Dana-Farber Cancer Institute

PALLAS Adjuvant Trial: A model of a successful academia/industry partnership.

Erica L. Mayer MD MPH
Dana-Farber Cancer Institute
Boston, MA

THE LANCET
Oncology

ARTICLES | VOLUME 22, ISSUE 2, P212-222, FEBRUARY 2021 Download Full Issue

Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study

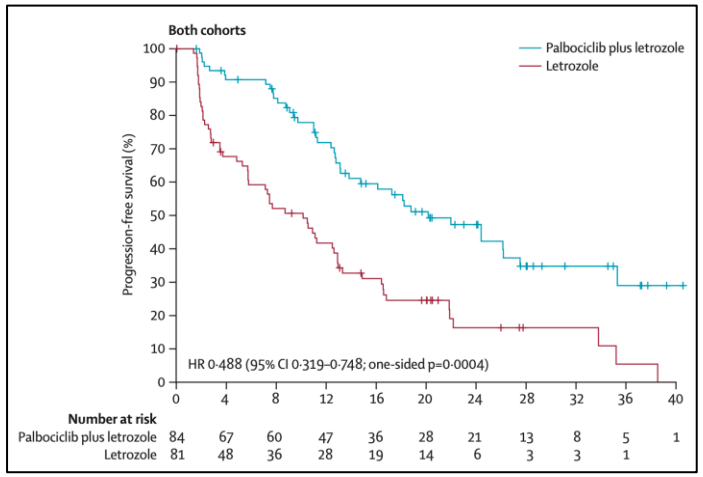
Erica L Mayer, MD • Amylou C Dueck, PhD • Prof Miguel Martin, MD • Gabor Rubovszky, PhD • Prof Harold J Burstein, MD • Meritxell Bellet-Ezquerra, MD • Kathy D Miller, MD • Nicholas Zdenkowski, PhD • Prof Eric P Winer, MD • Georg Pfeiler, MD • Prof Matthew Goetz, MD • Manuel Ruiz-Borrego, MD • Daniel Anderson, MD • Zbigniew Nowecki, MD • Prof Sibylle Loibl, MD • Prof Stacy Moulder, MD • Alistair Ring, FRCP • Florian Fitzal, MD • Tiffany Traina, MD • Prof Arlene Chan, MMed • Prof Hope S Rugo, MD • Julie Lemieux, MD • Fernando Henao, MD • Alan Lyss, MD • Silvia Antolin Novoa, MD • Prof Antonio C Wolff, MD • Marcus Vetter, MD • Daniel Egle, MD • Prof Patrick G Morris, MD • Prof Eleftherios P Mamounas, MD • Miguel J Gil-Gil, MD • Prof Aleix Prat, MD • Hannes Fohler, MVM • Otto Metzger Filho, MD • Magdalena Schwarz, MSc • Carter DuFrane, BA • Debora Fumagalli, MD • Kathy Puyana Theall, MD • Dongrui Ray Lu, MS • Cynthia Huang Bartlett, MD • Maria Koehler, MD • Christian Fesl, PhD • Prof Angela DeMichele, MD † • Prof Michael Gnant, MD † • Show less • Show footnotes

Published: January 15, 2021 • DOI: https://doi.org/10.1016/S1470-2045(20)30642-2 • Check for updates

- A global collaboration:
- Pfizer
- Austrian Breast Cancer Study Group (ABCSG)
- Alliance Foundation for Clinical Trials (AFT)
- ABCSG-42/AFT-05/BIG-14-03

