

**LBA2.PR Overall survival (OS) with palbociclib plus fulvestrant in women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC): Analyses from PALOMA-3**

M. Cristofanilli<sup>1</sup>, D.J. Slamon<sup>2</sup>, J. Ro<sup>3</sup>, I. Bondarenko<sup>4</sup>, S-A. Im<sup>5</sup>, N. Masuda<sup>6</sup>, M. Colleoni<sup>7</sup>, A. DeMichele<sup>8</sup>, S. Loi<sup>9</sup>, S. Verma<sup>10</sup>, H. Iwata<sup>11</sup>, N. Harbeck<sup>12</sup>, S. Loibl<sup>13</sup>, F. André<sup>14</sup>, K. Puyana Theall<sup>15</sup>, X. Huang<sup>16</sup>, C. Giorgetti<sup>17</sup>, C. Huang Bartlett<sup>18</sup>, N.C. Turner<sup>19</sup>

<sup>1</sup>Robert H. Lurie Comprehensive Cancer Center, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, <sup>2</sup>Geffen School of Medicine, UCLA - School of Medicine, Los Angeles, CA, USA, <sup>3</sup>Oncology, National Cancer Center, Goyang-si, Republic of Korea, <sup>4</sup>Dnipropetrovsk Medical Academy, City Multiple-Discipline Clinical Hospital #4, Dnipropetrovsk, Ukraine, <sup>5</sup>Cancer Research Institute, Seoul National University Hospital, Seoul, Republic of Korea, <sup>6</sup>Dept. of Surgery, Breast Oncology, NHO Osaka National Hospital, Osaka, Japan, <sup>7</sup>Divisione di Senologia Medica, Istituto Europeo di Oncologia, Milan, Italy, <sup>8</sup>Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA, <sup>9</sup>Peter MacCallum Cancer Centre, University of Melbourne, Melbourne, Australia, <sup>10</sup>Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada, <sup>11</sup>Department of Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan, <sup>12</sup>Dept. of Obstetrics and Gynecology, Brustzentrum der Universität München (LMU), Munich, Germany, <sup>13</sup>German Breast Group, C/o GBG Forschungs GmbH, Neu-Isenburg, Germany, <sup>14</sup>Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, <sup>15</sup>Pfizer Oncology, Pfizer Inc, Cambridge, MA, USA, <sup>16</sup>Pfizer Oncology, Pfizer Inc, San Diego, CA, USA, <sup>17</sup>Pfizer Oncology, Pfizer Inc, Milan, Italy, <sup>18</sup>Pfizer Oncology, Pfizer Inc, Collegeville, PA, USA, <sup>19</sup>Breast Cancer Now Research Centre, Royal Marsden Hospital and Institute of Cancer Research, London, UK

**Background:** Endocrine therapy (ET)—resistant ABC is dependent on cyclin dependent kinase (CDK) 4/6. In the prospective, randomized, double-blind, phase 3 PALOMA-3 study, the CDK4/6 inhibitor PAL in combination with FUL significantly improved progression-free survival (PFS) vs placebo (PBO)+FUL (median PFS, 11.2 vs 4.6 mo; absolute difference, 6.6 mo; hazard ratio [HR] 0.50 [95% CI, 0.40–0.62]; P < 0.000001). Here, we report OS analysis with a median follow up of 44.8 mo.

**Methods:** HR+/HER2- ABC (N = 521) patients (pts) who had relapsed or progressed on prior ET were randomized 2:1 to PAL (125 mg/d orally, schedule 3/1) + FUL (500 mg per standard of care) or PBO+FUL. Primary endpoint was investigator-

assessed PFS. A key secondary endpoint was OS. OS analysis occurred when approximately 60% (n≈310) of the 521 pts died.

**Results:** Median OS improved with PAL+FUL vs PBO+FUL by an absolute difference of 6.9 mo (Table). In pts with sensitivity to prior ET, the absolute improvement in median OS was 10.0 mo with PAL+FUL vs PBO+FUL. In pts without visceral disease, median OS significantly improved with PAL+FUL vs PBO+FUL (11.5 mo). Time to end of the next-line treatment was 18.8 (PAL+FUL) and 14.1 (PBO+FUL) mo (HR 0.68 [95% CI, 0.56–0.84]; P < 0.0001). Improvements in median OS, although not statistically significant at the prespecified level, were shown with PAL+FUL vs PBO+FUL regardless of ESR1 mutation status or prior lines of therapy. Median time on subsequent therapy was similar in both arms; median time to chemotherapy was 17.5 (PAL+FUL) and 8.8 (PBO+FUL) mo (HR 0.58; P < 0.000001). No new safety signals were observed with longer follow-up.

