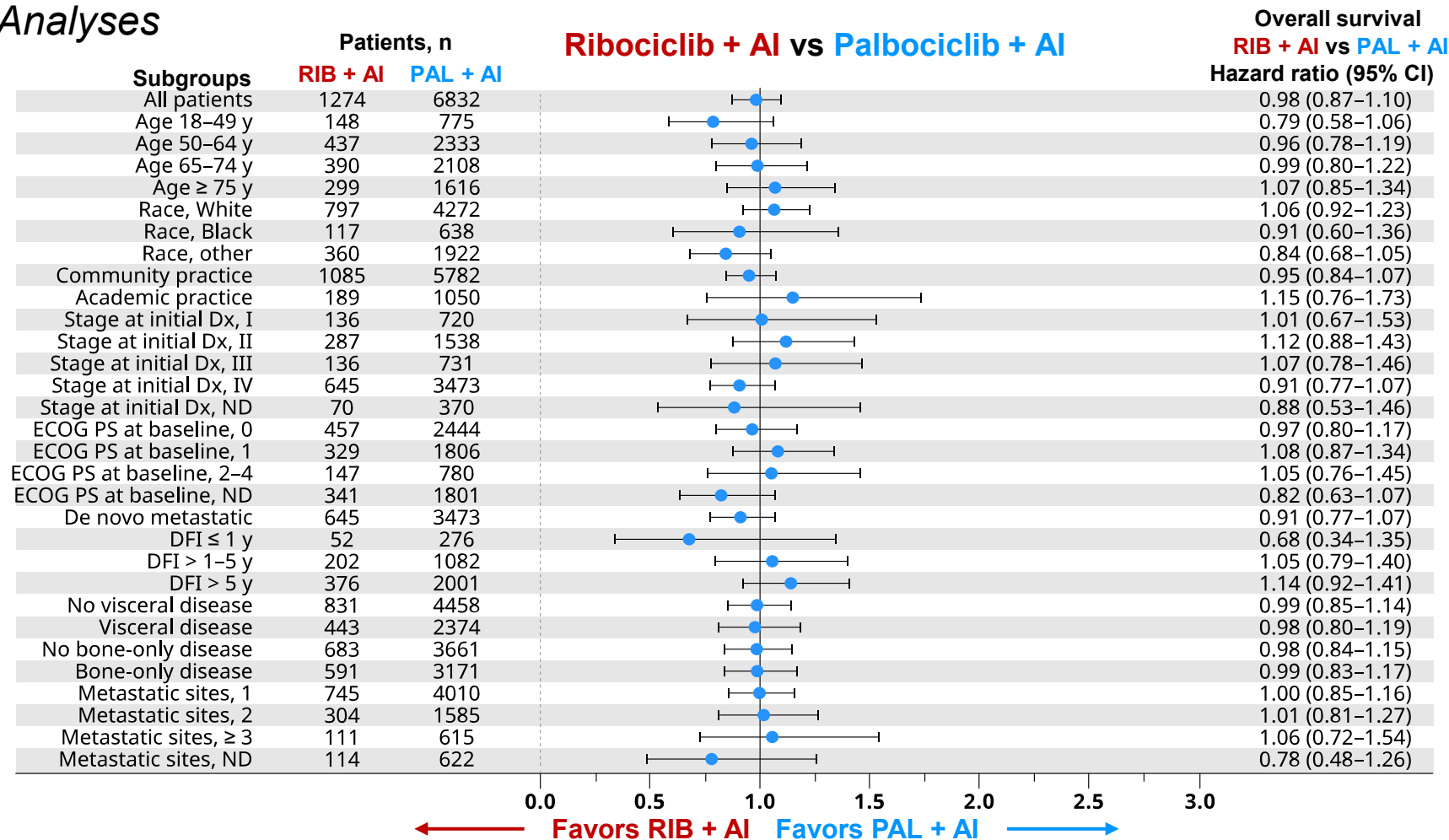
Exploratory Analyses



Observational retrospective analyses cannot establish causality between treatments and outcomes, and these analyses are not intended to demonstrate efficacy in particular subgroup. Small patient numbers is a limitation of this analysis. These results are not intended to be compared with clinical trials and should be interpreted in the context of the totality of evidence.

