GBG

GERMAN
BREAST
GROUP

Leading in Breast Cancer Research

ANNUAL SCIENTIFIC REPORT **2025**

Table of contents

Editorial

Twenty-three years ago, the GBG Forschungs GmbH was founded with the vision of advancing breast cancer research in Germany and sustainably improving patient care. Since then, we have witnessed remarkable progress in the treatment of breast cancer, and we are proud to have made a decisive contribution to improving patient survival and quality of life.

Our achievements in 2025 are reflected in our strong presence at major international conferences. Once again, GBG was represented at leading congresses such as ASCO, ESMO, ESMO Breast Cancer, the German Society for Senology, and the San Antonio Breast Cancer Symposium (SABCS). A particular highlight this year was SABCS, where GBG contributed seven oral and two poster presentations covering multiple clinical trials, alongside further involvement in additional presentations. More details on these achievements can be found in the “Congress Contribution” section.

Our ongoing commitment to excellence is reflected in an impact factor of 878.9 for 2025, based on a total of 39 publications in peer-reviewed journals. The year began with the publication of the overall survival results from the KATHERINE trial in the New England Journal of Medicine and concluded with the primary endpoint interim analysis of the DESTINY-Breast05 trial, also in the New England Journal of Medicine. These milestones underscore GBG’s ongoing commitment to high-quality, practice-changing research. A comprehensive overview of all 2025 publications is provided in the “Publications” section.

In 2025, GBG conducted 15 studies in active recruitment and 14 studies in follow-up, demonstrating our broad and sustained impact on clinical breast cancer research.

We are also pleased to present exclusive interviews with PD Dr. Laura Michel (NoLEEta trial), PD Dr. Mattea Reinisch (GeparPiPPa trial), Prof. Dr. Elmar Stickeler (OPTimal trial), and Prof. Dr. Thomas Decker (ELEMENT trial), all featured in the “Study Concepts in Focus” section.

Close collaboration with key opinion leaders and researchers remains a cornerstone of our work. Regular meetings of our Scientific Board and Subboards, as well as intensive cooperation with national and international collaborative trial organizations, are essential to furthering scientific progress in breast cancer research.

An overview of all currently recruiting and follow-up studies can be found in the corresponding sections. Additionally, the “Translational Research & Biobanking” section provides exciting insights into our translational research activities. Our updated GBG Study Finder is available on page 97.

We thank you for your ongoing collaboration and support. As we reflect on GBG’s accomplishments in 2025, we look forward to continuing our journey in 2026 – driven by innovation, competence, and partnership in the field of breast cancer therapy.

Yours sincerely,
Prof. Dr. Sibylle Loibl
on behalf of the GBG Team and the Subboards

About the GBG

The German Breast Group (GBG) is pleased to present the Annual Scientific Report (ASR) 2025, highlighting another year of significant achievements in breast cancer research. Our core values – innovation, expertise, and collaboration – continue to guide our mission. GBG remains steadfast in its commitment to advancing breast cancer research in Germany and beyond, managing clinical trials across the entire therapeutic spectrum, including prevention, neoadjuvant, adjuvant, local, and palliative treatment settings. Distinct from industry-sponsored research, GBG focuses on investigator-initiated trials (IITs), reflecting our dedication to addressing essential clinical and scientific questions that drive progress in breast cancer treatment. Adherence to the highest standards of the International Conference on Harmonization Good Clinical Practice (ICH-GCP) guidelines and regulatory requirements is fundamental to our work and underscores our unwavering commitment to scientific integrity.

OUR EXPERTISE

GBG offers a comprehensive range of services in breast cancer research. Our expertise spans the entire clinical trial process, from the initial design – developed by our specialized subboards of breast cancer experts – to project management, monitoring, data management, bioinformatics, and statistical analysis. We also ensure the international publication of trial results.

Beyond clinical trials, GBG is actively involved in translational research, biobanking, central pathology laboratory support, ongoing medical education, and rigorous quality assurance. Additionally, we provide end-to-end services for clinical studies sponsored by external partners or pharmaceutical companies, including project management, monitoring, data management, statistical evaluation, and medical expertise, both nationally and internationally.

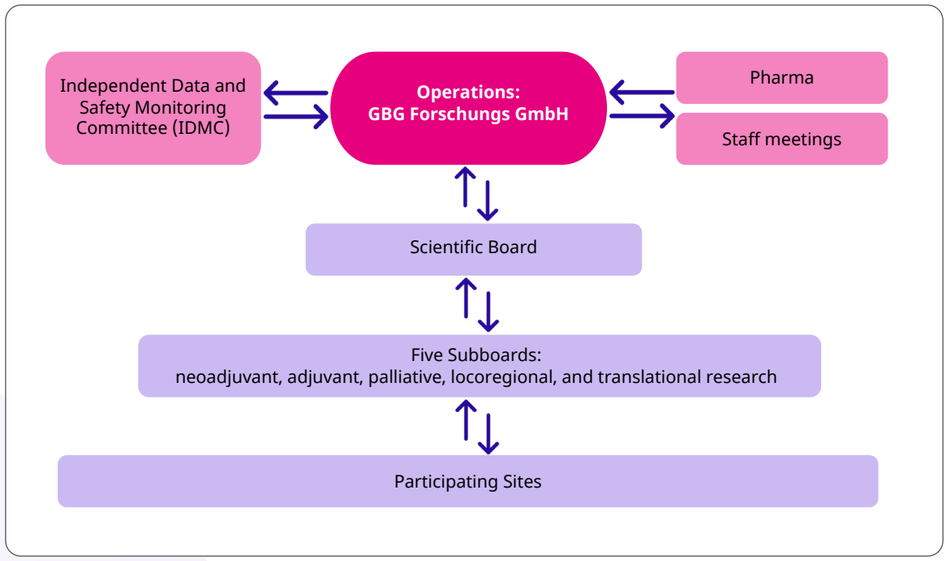


Figure 1: Structure of the German Breast Group

OUR INFRASTRUCTURE

At the core of GBG is a robust infrastructure that connects scientific concepts developed in regular subboard meetings with collaborating trial sites across a wide network of medical institutions. This interdisciplinary structure allows us to translate innovative ideas into practice efficiently. While official membership in GBG is not mandatory, physicians who actively participate in our trials become integral members of the study group. Our investigators, primarily based in gynecological departments of university hospitals, general hospitals, specialist practices, and general practices – provide invaluable insights and expertise to our research.

PATIENT RECRUITMENT AND IMPACT

The impact of our work is evident through a substantial body of publications on breast cancer treatment over recent decades. Our ongoing mission is to continuously improve treatment strategies and clinical guidelines, ultimately enhancing patient outcomes and reducing breast cancer mortality. The cumulative number of patients recruited into GBG studies reflects both the increasing impact of our research and the trust placed in us by physicians and patients alike.

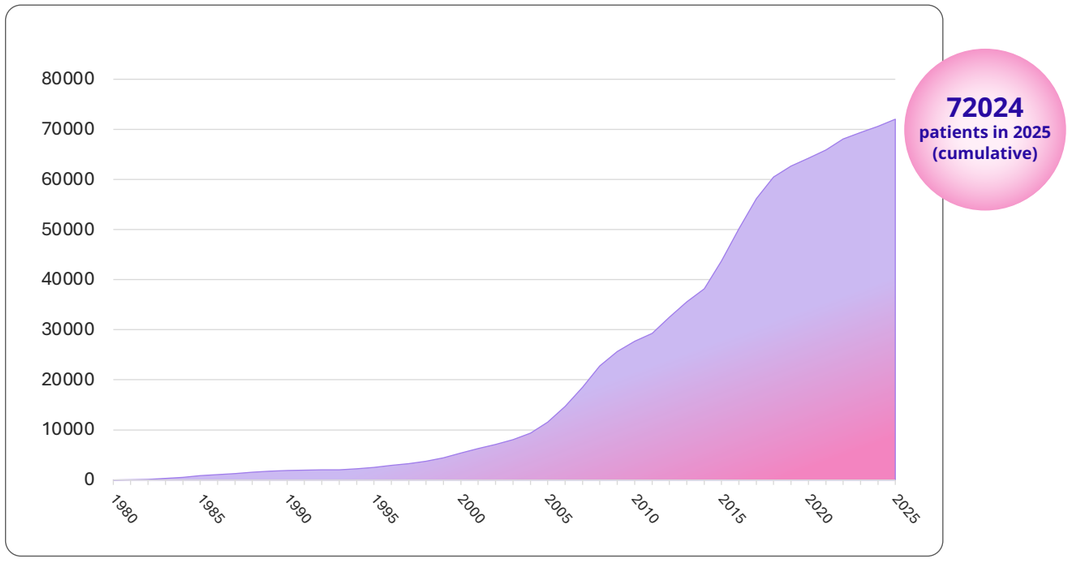


Figure 2: Cumulative patient recruitment

THE INDEPENDENT DATA AND SAFETY MONITORING COMMITTEE (IDMC)

Since its establishment in 2003, GBG has upheld the highest standards of safety and efficacy in clinical trials. Central to the commitment is the Independent Data and Safety Monitoring Committee (IDMC), which plays a vital role in ensuring the integrity and reliability of GBG-sponsored studies.

The IDMC is responsible for the comprehensive review of ongoing trials, focusing on key aspects such as:

- **Objectives and scientific impact: Rigorous evaluation of trial objectives, analysis of scientific findings, and detailed review of adverse events (AEs), serious adverse events (SAEs), and deaths unrelated to breast cancer, to ensure scientific integrity.**

- **Protocol modifications: Thorough assessment of all major protocol amendments, including changes to accrual goals, to guarantee alignment with the original study objectives.**

- **Efficacy Analyses: Active involvement in interim and final analyses of trial efficacy, conducted when the protocol-specified number of patients or events has been reached, ensuring robust evaluation of study outcomes.**

CONTINUOUS IMPROVEMENT AND PROACTIVE OVERSIGHT

By establishing the IDMC, GBG demonstrates a commitment to proactive and vigilant oversight, fostering continuous improvement in clinical trial conduct. The IDMC meets the evolving challenges of the dynamic scientific landscape, significantly contributing to the reliability and credibility of GBG-sponsored research. As we navigate the complexities of breast cancer research, the IDMC remains a testament to our dedication to safety, quality, and scientific rigor.

COOPERATIONS

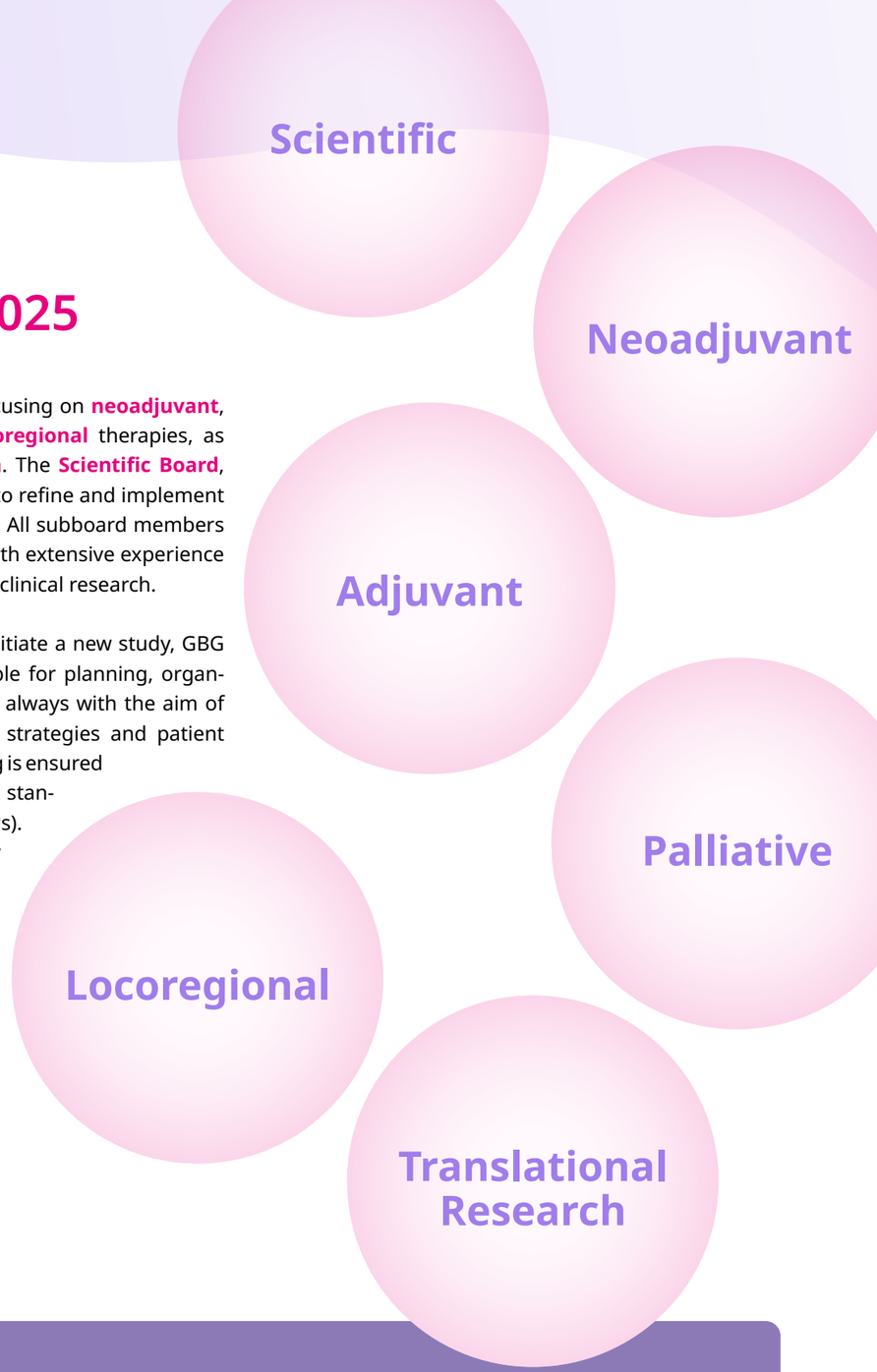
In 2025, we further expanded our international collaborations in our clinical trials.

As we begin another year of rigorous research, we would like to sincerely thank everyone who contributes to GBG's success, including trial participations, collaborators, and supporters.

Subboards 2025

Five subboards were active, focusing on **neoadjuvant**, **adjuvant**, **palliative**, and **locoregional** therapies, as well as **translational research**. The **Scientific Board**, reactivated in 2023, continued to refine and implement agreed-upon scientific projects. All subboard members are recognized professionals with extensive experience in breast cancer treatment and clinical research.

When a subboard decides to initiate a new study, GBG Forschungs GmbH is responsible for planning, organizing, and managing the trial – always with the aim of directly improving therapeutic strategies and patient benefit. Strict quality monitoring is ensured by adherence to GBG's internal standard operating procedures (SOPs). Each subboard meets annually in person and twice a year virtually.



