PARSIFAL-LONG: Extended follow-up of hormone receptor-positive/HER2-negative advanced breast cancer patients treated with fulvestrant and palbociclib vs letrozole and palbociclib in the PARSIFAL study

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Background: Parsifal Study

PARSIFAL (NCT02491983): An international, multicenter, phase II clinical trial assessing whether fulvestrant or letrozole was the optimal endocrine partner for palbociclib in patients with untreated, endocrine sensitive, HR[+] /HER2[-] advanced breast cancer

The trial failed to demonstrate an improvement in PFS of palbociclib + fulvestrant over palbociclib + letrozole, with a median follow-up of 32 months (IQR, 24.2-39.7).


IQR: Interquartile range (25% and 75%); HR: hazard ratio; No.: number of patients; mo: months
## Parsifal-Long: Methods

<table>
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<th><strong>Design</strong></th>
<th>Extended follow-up of an international, multicenter study that included patients from the prospective PARSIFAL study</th>
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<td><strong>Primary Objective</strong></td>
<td>Compare extended efficacy, in terms of OS, of palbociclib + fulvestrant vs. palbociclib + letrozole</td>
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| **Secondary Objectives** | • Extended PFS of palbociclib + fulvestrant vs. palbociclib + letrozole  
• Extended efficacy in combined treatment arms, by PFS and OS  
• Identification of new prognostic and predictive markers |
| **Statistical Considerations** | • Planned recruitment of at least 388 patients with 195 deaths  
• The 2-sided stratified log-rank test ($\alpha = 0.05$) had a 70% power to detect a hazard ratio $\leq 0.70$ in favor of fulvestrant + palbociclib arm |

OS: overall survival; PFS: progression-free survival
Results: Patient Demographics

This analysis includes all patients from 32 of the 47 original sites.

Patients signed a new informed consent form, if applicable, according to local regulations.

389 patients (80.5%) from the PARSIFAL study were included.

Median follow-up of 59.7 months (IQR, 36.3-72.9).

Demographic and baseline disease characteristics were similar between the PARSIFAL-LONG and the overall PARSIFAL intention-to-treat population.

IQR: Interquartile range (25% and 75%)
**Results:** Extended PFS and OS by treatment arm (n= 389)

Median follow-up: 59.7 months. Data cutoff: May 2023.

**Progression-Free Survival**

- **Median PFS (months)**
  - **F+P:** 31.4 (95%CI: 24.4-44.2)
  - **L+P:** 34.5 (95%CI: 27.6-44.9)
  - Hazard ratio: 1.00 (95%CI: 0.78-1.29),

- **p=0.985**

**Overall Survival (OS)**

- **Median OS (months)**
  - **F+P:** 68.5 (95%CI: 54.3-81.6)
  - **L+P:** 61.9 (95%CI: 55.7-71.3)
  - Hazard ratio: 0.94 (95%CI: 0.72-1.23),

- **p=0.635**

F: fulvestrant; L: letrozole; n (%), number of patients (percentage based on N); N: number of patients; OS: overall survival; P: palbociclib; PFS: progression-free survival
Results: PFS and OS of both cohorts combined (n=389)

Median follow-up: 59.7 months

Progression-Free Survival

PFS Events: 241 (62.0%)
Median PFS: 33.2 months, 95%CI: 27.7-39.5
5-year PFS rate: 35.3%, 95%CI: 30.2-40.3

Overall Survival

OS Events: 213 (54.8%)
Median OS: 65.4 months, 95%CI: 57.8-72

n (%), number of patients (percentage based on N); N: number of patients; OS: overall survival; PFS: progression-free survival
**Results:** Post-progression Survival by PFS duration (< 6, 6 - 12, and ≥12 months) for progressing patients (n=229)

- **≥12:** 27 mo. (95%CI: 24.1-31.1)
- **<12 to ≥6:** 19.2 mo. (95%CI: 8.6-24.5)
- **<6:** 18 mo. (95%CI: 8.6-24.7)

**Events per cohort:**
- ≥12: 103 (65.2%)
- <12 to ≥6: 34 (94.4%)
- <6: 27 (77.1%)

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Conclusions

- Extended follow-up confirmed no difference between letrozole and fulvestrant when combined with palbociclib
- mPFS was 33.2 months (95%CI, 27.7-39.5) and mOS was 65.4 mo (95%CI, 57.8-72.0), which is consistent with data for other CDK4/6 inhibitors
- Additional follow-up is planned with a data cutoff date of January 2024
- Early progression (<12 months) on a CDK4/6i regimen is a strong clinical marker of a less favorable outcome
We would like to extend our deepest gratitude all the patients and their families.

We would like to thank the investigators and personal from our participating sites, Pfizer, and the study team at MEDSIR.

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