P-VERIFY: Overall Survival After sIPTW Analysis by Subgroups (2 of 3)

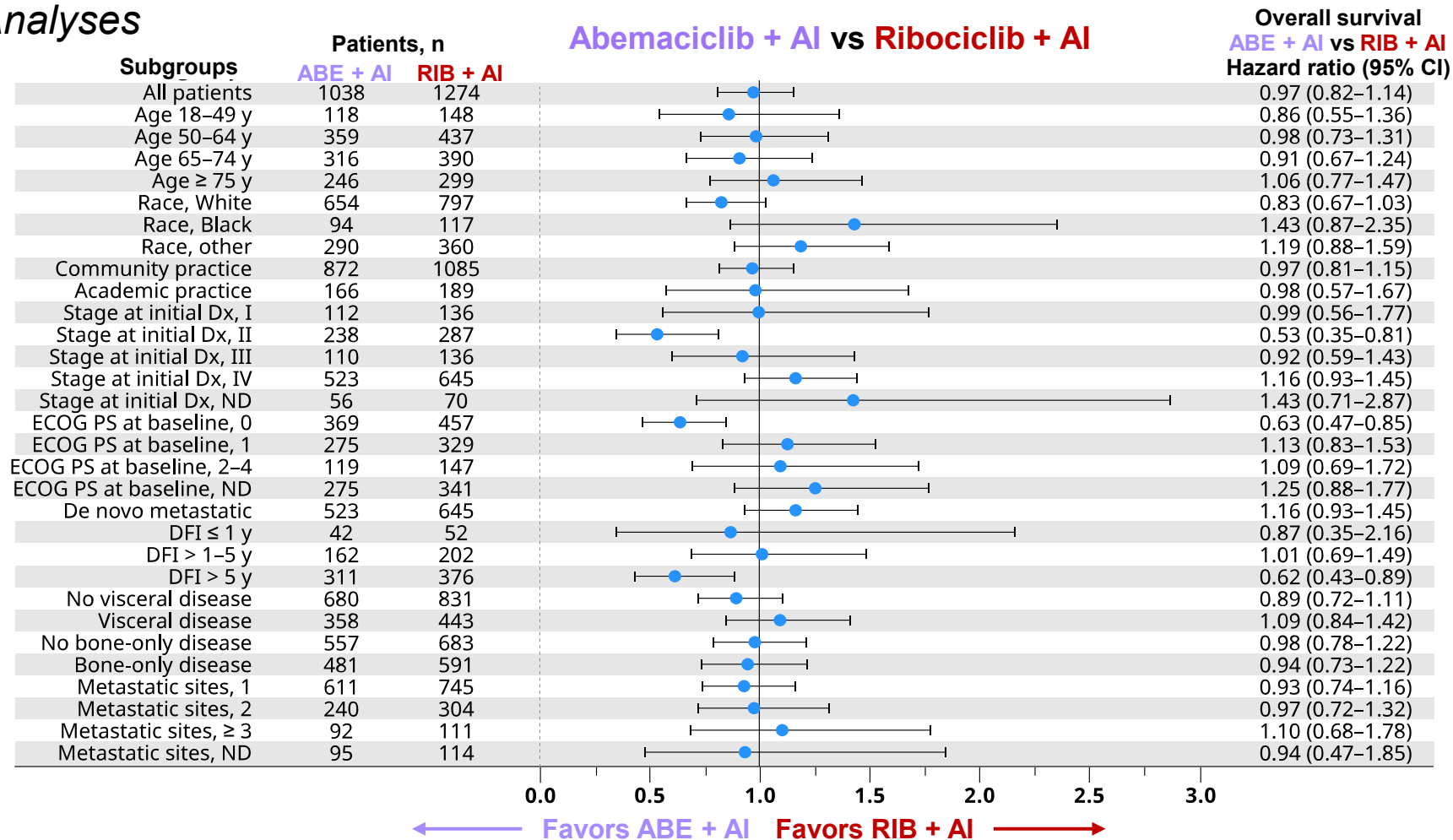
Exploratory Analyses



Observational retrospective analyses cannot establish causality between treatments and outcomes, and these analyses are not intended to demonstrate efficacy in particular subgroup. Small patient numbers is a limitation of this analysis. These results are not intended to be compared with clinical trials and should be interpreted in the context of the totality of evidence.

P-VERIFY: Overall Survival After sIPTW Analysis by Subgroups (3 of 3)

Exploratory Analyses



Observational retrospective analyses cannot establish causality between treatments and outcomes, and these analyses are not intended to demonstrate efficacy in particular subgroup. Small patient numbers is a limitation of this analysis. These results are not intended to be compared with clinical trials and should be interpreted in the context of the totality of evidence.

P-VERIFY: Overall Survival

Sensitivity Analyses

Multivariable Cox proportional hazards regression analysis showed no significant differences in OS between treatment groups.

Adjusted hazard ratios were as follows:

- **0.94** (95% CI, 0.84-1.06; $P=0.3216$) when comparing the **ribociclib group** versus the **palbociclib group**
- **0.94** (95% CI, 0.84-1.07; $P=0.3603$) when comparing the **abemaciclib group** versus the **palbociclib group**
- **1.00** (95% CI, 0.85-1.17; $P=0.9851$) when comparing the **abemaciclib group** versus the **ribociclib group**

After 1:1 exact matching, there were no significant differences in OS between treatment groups.

Adjusted hazard ratios were as follows:

- **0.99** (95% CI, 0.85-1.15; $P=0.8519$) when comparing the **ribociclib group** versus the **palbociclib group**
- **0.95** (95% CI, 0.80-1.13; $P=0.5898$) when comparing the **abemaciclib group** versus the **palbociclib group**
- **0.96** (95% CI, 0.75-1.24; $P=0.7630$) when comparing the **abemaciclib group** versus the **ribociclib group**

Observational retrospective analyses cannot establish causality between treatments and outcomes, and these analyses are not intended to demonstrate efficacy in particular subgroup. Small patient numbers is a limitation of this analysis. These results are not intended to be compared with clinical trials and should be interpreted with caution in the context of the totality of evidence.

P-VERIFY: Overall Survival

Subanalysis of Patients Who Started Index Treatment in 2017 or Later

This subanalysis included 5735 patients treated with palbociclib plus AI, 1279 treated with ribociclib plus AI, and 1036 treated abemaciclib plus AI

After sIPTW, the adjusted hazard ratios were as follows:

- **1.00** (95% CI, 0.89-1.13; $P=0.9728$) for the **ribociclib group** versus the **palbociclib group**
- **0.96** (95% CI, 0.84-1.09; $P=0.5326$) for the **abemaciclib group** versus the **palbociclib group**
- **0.96** (95% CI, 0.81-1.13; $P=0.6077$) for the **abemaciclib group** versus the **ribociclib group**

Observational retrospective analyses cannot establish causality between treatments and outcomes, and these analyses are not intended to demonstrate efficacy in particular subgroup. Small patient numbers is a limitation of this analysis. These results are not intended to be compared with clinical trials and should be interpreted with caution in the context of the totality of evidence.