We are looking for motivated young colleagues with experience whom we would like to welcome into our subboards and actively integrate into our projects in a collaborative manner.

Subboards 2025

Scientific


Dr. V. Nekljudova, Neu-Isenburg


Prof. Dr. F. Marmé, Mannheim


Prof. Dr. D. Krug, Kiel


Dr. J. Holtschmidt, Neu-Isenburg


Dr. T. Link, Dresden


PD Dr. M. Reinisch, Mannheim


Prof. Dr. S. Loibl, Neu-Isenburg


Prof. Dr. K. Rhiem, Köln


Prof. Dr. C. Denkert, Marburg


PD Dr. L. Michel, Heidelberg


Prof. Dr. M. van Mackelenbergh, Kiel

Neoadjuvant


Prof. Dr. A. Schneeweiss, Heidelberg


Prof. Dr. C. Solbach, Frankfurt am Main


Prof. Dr. V. Bjelic-Radisic, Witten-Herdecke


Prof. Dr. J. U. Blohmer, Berlin


Prof. Dr. C. Denkert, Marburg


Prof. Dr. P. Fasching, Erlangen


Prof. Dr. M. Untch, Berlin


Dr. C. Hanusch, München


Dr. T. Link, Dresden


Prof. Dr. A. Hartkopf, Tübingen


Dr. Niklas Gremke, Marburg


PD Dr. M. Reinisch, Mannheim


Prof. Dr. J. Huober, St. Gallen


Prof. Dr. Maria Margarete Karsten, Berlin


Prof. Dr. S. Loibl, Neu-Isenburg


Prof. Dr. K. Rhiem, Köln

Subboards 2025

Adjuvant


Prof. Dr. M. Untch, Berlin


Prof. Dr. C. Denkert, Marburg


Prof. Dr. W. Janni, Ulm


Prof. Dr. E. Stickeler, Aachen


Prof. Dr. S. Loibl, Neu-Isenburg


Prof. Dr. M. Schmidt, Mainz


Prof. Dr. F. Marmé, Mannheim


Dr. S. Schmatloch, Kassel


PD Dr. M. Reinisch, Mannheim


Prof. Dr. T. Reimer, Rostock


PD Dr. L. Michel, Heidelberg

Palliative


Prof. Dr. M. Thill, Frankfurt am Main


Prof. Dr. C. Denkert, Marburg


Prof. Dr. T. Decker, Ravensburg


Prof. Dr. M. Schmidt, Mainz


Prof. Dr. S. Loibl, Neu-Isenburg


Dr. Athina Kostara, Düsseldorf


Dr. Carlo Fremd, Heidelberg


Prof. Dr. V. Müller, Hamburg

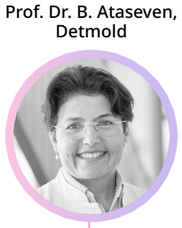
Prof. Dr. C. Mundhenke, Bayreuth


Dr. K. Lübbe, Hannover

Subboards 2025

Locoregional


Prof. Dr. S. Loibl,
Neu-Isenburg


Prof. Dr. B. Ataseven,
Detmold


PD Dr. I. Bekes,
St. Gallen


Prof. Dr. T. Kühn,
Esslingen


Prof. Dr. C. Denkert,
Marburg


Prof. Dr. D. Krug,
Kiel


Prof. Dr. B. Gerber,
Rostock

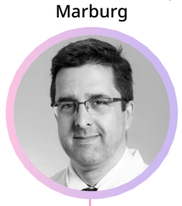

Dr. J. Holtschmidt,
Neu-Isenburg


Prof. Dr. J. Heil,
Heidelberg


Prof. Dr. M. Golatta,
Heidelberg

Translational Research


Prof. Dr. M. van Mackelenbergh,
Kiel


Prof. Dr. C. Denkert,
Marburg


Prof. Dr. P. Fasching,
Erlangen


Prof. Dr. E. Stickeler,
Aachen


Prof. Dr. T. Fehm,
Düsseldorf


Prof. Dr. C. Schem,
Hamburg


Prof. Dr. T. Karn,
Frankfurt am Main


Prof. Dr. A. Noske,
Zürich

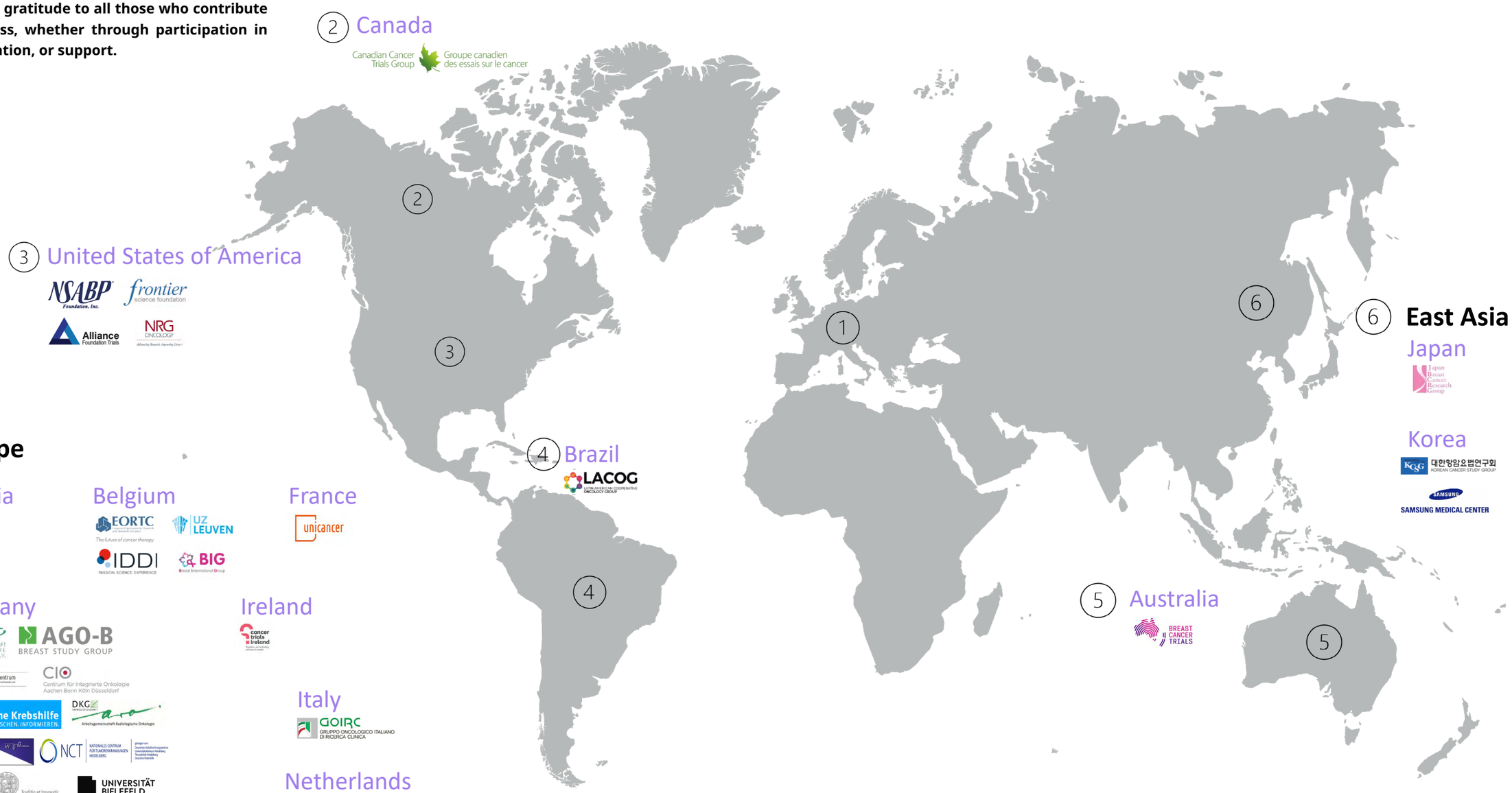

Prof. Dr. V. Müller,
Hamburg


Prof. Dr. S. Loibl,
Neu-Isenburg


Prof. Dr. F. Marmé,
Mannheim

Cooperations with other study groups

As we embark on another year of meticulous research, we express our gratitude to all those who contribute to GBG's success, whether through participation in trials, collaboration, or support.



1 Europe

Austria

Belgium

France

Germany

Ireland

Italy

Netherlands

United Kingdom

2 Canada

3 United States of America

4 Brazil

5 Australia

6 East Asia

Japan

Korea

Spain

Switzerland

Sweden

Peer-reviewed articles in 2025

IF 4.6 Bardia A, Rugo HS and Brufsky A. Q-TWiST Analysis to Assess Benefit-Risk of Sacituzumab Govitecan in Previously Treated Patients With Metastatic Triple-Negative Breast Cancer. JCO Oncol Pract. 2025; OP2400806.
Click here for more info

IF 65.4 Burstein HJ, Curigliano G and Panelists of the St. Gallen International Breast Cancer Consensus 2025. Tailoring treatment to cancer risk and patient preference: the 2025 St Gallen International Breast Cancer Consensus Statement on individualizing therapy for patients with early breast cancer. Ann Oncol. 2025; 36(12):1433-1446.
Click here for more info

IF 35.9 Conforti F, Holtschmidt J and Loibl S. Distant disease-free survival as a surrogate endpoint for overall survival in randomised trials of neoadjuvant therapy for early breast cancer: a pooled analysis of GBG and AGO-B Study Group trials. Lancet Oncol. 2025; 26(12):1584-1597.
Click here for more info

IF 7.1 Dauccia C, Alice Franzoi M and APHINITY Steering Committee and Investigators. Body mass index and weight changes in patients with HER2+ early breast cancer: A sub-analysis of the APHINITY trial. Eur J Cancer. 2025; 223:115489.
Click here for more info

IF 19.4 Denk D, Singh A and Greten FR. Effect of the mitophagy inducer urolithin A on age-related immune decline: a randomized, placebo-controlled trial. Nat Aging. 2025; 5(11):2309-2322.
Click here for more info

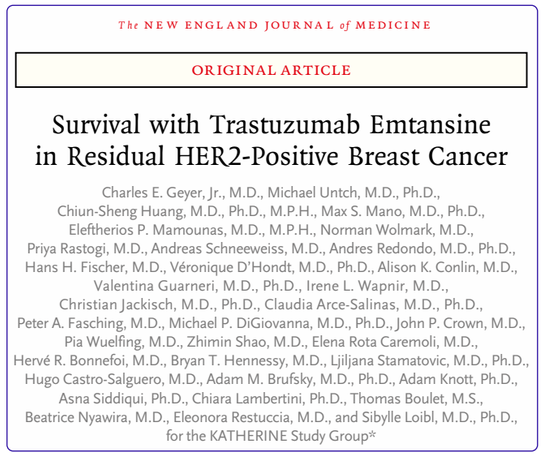
IF 88.5 Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Extending the duration of endocrine treatment for early breast cancer: patient-level meta-analysis of 12 randomised trials of aromatase inhibitors in 22 031 postmenopausal women already treated with at least 5 years of endocrine therapy. Lancet. 2025; 406(10503):603-614.
Click here for more info

IF 7.6 Galas K, Gleitsmann M and Loibl S. Effects of pregnancy on breast cancer immunology: immune biomarker and TIL quantification. NPJ Breast Cancer. 2025; 11(1):43.
Click here for more info

IF 8.3 García-Estévez L, Bardia A and Cortés J. The association of high body mass index with the safety and efficacy of sacituzumab govitecan in patients with metastatic triple-negative breast cancer from the ASCENT study. ESMO Open. 2025; 10(6):105294.
Click here for more info

IF 7.9 Geyer CE Jr, Loibl S. Switching to T-DM1 remains justified in patients with HER2- residual invasive breast cancer after neoadjuvant therapy. Breast. 2025; 81:104450.
Click here for more info

IF 78.5 Geyer CE Jr, Untch M and Loibl S; KATHERINE Study Group. Survival with Trastuzumab Emtansine in Residual HER2+ Breast Cancer. N Engl J Med. 2025; 392(3):249-257.


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Survival with Trastuzumab Emtansine in Residual HER2-Positive Breast Cancer

Charles E. Geyer, Jr., M.D., Michael Untch, M.D., Ph.D., Chiun-Sheng Huang, M.D., Ph.D., M.P.H., Max S. Mano, M.D., Ph.D., Eleftherios P. Mamounas, M.D., M.P.H., Norman Wolmark, M.D., Priya Rastogi, M.D., Andreas Schneeweiss, M.D., Andres Redondo, M.D., Ph.D., Hans H. Fischer, M.D., Véronique D'Hondt, M.D., Ph.D., Alison K. Conlin, M.D., Valentina Guarneri, M.D., Ph.D., Irene L. Wapnir, M.D., Christian Jackisch, M.D., Ph.D., Claudia Arce-Salinas, M.D., Ph.D., Peter A. Fasching, M.D., Michael P. DiGiovanna, M.D., Ph.D., John P. Crown, M.D., Pia Wuelfing, M.D., Zhimin Shao, M.D., Elena Rota Caremoli, M.D., Hervé R. Bonnefoi, M.D., Bryan T. Hennessy, M.D., Ljiljana Stamatovic, M.D., Ph.D., Hugo Castro-Salguero, M.D., Adam M. Brufsky, M.D., Ph.D., Adam Knott, Ph.D., Asna Siddiqui, Ph.D., Chiara Lambertini, Ph.D., Thomas Boulet, M.S., Beatrice Nyawira, M.D., Eleonora Restuccia, M.D., and Sibylle Loibl, M.D., Ph.D., for the KATHERINE Study Group*

Click here for more info

IF 52.7 Gremke N, Besong I and Stiewe T. Targeting PI3K inhibitor resistance in breast cancer with metabolic drugs. Signal Transduct Target Ther. 2025; 10(1):92.
Click here for more info

IF 5.6 Häberle L, Erber R and Fasching PA. Prediction of pathological complete response after neoadjuvant chemotherapy for HER2- breast cancer patients with routine immunohistochemical markers. Breast Cancer Res. 2025; 27(1):13.
Click here for more info

IF 5.6 Hahnen E, Hauke J and Loibl S. *BRCA1/2* and Other Predisposition Genes in High-Risk Hormone Receptor+/Human Epidermal Growth Factor Receptor 2- Breast Cancer Treated With Endocrine Therapy With or Without Palbociclib: A Secondary PENELOPE-B Study Analysis. JCO Precis Oncol. 2025; 9:e2400742.
Click here for more info

IF 5.6 Hahnen E, Hauke J and Loibl S. Reply to: Germline and Somatic *BRCA1/2* Mutations in Breast Cancer Treatment Strategies. JCO Precis Oncol. 2025; 9:e2500588.
Click here for more info