**Conclusions:** In HR+/HER2- ABC pts, PAL+FUL showed a clinically meaningful improvement in OS (6.9 mo vs PBO+FUL), especially in pts with sensitivity to prior ET. The absolute difference of PFS gain was maintained in OS.

**Clinical trial identification:** NCT01942135.

**Editorial acknowledgement:** Editorial support was provided by Jennifer Fetting, PhD, and Kevin O'Regan, PhD, of Complete Healthcare Communications, LLC (North Wales, PA), a CHC Group company, and funded by Pfizer Inc.

**Legal entity responsible for the study:** Pfizer Inc.

**Funding:** Pfizer Inc.

**Disclosure:** M. Cristofanilli: Honoraria: Pfizer. D.J. Slamon: Consulting or advisory role: Bayer, Eli Lilly, Novartis, BioMarin. S-A. Im: Consulting or advisory role: AstraZeneca, Hanmi Corp., Novartis, Roche, Pfizer. N. Masuda: Honoraria: Chugai, AstraZeneca, Pfizer, Takeda; Research funds: Chugai, AstraZeneca, Kyowa-Kirin, MSD, Novartis, Pfizer, Eli Lilly, Daiichi-Sankyo. A. DeMichele: Consulting or advisory role: Pfizer, Novartis; Research funds: Pfizer, Novartis, Johnson & Johnson, Calithera, Incyte, Genentech. S. Loi: Research funds: Merck, Novartis, Roche-Genentech. S. Verma: Consulting or advisory role: Pfizer, Novartis, Roche, AstraZeneca, Amgen, Eli Lilly. H. Iwata: Honoraria: AstraZeneca, Chugai, Eisai, Novartis; Consulting or advisory role: Chugai, Daiichi-Sankyo. N. Harbeck: Honoraria: Lilly, Novartis, Pfizer. S. Loibl: Research funds: Pfizer, Novartis. F. André: Research funds: AstraZeneca, Novartis, Pfizer, Eli Lilly. K. Puyana Theall, X. Huang, C. Huang Bartlett: Pfizer employee and shareholder. C. Giorgetti: Consulting role and shareholder: Pfizer. N.C. Turner: Honoraria: Pfizer; Consulting or advisory role: Pfizer; Research funds: Servier, Pfizer, Eli Lilly, Roche, AstraZeneca. All other authors have declared no conflicts of interest.

**Table: LBA2\_PR OS in the ITT population and by subgroup**

Subgroup	n (%)	HR (95% CI)	PAL+FUL median OS (95% CI)	PBO+FUL median OS (95% CI)	1-sided P value	Interaction P value
ITT, stratified	521 (100)	0.81 (0.64–1.03)	34.9 (28.8–40.0)	28.0 (23.6–34.6)	0.043	–
ITT, unstratified	521 (100)	0.79 (0.63–1.00)	34.9 (28.8–40.0)	28.0 (23.6–34.6)	0.025	–
Sensitivity to previous endocrine therapy						
Endocrine sensitive	410 (78.7)	0.72 (0.55–0.94)	39.7 (34.8–45.7)	29.7 (23.8–37.9)	–	0.124
Endocrine resistant	111 (21.3)	1.14 (0.71–1.84)	20.2 (17.2–26.4)	26.2 (17.5–31.8)	–	–
Site of metastatic disease						
Visceral disease	311 (59.7)	0.85 (0.64–1.13)	27.6 (24.4–31.2)	24.7 (20.8–31.8)	–	0.442
Nonvisceral disease	210 (40.3)	0.69 (0.46–1.04)	46.9 (39.3–NE)	35.4 (24.6–NE)	–	–
Menopausal status at study entry						
Postmenopausal	413 (79.3)	0.73 (0.57–0.95)	34.8 (28.8–40.1)	27.1 (22.8–32.1)	–	0.251
Pre/perimenopausal	108 (20.7)	1.07 (0.61–1.86)	38.0 (24.4–NE)	38.0 (22.2–NE)	–	–

FUL=fulvestrant; HR=hazard ratio; ITT=intent-to-treat; NE=not estimable; OS=overall survival; PAL=palbociclib; PBO=placebo.

Downloaded from https://academic.oup.com/annonc/article-abstract/29/suppl\_8/ndy424.009/5141510 by guest on 22 September 2019