SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 10–13, 2024
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Primary results of the randomised phase IV trial comparing first-line ET plus palbociclib vs standard mono-chemotherapy in women with high risk HER2-/HR+ metastatic breast cancer and indication for chemotherapy - PADMA study

Sibylle Loibl[1], Marc Thill[2], Julia Rey[1], Beate Rautenberg[3], Vesna Bjelic-Radisic[4,5], Thomas Decker[6], Joachim Rom[7], Matthias Kögel[8], Kristina Lübbe[9], Axel Nacke[10], Nader Hirmas[1], Marianne Just[11], Volkmar Müller[12], Renu Buss-Steidle[13], Jürgen Terhaag[14], Christoph Mundhenke[15], Carsten Denkert[16], Johannes Holtschmidt[1], Marcus Schmidt[17]

on behalf of the PADMA investigators

1 German Breast Group, Neu-Isenburg, Germany; 2 Agaplesion Markus Hospital, Frankfurt am Main, Germany; 3 Department of Obstetrics and Gynecology, Hospital Freiburg, Germany; 4 Helios University Clinic Wuppertal, Germany; 5 University Witten/Herdecke, Germany; 6 Oncology Ravensburg, Germany; 7 Hospital Höchst Frankfurt am Main, Germany; 8 Hospital Worms, Germany; 9 Diakovere Henriettenstift, Breast Center, Hannover, Germany; 10 Oncology Bad Neuenahr, Germany; 11 Oncology specialist practice Bielefeld, Germany; 12 University Hospital Hamburg-Eppendorf, Germany; 13 Helios Hospital Pforzheim, Germany; 14 MVZ Eggenfelden, Germany; 15 Department of Gynecology and Obstetrics, Hospital Hohe Warte, Bayreuth, Germany; 16 Institute of Pathology, Philipps-University Marburg and University Hospital Marburg (UKGM) University Hospital Marburg, Germany; 17 Department of Obstetrics and Gynecology, University Medical Center Mainz, Germany

PADMA

GBG GERMAN BREAST GROUP

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Disclosure Information

Sibylle Loibl

I have the following relevant financial relationships to disclose:

Employee of: GBG Forschungs GmbH (German Breast Group)

Grants and/or honorarium for adboards and/or contracts from the following entities / all paid to institution: AZ, Abbvie, Agendia, Amgen, BionTech, Celgene/BMS, Cellcuity, DSI, Exact Science, Gilead, GSK, Incyte, Lilly, Medscape, Molecular Health, MSD, Novartis, Pierre Fabre, Pfizer, Relay, Roche, Sanofi, Seagen, Stemline/Menarini, Olema, Bayer, Bicycle, JAZZ Pharma

Support for attending meetings and/or travel: DSI, ESMO, SGBCC, ASCO, AGO Kommission Mamma