IF 2.6 Hamilton EP, Loibl S and Mayer IA. CAMBRIA-1 & CAMBRIA-2 phase III trials: camizestrant versus standard endocrine therapy in ER+/HER2- early breast cancer. Future Oncol. 2025; 21(7):795-806.
Click here for more info

IF 2.9 Hartmann S, Banys-Paluchowski M and Kuehn T; AXSANA Study Group. Lost axillary markers after neoadjuvant chemotherapy in breast cancer patients - data from the prospective international AXSANA (EUBREAST 3) cohort study (NCT04373655). Eur J Surg Oncol. 2025; 51(9):110253.
Click here for more info

IF 1.9 Holtschmidt J, Rhiem K and Loibl S. Molekulare Testungen zu therapeutischen Zwecken bei Brustkrebs – Hilfe für die klinische Praxis. Geburtshilfe Frauenheilkd 2025; 85(11): 1131-1136.
Click here for more info

IF 78.5 Jhaveri KL, Im SA and Turner NC. Overall Survival with Inavolisib in *PIK3CA*-Mutated Advanced Breast Cancer. N Engl J Med. 2025; 393(2):151-161.
Click here for more info

IF 7.9 Laakmann E, Schmidt M and Müller V. Clinical characteristics and prognostic factors in patients with breast cancer and leptomeningeal metastases from a large registry of BMBC. Breast. 2025; 81:104433.
Click here for more info

IF 8.3 Link T, Reinisch M and Loibl S. Long-term effect of neoadjuvant denosumab treatment in high-risk early breast cancer (GeparX). ESMO Open. 2025; 10(12):105915.
Click here for more info

IF 13.0 Liu X, Binicy B and Matikas A. Prevalence and prognosis of patients with breast cancer eligible for adjuvant abemaciclib or ribociclib: a nationwide population-based study. Lancet Reg Health Eur. 2025; 59:101471.
Click here for more info

IF 65.4 Loibl S, Martin M and Marmé F. Final survival results from the PENELOPE-B trial investigating palbociclib versus placebo for patients with high-risk HR+/HER2- breast cancer and residual disease after neoadjuvant chemotherapy. Ann Oncol. 2025; 36(7):832-837.
Click here for more info

IF 78.5 Loibl S, Park YH and DESTINY-Breast05 Trial Investigators. Trastuzumab Deruxtecan in Residual HER2+ Early Breast Cancer. N Engl J Med. 2025 Dec 10.
Click here for more info

IF 41.9 Loibl S, Untch M and Schneeweiss A. Durvalumab in Combination with Neoadjuvant Chemotherapy in Early Triple-Negative Breast Cancer (TNBC) – Long-term Analysis from the GeparNuevo Trial. J Clin Oncol. 2025.

IF 1.6 Maschmeyer G, Fehm T and Hilgendorf I. Onkopedia: What's New? Systemic Tumor Treatment in Pregnancy. Oncol Res Treat. 2025; 1-15.
Click here for more info

IF N.A. Matuschek C, Krug D and Loibl S. Neoadjuvante Strahlentherapie beim Mammakarzinom: Die NeoRad-Studie. Frauenarzt. 2025

IF 4.2 McArthur HL, Tolaney SM and Loibl S. TROPION-Breast04: a randomized phase III study of neoadjuvant datopotamab deruxtecan (Dato-DXd) plus durvalumab followed by adjuvant durvalumab versus standard of care in patients with treatment-naïve early-stage triple negative or HR-low/HER2- breast cancer. Ther Adv Med Oncol. 2025; 17:17588359251316176.
Click here for more info

IF 10.2 Mürdter TE, Schroth W and Schwab M. Supplementation of Tamoxifen with Low-Dose Endoxifen in Patients with Breast Cancer with Impaired Tamoxifen Metabolism (TAMENDOX): A Randomized Controlled Phase I/II Trial. Clin Cancer Res. 2025; 31(23):4903-4911.
Click here for more info

IF 8.3 Naughton MJ, Zahrieh DM and Mayer EL. Quality-of-life and symptom severity in the PALLAS randomized trial of palbociclib with adjuvant endocrine therapy in early breast cancer (AFT-05, ABCSG-42, BIG-14-03, PrE0109). ESMO Open. 2025; 10(6):105120.
Click here for more info

IF 9.7 O'Regan RM, Ren Y and Regan MM. Assessment of Adjuvant Endocrine Therapy With Ovarian Function Suppression by Breast Cancer Index. JAMA Netw Open. 2025; 8(11):e2540931.
Click here for more info

IF 2.1 Park-Simon TW, Müller V and Thill M. AGO Recommendations for the Diagnosis and Treatment of Patients with Early Breast Cancer: Update 2025. Breast Care (Basel). 2025; 1-19.
Click here for more info

IF 1.9 Pixberg C, Maurer C, Schneeweiss A. COGNITION-GUIDE – Genomics-Guided Targeted Post-Neoadjuvant Therapy in Patients with Early Breast Cancer: Study Design of a Multicenter, Open-Label, Umbrella Phase II Study. Geburtshilfe Frauenheilkd. 2025; 85(6):611-619.
Click here for more info

IF 2.9 Reimer T, Kuehn T and Thill M. AGO Breast Commission recommendations for the surgical therapy of breast cancer: Working Group on Gynecologic Cancers (AGO) update 2025. Eur J Surg Oncol. 2025; 51(11):110445.
Click here for more info

IF 2.1 Thill M, Janni W and Park-Simon TW. AGO Recommendations for the Diagnosis and Treatment of Patients with Locally Advanced and Metastatic Breast Cancer: Update 2025. Breast Care (Basel). 2025 Mar; 1-12.
Click here for more info

IF 78.5 Tolaney SM, Jiang Z and DESTINY-Breast09 Trial Investigators. Trastuzumab Deruxtecan plus Pertuzumab for HER2+ Metastatic Breast Cancer. N Engl J Med. 2025.
Click here for more info

IF 1.9 Untch M, Banys-Paluchowski M and Ditsch N. Treatment of Patients with Early Breast Cancer: 19th St. Gallen International Breast Cancer Consensus Discussed against the Background of German Treatment Recommendations. Geburtshilfe Frauenheilkd. 2025; 85(7):677-693.
Click here for more info

Peer-reviewed reviews in 2025

IF 4.0 Finn RS, Rugo HS and Slamon DJ. A Decade After Approval of the First CDK4/6 Inhibitor: A Look Back at Palbociclib's Journey from Discovery to Approval and What's Next in CDK Inhibition in Breast Cancer. Target Oncol. 2025;20(6):917-936.
Click here for more info

IF 7.9 Lukac S, Putz F and Leone JP. Artificial intelligence as treatment support in breast cancer: current perspectives. Breast. 2025;83:104564.
Click here for more info

IF 50 Zitvogel L, Derosa L and Kroemer G. Impact of the ONCOBIOME network in cancer microbiome research. Nat Med. 2025;31(4):1085-1098.
Click here for more info

GBG-PUBLICATIONS GRADING SYSTEM

To define international publication objectives and objectively measure our scientific output, we have established an internal GBG grading system:

- **7 GBG points for an accepted publication in a high-quality peer-reviewed journal with an impact factor greater than 5**
- **5 GBG points for an accepted publication in a journal with an impact factor less than 5**
- **3 GBG points for an oral presentation or poster discussion**
- **2 GBG points for a poster presentation at an international congress**

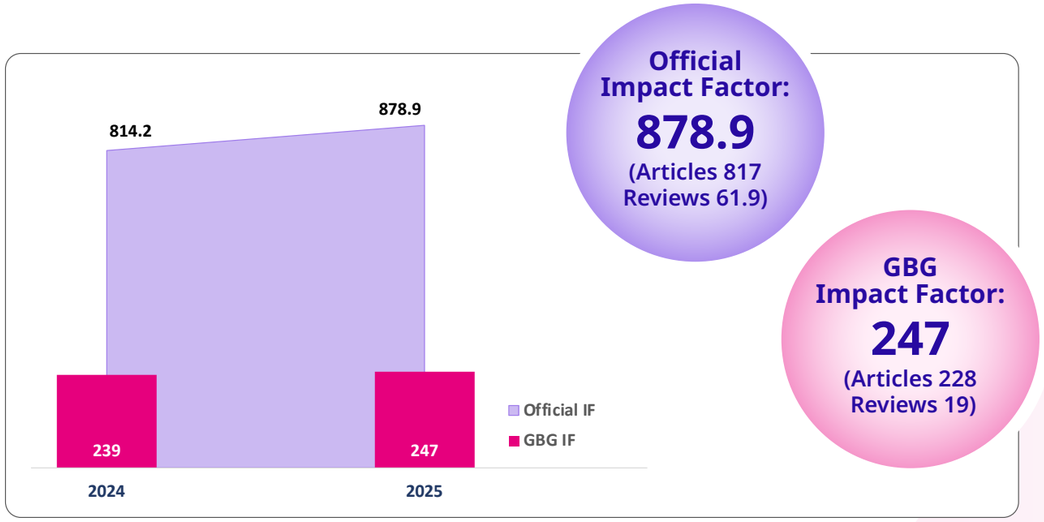


Figure 3: GBG and official Impact Factor (IF) in 2024 and 2025

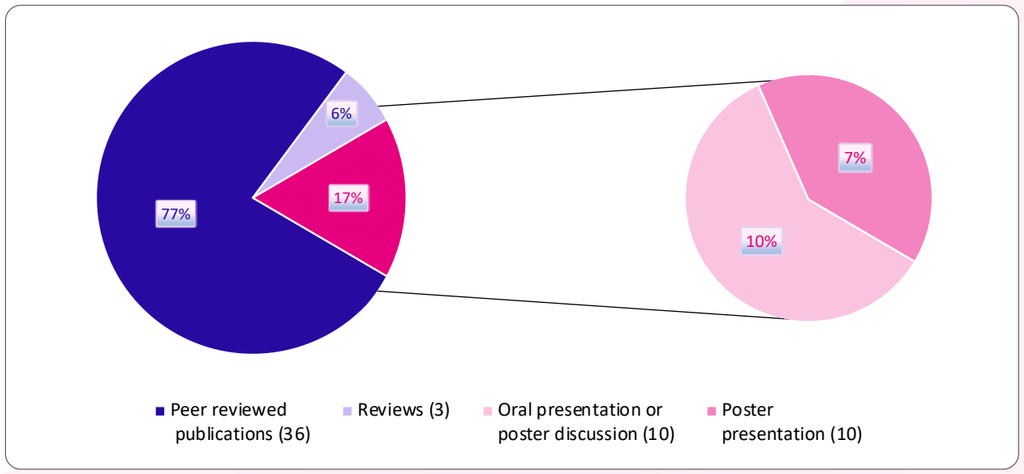


Figure 4: Overview of GBG's publications in 2025 and contribution to GBG impact factor in %

Congress Contributions

Sankt Gallen Breast Cancer Conference (SGBCC)
March 12-15, 2025

2025´congress participation started with Sankt Gallen Breast Cancer Conference (SGBCC), during which Sibylle Loibl had the honour to serve as Conference Chair together with Michael Gnant, Beat Thürlimann and Walter Weber.

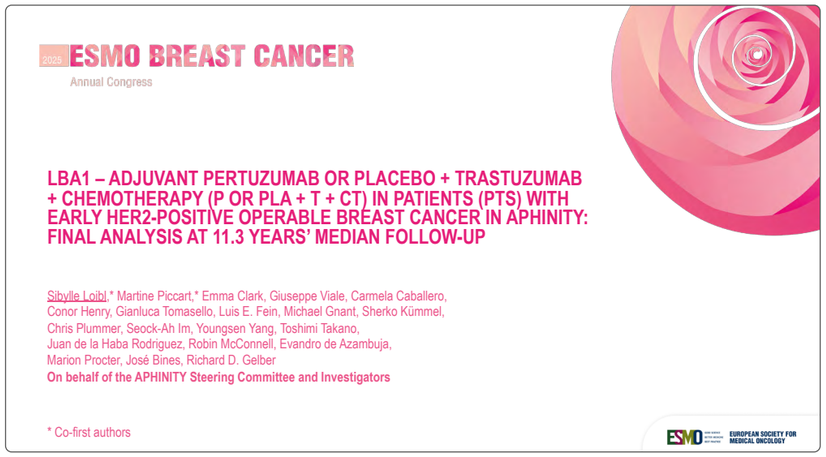
From l. to r.: C. Solbach, S. Loibl, L. Michel, M. v. Mackelenbergh

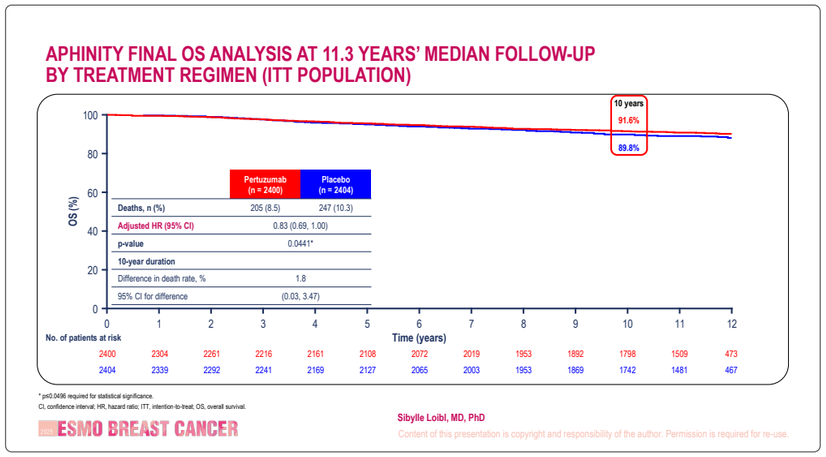
ESMO-Breast Cancer
May 14-17, 2025

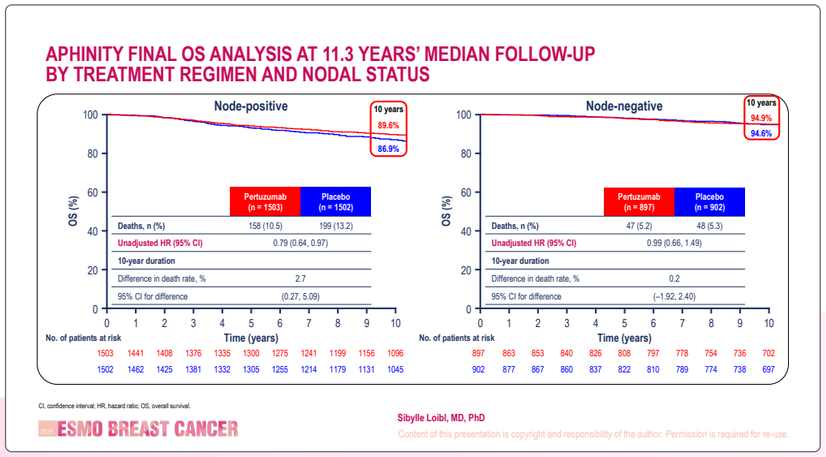
The ESMO Breast Cancer congress 2025 took place in Munich, bringing together leading international clinicians and researchers in breast oncology. We were able to present several oral and poster presentations showcasing current projects.