P-VERIFY: Strengths and Limitations^{1,2}

Strengths

- Strengths include the diversity of patients represented and the comprehensiveness of data collected in a US nationwide, longitudinal database
- In this database, EHR-derived data were validated using quality and performance assessment frameworks and date of death was a consensus mortality endpoint based on multiple sources and validated against the gold-standard National Death Index
- This study had a large sample size (N=9146), representing the largest real-world study conducted to date evaluating the comparative effectiveness of CDK4/6 inhibitors
- The consistency of findings across different comparative methods, including the unadjusted analysis, the primary analysis after sIPTW, and the sensitivity analysis using a multivariable regression model, contributed to the study's internal validity
- Findings remained consistent in the subanalysis of patients who started treatment in 2017 or later, when all CDK4/6 inhibitors were commercially available in the US

Limitations

- This study was a retrospective database analysis, which inherently carries the potential for treatment selection bias and inaccurate or incomplete data capture
- Although statistical methodologies were used to balance baseline characteristics between treatment groups, these methodologies cannot account for potential unmeasured confounders
- The statistical non-significant differences in OS between the 3 CDK4/6 inhibitors in the current analysis does not demonstrate noninferiority or equivalence, and a formal noninferiority or equivalence analysis would be needed to draw such conclusions
- The ribociclib and abemaciclib groups had small sample sizes and short follow-up times relative to the palbociclib group, which may cause point estimates to be unstable beyond 30 months of follow-up
- Results may not be generalizable to patient populations that were not represented in the Flatiron Health database

P-VERIFY: Authors' Conclusions

- This study represents the largest RW comparative analysis conducted to date of OS between the CDK4/6 inhibitors in combination with an AI
- This study suggests that there are no significant OS differences between 1L palbociclib, ribociclib, or abemaciclib used in combination with an AI for patients with HR+/HER2- mBC in routine clinical practice in the US; however, further research is needed

Enhanced Data Abstraction from Flatiron Health Enabled A Comprehensive Patient Analysis for P-VERIFY Using the Full Flatiron Health Dataset¹

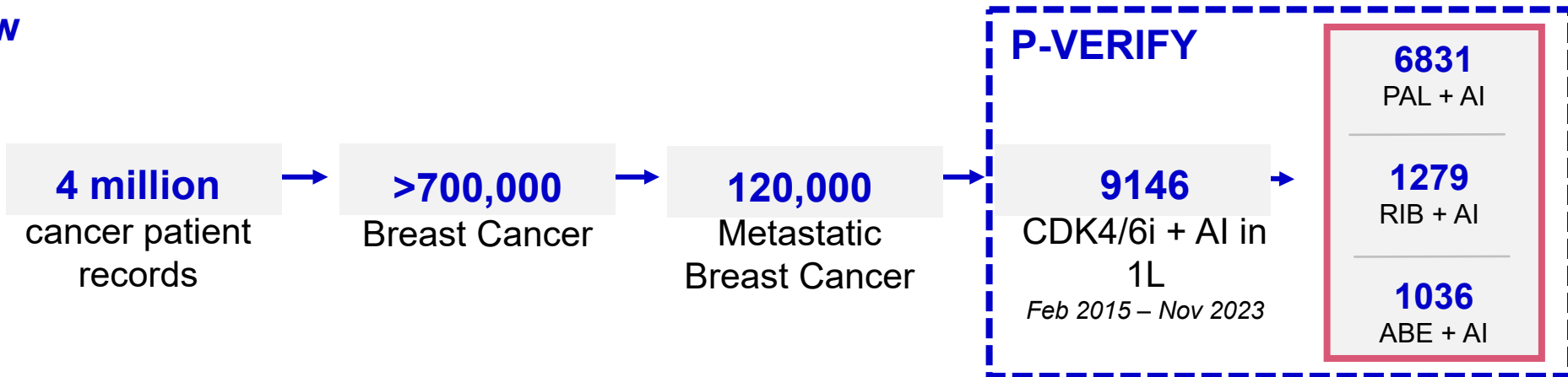
Previous Analyses (i.e. P-REALITY X)

