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ORIGINAL ARTICLE

Preliminary safety and efficacy of first-line pertuzumab combined with trastuzumab and taxane therapy for HER2-positive locally recurrent or metastatic breast cancer (PERUSE)

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Background: Pertuzumab combined with trastuzumab and docetaxel is the standard first-line therapy for HER2-positive metastatic breast cancer, based on results from the phase III CLEOPATRA trial. PERUSE was designed to assess the safety and efficacy of investigator-selected taxane with pertuzumab and trastuzumab in this setting.

Patients and methods: In the ongoing multicentre single-arm phase IIIb PERUSE study, patients with inoperable HER2-positive advanced breast cancer (locally recurrent/metastatic) (LR/MBC) and no prior systemic therapy for LR/MBC (except endocrine therapy) received docetaxel, paclitaxel or nab-paclitaxel with trastuzumab [8 mg/kg loading dose, then 6 mg/kg every 3 weeks (q3w)] and pertuzumab (840 mg loading dose, then 420 mg q3w) until disease progression or unacceptable toxicity. The primary end point was safety. Secondary end points included overall response rate (ORR) and progression-free survival (PFS).

Results: Overall, 1436 patients received at least one treatment dose (initially docetaxel in 775 patients, paclitaxel in 589, nab-paclitaxel in 65; 7 discontinued before starting taxane). Median age was 54 years; 29% had received prior trastuzumab. Median treatment duration was 16 months for pertuzumab and trastuzumab and 4 months for taxane. Compared with docetaxel-containing therapy, paclitaxel-containing therapy was associated with more neuropathy (all-grade peripheral neuropathy 31% versus 16%) but less febrile neutropenia (1% versus 11%) and mucositis (14% versus 25%). At this preliminary analysis (52 months' median follow-up), median PFS was 20.6 [95% confidence interval (CI) 18.9–22.7] months overall (19.6, 23.0 and 18.1 months with docetaxel, paclitaxel and nab-paclitaxel, respectively). ORR was 80% (95% CI 78%–82%) overall (docetaxel 79%, paclitaxel 83%, nab-paclitaxel 77%).

Conclusions: Preliminary findings from PERUSE suggest that the safety and efficacy of first-line pertuzumab, trastuzumab and taxane for HER2-positive LR/MBC are consistent with results from CLEOPATRA. Paclitaxel appears to be a valid alternative taxane backbone to docetaxel, offering similar PFS and ORR with a predictable safety profile.

ClinicalTrials.gov: NCT01572038.

Key words: pertuzumab, dual HER2 blockade, paclitaxel, HER2-positive, metastatic breast cancer, first line

Introduction

For patients with HER2-positive breast cancer, HER2-directed therapy is established as the standard of care. In the first-line metastatic setting, dual HER2 blockade demonstrated improved outcomes compared with a single HER2-directed therapy: progression-free survival (PFS) and overall survival (OS) were significantly improved with the addition of pertuzumab to trastuzumab plus docetaxel in the randomised phase III CLEOPATRA trial [1, 2]. These results led to regulatory approval of the regimen in Europe and the United States and its rapid adoption into treatment guidelines by the American Society of Clinical Oncology, the National Comprehensive Cancer Network and the Advanced Breast Cancer 4 guidelines [3–5].

In many countries, paclitaxel is considered the first-line taxane of choice for patients with metastatic breast cancer, and is preferred to docetaxel because of its more tolerable acute toxicity profile [6]. Particularly in older patients, the approved dose of docetaxel 100 mg/m^2 may not be considered appropriate [7]. There is no evidence that paclitaxel agents (solvent based or nanoparticle bound) are less effective than docetaxel; on the contrary, nab-paclitaxel demonstrated improved PFS compared with docetaxel in a prospective randomised trial [8]. Nanoparticle albumin-bound (nab)-paclitaxel appears to offer similar efficacy to docetaxel, with less frequent neutropenia but more frequent sensory neuropathy [9, 10]. A single-arm study ($N = 51$) evaluating weekly paclitaxel combined with trastuzumab and pertuzumab as first- or second-line therapy reported median PFS of 25.7 months and median OS of 33 months [11]. However, conclusions are limited by the small sample size.

