PERFORM

INTERIM RESULTS OF THE PERFORM STUDY

PALBOCICLIB PLUS ENDOCRINE THERAPY IN HR+/HER2- ADVANCED BREAST CANCER PATIENTS

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BACKGROUND

Endocrine-therapy (ET) combined with cyclin-dependent-kinase 4/6 inhibitors (CDK4/6i) is the 1st-line standard of care for HR+/HER2- advanced or metastatic breast cancer (ABC) patients based upon demonstrated efficacy and tolerability in pivotal phase III trials. A pooled analysis of results from the PALOMA clinical trials indicated palbociclib combination therapy to be effective and well tolerated in the subgroup of older patients (age 65-74 years and ≥75 years)[1]. These data were corroborated by a meta-analysis published by the FDA that evaluated the efficacy and safety of CDK4/6i plus an aromatase inhibitor in older women (age ≥75 years)[2]. The combination therapy demonstrated similar efficacy when compared with younger women, with slightly higher rates of grade 3/4 toxicities, dose modifications and a faster decrease from baseline in patient-reported outcomes[2]. As elderly patients accrued to clinical trials may not represent a general elderly cancer patient population, prospectively collected real world data on effectiveness, tolerability, treatment patterns and quality of life (QoL) over several treatment lines is of high medical interest in a real world setting.[3]

CONCLUSION

The second interim analysis of the PERFORM study gives first insights into patient characteristics and effectiveness of 1st-line treatment with palbociclib + ET in a real-world setting. Patients ≥75 years of age presented more often with *de novo* ABC, with worse ECOG PS at start of 1st-line treatment and required dose modifications more frequently than patients <75 years. Nevertheless, 12-months PFS rate, ORR and CBR of 1st-line treatment with palbociclib + ET were comparable between the age-related subgroups. These findings are in line with results of clinical trials and further support the use of palbociclib-based treatment, irrespective of age.

METHODS

Overall, 1,900 patients receiving 1st-line palbociclib + ET will be enrolled in the prospective non-interventional study PERFORM at 320 sites across Germany and Austria. The primary endpoint is progression-free survival (PFS). Secondary objectives include treatment patterns, effectiveness (including outcomes in second- and third-line treatment), treatment expectation/satisfaction, potential impact of socioeconomic status and QoL as well as patterns of biomarker analyses and genetic testing. During 1st-line treatment with palbociclib + ET, tumor response assessments are documented in the electronic case report form (eCRF), according to clinical routine. Two years after first-patient-in, the second interim analysis was conducted, focusing on patient- and disease-characteristics, dose modifications and response in all evaluable patients and in corresponding age-related subgroups.

RESULTS

Patient characteristics

In total, 938 patients were enrolled between 10/2020 and 09/2022 and 704 were followed for ≥6 months. Of these, 624 patients were evaluable (i.e., treated with at least one dose of palbociclib and not violating any in- and exclusion criteria). Median age was 68 years (range 33-89) and 92% (n=574) of the primarily female population (99.4%, n=620) were postmenopausal. 11,4% (n=71) of all patients had an Eastern Cooperative Oncology Group performance status (ECOG PS) ≥2 at inclusion **(Table 1)**. In total, 241 (38.6%) patients presented with *de novo* ABC and 383 (61.4%) had relapsed from EBC with a median time from primary diagnosis to inclusion of 8.26 years (range 0.3-41) **(Table 2)**. 29.7% of patients (n=185) were ≥75 years of age at inclusion. Of these, 21.6% (n=40) had an ECOG performance status of ≥2 compared to 7.1% (n=31) of patients <75 years. The rate of *de novo* ABC was higher in patients ≥75 years (44.3%, n=82) than in patients <75 years (36.2%, n=159), whereas the number and distribution of metastases was comparable **(Table 3)**.