- Based upon a **random subset** of all available patients in the Flatiron Health network of sites which met inclusion /exclusion criteria of the study
- This limitation was due to the **previous data technology abstraction process which, still required some level of manual chart review**
- **Time for data delivery:** ~ 9+ months

As of June 2024²⁻⁴

- Flatiron Health released a new dataset offering **advanced AI abstraction technology**
- **AI abstraction allows for ALL patients** to be accessible in near real time, with availability of similar clinical and demographic variables
- **Validation studies support data quality** in this newly released dataset

Dataset Overview



ABE=abemaciclib; AI=aromatase inhibitor; AI=artificial intelligence; CDK4/6=cyclin-dependent kinase 4/6; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; MBC=metastatic breast cancer; PAL=palbociclib; RIB=ribociclib. 1. Pfizer. Data on File. 2. Castellanos EH, et al. *JCO Clin Cancer Inform.* 2024;8:e2300046. 3. Estevez M, et al. *Cancers (Basel).* 2022;14(13):3063. 4. Benedum CM, et al. *Cancers (Basel).* 2023;15(6):1853.



Additional Information

Additional SABCS 2024 Breast Cancer Studies

Title	Abstract ID
Liquid biopsy DNADX assay in advanced HR+/HER2-negative breast cancer after progression on CDK4/6 and aromatase inhibitors: a correlative analysis from the PACE phase II randomized trial	PS2-09
Molecular characterization of the NeoPalAna endocrine resistant (ET-R) cohort: Implications for CDK4/6 inhibitor (CDK4/6i) and ET resistance mechanisms in primary estrogen receptor positive (ER+) and HER2 negative (HER2-) breast cancer (BC)	PS12-03
Real-world effectiveness and economic outcomes of first-line CDK4/6 inhibitors in combination with AI for HR+/HER2- metastatic breast cancer in a US Medicare eligible population	P1-10-03
Thymidine kinase activity as a prognostic and predictive biomarker in the phase II PACE trial of CDK4/6 inhibition beyond progression	P2-07-25
A011801 (CompassHER2 RD): Postneoadjuvant T-DM1 + tucatinib/placebo in patients with residual HER2-positive invasive breast cancer	P2-10-19
Tucatinib, trastuzumab and capecitabine with brain and/or spinal radiotherapy (XRT) in patients with HER2+ metastatic breast cancer and leptomeningeal disease: A multi-centre phase II, single arm feasibility study	P3-08-22
Subtype by PAM50 changes after neoadjuvant endocrine therapy, from a phase III randomized, double-blind, neoadjuvant study of hormonal therapy plus palbociclib versus hormonal therapy plus placebo in women with operable, hormone sensitive and HER2-negative primary breast cancer	P4-04-28
Quality of life with palbociclib plus tamoxifen in hormone receptor-positive, HER2-negative metastatic breast cancer: Results from NCCH1607/PATHWAY, an Asian international double-blind randomized phase 3 trial	P4-07-19
CDK 4/6 inhibitor switching and associated dosing patterns in Swedish HR+/HER2- MBC patients	P4-07-26
Potential risk factors for health-related quality of life (HRQoL) in palbociclib (PAL) plus endocrine therapy (ET) and ET alone patients with HR+/HER2- advanced breast cancer (ABC): exploratory analysis from 6-month longitudinal study (JBCRG-26)	P4-10-03
Real-world palbociclib dose adjustments and outcomes in HR+/HER2- metastatic breast cancer: Flatiron database analysis (P-REALITY X)	P4-10-04
Real-world effectiveness of palbociclib plus an aromatase inhibitor in HR+/HER2- mBC patients living in disadvantaged neighborhoods	P4-12-04
Safety and preliminary efficacy of tucatinib and alpelisib in patients with HER2-positive PIK3CA-mutated metastatic breast cancer	P5-03-10