Palbociclib Clinical Development Timeline

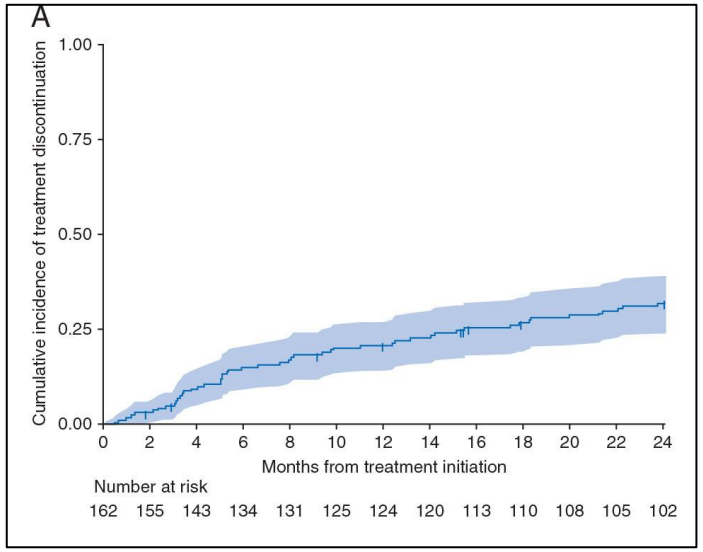
1990's – substantial preclinical development led to identification of CDK4/6i for breast cancer



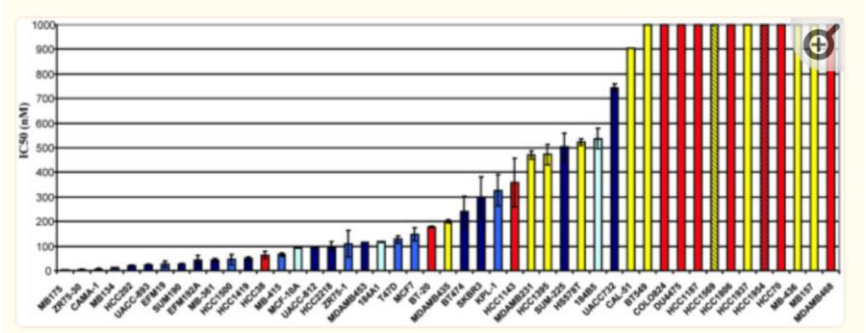
2012: first clinical presentation of data on palbociclib at SABCS

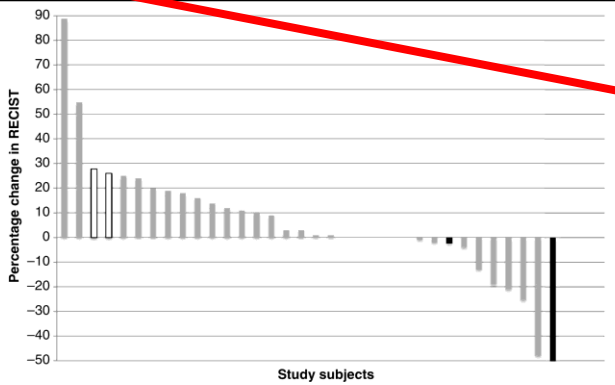
2013: phase 2 study of monotherapy presented at ASCO

2015: PALOMA-3
2015 PALOMA-2
2015 initial FDA approval for advanced breast cancer



2017: pilot DFCI adjuvant palbociclib study presented at SABCS





2013: Initial development of the PALLAS trial begins

Finn et al, Breast Cancer Res 2009; Finn et al. Lancet Oncol 2015; DeMichele et al, Clin Cancer Res 2015; Turner et al NEJM 2015; Finn et al NEJM 2016; Mayer et al, Ann Oncol 2019

PALLAS Trial Development

- Significant interest in adjuvant trial design shared between senior breast cancer leaders and pharma colleagues – over lunch, around a table at SABCS, coffee between ASCO sessions.
  - Importance of in-person contact and friendship

- *"Our interests are similar to yours and most importantly we would like to hear your proposal re how to set up the trial efficiently and select those patients who have both the most need for additional therapy and highest likelihood of responding to palbociclib. We would be very open to work through the Intergroup Alliance with NCI support and are looking for most efficient trial with highest focus on both patients and science." – Pfizer, April 2023*

PALLAS Trial Development

- US: Senior colleagues mentored junior colleagues
  - Eric Winer -> Erica Mayer at DFCI, Peter O'Dwyer -> Angie DeMichele at U Penn
- Rest of World – great political effort by Michael Gnant of ABCSG to harness the global research networks.

