SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM®
DECEMBER 5-9, 2023 | @SABCSSanAntonio

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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Disclosure Information

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Antonio Llombart-Cussac, MD, PhD

- **Consulting/Advisor**: Roche, AstraZeneca, Seagen, Daiichi Sankyo, Eli Lily, Merck Sharp&Dohme, GSK, Gilead, Menarini, ExactSicences, Novartis, Agendia, Pfizer.
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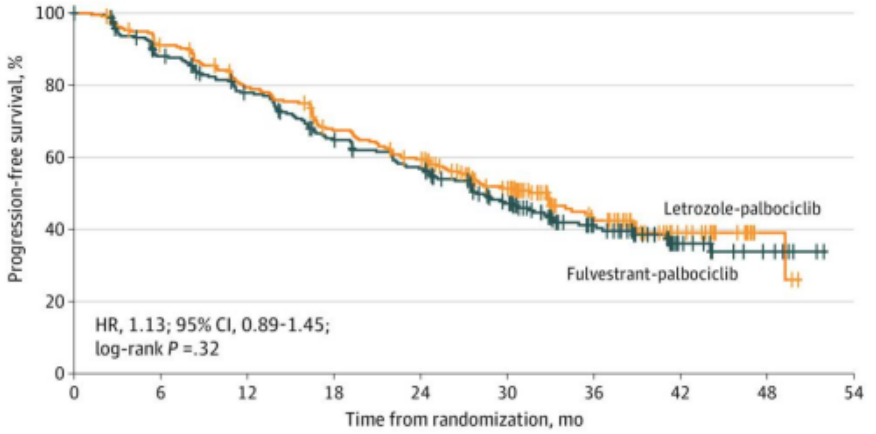
- **Patents**: HER2 as a predictor of response to dual HER2 blockade in the absense of cytotoxic therapy. Aleix Prat, Antonio Llombart, Javier Cortés. US 2019/0338368 A1.

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



No. at risk

Fulvestrant-palbociclib	243 (100)	204 (84)	174 (72)	141 (58)	121 (50)	86 (35)	51 (21)	20 (8)	7 (3)	0 (0)
Letrozole-palbociclib	243 (100)	212 (87)	182 (75)	151 (62)	131 (54)	92 (38)	51 (21)	23 (9)	3 (1)	0 (0)

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).

Llombart-Cussac A, et al. *JAMA Oncol*. 2021 Dec 1;7(12):1791-1799.

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

Parsifal-Long: Methods

Design	Extended follow-up of an international, multicenter study that included patients from the prospective PARSIFAL study
Primary Objective	Compare extended efficacy, in terms of OS, of palbociclib + fulvestrant vs. palbociclib + letrozole
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 ≤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**

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

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

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

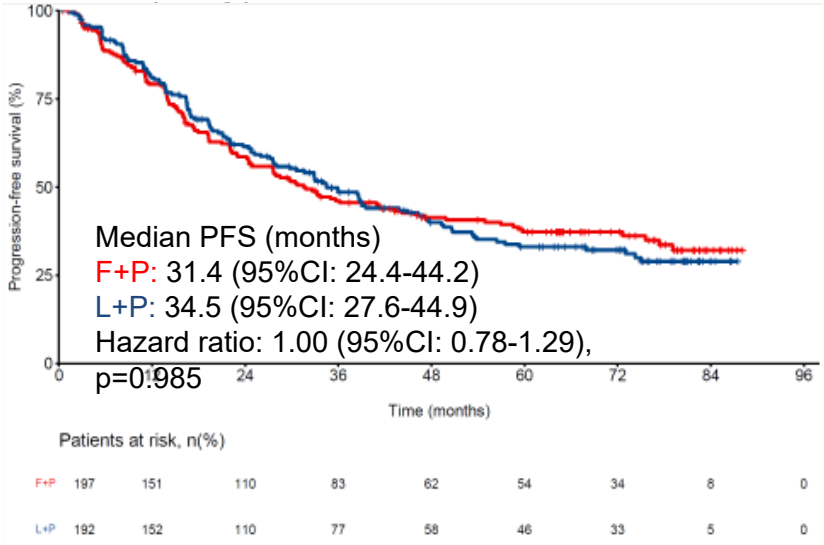
Demographic and baseline disease characteristics were similar between the PARSIFAL-LONG and the overall PARSIFAL intention-to-treat population