The PERtUzumab global SafEty (PERUSE) study was initiated to assess the safety and efficacy of three widely used taxanes in combination with dual HER2 targeting in the first-line locally recurrent/metastatic breast cancer (LR/MBC) setting. Here we report preliminary safety and efficacy analyses representing a snapshot of current data from this ongoing study, with a particular focus on subgroup analyses according to the taxane backbone combined with pertuzumab and trastuzumab. Data entry and cleaning will continue until database lock for the final analysis (prespecified ≥60 months after last patient enrolment), which is expected in 2020.

Patients and methods

PERUSE (NCT01572038) is a global open-label single-arm phase IIIb study evaluating the safety and tolerability of pertuzumab in combination with trastuzumab and a taxane. Eligible patients were male or female, aged ≥18 years, with HER2-positive LR/MBC not amenable to curative resection. HER2 positivity was defined as 3+ staining by immunohistochemistry or positive by *in situ* hybridisation according to local assessment of the primary tumour and/or metastatic site. All patients had to have at least one measurable lesion and/or non-measurable disease evaluable according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Patients with central nervous system metastases were eligible if they were stable for ≥3 months preceding screening after receiving local therapy without anti-HER2 therapy. Patients were required to have Eastern Cooperative Oncology Group performance status ≤2, life expectancy ≥12 weeks, left ventricular ejection fraction (LVEF) ≥50% and to have received no prior systemic therapy (except ≤2 lines of endocrine therapy, one of which may have been in combination with everolimus) for LR/MBC. Any prior anti-HER2 agent (approved or investigational) other than (neo)adjuvant trastuzumab and/or lapatinib was prohibited. Patients with disease progression during (neo)adjuvant trastuzumab and/or lapatinib therapy were excluded, as were patients with recurrence within 6 months of completing (neo)adjuvant non-hormonal systemic therapy. Additional exclusion criteria included history of persistent grade ≥2 haematological toxicity related to previous (neo)adjuvant therapy, ongoing grade ≥3 peripheral neuropathy or inadequate organ function.

Investigators selected their preferred taxane agent (docetaxel, paclitaxel or nab-paclitaxel), administered weekly or every 3 weeks (q3w) according to local prescribing information and/or recognised guidelines. Taxane therapy was given in combination with pertuzumab (Perjeta®, F. Hoffmann-La Roche Ltd, Basel, Switzerland) 840 mg as a loading dose, reduced to 420 mg for subsequent cycles administered q3w, and trastuzumab (Herceptin®, F. Hoffmann-La Roche Ltd) 8 mg/kg as a loading dose, reduced to 6 mg/kg for subsequent cycles administered q3w. The protocol allowed switching to an alternative taxane during treatment. Study medication was administered until unacceptable toxicity, disease progression, withdrawal of consent or death, whichever occurred first.

LVEF was assessed by either echocardiography (preferred) or multigated acquisition scan within 42 days of enrolment and every three treatment cycles (≤7 days before study drug administration) thereafter. In the event of an LVEF measurement ≤45%, a strict algorithm for treatment interruption, continuation or permanent discontinuation was implemented (supplementary Figure S1, available at *Annals of Oncology* online). Adverse events (AEs) were coded according to the Medical Dictionary for Regulatory Activities (version 21.0) and severity was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0). Patients participating in the PERUSE study will be followed up until at least 60 months after enrolment of the last patient or until all patients in the study have withdrawn consent or died, whichever occurs first.

The primary objective of PERUSE is to evaluate the safety and tolerability of pertuzumab in combination with trastuzumab and a taxane. Safety outcome measures include the incidence and severity of AEs and LVEF measurements. Secondary outcome measures include PFS, OS, overall response rate (ORR), clinical benefit rate, duration of response, time to response and patient-reported outcomes.

Investigators assessed tumour response using computed tomography or magnetic resonance imaging scans (and isotope bone scan if indicated) according to RECIST (version 1.1). Objective responses were confirmed ≥4 weeks after initial documentation. Tumour assessments were carried out every three cycles for the first 3 years, and every six cycles thereafter in patients who remained progression free.

Safety analyses were based on the safety population, comprising all enrolled patients who received at least one dose of study treatment. In the present analysis, patients were allocated to each taxane subgroup according to the first taxane they received during study therapy. PFS was estimated using the Kaplan–Meier method in the intent-to-treat (ITT) population, defined as all enrolled patients. ORR analysis was based on the best (confirmed) overall response as assessed by investigators in all enrolled patients with measurable disease at baseline. The number and proportion of responders and non-responders in patients with measurable disease were reported for each treatment group, together with two-sided 95% confidence intervals (CIs). Patients without a post-baseline tumour assessment were considered to be non-responders. Subgroup analyses according to the type of taxane were prespecified in the protocol.

