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

Presentation Number: LBA2_PR
Lecture Time: 17:00 - 17:15
Speakers: Massimo Cristofanilli (Chicago, US)
Session Name: Presidential Symposium 1
Location: Hall A2 - Room 18, ICM München, Munich, Germany
Date: 20.10.2018
Time: 16:30 - 18:20

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 (11.33 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.
Table. OS in the ITT Population and by Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>HR (95% CI)</th>
<th>PAL+FUL median OS (95% CI)</th>
<th>PBO+FUL median OS (95% CI)</th>
<th>1-sided P value</th>
<th>Interaction P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT, stratified</td>
<td>521 (100)</td>
<td>0.81 (0.64–1.03)</td>
<td>34.9 (28.8–40.0)</td>
<td>28.0 (23.6–34.6)</td>
<td>0.043</td>
<td>–</td>
</tr>
<tr>
<td>ITT, unstratified</td>
<td>521 (100)</td>
<td>0.79 (0.63–1.00)</td>
<td>34.9 (28.8–40.0)</td>
<td>28.0 (23.6–34.6)</td>
<td>0.025</td>
<td>–</td>
</tr>
</tbody>
</table>

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) | – | – |
| 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.

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.

Funding: Pfizer (NCT01942135)

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.