Patents planned, issued or pending: EP14153692.0 / EP21152186.9 / EP15702464.7

Royalties to institution: VM Scope

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

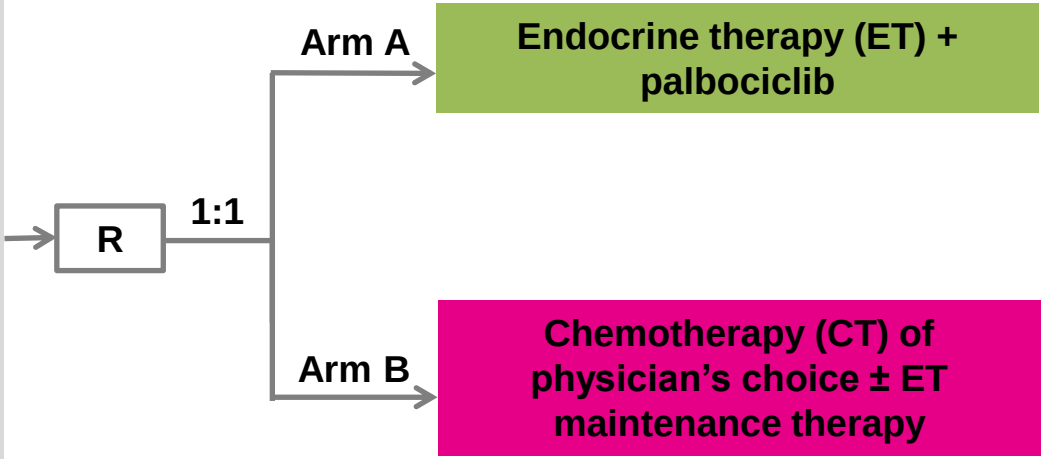
Background

- International guidelines have recommended endocrine treatment (ET) with CDK4/6i as 1st line treatment in HR+/HER2- metastatic breast cancer (mBC) for several years.
- Due to the lack of prospective data comparing ET with standard-of-care chemotherapy in this setting, many patients still received chemotherapy as 1st line treatment for HR+/HER2- mBC when the PADMA trial was initiated.
- The PADMA study (NCT03355157; GBG 93) is the first prospective, randomized, open-label, multi-center, phase IV trial to compare CDK4/6 inhibitor + ET with standard mono-chemotherapy +/- maintenance ET as first-line therapy in patients with high-risk mBC and a chemotherapy indication.

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

PADMA Study Design

Patient Population
N=150
- HR-positive/HER2-negative
- Female or male
- Indication for mono-chemotherapy
- No prior treatment for metastatic/relapsed disease
- No asymptomatic bone-only, oligo-metastatic disease
- No uncontrolled/untreated CNS metastases
- Live-expectancy >6 months



Stratification:
- Endocrine resistant vs endocrine sensitive
- Symptomatic vs asymptomatic metastatic disease

ET with palbociclib: AI or fulvestrant ± GnRHa
ET maintenance: tamoxifen, AI or fulvestrant ± GnRHa
CT: paclitaxel, capecitabine, epirubicin, or vinorelbine

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

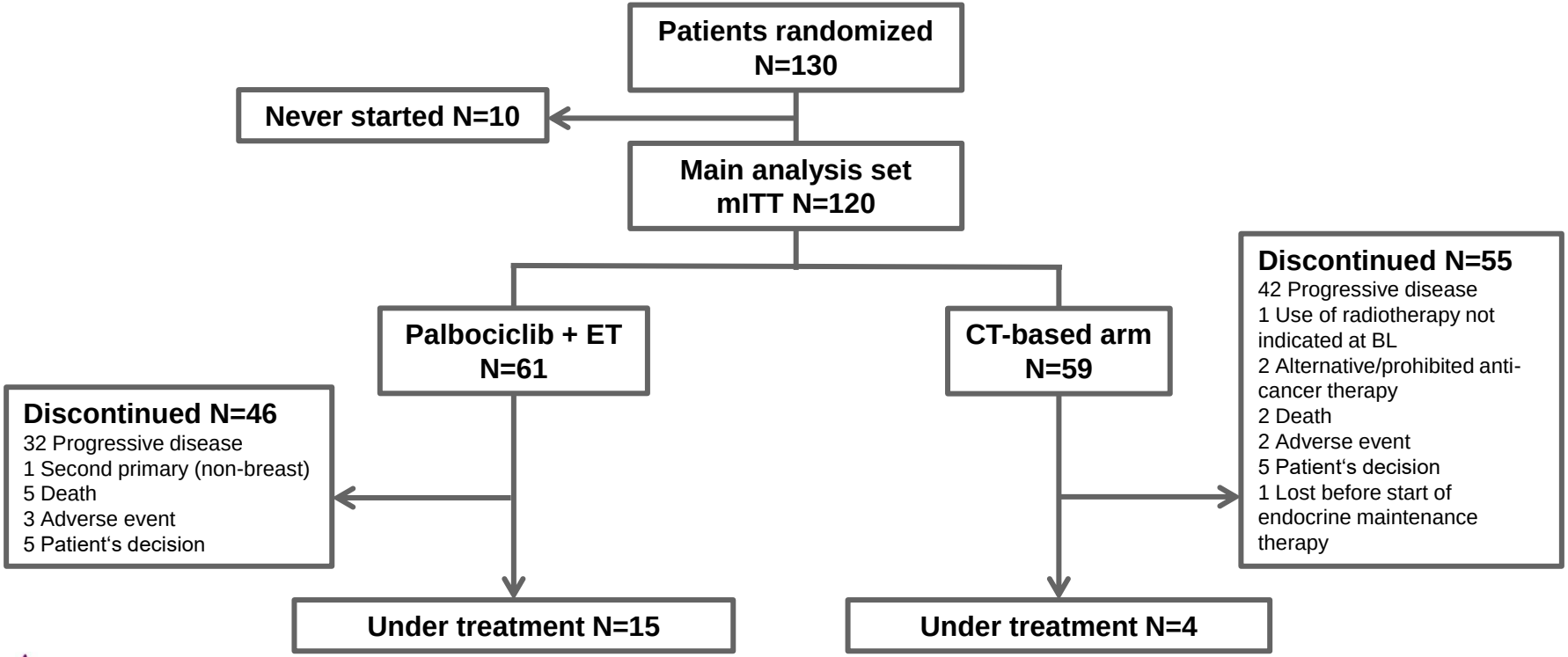
Study Endpoints

- **Primary endpoint:**
  - Time-to-treatment failure (TTF) defined as time from randomization to discontinuation of treatment due to disease progression, treatment toxicity, patient's preference, or death.

