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

Antonio Llombart Cussac[1,2], José Manuel Pérez-García[1,3], Meritxell Bellet[4], Florence Dalenc[5], Miguel Gil-Gil[6], Manuel Ruiz-Borrego[7], Joaquín Gavila[8], Peter Schmid[9], Pilar Zamora[10], Duncan Wheatley[11], Eduardo Martínez-de Dueñas[12], Kepa Amillano[13], Antonio Anton[14], Paul Cottu[15], Gemma Viñas[16], Thierry Petit[17], Petra Tesarová[18], Juan Cueva[19], Marco Colleoni[20], Maria Purificación Martínez del Prado[21], Raquel Andres[22], Elena Aguirre[23], Marta Díaz[1], Susana Vitorino[1], Miguel Sampayo-Cordero[1], Javier Cortés[1,3,25]

1) Medica Scientia Innovation Research, Barcelona, Spain and Ridgewood, New Jersey, USA; 2) Hospital Arnau de Vilanova, Universidad Católica, Valencia, Spain; 3) International Breast Cancer Center, Pangaea Oncology, Quiron Group, Barcelona, Spain; 4) Vall d'Hebrón University Hospital, and Vall d'Hebrón Institute of Oncology (VHIO), Barcelona, Spain; 5) Oncopole Claudius Regaud, IUCT-, CRCT, Inserm, Department of Medical Oncology, Toulouse, France; 6) Medical Oncology Department, Institut Catalá d' Oncología, Insitut d'Investigació Biomèdica Bellvitge, Barcelona, Spain; 7) Hospital Universitario Virgen del Rocío, Sevilla, Spain 8) Medical Oncology Department, Fundación Instituto Valenciano de Oncología, Valencia, Spain; 9) Barts Experimental Cancer Medicine Centre, Barts Cancer Institute, Queen Mary University of London, and Barts Hospital, NHS Trust, London, United Kingdom; 10) Centro de Investigación Biomédica en Red de Oncología, Madrid, Spain; 11) Royal Cornwall Hospitals NHS Trust, Truro, United Kingdom; 12) Medical Oncology Department, Consorcio Hospitalario Provincial de Castellón, Castellón, Spain; 13) Medical Oncology Department, Hospital Universitari Sant Joan de Reus, Reus, Spain; 14) Department of Medical Oncology, Hospital Universitario Miguel Servet, IIS Aragón, Universidad de Zaragoza, Spain; 15) Oncologie Médicale, Institut Curie, PSL Research University, Paris, France; 16) Medical Oncology, Catalan Institute of Oncology, Hospital Universitari Dr. Josep Trueta, Girona, Spain; Precision Oncology Group (OncoGIR-Pro), Institut d'Investigació Biomèdica de Girona (IDIBGI), Salt, Spain; 17) Department of Medical Oncology, Centre Paul Stauss, Strasbourg, France; 18) Department of Oncology, 1st Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; 19) Complexo Hospital Universitario de Santiago de Compostela, Santiago de Compostela, Spain; 20) Division of Medical Senology, Istituto Europeo di Oncologia (IEO), IRCCS, Milano, Italy; 21) Medical Oncology Department, Hospital Universitario Basurto, Bilbao, Spain; 22) Oncology Department, Hospital Lozano Blesa, Zaragoza, Spain; 23) Instituto Oncológico, Quriónsalud Zaragoza, Zaragoza, Spain; 24) Department of Medical Oncology, Hospital Universitario Miguel Servet, IIS Aragón, Universidad de Zaragoza, Spain; 25) Universidad Europea de Madrid, Madrid, Spain

Disclosure Information

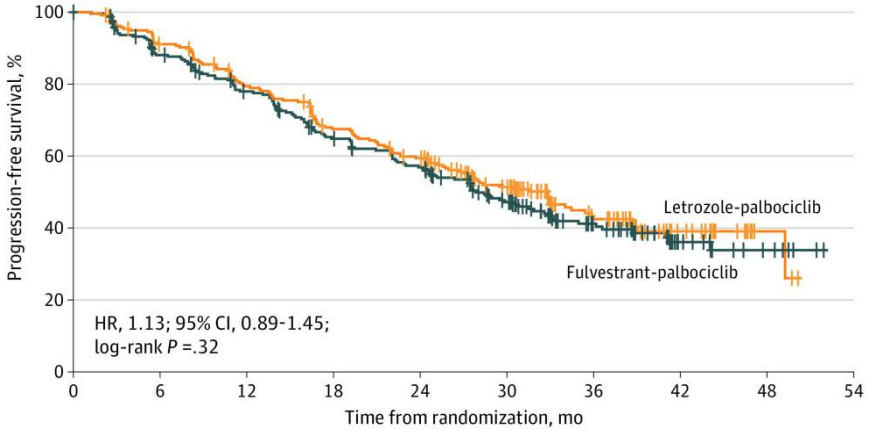
San Antonio Breast Cancer Symposium®
December 5-9, 2023 | San Antonio, TX | @SABCSSanAntonio