Effectiveness

At the second interim analysis, median PFS [95%CI 19.9, NA] could not yet be estimated because median was not reached yet **(Figure 1)**. At 12 months, median PFS rate was 71.7% and the overall response rate (ORR) and clinical benefit rate (CBR) were 33.2% and 57.4%, respectively **(Table 4)**. Notably, 12-month PFS rate, ORR and CBR were similar across age subgroups: the 12-month PFS rate was 71.1% for patients <75 years and 73.4% for patients ≥75 years. The ORR was 33.9 % vs. 31.4% and the CBR 58.5 % vs. 54.6%, respectively **(Table 4)**.

Treatment modifications

Therapy modifications were performed in 65.2% (n=407) of all patients, with treatment interruption between cycles documented for 42.9% (n=268), and dose modification for 35.6% (n=222) of patients, respectively. Therapy modifications were required numerically more often in patients ≥75 years (74.1%, n=137) than <75 years (61.5%, n=270). Treatment interruptions between cycles were performed in 47.6% (n=88) vs 41.0% (n=180) and dose modifications in 45.4% (n=84) vs 31.4% (n=138) of patients, respectively. In both subgroups, >70% of patients were still on treatment at database cut. Treatment discontinuation rates were comparable in both age groups (28.6% (n=53) of patients ≥75 years vs 27.3% (n=120) of patients <75 years), however a serious adverse event as reason for treatment discontinuation was more frequent in patients ≥75 years (9.2%, n=17 vs 3.0%, n=13) **(Table 5)**.

Table 1: Patient characteristics at start of 1st-line treatment (n=624).

Characteristics	n (%)
Age at start of first-line treatment [years]	
Median (Q1–Q3)	68 (59 – 77)
Min–Max	33 – 89
Missing	0
Age group	
<65 years	259 (41.5)
65-74 years	180 (28.8)
75-79 years	99 (15.9)
≥80 years	86 (13.8)
Sex	
Female	620 (99.4)
Male	4 (0.6)
Menopausal status	
Pre-/Perimenopausal	46 (7.4)
Postmenopausal	574 (92.0)
Not derivable	4 (0.6)
ECOG Performance Status	
0	280 (44.9)
1	261 (41.8)
2	58 (9.3)
3	13 (2.1)
4	0 (0.0)
No assessment done	12 (1.9)

Table 2: Disease characteristics at inclusion by *de novo* advanced disease.

	Total (n=624, n (%))	Yes (n=241 (38.6%), n (%))	No (n=383 (61.4%), n (%))
Tumor stage at ABC diagnosis			
Locoregionally advanced	33 (5.3)	15 (6.2)	18 (4.7)
Metastatic	361 (57.9)	57 (23.7)	304 (79.4)
Locoregionally advanced and metastatic	228 (36.5)	169 (70.1)	59 (15.4)
Missing	2 (0.3)	0 (0.0)	2 (0.5)
Time since initial diagnosis [years]			
N	624	241	383
Mean (±SD)	6.24 (±7.70)	0.28 (±1.66)	10.0 (±7.64)
Median (Q1/Q3)	3.2 (0.12/10.45)	0.10 (0.06/0.15)	8.26 (3.99/14.24)
Min–Max	0.0-41.2	0.0-23.7	0.3-41.2
Number of metastatic sites present at inclusion			
0	52 (8.3)[1]	18 (7.5)[1]	34 (8.9)[1]
1	376 (60.3)	145 (60.2)	231 (60.3)
2	122 (19.6)	50 (20.7)	72 (18.8)
3	54 (8.7)	17 (7.1)	37 (9.7)
≥4	20 (3.2)	11 (4.6)	9 (2.3)
Disease site present at inclusion			
Visceral	287 (46.0%)	106 (44.0%)	181 (47.3%)
Non-visceral only (excl. bone only)	73 (11.7%)	26 (10.8%)	47 (12.3%)
Bone only	212 (34.0%)	91 (37.8%)	121 (31.6%)
No metastases present at inclusion	52 (8.3%)	18 (7.5%)	34 (8.9%)

[1]For some patients, metastases may not be present anymore at inclusion due to e.g. surgery.