- **Secondary endpoints:**
  - Progression-free survival (PFS)
  - Overall survival (OS)
  - Safety, tolerability, treatment compliance
  - Time-to-first subsequent treatment (TFST) and further time-to-event endpoints
  - Patient-reported QoL
  - Daily Monitoring of Treatment Impact (DMTI): call tracking/geofencing with passive collection of information about frequency and duration of phone calls/visits to study site, respectively

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Study Treatment and Analysis Populations



This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Baseline Characteristics

	Palbociclib+ET N=61	CT-based N=59	Overall N=120
Median age in years (range)	63 (42.0-85.0)	62 (31.0-80.0)	62 (31.0-85.0)
Postmenopausal status	54 (88.5%)	52 (88.1%)	106 (88.3%)
Liver metastases	28 (45.9%)	22 (37.3%)	50 (41.7%)
Endocrine resistant*	17 (27.9%)	21 (35.6%)	38 (31.7%)
Metastasis at initial diagnosis	20 (33.3%)	24 (40.7%)	44 (37.0%)
Prior (neo)adjuvant CT	29 (47.5%)	25 (42.4%)	54 (45.0%)
HER2-low (IHC 1-2)**	41 (73.2%)	30 (58.8%)	71 (66.4%)
Pathogenic variants (tissue)***			
- *PIK3CA*	11 (18.0%)	16 (27.1%)	27 (22.5%)
- *BRCA1/2*	3 (4.9%)	4 (6.8%)	7 (5.8%)
- *ESR1*	1 (1.6%)	1 (1.7%)	2 (1.7%)

* According to clean data; endocrine resistant = relapse on or within 12 months of end of adjuvant ET
** From metastasis (N=47), otherwise if available from initial diagnosis (N=24)
*** Tested in 81 patients.

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

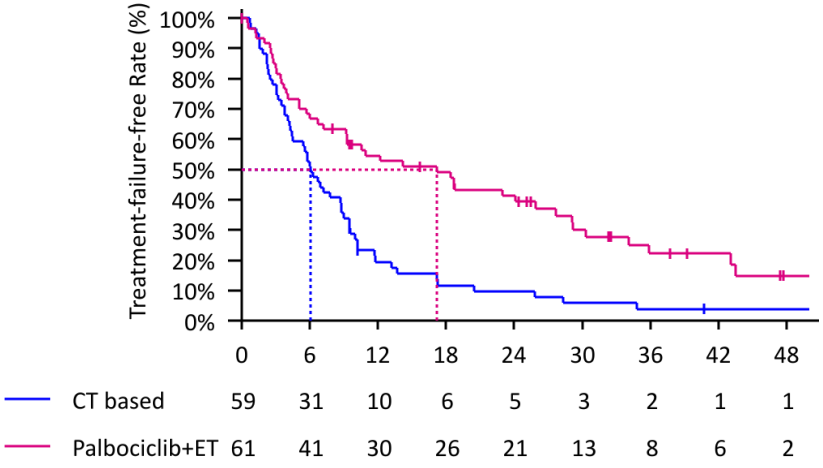
Study Treatment as Treated

	Palbociclib+ET N=62*	CT-based N=58
Type of treatment of physician's choice CT		
- Capecitabine	-	40 (69.0%)
- Paclitaxel		17 (29.3%)
- Vinorelbine		1 (1.7%)
Received ET maintenance post CT	-	13 (22.4%)
Type of ET**		
- Aromatase inhibitor	48 (77.4%)	9 (15.5%)
- Tamoxifen	-	3 (5.2%)
- Fulvestrant	14 (22.6%)	1 (1.7%)
Median duration palbociclib or CT, weeks (range)	51.0 (1.0-322.0)	19.5 (2.0-122.0)