Rest of World: Lead Network: ABCSG (Austria)

- SOLTI (Spain)
- GEICAM (Spain)
- NCT (Australia)
- Irish
- SAKK (Swiss)
- GBG (German)
- Breast International Group (BIG)

USA: Lead Network: Alliance Foundation for Clinical Trials

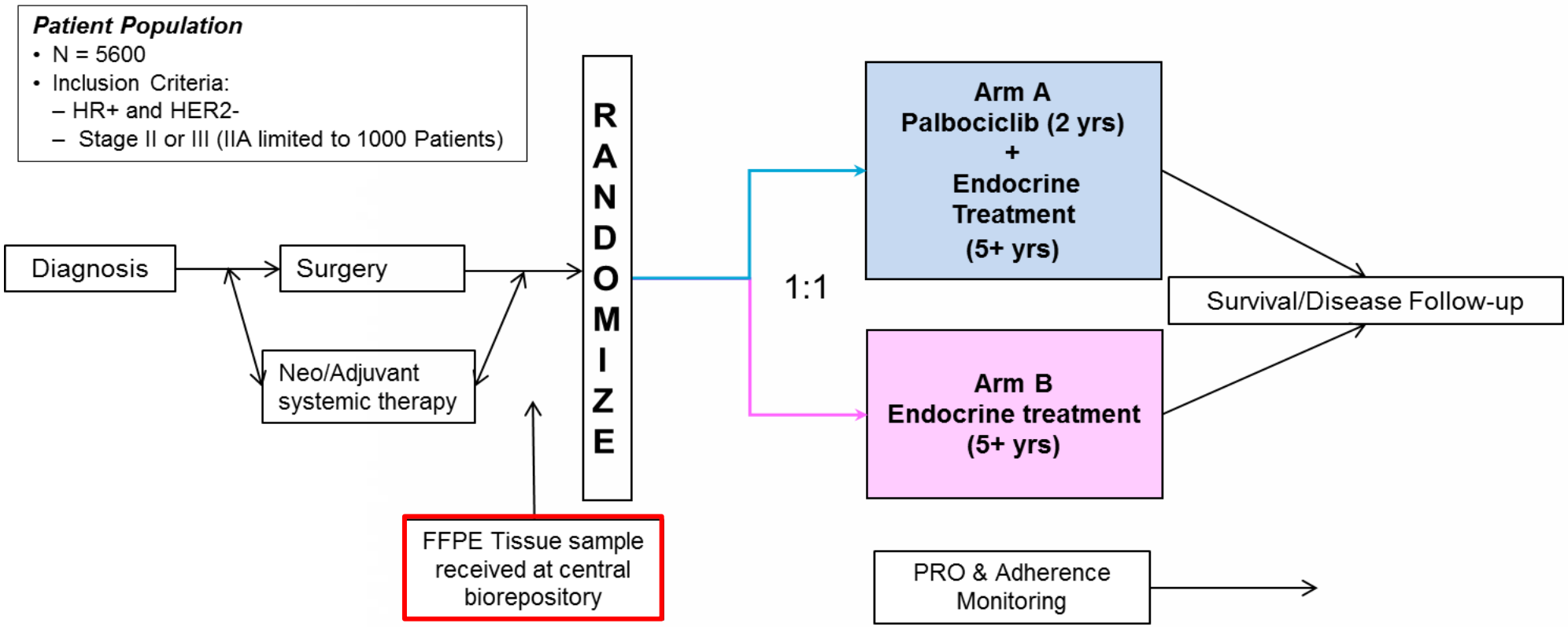
- prECOG
- NSABP

PALLAS Trial Development

- Protocol development was a TEAM EFFORT
  - Working calls twice a month, academia and industry present on all. F2F at all major meetings.
  - Drafts shared and edited together.
  - Ability to endorse transformative aspects of protocol design, ie mandatory biospecimen collection and analysis, first time ever in a breast cancer trial of this scale
  - Seats at the table together for Executive Committee, Steering Committee, authorship slots on every abstract/manuscript