Table 3: Patient and disease characteristics at inclusion by age.

	Total (n=624, n (%))	<75 years (n=439 (70.4%), n (%))	≥75 years (n=185 (29.6%), n (%))
Age at start of first-line treatment [years]			
Median (Q1–Q3)	68 (59 – 77)	62 (56 – 69)	80 (78 – 83)
Min–Max	33 – 89	33 – 75	75 – 89
Missing	0	0	0
Sex			
Female	620 (99.4)	436 (99.3)	184 (99.5)
Male	4 (0.6)	3 (0.7)	1 (0.5)
Menopausal status			
Pre-/Perimenopausal	46 (7.4)	46 (10.5)	0 (0.0)
Postmenopausal	574 (92.0)	390 (88.8)	184 (99.5)
Not derivable	4 (0.6)	3 (0.7)	1 (0.5)
ECOG Performance Status			
0	280 (44.9)	255 (51.3)	55 (29.7)
1	261 (41.8)	175 (39.9)	86 (46.5)
≥2	71 (11.4)	31 (7.1)	40 (21.6)
No assessment done	12 (1.9)	8 (1.8)	4 (2.2)
De novo advanced disease			
Yes	241 (38.6)	159 (36.2)	82 (44.3)
No	383 (61.4)	280 (63.8)	103 (55.7)
Tumor stage at ABC diagnosis			
Locoregionally advanced	33 (5.3)	19 (4.3)	14 (7.6)
Metastatic	361 (57.9)	268 (61.0)	93 (50.3)
Locoregionally advanced and metastatic	228 (36.5)	150 (34.2)	78 (42.2)
Missing	2 (0.3)	2 (0.5)	0 (0.0)
Number of metastatic sites present at inclusion			
0	52 (8.3)[1]	31 (7.1)[1]	21 (11.4)[1]
1	376 (60.3)	263 (59.9)	113 (61.1)
2	122 (19.6)	86 (19.6)	36 (19.5)
3	54 (8.7)	44 (10.0)	10 (5.4)
≥4	20 (3.2)	15 (3.4)	5 (2.7)
Disease site present at inclusion			
Visceral	287 (46.0%)	208 (47.4%)	79 (42.7%)
Non-visceral only (excl. bone only)	73 (11.7%)	49 (11.2%)	24 (13.0%)
Bone only	212 (34.0%)	151 (34.4%)	61 (33.0%)
No metastases present at inclusion	52 (8.3%)	31 (7.1%)	21 (11.4%)

[1]For some patients, metastases may not be present anymore at inclusion due to e.g. surgery.

Figure 1: Progression-free survival of first-line treatment (n=624).

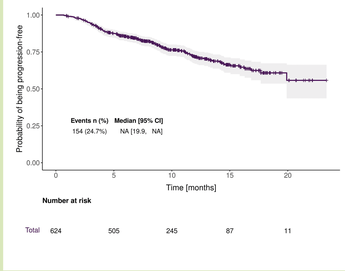

Table 4: Response in total and by age.

	Total (n=624, n(%))	<75 years (n=439 (70.4%), n(%))	≥75 years (n=185 (29.6%), n(%))
Best response			
CR	22 (3.5)	15 (3.4)	7 (3.8)
PR	185 (29.6)	134 (30.5)	51 (27.6)
SD ≥24 weeks	151 (24.2)	108 (24.6)	43 (23.2)
SD <24 weeks	97 (15.5)	68 (15.5)	29 (15.7)
Non-CR/Non-PD[a]	1 (0.2)	1 (0.2)	0 (0.0)
Non-PD (acc. to PI)[b]	2 (0.3)	2 (0.5)	0 (0.0)
PD	54 (8.7)	37 (8.4)	17 (9.2)
Missing[c]	112 (17.9)	74 (16.9)	38 (20.5)
ORR (%)	33.2	33.9	31.4
Missing[c]	112 (17.9)	74 (16.9)	38 (20.5)
CBR[a] (%)	57.4	58.5	54.6
Missing[c]	112 (17.9)	74 (16.9)	38 (20.5)
DCR (%)	72.9	74.0	70.3
Missing[c]	112 (17.9)	74 (16.9)	38 (20.5)
PFS			
6-month rate [95% CI]	85.6% [82.5, 88.2]	85.8% [82.1, 88.8]	85.0% [78.9, 89.5]
12-month rate [95% CI]	71.7% [67.1, 75.7]	71.1% [65.5, 75.9]	73.4% [64.9, 80.2]
18-month rate [95% CI][c]	60.8% [53.7, 67.2]		