IQR: Interquartile range (25% and 75%)

Results: Extended PFS and OS by treatment arm (n= 389)

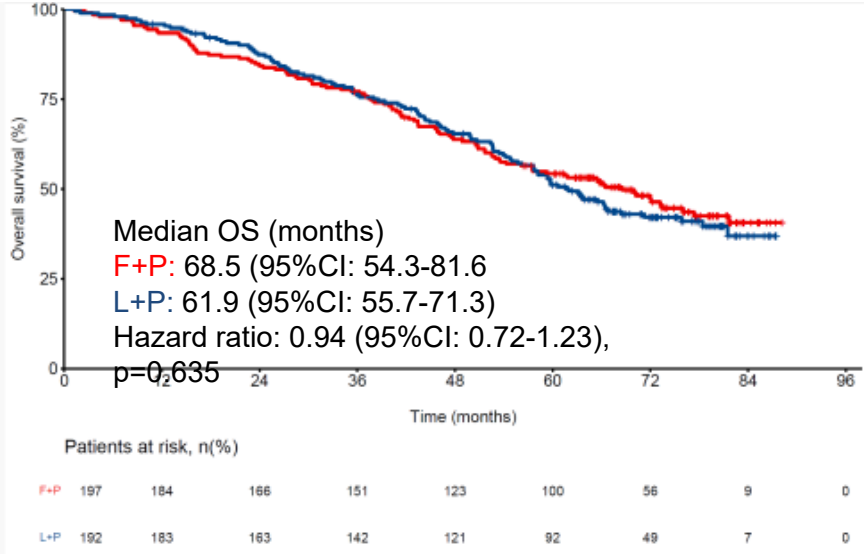
Median follow-up: 59.7 months. Data cutoff: May 2023.

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

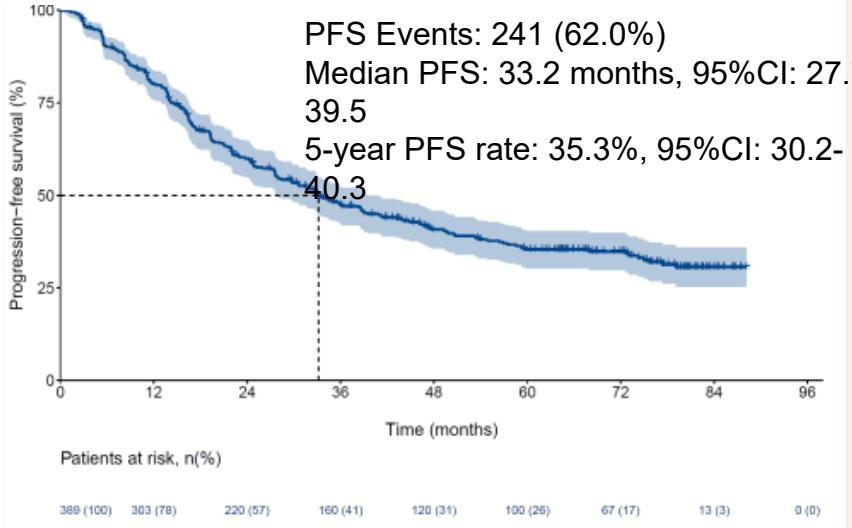
F: fulvestrant; L: letrozole; n (%), number of patients (percentage based on N); N: number of patients; OS: overall survival; P: palbociclib; PFS: progression-free survival

Results: PFS and OS of both cohorts combined (n=389)