- *"The relationships I had with Maria and Cynthia were so valuable. They were involved in how the drug was developed. They were very creative and took a lot of feedback. They also helped junior people like me understand how things worked*." – PALLAS co-PI

PALLAS SCHEMA



Arm A: palbociclib at a dose of 125 mg once daily, Day 1-21 in a 28-day cycle for total duration of 2 years, in addition to standard adjuvant endocrine therapy
Arm B: standard adjuvant endocrine therapy (AI, tamoxifen, LHRH agonists)

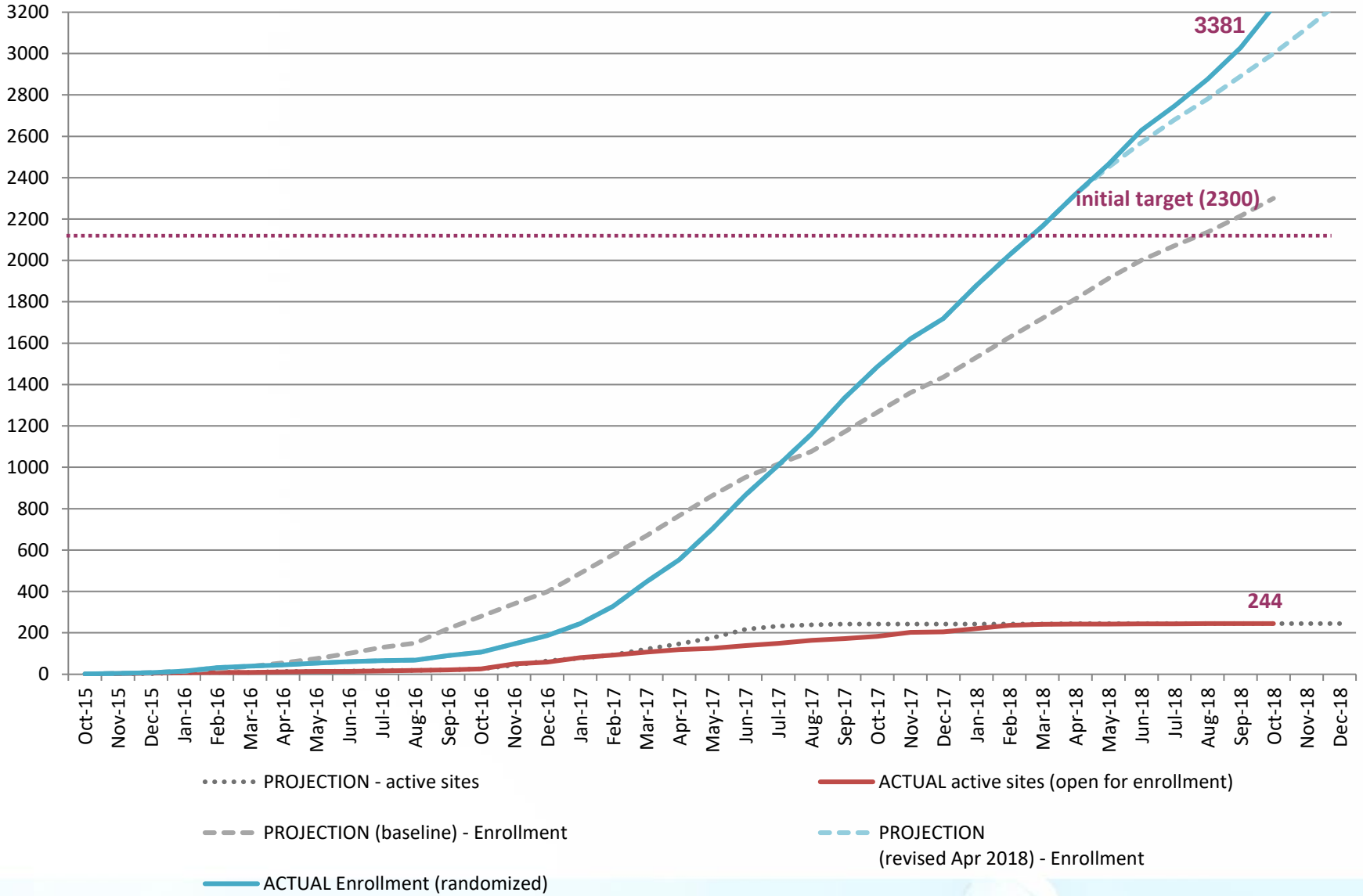
Stratification Factors:
•Anatomic stage (IIA vs IIB/III), assessed by pathologic staging or by clinical staging if pre-operative therapy was given with the higher stage determining eligibility,
•Neo/adjuvant chemotherapy (yes vs no),
•Age (≤ 50 vs > 50 years),
•Geographic region (North America vs Europe vs Other)