All analyses are descriptive. No formal statistical hypothesis tests were carried out. There were no adjustments for multiplicity of end points or comparisons within subgroups.

The study was carried out in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki, and all patients provided written informed consent. The protocol and all accompanying materials provided to patients were approved by independent ethics committees at the participating institutions. An independent data monitoring committee reviewed study data at prespecified intervals during enrolment and then annually after completion of enrolment.

Results

Patient population

Between 11 May 2012 and 16 September 2014, 1667 patients were screened, of whom 1436 were enrolled from sites in Europe ($N=1009$), Asia ($N=177$), South America ($N=121$), Africa ($N=71$), Canada ($N=34$) and Australia ($N=24$). A total of 1436 patients received pertuzumab, 1435 received trastuzumab and 1429 received a taxane. One patient discontinued therapy immediately after the first pertuzumab administration and therefore received neither trastuzumab nor taxane; six additional patients discontinued all study treatments before receiving their first taxane dose. The initial taxane selected by the investigator was docetaxel in 775 patients (54%), paclitaxel in 589 patients (41%) and nab-paclitaxel in 65 patients (5%). Although information on paclitaxel treatment schedule was not collected, approximately two-thirds of patients received two or more doses per cycle, suggesting that a weekly paclitaxel regimen was administered. There were some notable differences between countries in chemotherapy selection: docetaxel was selected for all patients in Africa, Poland, Finland and Estonia, whereas in Germany, Israel, Ukraine, Belgium, Canada, The Netherlands, Peru, Argentina, Hong Kong and Ecuador, ≥60% of patients received paclitaxel chemotherapy. More than half of all patients receiving nab-paclitaxel were treated in Germany or Australia. A total of 52 patients (4%) switched taxane at least once during the study (25 from docetaxel to paclitaxel, 16 from paclitaxel to docetaxel).

Baseline characteristics and prior therapy are summarised in Table 1 and supplementary Table S1, available at *Annals of Oncology* online. The main differences between the chemotherapy subgroups were the slightly older age and worse performance status in the paclitaxel subgroup, and the higher proportion of patients with *de novo* metastatic disease in the docetaxel subgroup.

Treatment exposure

At the data cut-off for this preliminary analysis (16 March 2018), the median duration of follow-up was 52.2 months (95% CI 51.5–52.7). The median duration of anti-HER2 therapy was 24 cycles (range 1–99) (16 months) for both pertuzumab and trastuzumab. The median duration of taxane exposure was six cycles (range 1–70), corresponding to 4.0 months (3.8, 4.2 and 3.9 months for docetaxel, paclitaxel and nab-paclitaxel, respectively) (supplementary Table S2, available at *Annals of Oncology* online). Treatment was ongoing in 270 patients, of whom 75 had discontinued at least one of the component drugs, predominantly taxane (73 patients). Of the 1166 patients who had discontinued all study treatment, 348 remained in follow-up. Disease progression was the most common reason for discontinuing pertuzumab (57%) and trastuzumab (56%), with only 9% of patients discontinuing either anti-HER2 agent because of AEs (supplementary Table S3, available at *Annals of Oncology* online). In contrast, reasons for discontinuing taxane therapy were more varied (AEs in 18%, investigator decision or disease progression each in 17%, and 'other' reason in 30%).

Safety

In the overall population, the most common AEs (any grade) were diarrhoea (68%), alopecia (48%), nausea (35%) and fatigue (32%). Although these AEs were among the most common with all three chemotherapy backbones, some differences in safety profile were apparent between the subgroups. Neuropathy and epistaxis were more common with paclitaxel and nab-paclitaxel than with docetaxel, whereas febrile neutropenia and mucosal inflammation were more common with docetaxel than with either paclitaxel formulation (supplementary Table S4, available at *Annals of Oncology* online).