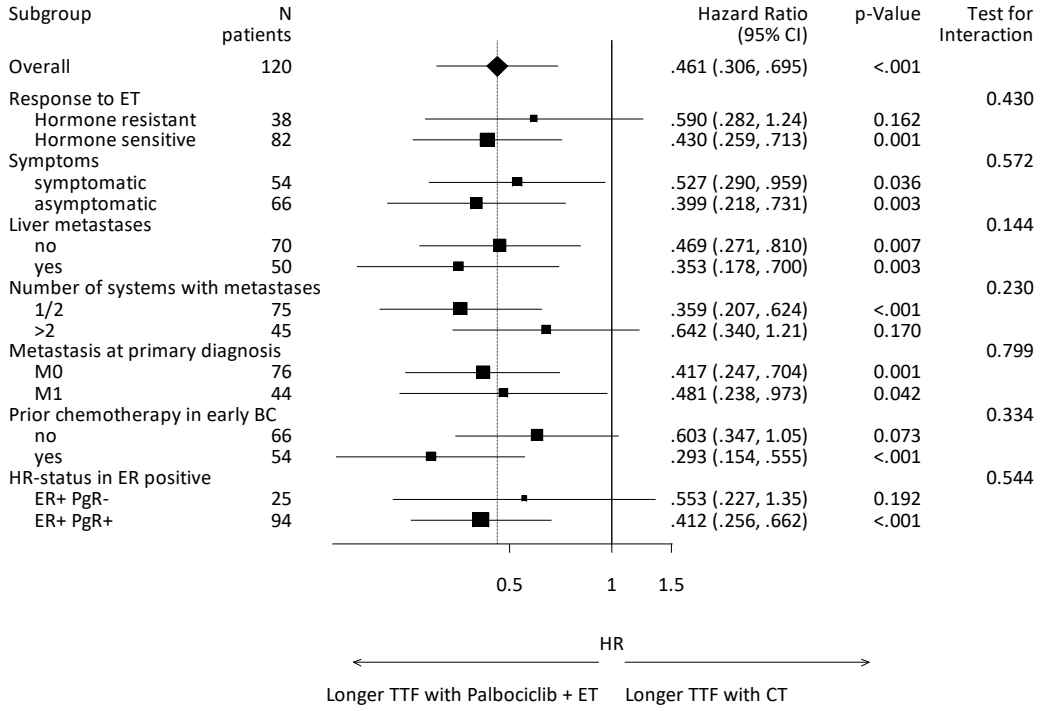
*one patient randomized to CT-based arm received palbociclib + ET.
**pre- or perimenopausal women receiving AI or fulvestrant required GnRH analogue or ovarian ablation.

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Primary Endpoint



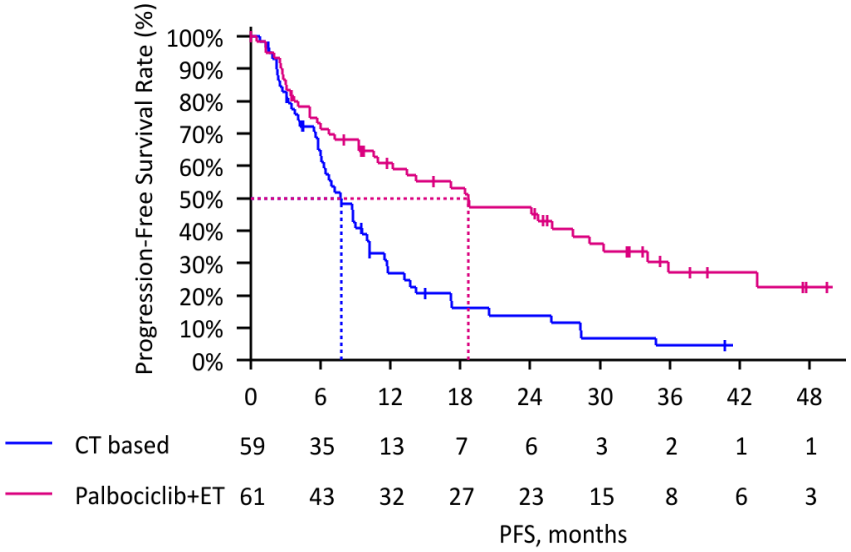
	Palbociclib + ET	CT
TTF events, N (%)	45 (73.8)	55 (93.2)
Median TTF months	17.2	6.1
HR 0.46: 95% CI (0.31-0.69), p<0.001 (log-rank)		