PALLAS Final Global Enrollment Numbers: a huge success!

406 centers, 21 countries
Accrual Sept 1 2015 - Nov 30 2018
Almost 6,000 patients randomized in 3 years

	US	Non-US	Total
FPI	01-Sep-2015	28-Oct-2015	
Patients screened	2862	3844	6706
Screen Failures	450 (15.7%)	462 (12.0%)	912 (13.6%)
Patients randomized	**2412**	**3381**	**5793**
Stage IIA Patients	461	571	1032

Projection vs. Actual Enrollment & Active Sites (Non-US)



AFT-05 (PALLAS) BIOSPECIMEN COHORT

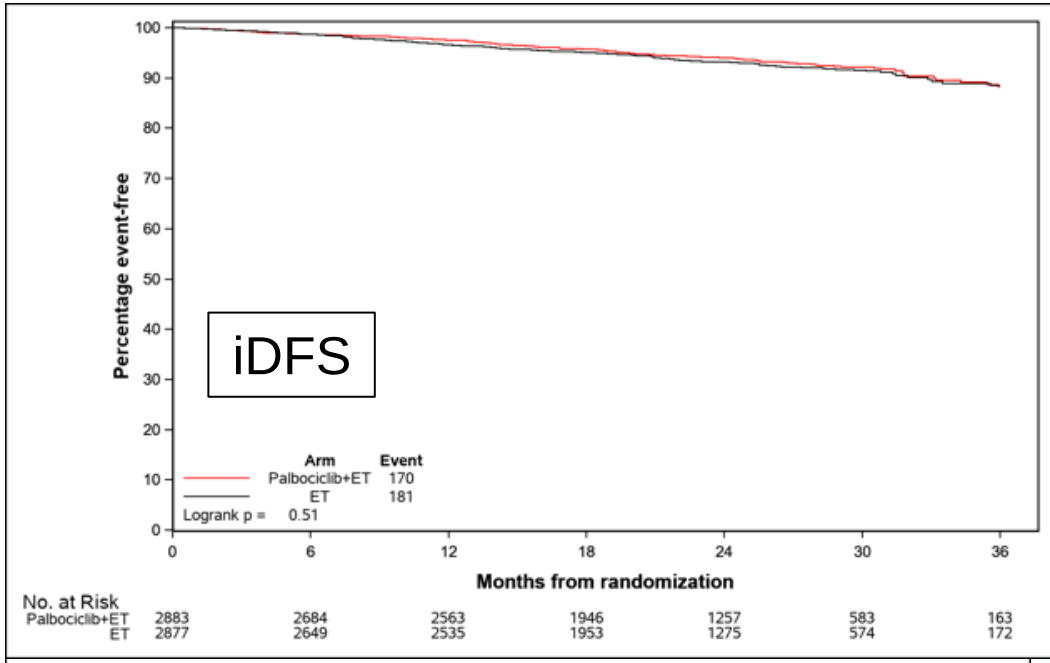
* NOT filtered for screen failures and withdrawn patients