The most common grade ≥3 AEs were neutropenia (10%), diarrhoea (8%) and febrile neutropenia (6%). The incidences of grade ≥3 neutropenia and febrile neutropenia were highest with docetaxel and lowest with nab-paclitaxel (Figure 1). The incidences of grade ≥3 diarrhoea and other grade ≥3 AEs were generally similar in the three taxane subgroups. Fatal AEs were reported in 16 patients (2%) in the docetaxel subgroup [infections in 0.6%, cardiac disorders in 0.5%, hepatic failure in 0.3% and neutropenia, acute respiratory distress syndrome, hypoglycaemia, spontaneous abortion (although not fatal for the patient), delirium and unexplained death each in 0.1%], 19 patients (3%) in the paclitaxel subgroup (infections and unexplained death each in 0.8%, cardiac disorders in 0.5%, pancreatitis and haematological AEs each in 0.3% and hepatic encephalopathy, ischaemic stroke and bronchial aspiration each in 0.2%) and one patient (2%) in the nab-paclitaxel subgroup (pneumonitis).

The AEs most commonly leading to treatment discontinuation for both pertuzumab and trastuzumab were ejection fraction decreased (2.3%), cardiac failure (0.8%) and left ventricular dysfunction (0.6%). For taxane discontinuation, the most common AEs were peripheral neuropathy (3.7%), paraesthesia, peripheral sensory neuropathy (both 1.7%), fatigue (1.2%) and diarrhoea (1.1%).

In the overall safety population across all timepoints, LVEF remained above 50% in most patients (86%). In 24 patients (2%), the worst recorded LVEF was 45%–50% with a decrease from baseline of <10% points; in 69 patients (5%), the worst recorded LVEF was 45%–50% with a decrease from baseline of ≥10% points. Sixty patients (4%) had an LVEF <45%. LVEF measurements were missing in 46 patients (3%), 35 of whom discontinued from the study before the scheduled date of their first post-baseline LVEF assessment. There was no recognisable pattern for the timing of LVEF decrease.

Efficacy

Best overall response was evaluable in 1199 patients with measurable disease at baseline. The ORR was 80% (95% CI 78% to 82%), including confirmed complete responses in 15%. An additional 15% of patients had stable disease as their best overall response. ORRs were similar in the three taxane subgroups (Table 2).

At the data cut-off date, PFS events had been recorded in 986 patients (69%). Median PFS was 20.6 months (95% CI 18.9–22.7) in the ITT population (Figure 2A). Median PFS according to the initial taxane was 19.6 months (95% CI 16.9–21.8) with

Table 1. Baseline characteristics and treatment history overall and by taxane subgroup

Characteristics	All patients (*N* = 1436)	Docetaxel (*N* = 775)	Paclitaxel (*N* = 589)	Nab-paclitaxel (*N* = 65)
Age, years				
Median (range)	54 (23–87)	53 (23–82)	56 (26–87)	53 (31–81)
≥65	312 (22)	137 (18)	158 (27)	14 (22)
≥75	81 (6)	29 (4)	46 (8)	4 (6)
ECOG PS[a]				
0	851 (59)	487 (63)	320 (54)	43 (66)
1	521 (36)	267 (34)	229 (39)	21 (32)
2	63 (4)	20 (3)	40 (7)	1 (2)
Sex				
Female	1429 (100)	772 (100)	587 (100)	63 (97)
Male	7 (<1)	3 (<1)	2 (<1)	2 (3)
Stage at initial diagnosis				
I	116 (8)	54 (7)	56 (10)	5 (8)
II	395 (28)	193 (25)	184 (31)	18 (28)
III	400 (28)	219 (28)	148 (25)	29 (45)
IV	509 (35)	298 (38)	196 (33)	13 (20)
Not done	16 (1)	11 (1)	5 (1)	0
Median time since initial breast cancer diagnosis, months (range)	26.5 (0.2–383.0[b])	19.2 (0.2–383.0)	28.1 (0.3–366.2)	33.5 (0.3–283.8)
Hormone receptor status[b]				
ER and/or PgR positive	918 (64)	491 (63)	377 (64)	46 (71)
ER and PgR negative	512 (36)	279 (36)	211 (36)	19 (29)
Metastatic sites				
Visceral	1000 (70)	552 (71)	401 (68)	42 (65)
Prior chemotherapy	680 (47)	348 (45)	293 (50)	36 (55)
Neoadjuvant	219 (15)	115 (15)	92 (16)	12 (18)
Adjuvant	516 (36)	265 (34)	222 (38)	26 (40)
Metastatic/advanced	2 (<1)	1 (<1)	1 (<1)	0
Other[c]	1 (<1)	0	1 (<1)	0
Type of chemotherapy				
Anthracycline	570 (40)	301 (39)	241 (41)	26 (40)
Taxane	380 (26)	187 (24)	170 (29)	21 (32)
Endocrine therapy	409 (28)	201 (26)	181 (31)	24 (37)
Neoadjuvant	8 (1)	5 (1)	3 (1)	0
Adjuvant	348 (24)	173 (22)	154 (26)	18 (28)
Metastatic/advanced	92 (6)	43 (6)	42 (7)	7 (11)
Other	4 (<1)	1 (<1)	3 (1)	0
Trastuzumab	416 (29)	212 (27)	176 (30)	26 (40)
Neoadjuvant	81 (6)	43 (6)	33 (6)	5 (8)
Adjuvant	381 (27)	195 (25)	159 (27)	25 (38)
Metastatic/advanced	3 (<1)	0	2 (<1)	1 (2)
Other	6 (<1)	1 (<1)	5 (1)	0
Radiotherapy	661 (46)	332 (43)	289 (49)	36 (55)
Surgery	1109 (77)	579 (75)	472 (80)	53 (82)