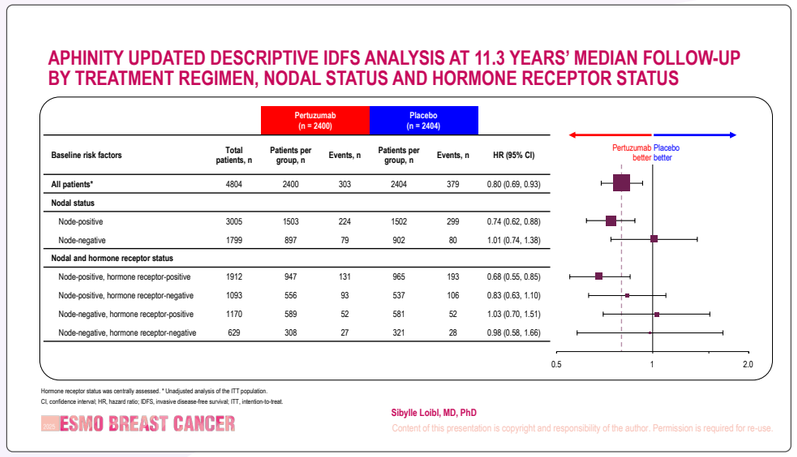
Sibylle Loibl presented the final results from the phase III APHINITY trial (NCT01358877). This randomized, placebo-controlled study investigated the efficacy of adding pertuzumab (P) to trastuzumab (T) and chemotherapy (CT) in patients with either node-positive or high-risk-node negative-HER2+ breast cancer in the adjuvant setting. Previous analyses had demonstrated a significant improvement in the primary endpoint invasive disease-free survival, (iDFS), establishing pertuzumab as standard of care and leading to its approval in this setting. Until now, no significant benefit in overall survival (OS) had been observed.

At the currently presented final analysis, after a median follow-up of 11.3 years, a significant improvement in OS was demonstrated for the overall population (hazard ratio [HR] 0.83, 95% CI 0.69 – 1.0), primarily driven by the node-positive cohort (HR 0.79, 95% CI 0.64 - 0.97), corresponding to an absolute benefit of 2.7%. The maintained clinically meaningful iDFS improvement was only attributable to the node-positive cohort. No new cardiac safety signals were observed during longer follow-up.









More information

Vesna Bjelic-Radisic and Stefan Lukac presented data from the PADMA trial on Quality of Life (QoL) and treatment related physician contacts (PADMA Phone). PADMA was a randomized, open-label, multicenter, prospective study comparing palbociclib (Palb) plus endocrine treatment (ET) versus standard mono-CT with or without maintenance ET as first-line treatment for patients (pts) with high-risk HER2-/HR+ metastatic breast cancer. Both primary endpoint (time to treatment failure, TTF) and secondary endpoint (progression-free survival, PFS) were significantly improved in the Palb/ ET arm. A total of 130 patients were randomized to receive either Palb/ET or standard mono-CT +/-subsequent maintenance ET, 120 initiated study treatment. Disease progression, unacceptable toxicity or withdrawal of consent were the primary reasons for discontinuation or change of treatment.

For the PADMA QoL analysis, FACT-B questionnaires were used to assess patient well-being, with two daily FACT-B derived questions (side effects and satisfaction) and QoL measured at baseline, each cycle for 6 months, and then every other cycle until end of treatment. Patients treated with Palb/ET experienced statistically significant QoL improvements, particularly in physical and psychological domains. Additional analysis showed that Palb/ET patients required fewer medical consultations, resulting in positive impact on carbon footprint, better QoL, and longer TTF and PFS. These patient-centric outcomes further support the use of CDK4/6 inhibitors plus ET as first-line treatment in high-risk HER2-/HR+ metastatic breast cancer.

Find the PADMA QoL poster as download here

Find the PADMA Phone poster as download here

A further presentation covered long-term survival factors from the Brain metastases in the Breast Cancer Registry (BMBC) for patients with HER2+ breast cancer and brain metastases. Since approximately 50% of patients with HER2+ metastatic breast cancer develop brain metastases, real world insights are needed in this growing cohort. This sub-analysis focused on factors associated with long-term survival. Long term survivors were younger at time of primary diagnosis (median age 48.0 years; range: 24.0-78.0 years) and at the first central nervous system (CNS) metastasis (median age 52.0 years; range: 25.0-85.0 years), compared to short term survivors (median age at breast cancer diagnosis 53.0 years; range: 20.0-92.0 years, median age of diagnosis of CNS metastases 58.0 years; range: 22.0-93.0 years). Positive hormone receptor status, better performance status at CNS metastases diagnosis, and fewer CNS lesions were linked to longer survival. Moreover, long-term survivors had fewer leptomeningeal and extracranial metastases at CNS metastasis diagnosis, with a significantly higher proportion of asymptomatic CNS metastases. Treatment with HER2-targeted therapy was also significantly associated with improved long-term survival.

Find this poster as download here

From l. to r.: S. Schöffel, A. Rossberg, B. Freitag, S. Loibl, V. Nekljudova, J. Holtschmidt, N. Hirmas

Further congress contributions and contributions with GBG participation are listed below:

Special Symposium: Antibody-drug conjugates (ADCs) resistance: What do we know? – Payload and antibody in predicting resistance to ADCs, presented by Sibylle Loibl

For more information please visit our website

American Society of Clinical Oncology (ASCO)
May 30-June 03, 2025

Contributions with GBG participation:

Turner N et al., INAVO120: Phase III trial final overall survival (OS) analysis of first-line inavolisib (INAVO)/placebo (PBO) + palbociclib (PALBO) + fulvestrant (FULV) in patients (pts) with *PIK3CA*-mutated, hormone receptor-positive (HR+), HER2-negative (HER2–), endocrine-resistant advanced breast cancer (aBC), oral presentation

Tolaney S et al., Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for first-line (1L) treatment of patients (pts) with human epidermal growth factor receptor 2–positive (HER2+) advanced/metastatic breast cancer (a/mBC): Interim results from DESTINY-Breast09, oral presentation

From l. to r.: J. Holtschmidt, A. Rossberg, F. Marmé, S. Loibl, V. Nekljudova, B. Freitag

German Society for Senology (DGS)
June 26-28, 2025

Congress contributions and contributions with GBG participation:

Von Kroge P., et al. Long-term survival of HER2+ breast cancer patients with brain metastases: final analysis of the Brain Metastases In Breast Cancer Registry (BMBC); poster presentation

Fröhlich S. et al., Surgical axillary staging in elderly patients with initially node-positive breast cancer after neoadjuvant chemotherapy - data from the prospective AXSANA study; poster presentation

Japanese Breast Cancer Society (JBCS)
July 10-12, 2025

Congress contribution:

Loibl S., Breast Cancer Therapy in Young Adults-Differences between Asia and the West: Bridging across the Pacific, oral presentation

ESMO
October 17-21, 2025

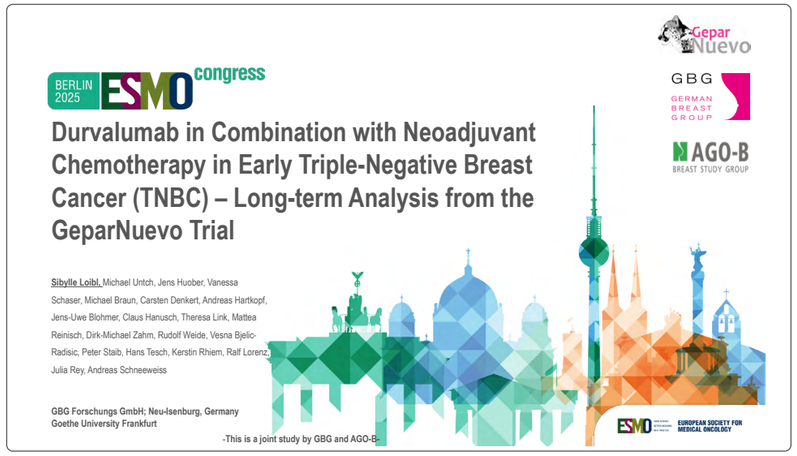
The annual ESMO congress, organized by the European Society for Medical Oncology (ESMO), provides a multidisciplinary platform for sharing the latest advances in cancer treatment and research with an international community of specialists. This year's conference was rich in reports from major phase III breast cancer trials, including primary endpoint analyses from DESTINY-Breast05, TROPION-Breast02 und ASCENT-03.

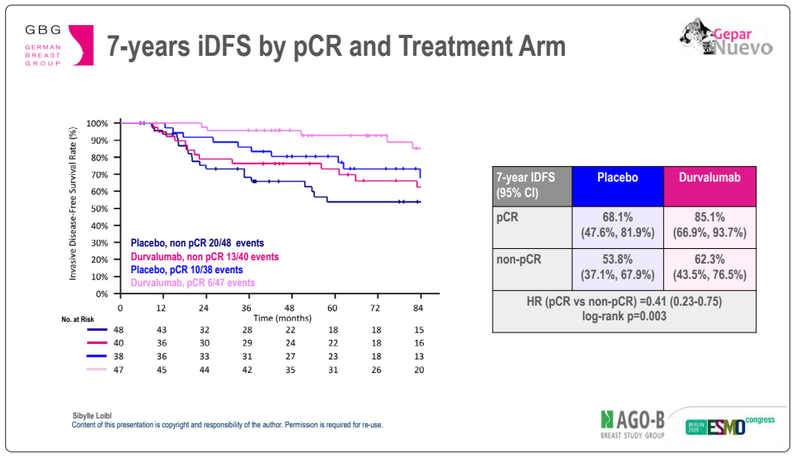
A definitive highlight of this year was the presentation of the primary endpoint analysis from the DESTINY-Breast05 trial, in which GBG participated. This global, multicenter, randomized, open-label, phase III study compared trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1) in patients with high-risk, HER2+ primary breast cancer who had residual invasive disease in the breast or regional lymph nodes following neoadjuvant chemotherapy. Charles Geyer (NSABP) presented results from the first interim efficacy analysis, which showed a statistically significant and clinically meaningful improvement in iDFS with adjuvant T-DXd compared to T-DM1, with a 3-year iDFS of 92.4% versus 83.7% (HR = 0.47, 95% CI: 0.34–0.66; p < 0.0001), corresponding to a 53% relative reduction in the risk of invasive disease recurrence or death.

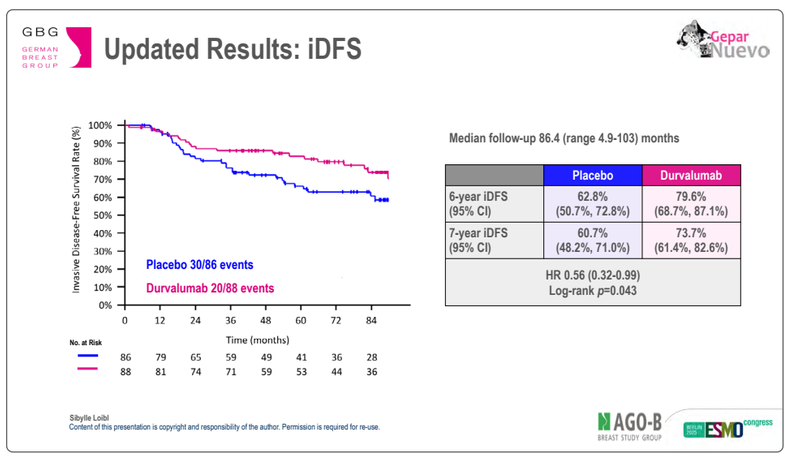
T-DXd demonstrated superior efficacy and a manageable safety profile, positioning it as a likely new standard of care in the post-neoadjuvant setting for high-risk, HER2+ early breast cancer with invasive residual disease after neoadjuvant treatment. Following the compelling DESTINY-Breast05 data presented at ESMO, the FDA has already granted breakthrough designation for T-DXd.

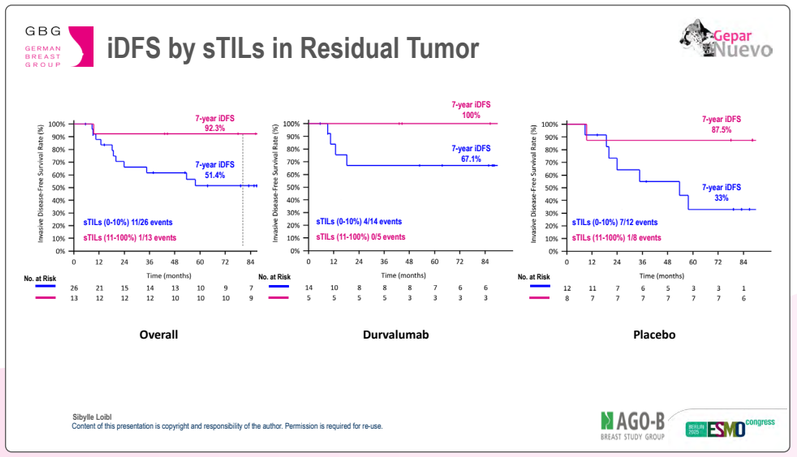
Sibylle Loibl also presented long-term survival data from the GeparNuevo trial at ESMO 2025 in Berlin. The phase II GeparNuevo study examined the addition of anti-PD-L1 checkpoint inhibitor (CPI) durvalumab to neoadjuvant chemotherapy (NACT) in patients with early triple-negative breast cancer (TNBC). While the addition of durvalumab increased the primary endpoint of pathological complete response (pCR) by 9.2%, this did not reach statistical significance. Nevertheless, the trial showed significant improvements in secondary endpoints: iDFS, distant disease-free survival (DDFS), and OS compared to placebo, as demonstrated in previous analyses. After a median follow-up of 86.4 months, these benefits in iDFS, DDFS and OS were sustained. Survival improvements were observed regardless of response to NACT (pCR/non-pCR) and were achieved without adjuvant continuation of durvalumab. Notably, among patients achieving pCR, the 7-year OS was 100% in the durvalumab arm versus 82.5% in the placebo arm (log-rank p=0.0053). In 39 out of 71 patients who did not achieve pCR, stromal tumor-infiltrating lymphocytes (sTILs) in residual disease could be evaluated. Patients with initially affected nodes derived greater iDFS benefit from durvalumab (HR 0.33, CI 0.144-0.771, p=0.01; interaction p=0.045) upon preplanned subgroup analysis.

GeparNuevo was the first trial to demonstrate a survival benefit with PD-L1 inhibition in early TNBC and remains unique in proving this benefit without adjuvant checkpoint inhibition. These findings support further investigation of adjuvant CPI and its impact on long-term survival in early TNBC.