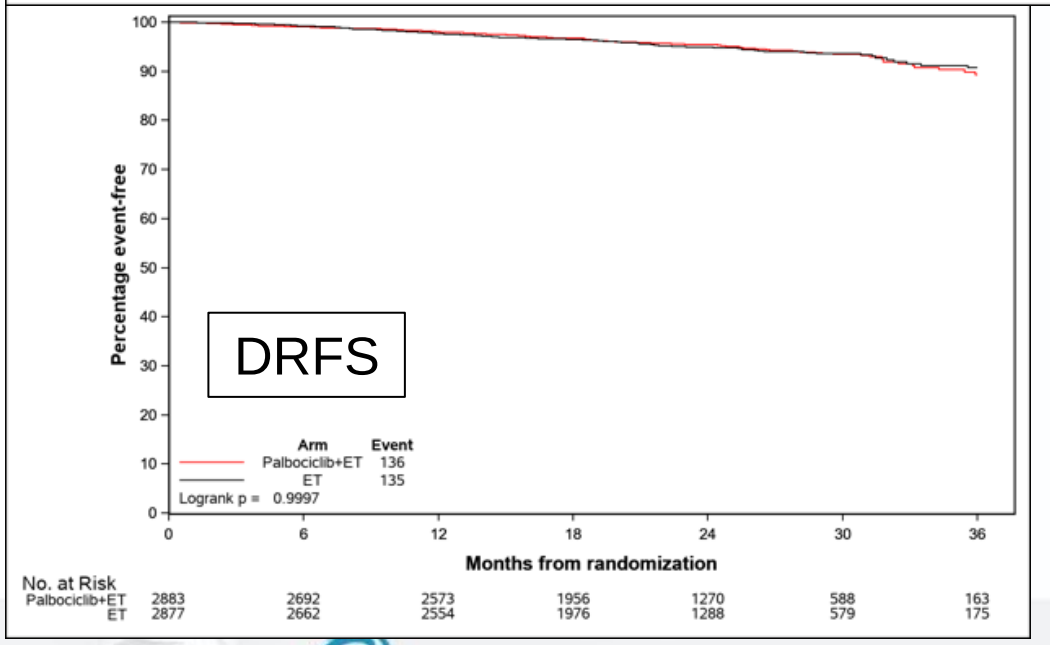
PALLAS: Efficacy

- At IA2 (May 2020), the test statistic comparing iDFS crossed the pre-specified futility boundary, leading the IDMC to recommend discontinuation of palbociclib in Arm A patients and moving all patients to follow-up.

- The presented data reflect 351 iDFS events, the majority (65·5%) being distant recurrences.

- At a median follow-up of 23.7 months, no significant difference in iDFS was observed, with 3-year iDFS of 88·2% with palbociclib + ET, and 88·5% with ET alone (HR 0·93, 95% CI 0·76-1·15; log-rank p = 0·51). The result was also consistent for DRFS.