[a]Non-CR/Non-PD – was documented when assessed according to RECIST
[b] Non-PD (acc. to PI) – was documented when 1L therapy was started but due to organizational reasons stagings planned before start of 1L were delayed and revealed further metastases that were most likely already present before start of of therapy
[c]CBR: proportion of patients with best overall response of CR, PR, or SD. SD must last for 24 weeks or more (since start of treatment) to be counted as response.
[c]For those patients at data cut for 1A no response assessment was documented as yes.
[c]Due to low patient numbers the 18-month PFS rate is not shown for the two subgroups

Table 5: Treatment modifications in total and by age.

	Total (n=624, n(%))	<75 years (n=439 (70.4%), n(%))	≥75 years (n=185 (29.6%), n(%))
Palbociclib treatment status			
Treatment ongoing	451 (72.3)	319 (72.7)	132 (71.4)
Treatment discontinued	173 (27.7)	120 (27.3)	53 (28.6)
(Serious) Adverse Event	30 (4.8)	13 (3.0)	17 (9.2)
Progressive disease	106 (17.0)	83 (18.9)	23 (12.4)
Other	37 (5.9)	24 (5.5)	13 (7.0)
Therapy modifications palbociclib			
Yes	407 (65.2)	270 (61.5)	137 (74.1)
Dose modification[1]	222 (35.6)	138 (31.4)	84 (45.4)
Interruption within cycle[1]	168 (26.9)	120 (27.3)	48 (25.9)
Interruption between cycle[1]	268 (42.9)	180 (41.0)	88 (47.6)
Skipped cycle[1]	58 (9.3)	37 (8.4)	21 (11.4)
No	217 (34.8)	169 (38.5)	48 (25.9)

[1]Multiple answers possible

Abbreviations:

ABC: Advanced Breast Cancer | CDK4/6i: Cyclin-dependent-kinase 4/6 inhibitor | CBR: Clinical Benefit Rate | DCR: Disease Control Rate | eCRF: Electronic Case Report Form | EBC: Early Breast Cancer | ECOG PS: Eastern Cooperative Oncology Group performance status | ET: Endocrine therapy | ET: Endocrine therapy | HER2: Human-epidermal-growth-factor-receptor 2 | HR: Hormone receptor | ORR: Overall response rate | PFS: Progression-free survival | PRO: Patient reported Outcomes | Q: Quartile | QoL: Quality of life | SD: Standard deviation

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Conflicts of Interest:

Michael Patrick Lux, Rupert Bartsch, Julia Radosa: Advisory/Consultancy, Speaker-Bureau/Expert testimony, Travel/Accomodation/Expenses

Denise Wrobel, Thomas Fietz, Thomas Decker: Advisory/Consultancy

Esther Glastetter, Johanna Buncke, Anne Adams, Emanuele Zanucco: Full/Part-time employments

Sandra Maria Woerner, Katja Gratzke, Mustafa Deryal, Jan Knoblich, Christoph Losem, Volker Petersen, Uwe Rhein, Jochen Wilke, Björn Schöttker: No COI

Georg Pfeiler: Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accomodation/Expenses; Research Grant

Acknowledgements:

The non-interventional study PERFORM is sponsored by Pfizer Pharma GmbH.

ESMO congress 2023
20. – 24. October 2023, Madrid
Final Publication Number: 401P