At ESMO, data from the Brain metastases Breast Cancer (BMBC) Registry on HER2 immunohistochemistry (IHC) status of CNS metastases were shown by Elena Laakmann as poster presentation. The impact of HER2 IHC status of CNS metastases in HER- metastatic breast cancer (detected by FISH) remains insufficiently understood. Systemic treatment with antibody-drug conjugate (ADC) T-Dxd is effective and approved not only for HER2+ disease, but also for HER2-low, and more recently, HER2-ultralow breast cancer. However, data on the HER2-low and -ultralow status specifically in brain metastases (BM) are limited. This analysis evaluated the HER2 IHC status of BMs and compared clinical characteristics and survival outcomes across different HER2 IHC-defined cohorts. Among patients with brain metastases, 39.2% were diagnosed with IHC 3+ status (103 cases), 35.4% with IHC 0, 11.0% with IHC 1, 10.3% with IHC ultralow, and 4.2% with IHC 2+. Significant differences in median OS (mOS) were observed among HER2-IHC cohorts (p=0.0064). Patients with HER2 3+ brain metastases had the highest mOS (35.4 months, 95% CI 17.7-46.0), followed by HER2 ultralow (22.7 months, 95% CI 8.0-28.6) and HER2 1+/2+ (16.5 months, 95% CI 13.2-36.2). The lowest survival was observed in patients with HER2 0 brain metastases (13.1 months, 95% CI 7.5-21.7). These findings suggest that HER2 IHC status of CNS metastases is significantly associated with OS and may serve as a valuable biomarker for future therapeutic decision-making, especially regarding the use of ADCs targeting HER2. Notably, 65% of patients with brain metastases may potentially benefit from such HER2-targeted therapies.

Further congress contributions and contributions with GBG participation are listed below:

Loibl S., et al. Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for patients (pts) with HER2+ advanced/metastatic breast cancer (a/mBC): Additional analyses of DESTINY-Breast09 in key subgroups of interest; oral presentation

Rugo H.S., et al. Capivasertib plus fulvestrant as first and second-line endocrine-based therapy in *PIK3CA*/AKT1/PTEN-altered hormone receptor-positive advanced breast cancer: Subgroup analysis from the phase 3 CAPItello-291 trial; poster presentation

For more information please visit our website

German Society for Hematology and Medical Oncology (DGHO)
October 24-27, 2025

Congress contributions and contributions with GBG participation:

Loibl S., et al. A randomized phase III study of first-line saruparib (AZD5305) plus camizestrant vs CDK4/6i plus physician's choice endocrine therapy or CDK4/6i plus camizestrant in patients with HR+/HER2- advanced breast cancer with *BRCA1/BRCA2/PALB2* mutations (EvoPAR-Breast01); poster presentation

Decker T., et al. Phase II study evaluating the addition of Elacestrant to Olaparib (Standard PARP-Inhibitor) compared to olaparib monotherapy in patients with HR+/HER2- locally advanced or metastatic breast cancer with germline *BRCA1/2* mutations – ELEMENT; poster presentation

San Antonio Breast Cancer Symposium (SABCS)
December 9-12, 2025

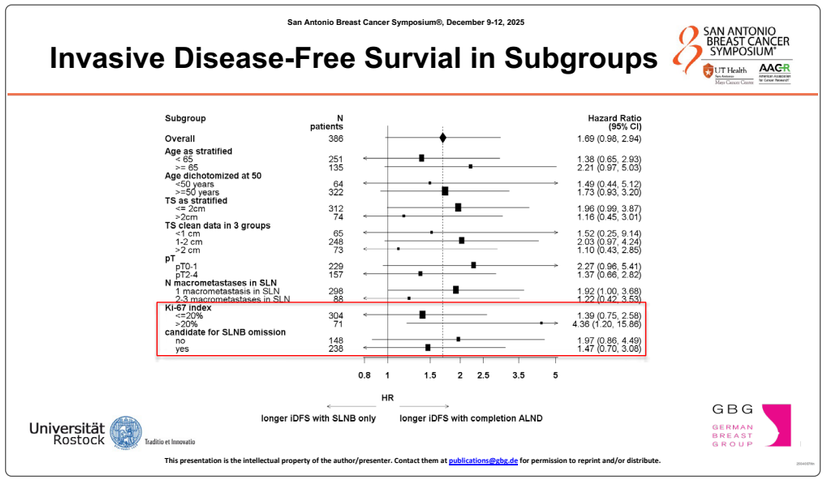
The year ended on a high note for the GBG, with eight internal contributions and an additional eleven presentations with GBG participation – delivered as oral, rapid-fire, or poster presentations at the San Antonio Breast Cancer Symposium (SABCS) in Texas. Overall, there was a remarkable level of participation from German research groups at this year's conference.

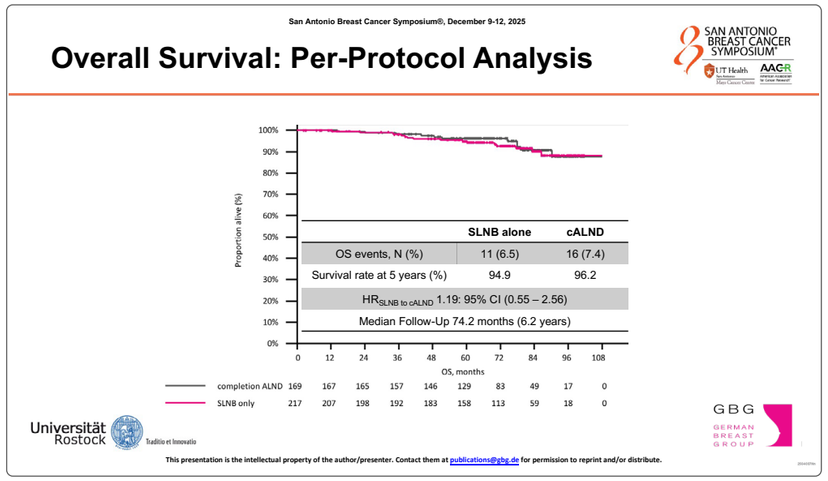
A highlight was the oral presentation by Toralf Reimer (General Session 2), presenting results from the second randomization of the Intergroup-Sentinel-Mamma (INSEMA) trial. This study primarily investigated the omission of sentinel lymph node biopsy (SLNB) in clinically node-negative (cN0) patients (Rando1). The primary endpoint analysis for the first randomization was presented at SABCS 2024, demonstrating non-inferiority of omitting SLNB in cN0 patients undergoing breast-conserving surgery (BCS) with regard to iDFS. These findings, together with data from previous trials, led to changes in international guidelines issued by ASCO and AGO in 2025.

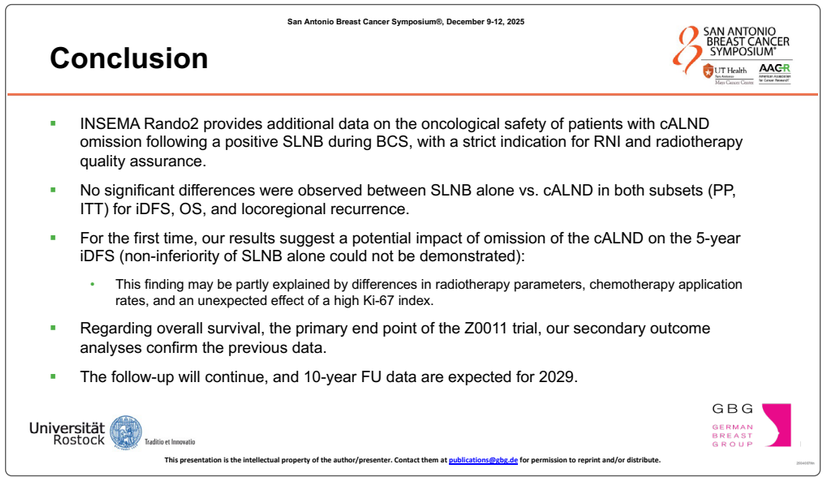
Patients with 1-3 involved lymph nodes in the SLNB arm of INSEMA were randomized a second time (1:1) to either SLNB alone or completion axillary lymph node dissection (cALND) (Rando2) to assess the non-inferiority of SLNB alone compared to cALND in terms of iDFS. The analysis of this key secondary endpoint was presented at this year's meeting. The non-inferiority margin was set at a 5-year iDFS greater than 76.5% (HR < 1.271) for SLNB alone, with anticipated 5-year iDFS of 81% for the cALND arm.

In the per protocol (PP) analysis, non-inferiority for SLNB alone versus cALND could not be demonstrated (HR of 1.69, 95% CI: 0.98-2.94). The estimated 5-year iDFS rates were 86.6% (81.0%-90.7%) in the SLNB-alone arm and 93.8% (88.7%-96.6%) in the cALND arm (log-rank p=0.058). OS rates at 5 years were similar, at 94.9% for the SLNB-only group versus 96.2% for the cALND group. In the intention-to-treat (ITT) analysis, no significant differences in iDFS were observed (HR 1.26, 0.80-1.99). Locoregional recurrences (LRR) were rare in both arms, with a 5-year cumulative incidence of 1.1% in the SLNB alone arm compared to 0.0% with cALND arm (p=0.405).

In summary, no significant differences were observed between SLNB alone and cALND regarding iDFS, OS, and LRR in either the PP or ITT populations. However, the data suggest that omission of cALND may impact 5-year iDFS, as non-inferiority of SLNB alone could not be confirmed and iDFS was numerically lower. Results for OS are consistent with previous findings such as those from ACOSOG Z001. Long-term follow-up is ongoing, with 10-year data expected in 2029.







Link full presentation

Immediately following, Guido Hildebrandt from the University of Rostock presented an additional analysis from the INSEMA trial, focussing on the comparability of applied radiotherapy among patients who underwent breast-conserving surgery with or without SLNB in the first randomization.

The analysis recorder the distribution of doses in ipsilateral axillary levels I-III and regional nodal irradiation (RNI). According to the protocol, whole-breast irradiation (WBI) was mandatory, while RNI was permitted only for patients with 4 or more involved lymph nodes. This pre-scheduled secondary analysis included 5,154 patients from 108 radiotherapy (RT) centers; of these, 4890 patients (95.7%) received postoperative WBI in line with the protocol. There were no significant differences between randomized groups regarding the RT technique employed, fractionation schedule, and boost application. However, median and average doses for each axillary level differed

significantly between groups, with higher median doses observed in the SLNB arm compared to the no SLNB arm at level I (91.4% versus 86.3%; p<0.001), level II (37.8% versus 24.3%; p<0.001), and level III (5.2% versus 4.5%; p=0.003). RNI including supra-/infraclavicular and/or parasternal nodes was performed in 87 patients (4.0%) in the SLNB arm, even though only 8 patients actually had 4 or more positive lymph nodes. In contrast, only 5 patients (0.9%) in the no SLNB arm received RNI (p<0.001).

In conclusion, approximately 50% of INSEMA patients received a potentially therapeutic dose at axillary level I. Patients in the SLNB arm received higher incidental axillary dose and more frequent RNI than those in the no SLNB arm. In the no SLNB group, fewer than 1% received RNI. This analysis demonstrates that omission of SLNB was not compensated by escalated axillary RT, nor was such compensation necessary.

Link full presentation

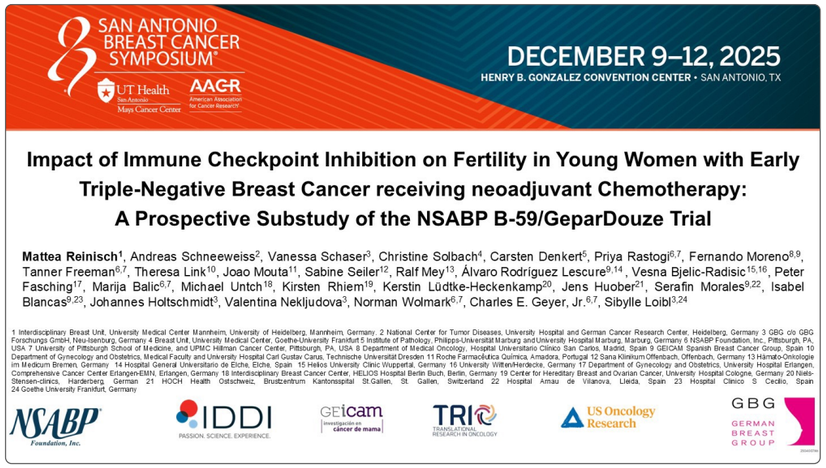
Mattea Reinisch presented the world's first analysis of the impact of neoadjuvant CPI therapy on ovarian function in young women, in combination with chemotherapy for early TNBC, as part of the NSABP-B59/GeparDouze-Ovarian substudy.

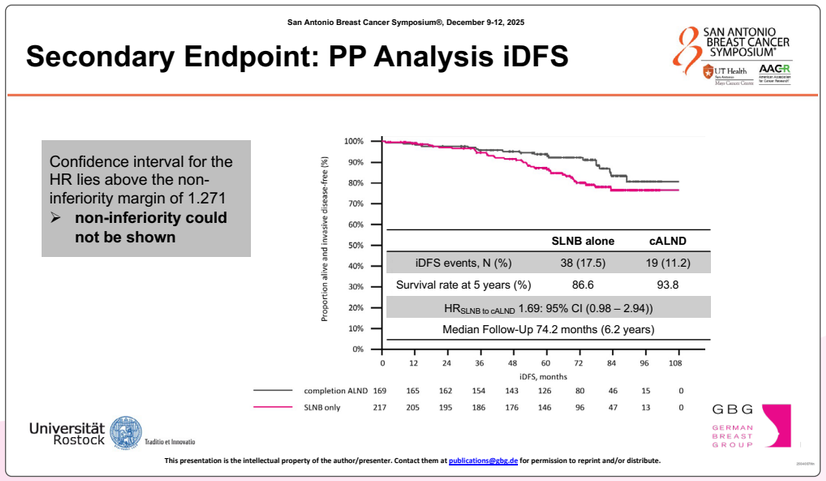
Women aged 45 years or younger who had not undergone hysterectomy or oophorectomy were enrolled. All participants received NACT comprising anthracycline, cyclophosphamide, taxane, and carboplatin, together with atezolizumab (CTA) or placebo (CT). The primary objective was to assess the rate of chemotherapy-induced ovarian failure (CIOF), defined by postmenopausal levels of follicle-stimulating hormone (FSH>25.8 IU/l) and estradiol (E2<5 pg/ml). Additional assessment included anti-Mullerian hormone (AMH) levels and the rate of amenorrhea. During chemotherapy, E2 levels declined and subsequently increased after end of trial (EOT), through not to baseline values in either arm. In the CTA group, median FSH values continued to rise after EOT and remained with the postmenopausal range at 24 months. At EOT, 34.2% of patients experienced CIOF (CTA: 40.6%, CT: 26.8%; p=0.13). Two years after EOT, 10% of participants had persistent CIOF, with a trend toward a higher rate in those receiving atezolizumab (CTA: 7.5%; CT: 2.5%; p=0.06).