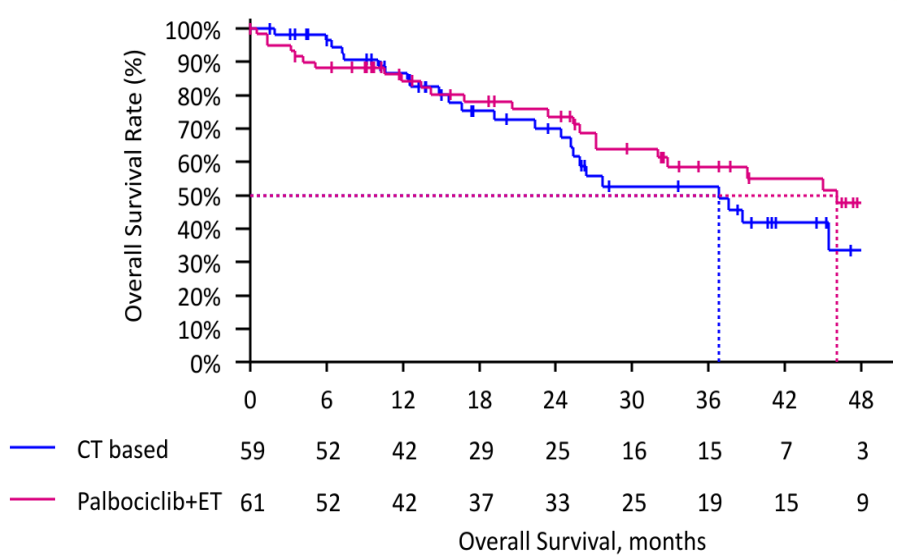
Median follow-up of 36.8 (range 0-74.4) months

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Secondary Endpoints



	Palbociclib + ET	CT
PFS events, N (%)	40 (65.6)	50 (84.7)
Median PFS months	18.7	7.8
HR 0.45 95% CI (0.29-0.70), p<0.001 (log-rank)		



	Palbociclib + ET	CT
OS events, N (%)	25 (41.0)	24 (40.7)
Median OS months	46.1	36.8
Proportional hazard cannot be assumed		

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Safety

Patients with treatment-related adverse events (TRAE)

	Palbociclib+ET N=62		CT based N=58	
	Any grade	**Grades 3-4**	**Any grade**	**Grades 3-4**
Any TRAE	60 (96.8%)	37 (59.7%)	55 (94.8%)	16 (27.6%)
Any hematological TRAE	**60 (96.8%)**	**34 (54.8%)**	**34 (58.6%)**	**4 (6.9%)**
Any non-hematological TRAE	51 (82.3%)	12 (19.4%)	54 (93.1%)	13 (22.4%)
Treatment-related SAE	7 (11.3%)	5 (8.1%)	6 (10.3%)	6 (10.3%)
Treatment-related death	**1 (1.6%)**	**-**	0 (0.0%)	-

- Hematological toxicity significantly higher in the palbociclib + ET arm compared to CT-based arm (96.8% vs. 58.6%; p<0.001). Comparable non-hematological toxicity.
- One treatment-related death (septic shock; palbociclib + ET arm).

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Conclusions

- The PADMA trial in high-risk HR+/HER2- mBC met its primary endpoint and shows a statistically significant and clinically meaningful improvement in Time To Treatment Failure and PFS for palbociclib + ET over mono-CT (± ET maintenance) as first-line therapy
  - Median TTF 17.2 vs 6.1 months ; HR 0.46, 95% CI (0.31-0.69), p<0.001
  - Median PFS 18.7 vs 7.8 months; HR 0.45, 95% CI (0.29-0.70), p<0.001
- After a median follow-up of 36.8 months there was a numerical trend for an improved OS for palbociclib + ET 46.1 vs 36.8 months
- No new safety signals were observed
- These results support existing international guidelines advocating the use of ET + CDK4/6i as standard first-line treatment of patients with HR+/HER2- mBC.

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.

Acknowledgements

- All patients and their families, all participating sites, and IDMC
- Pfizer for Drug Supply and Financial Support
- Molecular Health Financial Support

Cooperating partner

Central Pathology Marburg:
Carsten Denkert
Paul Jank

Funders:
Pfizer
Molecular Health

More information and downloads here:
www.gbg.de

GBG

Members of the Subboard and GBG Team

PM and Monitoring:
Konstantin Reißmüller
Steffen Kiehl
Translational Research:
Bärbel Felder
Stefanie Lettkemann
Data Management:
Ronak Salehi, Sabine Kleinefeld
Medical Team:
Sabine Seiler, Nader Hirmas
Medical Writing:
Alena Gribko

This presentation is the intellectual property of the author/presenter. Contact them at publications@gbg.de for permission to reprint and/or distribute.