Geriatric Assessment: The G8 Questionnaire

Back →

- Identifies older patients with cancer who could benefit from a comprehensive geriatric assessment¹
- Healthcare professional-administered¹
- **8 ITEMS including¹:**
 - Appetite, weight loss, BMI
 - Mobility
 - Mood and cognition
 - Number of medications
 - Patient-related health
 - Age categories

• **Score <14 (total range 0–17) indicates patient should undergo full geriatric evaluation¹**

Benefits: The G8 tool has been found predictive for chemotherapy-related toxicity and prognostic for survival in mostly solid tumors²

Limitations: Does not include social environment and biological variables.¹ However, sensitivity is ~87% which is in line with other clinical tools e.g. mammography²

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
		3 : no weight loss
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not go out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m ²))	0 : BMI < 19
		1 : BMI = 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
TOTAL SCORE		0 – 17

BMI=body mass index.

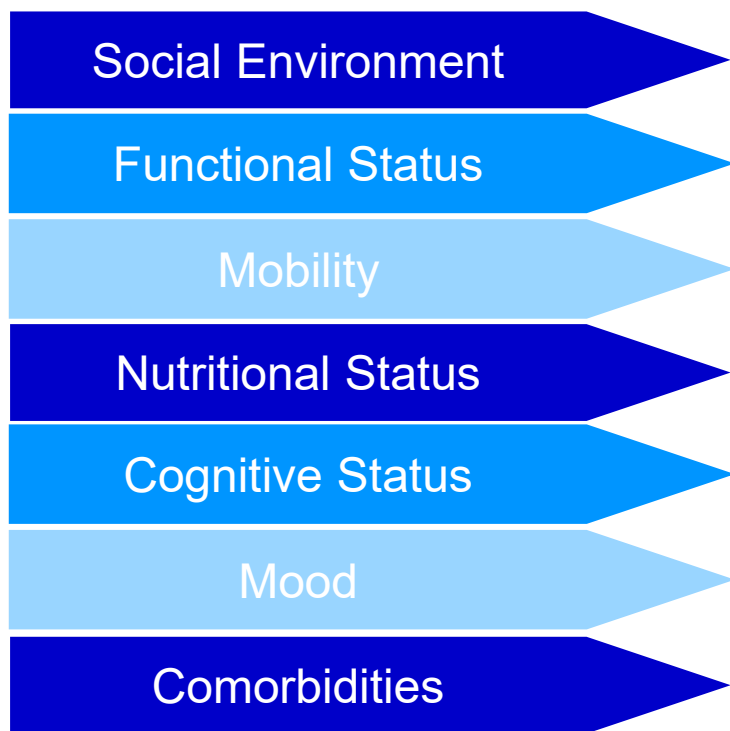
1. Bellera CA, et al. *Ann Oncol.* 2012;23:2166-2172. 2. Kenis C, et al. *J Clin Oncol.* 2014;32:19-26.

Geriatric Assessment: The Geriatric COre DatasEt (G-CODE)

Back →

- Defined by the French cooperative group DIALOG in order to give a minimal and standardized geriatric description of older patients included in clinical trials
- Physician-administered

7 GERIATRIC DOMAINS, 10 ITEMS



1. Do you live alone?
2. Do you have a person or caregiver able to provide care and support?
3. Activities of Daily Living (ADL; abnormal if <6/6)
4. Instrumental ADL (IADL; abnormal if <4/4)
5. Timed Up and Go test (TUG; abnormal if >20 seconds)
- 6–7. BMI (<21) and Weight loss (>10%) during the last 6 months
8. Mini-Cog™ (3 words and clock drawing tests; abnormal if <4/5)
9. Mini-Geriatric Depression Scale (Mini-GDS; abnormal if ≥1/4)
10. Updated Charlson comorbidity index score²

BMI=body mass index.

1. Paillaud E, et al. *Eur J Cancer*. 2018;103:61-68. 2. Quan H, et al. *Am J Epidemiol*. 2011;173(6):676-682