Antonio Llombart-Cussac, MD, PhD

- **Consulting/Advisor**: Roche, AstraZeneca, Seagen, Daiichi Sankyo, Eli Lily, Merck Sharp&Dohme, GSK, Gilead, Menarini, ExactSicences, Novartis, Agendia, Pfizer.
- **Honararia**: Roche, Novartis, Pfizer, Lilly, Daiichi Sankyo
- **Research funding to the Institution**: Roche, AstraZeneca, Eisai, F. Hoffman-La Roche, Guardant Health, Merck Sharp&Dohme, Pfizer.
- **Travel, accomodations, expenses**: Roche, Novartis, Pfizer, Daiichi Sankyo, AstraZeneca, Gilead.
- **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

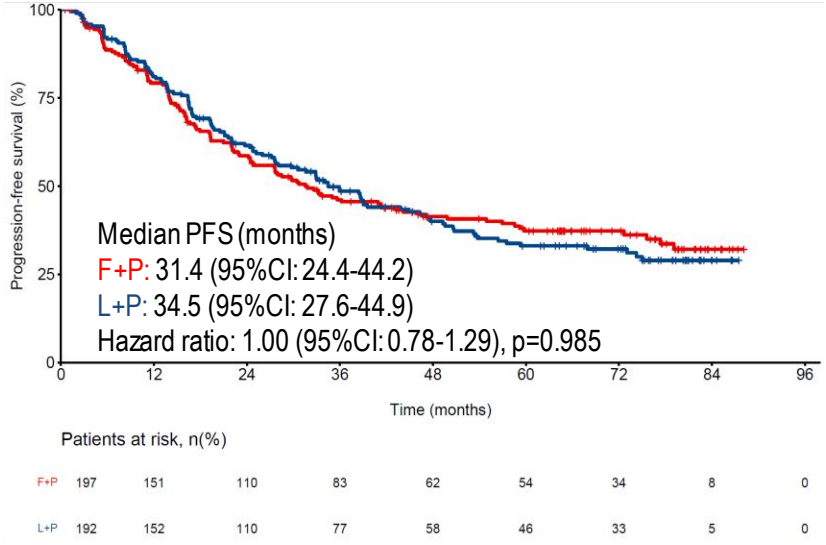
Demographic and baseline disease characteristics were similar between the PARSIFAL-LONG and the overall PARSIFAL intention-to-treat population

IQR: Interquartile range (25% and 75%)

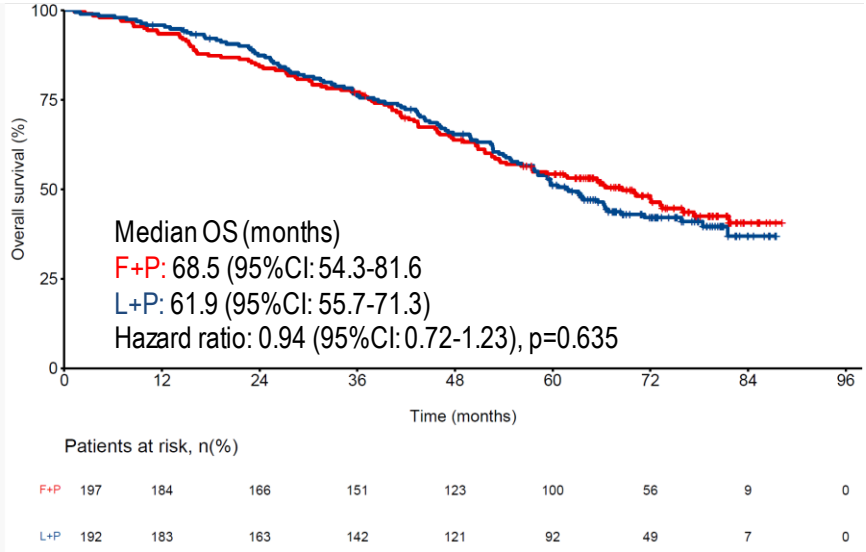
Results: Extended PFS and OS by treatment arm (n= 389)

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

Progression-Free Survival (PFS)



Overall Survival (OS)

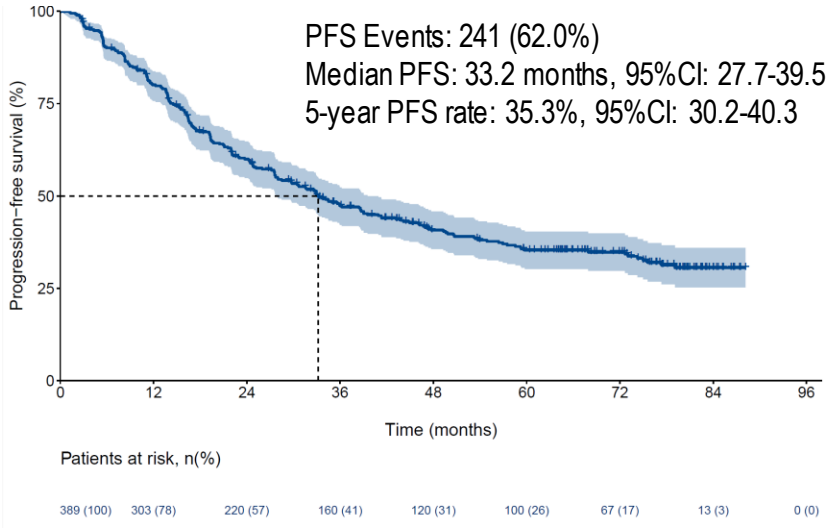


F: fulvestrant; L: letrozole; n (%), number of patients (percentage based on N); N: number of patients; OS: overall survival; P: palbociclib; PFS: progression-free survival