[a]Missing in one patient in the docetaxel subgroup.
[b]Unknown in six patients (five in the docetaxel subgroup and one in the paclitaxel subgroup; two patients with unknown ER and PgR, four patients negative for one receptor and unknown for the other).
[c]Locally advanced.
All data are *N* (%) unless otherwise indicated.
ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; PgR, progesterone receptor.

docetaxel, 23.0 months (95% CI 19.8–25.8) with paclitaxel and 18.1 months (95% CI 12.2–32.3) with nab-paclitaxel (Figure 2B).

Further subgroup analyses according to hormone receptor status are shown in Figure 2C and D. In the hormone receptor-positive subgroup, median PFS was 19.8 months (95% CI 16.6–23.3) with docetaxel, 22.7 months (95% CI 19.2–25.8) with paclitaxel and 15.4 months (95% CI 10.2–31.6) with nab-paclitaxel. In the hormone receptor-negative subgroup, median

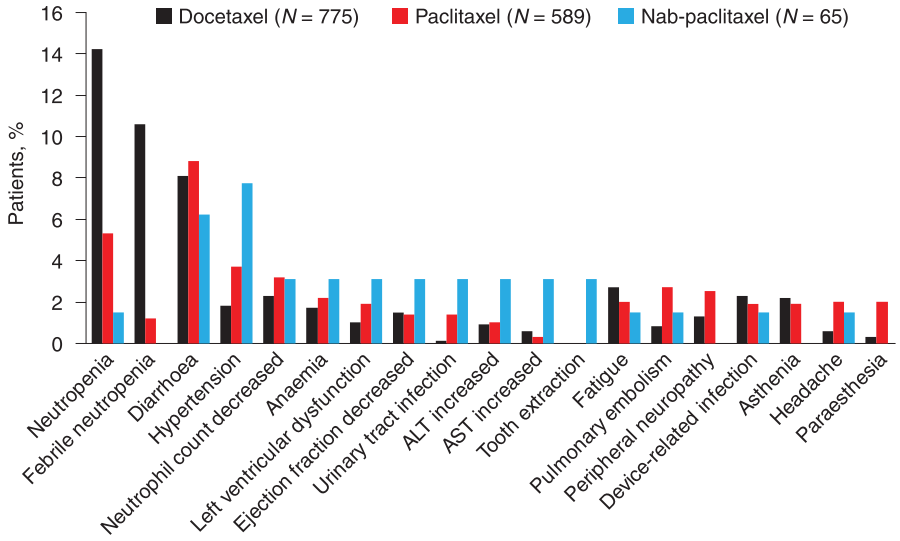

Figure 1. Most common (>2% of patients in any subgroup) grade ≥3 adverse events by initially selected taxane. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 2. Best overall response in patients with measurable disease at baseline

Response, *N* (%)	All patients (*N* = 1199)	Docetaxel (*N* = 657)	Paclitaxel (*N* = 483)	Nab-paclitaxel (*N* = 53)
ORR [95% Clopper–Pearson CI]	959 (80) [78–82]	517 (79) [75–82]	400 (83) [79–86]	41 (77) [64–88]
Complete response	175 (15)	89 (14)	83 (17)	3 (6)
Partial response	784 (65)	428 (65)	317 (66)	38 (72)
Stable disease	180 (15)	108 (16)	62 (13)	9 (17)
Progressive disease	50 (4)	25 (4)	19 (4)	3 (6)
Not evaluable	10 (1)	7 (1)	2 (<1)	0

Patients with complete or partial response were considered as responders. Patients without a post-baseline tumour assessment were considered as non-responders. Patients with no post-baseline tumour assessment who discontinued treatment because of clinical progression were considered to have progressive disease as best overall response (*N* = 2).
CI, confidence interval; ORR, overall response rate.