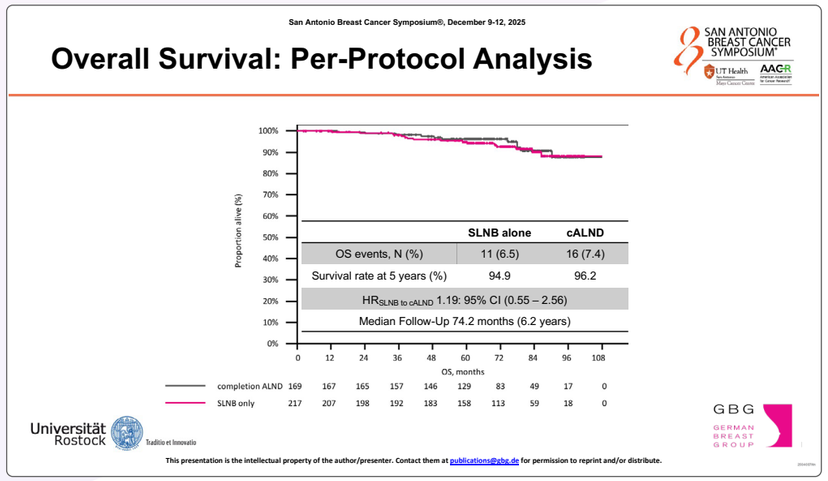
Mattea Reinisch presenting at SABCS 2025

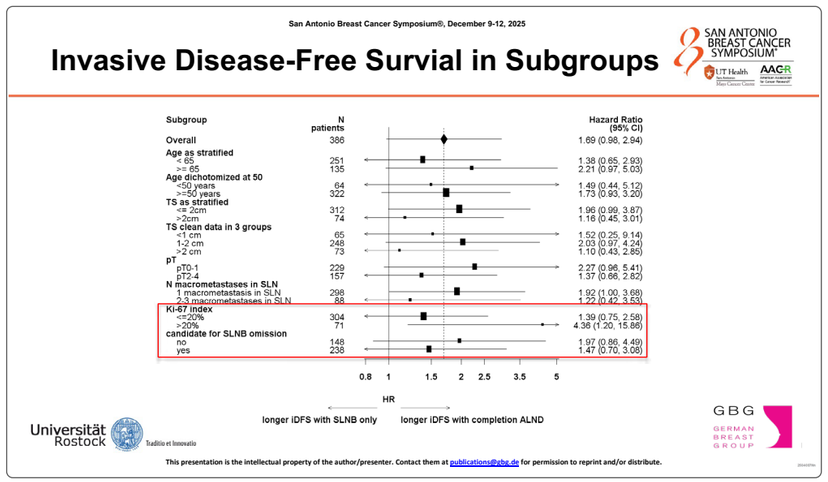
The proportion of patients experiencing amenorrhea was highest at EOT: 64.9% in the CT arm and 62.9% in the CTA arm declined to approximately 33% after 12 months of follow-up and remaining stable thereafter. At baseline AMH levels below 0.22 – indicative of severely impaired ovarian reserve – were observed in only a small fraction of patients (8.6% in the CTA group, 12.7% in the CT group). However, at EOT, all patients exhibited AMH <0.22, with no recovery detected up to two years post-treatment and no significant difference between the two treatment groups.

In summary, E2, FSH and AMH levels all decreased to menopausal ranges by EOT. While E2 and FSH partially recovered during follow-up, AMH remained below the threshold for severely reduced ovarian function even 24 months after EOT. These findings enhance our understanding of the impact of CPI on fertility in young women when administered with NACT for early TNBC, and provide important information for fertility counselling.

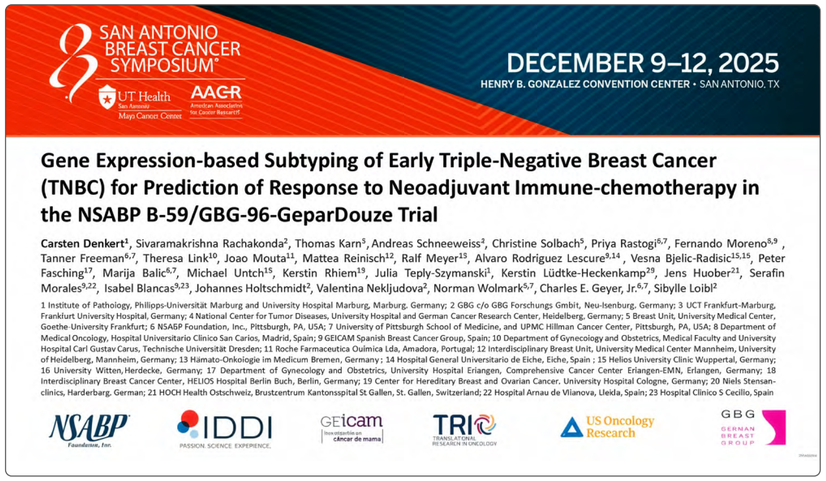


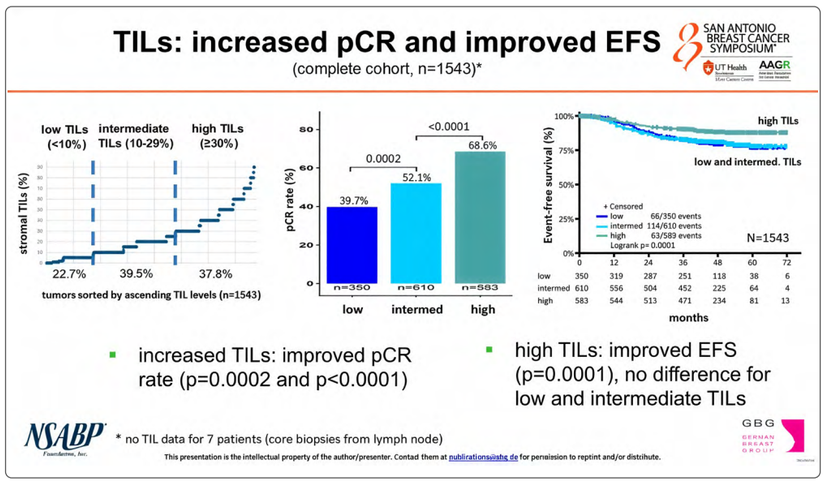






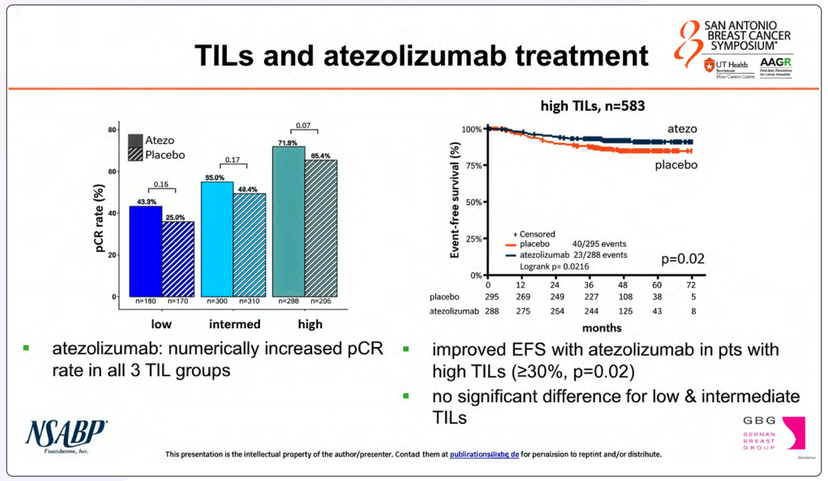
In summary, both TIL levels and TNBC subtypes are significant for predicting pCR and EFS in the NSABP-B59/GeparDouze cohort. A positive effect of atezolizumab on survival was observed in subgroups with immune-activated tumors (BLIA) and in patients with high TILs (≥ 30%, most of which were BLIA tumors). Tumors with intermediate TILs were more heterogenous, including both BLIA and BLIS subtypes. Therefore, evaluating TNBC subtype in tumors with intermediate TIL levels may be relevant for predicting immunotherapy benefit.

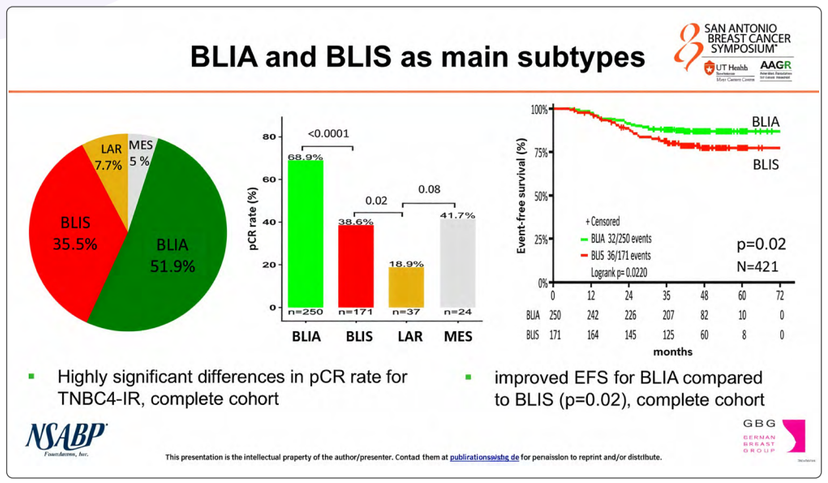


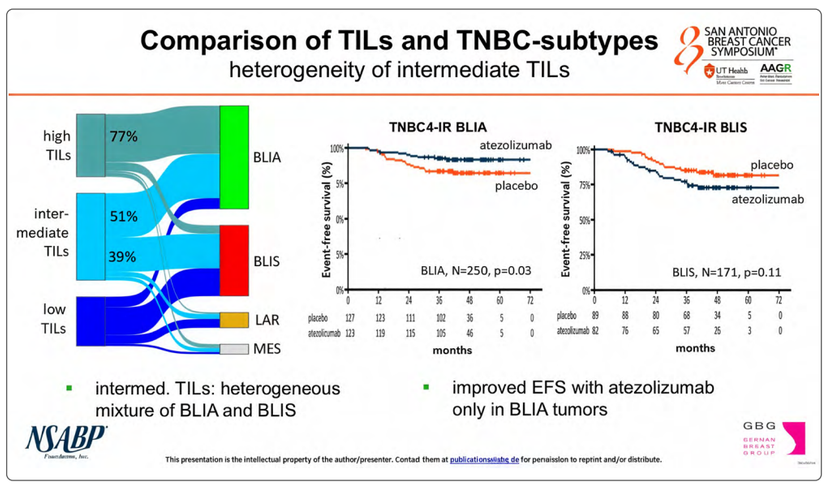


Link full presentation

Carsten Denkert presented data on gene expression-based subtyping of eTBNC and on analyses of tumor-infiltrating lymphocyte (TIL) levels and their relevance for response to neoadjuvant immunochemotherapy in the NSABP-B59/GeparDouze trial. Building on earlier analyses from the GeparNuevo trial, this study provided the first biomarker-based subtyping of TNBC and evaluation of predictive signatures. Within the full cohort n=1,543), TIL levels were categorized as low (<10%), intermediate (10-29%), or high (≥30%) and assessed in relation to pCR, event-free survival (EFS), and response to atezolizumab. In a biomarker subcohort of 482 patients, gene expression analysis (HTG Edge) was used to assign tumors to TNBC subtypes: 51.8% were “basal-like immune-activated” (BLIA), 35.5% “basal-like immunosuppressed” (BLIS), 7.7% “luminal androgen receptor” (LAR) and 5.0% “mesenchymal” (MES). Overall, BLIA tumors were assocciated with superior survival compared to BLIS tumors. Notably, EFS was significantly improved with atezolizumab in BLIA tumors, but was numerically lower with atezolizumab in BLIS tumors. This mirrors the observation that most tumors with high TILs also belonged to BLIA subtype.







Link full presentation

Brooke M. Felsheim presented a pooled analysis of the BrighTNess, CALGB 40603, and GeparSixto trials investigating the impact of adding neoadjuvant carboplatin on pCR and survival in early TNBC. While introducing carboplatin to NACT has been shown to increase pCR rates, its integration into standard NACT regimens has been inconsistent. With carboplatin added to both arms in the KEYNOTE-522 trial, this approach is now widely adopted. Given the associated toxicities, it remains essential to fully delineate carboplatin's therapeutic benefit and to identify biomarkers that can predict response. In the pooled dataset of three randomized clinical trials (n=1,084), the addition of neoadjuvant carboplatin was significantly associated with increased pCR rates (odds ratio [OR] of 1.89, 95% CI: 1.41-2.55, p < 0.001) and improved EFS (HR of 0.71, 95% CI: 0.54-0.93, p = 0.01), but not OS (HR of 0.93, 95% CI = 0.65-1.31, p = 0.66). Patients with germline *BRCA1/2* (*gBRCA*) wildtype (n=813) and mutant status (n = 137) both benefited in terms of EFS (WT: HR of 0.73, 95% CI: 0.55-0.96, p= 0.024 and mutant: HR of 0.50, 95% CI: 0.25-1.00, p = 0.05) but not OS. Wildtype *gBRCA* patients had significantly higher pCR rates with carboplatin compared to without, while in the mutant group, carboplatin did not increase pCR (WT: HR of 2,13 95% CI: 1.59-2.85, p= <0.001 and mutant: HR of 1.01, 95% CI: 0.48-2.10, p=0.987). Among eight gene expression signatures, all six immune signatures correlated with increased pCR rates; four (IgG, CD8, CD274, and Immune1) were associated with higher pCR and improved EFS and OS. No interaction between carboplatin and any tested markers predicted pCR, EFS, or OS.

The findings support incorporating neoadjuvant carboplatin into regimens for early TNBC and underscore the prognostic significance of the tumor immune micro-environment.