Efficacy population: Intent-to-treat (ITT) principle, with patients withdrawing consent for all analysis excluded

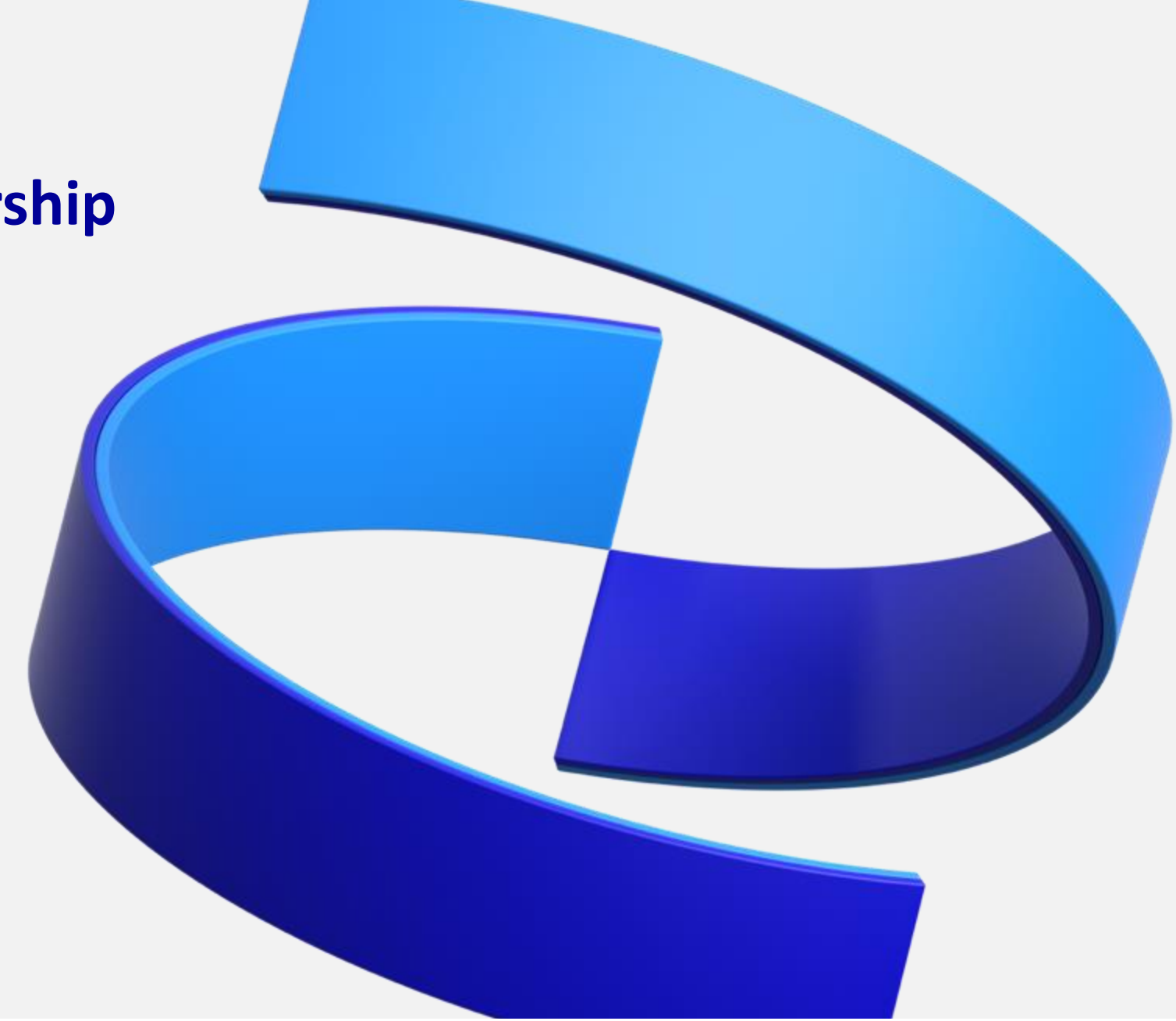
PALLAS References

1. Mayer et al, Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study. Lancet Oncol 2021
2. Gnant et al, Adjuvant Palbociclib for Early Breast Cancer: The PALLAS Trial Results (ABCSG-42/AFT-05/BIG-14-03). JCO 2022
3. Naughton et al, Quality of life and symptom severity in the PALLAS randomized trial of palbociclib with adjuvant endocrine therapy in early breast cancer (AFT-05). SABCS 2021
4. Shinn et al, Adherence with adjuvant endocrine therapy with or without Palbociclib in the PALLAS trial, SABCS 2021
5. Pfeiler et al, Safety of adjuvant CDK4/6 inhibitors during the COVID-19 pandemic. Lancet Oncol 2022.
6. Mayer et al, Treatment Exposure and Discontinuation in the PALbociclib CoLlaborative Adjuvant Study of Palbociclib With Adjuvant Endocrine Therapy for Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Early Breast Cancer (PALLAS/AFT-05/ABCSG-42/BIG-14-03). JCO 2022
7. DeMichele et al, Adjuvant palbociclib for ER+ breast cancer (PALLAS Trial (ABCSG-42/AFT-05/PrE0109/BIG-14-13): A preplanned analysis of the stage IIA cohort. ASCO Virtual Plenary 2022
8. Yuan et al, Development and Validation of a Composite Biomarker Predictive of Palbociclib + Endocrine Treatment Benefit in Early Breast Cancer: PENELOPE-B and PALLAS Trials. SABCS 2022
9. Pfeiler et al, Impact of BMI in Patients With Early Hormone Receptor-Positive Breast Cancer Receiving Endocrine Therapy With or Without Palbociclib in the PALLAS Trial. JCO 2023
10. Kantor et al, Racial and Ethnic Differences in Clinical Outcomes among North American Patients with Hormone Receptor-Positive, HER2-negative, Early Breast Cancer in the PALLAS Trial (AFT-05). SABCS 2023
11. Nader-Marta et al, Clinical characterization, prognostic and predictive values of HER2-low in early breast cancer in the PALLAS trial, SABCS 2023
12. Agostinetto et al, The impact of drug-drug interactions between palbociclib and proton pump inhibitors on clinical outcome of patients with hormone receptor positive, HER2-negative, early breast cancer: an analysis of the PALLAS study. SABCS 2023