PFS was 17.8 months (95% CI 15.0–22.8) with docetaxel, 24.2 months (95% CI 17.9–29.7) with paclitaxel and 32.3 months (95% CI 9.1–not evaluable) with nab-paclitaxel.

OS results were not mature at this data cut-off. Among the 545 patients (38%) who had died at the time of data cut-off, the majority (462; 85%) had died from disease progression.

Discussion

The PERUSE study population of 1436 patients treated with trastuzumab, pertuzumab and taxane therapy represents the largest population treated in this setting reported to date. PERUSE includes patients representative of routine oncology practice, such as those who may not be suitable for docetaxel therapy and a substantial proportion (45% of patients initially diagnosed with early breast cancer) previously treated with trastuzumab (29% of the overall population compared with 12% in CLEOPATRA [1]). Preliminary findings suggest that the safety and efficacy of first-line pertuzumab combined with trastuzumab and standard taxane therapy for HER2-positive LR/MBC are consistent with results from the phase III CLEOPATRA trial [1, 2]. Preliminary PFS results suggest activity for all three combinations in line with the 18.5-month median PFS observed in CLEOPATRA with pertuzumab, trastuzumab and docetaxel [1]. In PERUSE, median PFS was 20.6 months overall and 19.6, 23.0 and 18.1 months in the docetaxel, paclitaxel and nab-paclitaxel subgroups, respectively. ORRs were also similar in the two trials (80% in both CLEOPATRA and overall in PERUSE; 79%, 83% and 77% in the docetaxel, paclitaxel and nab-paclitaxel subgroups, respectively, of PERUSE), although we acknowledge the limitations of cross-trial comparisons.

The safety profile of pertuzumab, trastuzumab and taxane regimens in PERUSE was also generally consistent with results from CLEOPATRA, characterised by all-grade diarrhoea, alopecia, nausea and fatigue and grade ≥3 diarrhoea and haematological toxicities. However, there was a notably lower incidence of neutropenia and febrile neutropenia in PERUSE compared with CLEOPATRA. This may be partly explained by the chemotherapy backbone, as incidences of febrile neutropenia were less