Median follow-up: 59.7 months

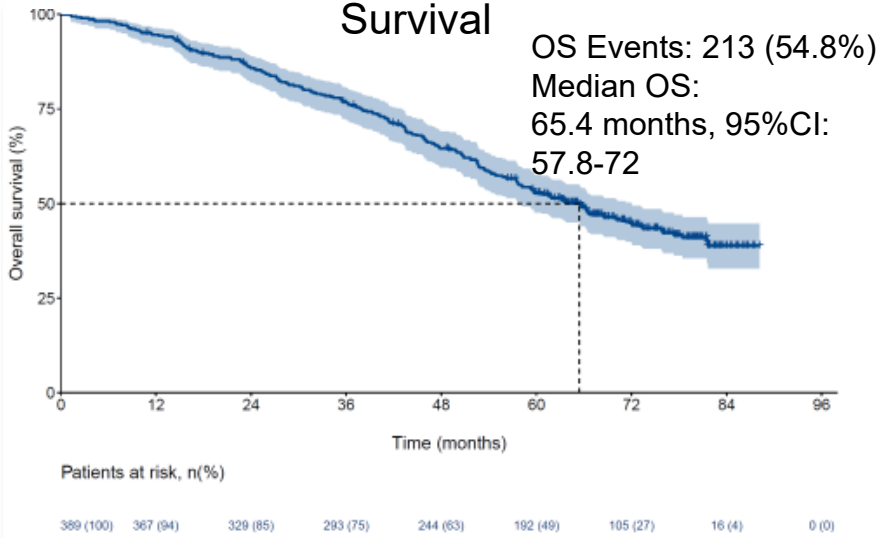
Progression-Free Survival

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



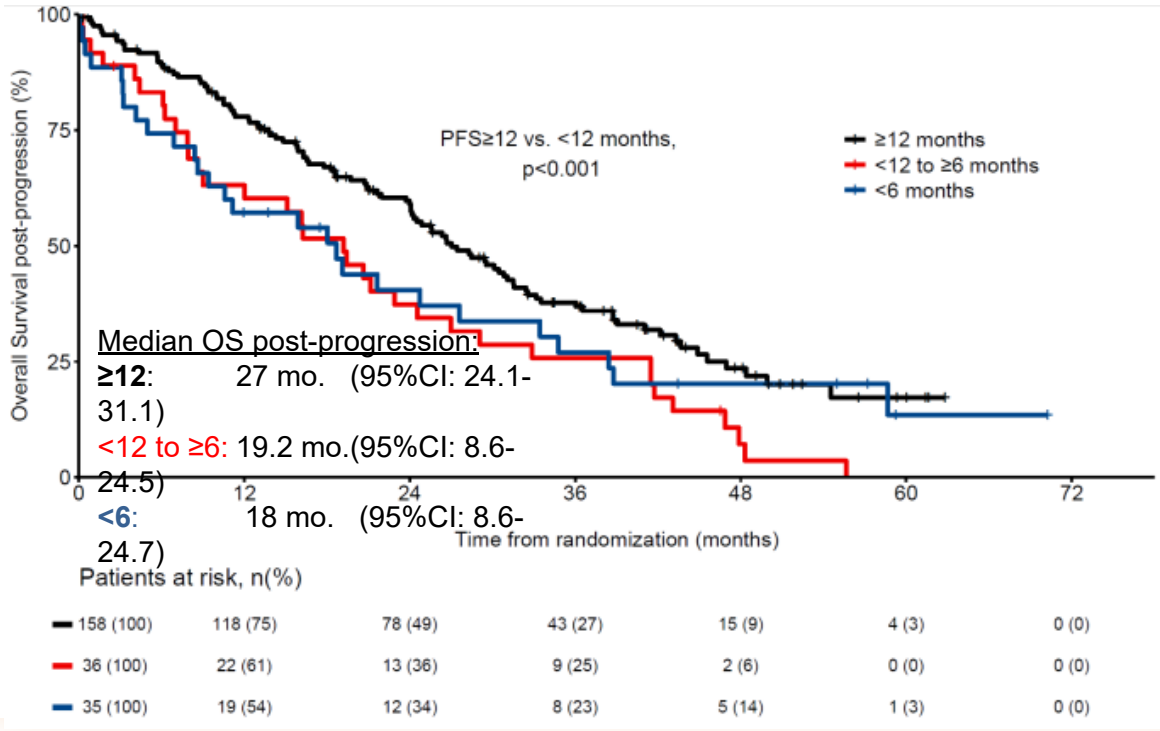
Overall Survival

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)



Median OS post-progression:
≥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%)

n (%), number of patients (percentage based on N); N: number of patients; mo.: months; OS: overall survival; PFS: progression-free survival

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

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Presentation

Lay Language Summary

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