Link full presentation

Carsten Denkert presented data on core needle on-treatment biopsies (OTB) after 2-4 cycles of neoadjuvant systemic treatment (NST) for residual invasive cancer, focusing on Ki67, sTILs, and their predictive value for treatment outcome and survival. Early assessment of NST efficacy can prevent ineffective therapies and allow for early adjustment. The study included patients with evaluable OTBs (n=449) from the neoadjuvant clinical trials GeparSixto (n=47), GeparSepto (n=194), GeparNuevo (n=99), GeparX (n=47), and GeparOLA (n=62). Tumor beds, residual cancer (cellularity of viable invasive cancer cells >0 [OTB+] vs. 0 [OTB-]), Ki67, and sTILs were retrospectively assessed and correlated with clinical outcomes. Most tumors were cT2 (55%), of no particular kind (88%), G3 (66.1%), and clinically node-negative (69.6%). TNBC was the most frequent subtype (n=257, 57.2%), followed by HR+/HER2- (n=108, 24.1%) and HRany/HER2+ BC (n=84, 18.7%). Tumor bed was identified in 79.1% (355/449) of OTBs. The remaining OTBs showed unspecific (10%), or unclear alterations (6.2%) or no signs of tumor bed (4.7%). After NST, OTB+ was present in 60% (213/355), with a low pCR rate (20.2%, 43/213), while OTB- was find in 40% (142/355) and had a high pCR rate (73.9%, 105/142). In multivariate analysis, OTB+ was linked to markedly decreased odds of pCR (OR of 0.111, 95% CI: 0.063-0.196, p<0.001), independent of nodal stage, subtype, and grade. By subtype, pCR rates for OTB+ were 48% for HER2+ (12/25), 21.6% for TNBC (24/111), and 9.1% for HR+/HER2- (7/77). Presence of OTB+ was strongly associated with worse DFS and OS (DFS: HR of 2.59, 95% CI: 1.72-3.91; OS: HR of 3.99, 95% CI: 2.09-7.59, log-rank p< 0.001 respectively),

with significance maintained in multivariate analysis (DFS: HR of 2.37, 95% CI: 1.52-3.68; OS: HR of 3.76, 95% CI: 1.91-7.40, p<0.001 respectively). OTB+ tumors had lower baseline Ki67 (median 39%) than OTB- (median 48%, p<0.001), and there was a 30% median absolute decrease in Ki67 from baseline to OTB, most pronounced in high-grade TNBC (median 37.5%, stratified signed rank test p=0.03). Baseline sTILs were lower in OTB+ (median 10%) than OTB- (median 20%, p<0.001). After NST, patients achieving pCR had a median absolute increase in sTILs (5%), while those without pCR saw no change.

Find this poster as download here

Johannes Holtschmidt presented on prognostic markers in residual tumors after NACT for early TNBC, based on a pooled analysis from nine neoadjuvant GBG/AGO-B trials. After NACT for TNBC, residual invasive disease is associated with increased recurrence rates and worse OS. However, a lack of pCR does not always equate to poor prognosis. To refine outcome prediction, this analysis considered proliferation (Ki67) and TILs in residual invasive tumor. Across 3,017 TNBC patients receiving anthracycline/taxane-containing NACT in nine GBG/AGO-B trials (GeparTrio, GeparQuattro, GeparQuinto, GeparSixto, GeparSepto, GeparOcto, GeparNuevo, GeparOla, and GeparX), 1,505 had residual disease; 640 were evaluable for TILs and Ki67. Endpoints included distant disease-free survival (DDFS; primary endpoint) and OS, assessed by landmark analysis. Persistently, elevated Ki67 (>15%) in residual tumors correlated with significantly worse DDFS (HR of 1.71; 95% CI 1.33-2.21; p<0.0001) and OS (HR of 2.02; 95% CI 1.51- 2.71; p<0.001). Conversely, high TILs (≥50%) in residual tumors predicted significantly better OS and a clear trend toward improved DDFS. When combining Ki67 (>15% versus ≤15%) and TILs (≥50% versus <50%), four distinct groups emerged. Those with low Ki67 and high TILs (≤15%/≥50%) had markedly improved survival compared to those with high Ki67 and low TILs (>15%/>50%) with a 5-year OS difference of 44.1%: 92.1% (84.9-99.9) versus 48.0% (37.4-61.7) HR of 7.57 (3.19-17.94) p<0.0001. Among patients with ypT1, ypN0 those meeting favorable criteria had numerically better survival.

In conclusion, low Ki67 in residual tumors was prognostic for improved DDFS and OS, especially when combined with high TILs, regardless of residual disease extent. The risk of death was over seven times higher for patients with Ki67>15% and TILs<50% compared to those with Ki67≤15% and TILs≥50% (abs. Δ of 44.1% for OS at 5y).

These results suggest that combined assessment of Ki67 and TILs in residual disease after NACT for TNBC can inform individualized risk evaluation and support personalized selection of post-neoadjuvant therapy.

Link full presentation

Johannes Holtschmidt presenting at SABCS 2025

Further congress contributions and contributions with GBG participation are listed below:

Educational Session by Sibylle Loibl: Moving on up: ADCs in early-stage breast cancer
Link full presentation

van Mackelenbergh M., et al. Evaluation of stable calcium isotope ratios in women undergoing neoadjuvant chemotherapy (NACT) with and without denosumab (GeparX); oral presentation
Link poster

Balic M., et al. Evaluation of a whole-exome sequencing tumor-informed circulating tumor DNA MRD assay in patients with early triple-negative breast cancer (TNBC) receiving neoadjuvant chemotherapy (NAC) with or without atezolizumab: A prospective sub study of the NSABP-B59/GBG-96-GeparDouze Trial; oral presentation

Loibl S., et al. Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients with high-risk human epidermal growth factor receptor 2-positive (HER2+) primary breast cancer (BC) with residual invasive disease after neoadjuvant therapy: Interim analysis of DESTINY-Breast05; oral presentation

DeMichele A., et al. Adjuvant Palbociclib for ER+ Breast Cancer in the PALLAS Trial (ABCSG-42/AFT-05/PrE0109/BIG-14-13): Post-Recurrence Treatment and Overall Survival; oral presentation

Malorni L., et al. Prognostic and predictive role of RBsig and CCNE1/RB1 gene-expression signatures for patients with early breast cancer treated with endocrine therapy with or without palbociclib in the PALLAS trial (ABCSG-42, AFT-05, BIG 14-03); poster presentation

Vetter M., et al. Predictors of early discontinuation of adjuvant palbociclib in early HR+/ HER2- breast cancer: final analysis of the PALLAS trial integrating patient-reported outcomes; poster presentation

Metzger O., et al. Exploratory analysis of palbociclib benefit in the PALLAS trial by SETERPR index and prior chemotherapy regimens (ABCSG-42/AFT-05/BIG-14-13); poster presentation

Nader-Marter G., et al. Long-term prognostic and predictive value of lobular histology in the PALLAS trial; poster presentation

Parsons H.A., et al. Tumor-informed circulating tumor DNA analysis to assess molecular residual disease for prognosis and prediction of benefit from palbociclib in the PALLAS trial; oral presentation

Salgado R., et al. Prognostic and predictive associations of manual, digital and AI-derived tumor infiltrating lymphocytes-scoring: A retrospective analysis from the Phase III APHINITY trial; oral presentation

Metzger O., et al. Central nervous system outcomes from the phase III PATINA trial (AFT-38); oral presentation

For more information please visit our website

From l. to r.: V. Nekljudova, A. Kostara , L. Michel, T. Link, M. Reinisch, S. Loibl

SAVE THE DATE!

The 24rd Annual Scientific Meeting

will take place in **Frankfurt/Main** on **March 11-12, 2027.**

GBG 114 ELEMENT
EU-CT-Nummer: 2023-504925-38-00

Interview with Prof. Dr. Thomas Decker

A phase II study evaluating the addition of elacestrant, an oral selective estrogen receptor degrader (SERD), to standard-of-care olaparib in patients with HR+, HER2- locally advanced or metastatic breast cancer with gBRCA1/2 mutations

What is the rationale for the ELEMENT study? In the context of antibody–drug conjugate (ADC) therapies moving to earlier lines in all breast cancer subtypes, what is the clinical aim of the ELEMENT trial?

The rationale for the ELEMENT study is based on the biological interplay between estrogen receptor (ER) signaling and DNA damage repair pathways in HR+, HER2- breast cancer with germline *BRCA1/2* mutations. While olaparib is an established standard of care in this population, development of resistances remain important clinical challenges.

Preclinical and translational data suggest that ER signaling can promote DNA repair capacity, potentially reducing the sensitivity of tumor cells to PARP inhibition. By adding elacestrant, an oral SERD that leads to potent ER degradation, the ELEMENT study aims to effectively suppress ER-driven survival pathways, thereby enhancing or prolonging the antitumor activity of olaparib.

In the broader treatment landscape, ADCs are indeed moving into earlier lines across breast cancer subtypes. However, ADCs are associated with cumulative toxicity, intravenous administration, and limited sequencing options. The clinical aim of ELEMENT is therefore to optimize targeted, chemotherapy-free oral treatment combinations that may preserve quality of life, and to delay the need for ADCs or chemotherapy.

ELEMENT study uses elacestrant as an oral selective estrogen receptor degrader (SERD) in the experimental arm in combination with standard olaparib therapy. What is the difference between the SERD elacestrant and conventional endocrine therapy options? What is the potential added value of elacestrant within the context of ELEMENT?

Conventional endocrine therapies, such as aromatase inhibitors or tamoxifen, primarily work by reducing estrogen levels or blocking estrogen binding to the receptor, but they do not eliminate the estrogen receptor itself. However, resistance frequently develops through *ESR1* mutations or ligand-independent ER activation, limiting the effectiveness of these approaches in later-line settings.

Elacestrant is an oral selective estrogen receptor degrader, which directly binds to ER and induces receptor degradation, resulting in deeper and more sustained ER pathway inhibition.

Within the context of ELEMENT, the potential added value of elacestrant lies in its ability to provide more complete ER pathway suppression compared with conventional endocrine agents, overcome common mechanisms of endocrine resistance, and potentially synergize with PARP inhibition by reducing ER-mediated DNA repair signaling.

This combination therefore represents a rational strategy to enhance efficacy without adding chemotherapy-related toxicity, while maintaining an all-oral regimen.

Which patients will be enrolled in ELEMENT and how many? In clinical practice, how can we identify potentially suitable patients for this study? Should we make more use of molecular testing such as NGS tumor sequencing? Do we consequently screen all patients with potential indication for PARP inhibitor therapy for germline BRCA1/2 mutations in Germany?

The ELEMENT study enrolls patients with HR+, HER2- locally advanced or metastatic breast cancer who harbor germline *BRCA1* or *BRCA2* mutations and are candidates for olaparib therapy. As a phase II trial, the study aims to enroll 176 patients in total (two thirds in the elacestrant arm, and one third in the standard arm).

In clinical practice, identifying suitable patients requires early and systematic molecular characterization, particularly germline *BRCA1/2* testing. All patients with HR+/HER2– metastatic disease who are being considered for PARP inhibitor therapy should be proactively evaluated rather than tested only after treatment exhaustion!

Broader use of NGS-based tumor sequencing can support flagging patients who may benefit from confirmatory germline testing, and this approach can additionally identify other actionable alterations (e.g., *ESR1* mutations, PI3K pathway alterations).

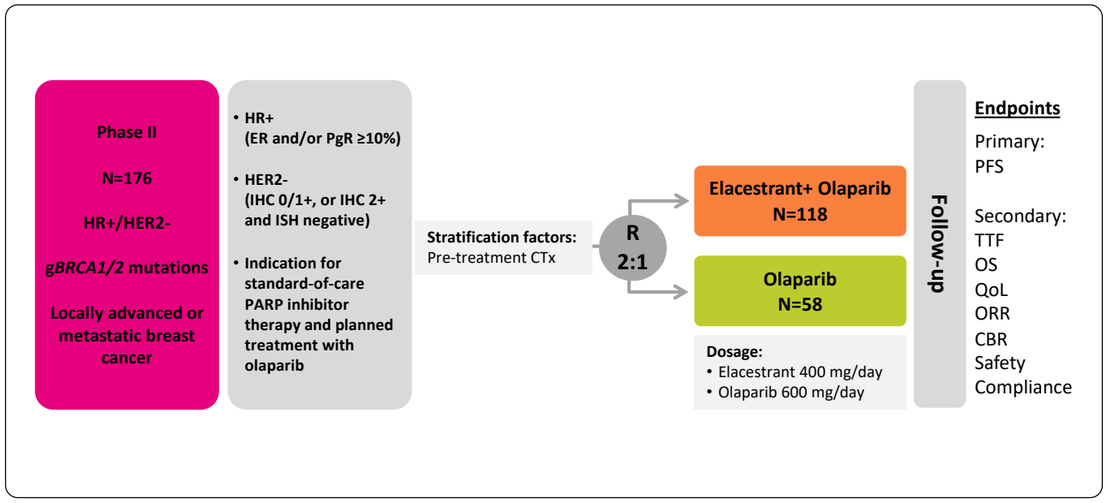
In Germany, current guidelines already recommend germline *BRCA1/2* testing for patients with HER2- metastatic breast cancer who may be eligible for PARP inhibitors. ELEMENT reinforces the importance of implementing these recommendations consequently and early, rather than selectively or late in the treatment journey.

Some clinicians still think that molecular testing is a measure of "last resort". Therefore, it is frequently used in situations after multiple lines of prior treatments, and physicians are disappointed with the clinical impact of molecular testing in this setting. Should we try to move molecular testing from later lines ideally to the 1st line setting?

Yes! Molecular testing should clearly be moved earlier in the treatment pathway, ideally at diagnosis of metastatic disease or even at high-risk early disease. The ELEMENT study exemplifies how early molecular identification enables rational, biomarker-driven treatment strategies, rather than reactive decision-making after resistance has developed. Disappointment with molecular testing outcomes is often a consequence of late timing, not lack of clinical relevance!

Contact Projectmanagement:
Dr. Laura Steinmann
element@gbg.de

Cooperationpartner/Sponsor:
GBG Forschungs GmbH



Study Design of the ELEMENT trial

GBG 105 GeparPiPPa
EU-CT-Nummer: 2022-501152-28

Interview with PD Dr. Mattea Reinisch

A randomized, open-label, phase II trial comparing neoadjuvant endocrine therapy in combination with trastuzumab, pertuzumab +/- the PI3K inhibitor inavolisib in patients with HER2+, HR+, PIK3CA mutant early breast cancer

What is the GeparPiPPa trial trying to investigate, and why was it created? Which patients qualify for the GeparPiPPa trial?

The GeparPiPPa trial is a randomized, open-label phase II study designed to evaluate the efficacy and safety of adding the PI3K inhibitor inavolisib to neoadjuvant endocrine therapy (ET) with dual anti-HER2 treatment (trastuzumab + pertuzumab) in patients with HR+/HER2+ and *PIK3CA*-mutated early breast cancer.

The rationale behind the trial is based on evidence that *PIK3CA* mutations – present in approximately 25–30% of HR+/HER2+ breast cancers – are associated with reduced sensitivity to standard anti-HER2 therapies and chemotherapy. The study therefore explores whether targeting this pathway can enhance tumor response and potentially offer a chemotherapy-sparing strategy for a defined molecular subgroup.

Eligible patients are patients with:

- Early-stage (non-metastatic), operable breast cancer
- HR+ and HER2+ disease based on local testing
- Confirmed *PIK3CA* mutation (central testing required)
- Tumor size cT1c–cT3, suitable for neoadjuvant treatment

Depending on menopausal status, patients receive tamoxifen or an aromatase inhibitor, with or without ovarian suppression.

One might think that trial participation could prolong the overall treatment duration for patients or might hinder standard of care treatment options. What is your view on this?