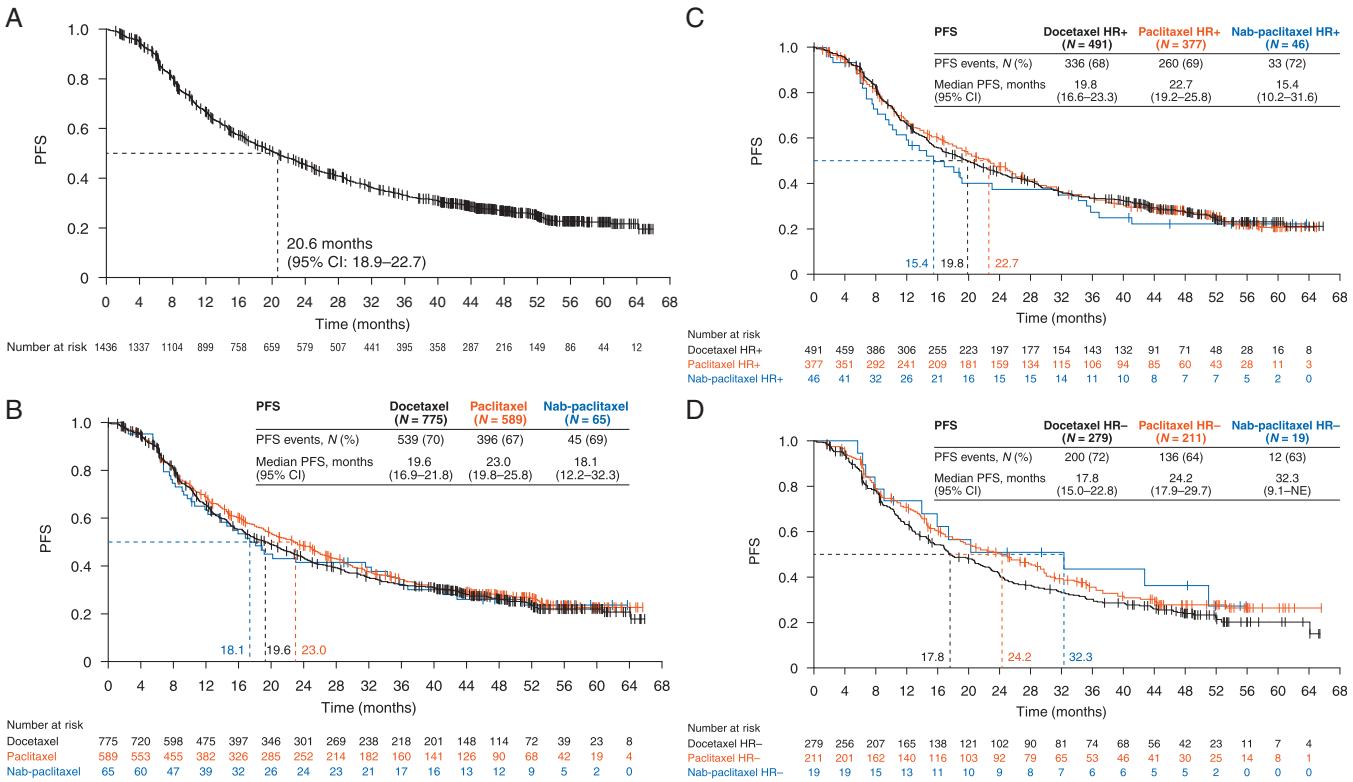

Figure 2. PFS: (A) overall; (B) by initially selected taxane; (C) by initially selected taxane in the HR-positive subgroup; and (D) by initially selected taxane in the HR-negative subgroup. CI, confidence interval; HR, hormone receptor; NE, not evaluable; PFS, progression-free survival.

different between CLEOPATRA (14%) and the docetaxel subgroup of PERUSE (11%). Furthermore, weekly taxane schedules may be associated with less neutropenia than q3w schedules [12, 13].

Focusing on differences between taxane subgroups within the PERUSE study, neuropathy was observed most frequently in the paclitaxel subgroup. However, febrile neutropenia was less common with paclitaxel-containing than docetaxel-containing regimens. These results are consistent with clinical experience of each chemotherapy. This more manageable safety profile, combined with the similar or better efficacy of weekly paclitaxel [13], contributes to many clinicians' preference for paclitaxel combination regimens instead of the approved docetaxel regimen.

PERUSE findings complement results from the CLEOPATRA trial, indicating that findings from a phase III trial can be replicated in the routine clinical practice setting. The results also expand upon recently published retrospective and real-world studies of patients treated with pertuzumab, trastuzumab and the investigator's chosen taxane in the United States, Italy and Turkey, which reported median PFS ranging from 17 to 29 months [14–17]. Strengths of PERUSE results compared with previous reports include the prospective nature of the study, the larger proportion of patients treated with paclitaxel instead of docetaxel, the more rigorous data collection and the regular schedule of tumour assessment according to RECIST (version 1.1).

A limitation of PERUSE is the single-arm open-label design lacking a control arm. Limitations of the preliminary analyses reported here include the exploratory nature of these subgroup analyses, which may be biased by differences in patient selection, regional oncology practice and confounding factors at baseline, the relatively few patients treated with nab-paclitaxel and the current absence of OS results. Nevertheless, ORR, PFS and more favourable tolerability with paclitaxel, despite the slightly older age, worse performance status and higher proportion of patients with recurrent metastatic disease, provide reassurance that paclitaxel (or nab-paclitaxel) is a reasonable alternative in patients for whom docetaxel may not be considered optimal or appropriate.

In conclusion, these results from the PERUSE study after a median follow-up of >4 years support the use of paclitaxel or nab-paclitaxel as alternatives to docetaxel in combination with first-line pertuzumab and trastuzumab for HER2-positive LR/MBC. Efficacy in the paclitaxel and nab-paclitaxel subgroups appeared similar to that observed with docetaxel; the more favourable safety profile suggests that paclitaxel or nab-paclitaxel may be valid alternatives to docetaxel with pertuzumab and trastuzumab. Final results from the PERUSE study are expected in 2020.

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