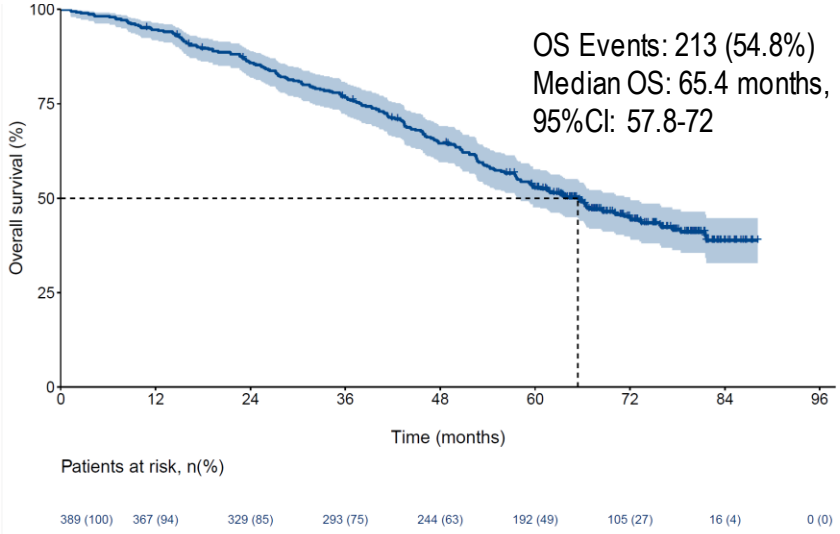
Results: PFS and OS of both cohorts combined (n=389)

Median follow-up: 59.7 months

Progression-Free Survival

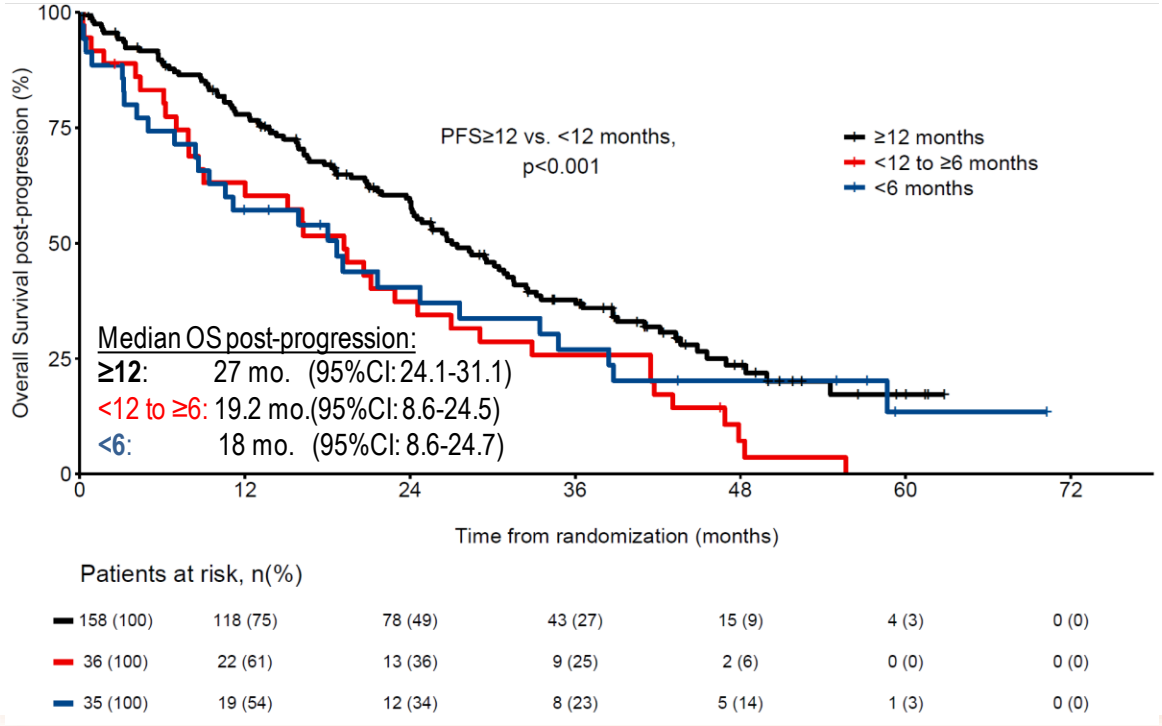


Overall Survival



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)



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

Acknowledgements

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.

Presentation

Lay Language Summary

To download today's presentation and its lay language summary scan the QR code*