13. Stover et al, Protocol-defined biomarker analysis in the PALLAS (AFT-05) adjuvant trial: Genomic subtype derived from RNA sequencing of HR+/HER2- early breast cancer. SABCS 2023 oral presentation

Lessons Learned from PALLAS

- Despite clinical results of PALLAS, the trial was exceptionally well run and shows power and efficiency of a global academic collaboration.
- Agreement to mandate biospecimen collection was transformative, and will generate substantial correlative discovery investigating the biology of HR+ breast cancer.
- Collaborative trials offer many opportunities for mentorship and professional growth. Shared partnerships allow junior faculty to have leadership roles, maintains pipelines in academic oncology and develops next generation of research leaders.
- Involvement of academic faculty in collaborative trial development keeps patients' needs front and center.
- A close relationship with industry partners can be a wonderful thing: requires transparency, communication, collaboration and trust.

Academia/Industry Partnership Learnings



Prash Gopalakrishna MD

Oncology Research & Development
Pfizer

Disclosures

Contents represent learnings based on collective professional experience across academia & Industry and are not limited to current role at Pfizer.

PPP: Advantages

Successful partnerships enhance drug development processes and facilitates innovation

- Access to Expertise, Innovative Ideas and Approaches
- Access to Patient Populations & Expanded Research Capabilities
- Enhanced Reputation
- Long-Term Relationships
- Reduced Regulatory Hurdles
- Cost Savings
- Accelerated Drug Development

PPP: Challenges

Successful partnerships require careful planning, clear communication, and a shared commitment

- Differing Objectives and Priorities
- Timelines and Speed; Quality control
- Recruitment and Retention Challenges
- Intellectual Property Issues; Data Sharing and Confidentiality
- Funding and Resource Constraints; Resource Allocation
- Cultural and Communication Differences
- Publication Timing