This is a valid concern, but in the case of the GeparPiPPa trial, participation does not meaningfully delay, hinder, or compromise standard-of-care treatment. The study backbone – dual anti-HER2 treatment with trastuzumab and pertuzumab in combination with ET – reflects an established treatment approach for this patient population. The investigational component is the addition of inavolisib, evaluated for its potential to enhance efficacy in *PIK3CA*-mutant disease.

For patients who do not achieve a complete clinical or pathological response, chemotherapy in combination with anti-HER2 therapy is recommended. In these cases, treatment is not prolonged but rather initiated approximately 18 weeks later, following completion of the neoadjuvant phase within the GeparPiPPa study. The overall duration of anti-HER2 therapy remains unchanged (one year in total) in accordance with current standards.

The key advantage of the GeparPiPPa trial lies in offering selected patients the opportunity to receive a chemotherapy-free neoadjuvant regimen, which would otherwise not be available outside the study setting.

Safety and tolerability are key secondary endpoints, so any toxicity or delay in surgery would be closely documented and managed. Moreover, the trial protocol allows starting ET already during the screening period, so patients are not left untreated while awaiting central *PIK3CA* testing results before being randomized in the study.

In summary, participation in the GeparPiPPa trial does not compromise standard of care, and it may contribute to more personalized and potentially less toxic treatment options.

What are the main objectives of this study? How many patients and sites are expected to participate in this study?

The primary objective is to compare the rate of pathological complete response (pCR; ypT0/is ypN0) after neoadjuvant treatment between patients who have received dual anti-HER2 treatment (pertuzumab + trastuzumab, fixed-dose combination SC) + ET with or without inavolisib. Key secondary objectives include safety and tolerability of the combination, breast-conserving surgery rate, invasive disease-free survival (iDFS) and overall survival (OS), as well as biomarker analyses (e.g., molecular predictors of response to PI3K inhibition)

Approximately 170 patients will be enrolled in the study from multiple European countries. So far, Germany, Spain, Italy and Romania are actively recruiting patients, and Slovakia and Poland will start recruiting patients soon. The estimated recruitment completion will be achieved at the end of 2026.

What were some challenges for recruitment so far in this study? How were these challenges alleviated?

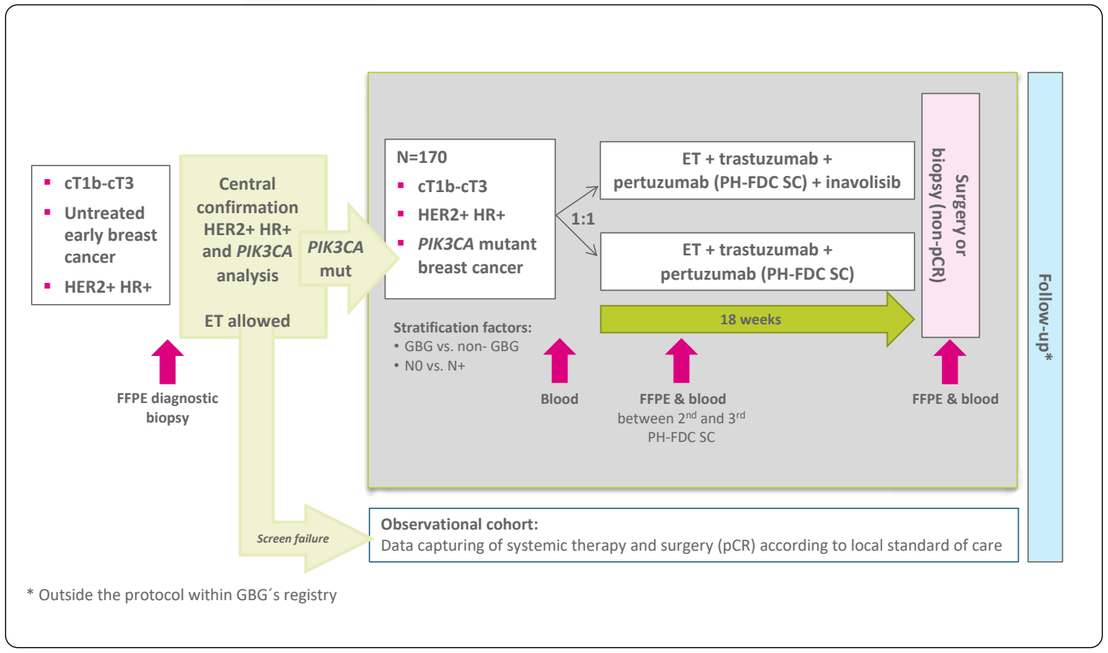
Recruitment for the GeparPiPPa trial has progressed steadily, although several challenges typical of biomarker-driven phase II studies have been encountered. The main difficulty lies in the strict molecular inclusion criteria, as only patients with HR+/HER2+ breast cancers with a *PIK3CA* mutation are eligible. This subgroup is relatively small and requires central molecular confirmation prior to treatment.

The central testing of *PIK3CA* mutation and HER2 and HR statuses is one of the key quality criteria of the study. This ensures reliable and standardized results for all participants, which is an important aspect for patient safety and data integrity. While this process can extend the time between biopsy and randomization, it is an essential step to guarantee the precision of patient selection. We were, however, able to optimize and speed up the turnaround time of central testing, which led to improved recruitment capabilities.

Logistical aspects such as the initially limited number of study sites and start-up procedures also caused some delays early on, but recruitment has accelerated as more centers and countries have become active.

Contact Projectmanagement:
Jana Roßney
geparpippa@gbg.de

Cooperationpartner/Sponsor:
GBG Forschungs GmbH



Study Design of the GeparPiPPa trial

GBG 121 NoLEEta
NCT 07237256

Interview with PD Dr. med. Laura Michel

NoLEEta
INTERMEDIATE-RISK BREAST CANCER

A phase III non-inferiority trial of chemotherapy de-escalation in HR+, HER2-, intermediate-risk early breast cancer treated with ribociclib in the adjuvant setting

Can you tell us about the study's rationale and how the trial design compares to that of other trials involving CDK4/6 inhibitors?

Adjuvant CDK4/6 inhibitors (abemaciclib and ribociclib) have meaningfully improved iDFS in early HR+/HER2− breast cancer as demonstrated by the MonarchE and NATALEE trials. Many patients at intermediate clinical risk are currently recommended chemotherapy based on clinicopathological criteria or genomic signatures, but the absolute benefit of chemotherapy in this subgroup is uncertain when CDK4/6 inhibitors are definitively given in the adjuvant setting. NoLEEta therefore asks a pragmatic and clinically important question — can we safely omit adjuvant chemotherapy in intermediate-risk patients who receive ribociclib in addition to ET?

To answer this question, patients will be randomized to receive adjuvant ribociclib and ET or standard chemotherapy followed by ribociclib and ET.

What are the main objectives of this study? How many patients and sites are expected to participate in this study? What is the best timepoint to screen patients for eligibility?

The primary objective is to demonstrate non-inferiority of ribociclib plus ET alone versus chemotherapy followed by the same regimen, with respect to invasive breast cancer–free survival (iBCFS). Key secondary endpoints include iDFS, distant disease-free survival (DDFS), and overall survival at 5, 8, and 10 years.

The NoLEEta trial will enroll approximately 3900 patients across multiple European sites as well as sites in Canada and Brazil over a 42-month recruitment period. Patients should be screened after curative surgery, ideally once final pathology and genomic test results are available. Screening must occur within 12 weeks post-surgery to allow for baseline assessments and randomization.

We understand the main focus is to investigate the additional value of adjuvant chemotherapy in an intermediate-risk population of patients receiving adjuvant CDK4/6 inhibitor treatment. Can you tell us about the planned main study procedures? And how long will patients be treated?

After surgery, patients are randomized to:

- Arm A: Ribociclib + ET
- Arm B: Chemotherapy → Ribociclib + ET

Chemotherapy regimen in the control arm must be chosen per investigator's decision (anthracycline-containing vs anthracycline-free regimen):

- AC/EC q2-3w for 3-4 cycles, followed by paclitaxel q1w for 12 weeks or docetaxel q3w for 3-4 cycles.
- Docetaxel/Cyclophosphamide q3w for 4-6 cycles.

Ribociclib is given for 3 years (400 mg daily), ET is given for at least 5 years (up to 7 years per standard of care). ET will consist of an aromatase inhibitor during ribociclib treatment. Premenopausal women receive concurrent GnRH agonists. After the end of ribociclib treatment, ET composition and duration (5 vs 7 years) are left to the physician's choice and according to local and international guidelines.

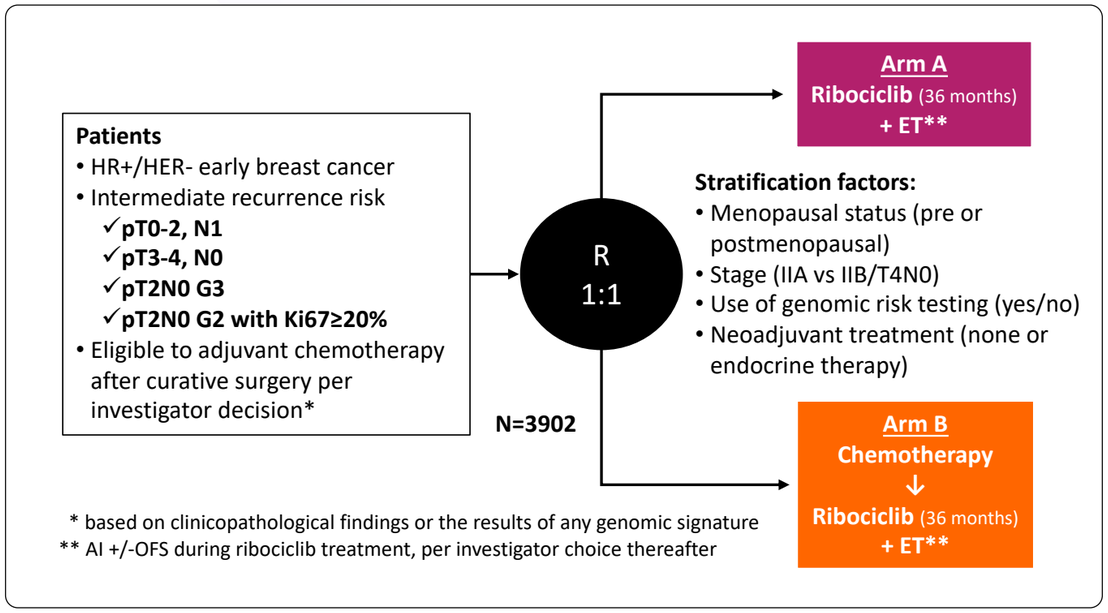
Routine safety, ECG, and laboratory monitoring are performed throughout treatment.

A large number of patients will be recruited for this trial. And what could be the clinical impact if the trial meets its primary endpoint?

Since CDK4/6 inhibitors have become a cornerstone of adjuvant therapy for most HR+/HER2-breast cancer patients, we now need to redefine which patient populations can safely omit chemotherapy. If NoLEEta meets its primary endpoint, it could transform adjuvant treatment for intermediate-risk HR+/HER2− disease, by showing that selected patients could omit chemotherapy without compromising efficacy. This would spare thousands of women the acute and long-term toxicities of chemotherapy and support a more personalized, less toxic standard of care.

Contact Projectmanagement:
Dr. Christin Wünsche
noleeta@gbg.de

Cooperationpartner/Sponsor:
GBG Forschungs GmbH/Unicancer



Study Design of the NoLEEta trial

GBG 125 OPTImaL
NCT 06476119

Interview with Prof. Dr. Elmar Stickeler

Solving a clinical dilemma – treatment optimization for patients with low stage triple-negative breast cancer with high stromal tumor-infiltrating lymphocytes

Can you tell us about the study's background and clinical rationale?

Triple-negative breast cancer (TNBC) is an aggressive disease subtype historically treated with polychemotherapy due to its high recurrence risk. However, in small, node-negative Stage I tumors (pT1a/b), the absolute survival benefit of adjuvant chemotherapy remains uncertain, and traditional systemic therapy may result in unbeneficial, significant toxicity in patients who may already have excellent outcomes with local therapy alone. Especially for patients with pT1a ("≤ 5 mm") tumors, recommendations on adjuvant chemotherapy are ambivalent, and many Stage I patients are potentially exposed to unnecessary harm.

At the same time, high levels of stromal tumor-infiltrating lymphocytes (sTILs) are a well-established biomarker of an active antitumor immune response and are strongly associated with favorable prognosis and lower risk of recurrence in TNBC. Higher TILs are linked to reduced distant recurrence and longer survival outcomes even without systemic therapy.

The OPTImaL study was therefore designed to address this clinical dilemma: can we safely omit adjuvant chemotherapy in patients with low-stage, node-negative TNBC and very high sTILs, sparing them the morbidity of cytotoxic therapy while preserving excellent long-term outcomes?

High TILs indicate a good prognosis. Only patients with very high TILs are eligible for OPTIMAL. What is the rationale for this, and what are further eligibility criteria for this trial?

A large body of evidence supports that increasing TIL levels correlate with improved distant relapse-free and overall survival compared to those with low levels.

The OPTImaL trial leverages this biology by enrolling patients whose surgical specimens show very high sTIL scores, defined by prespecified cut-offs, on standardized H&E stain assessments. This is based on the concept that in this subgroup, the immune system is already effectively controlling residual disease risk, potentially making cytotoxic adjuvant chemotherapy redundant.

Key eligibility criteria for OPTImaL include:

- Pathological Stage I TNBC (pT1a/b/c ≤ 2 cm and pN0, no nodal involvement) confirmed on surgical pathology
- sTIL score of ≥50% for patients ≥40 years at the time of TNBC diagnosis, and ≥ 75% for patients <40 years at the time of TNBC diagnosis by local and central review
- No prior neoadjuvant systemic therapy
- No lymphovascular invasion, other concurrent malignancies within 5 years, or other severe comorbidities

This design enriches the cohort for patients with a robust antitumor immune milieu, where minimal to no chemotherapy benefit is suspected.

If a patient is eligible, what are the expected study procedures, and how are treatment decisions made?

In OPTImaL, patients with resected Stage I TNBC and high sTILs are typically offered a structured pathway that includes:

1. Post-surgical evaluation and sTIL assessment: Pathology confirms TNBC, stage pT1a/b/c pN0, and quantifies sTILs according to standardized guidelines.
2. Patient-clinician discussion of risks/benefits: patients receive detailed counseling on the potential benefits and risks of adjuvant chemotherapy versus observation.
3. Shared treatment decision: Unlike a classic randomized trial, OPTImaL allows patients (in consultation with their physician) to choose to undergo standard adjuvant chemotherapy (control cohort) or omission of chemotherapy (optimization cohort), reflecting real-world preferences and optimizing external validity. In the optimization cohort, patients will be treated with surgery and adjuvant radiotherapy following local/national guidelines, while chemotherapy will be omitted. In the control cohort, patients will receive adjuvant chemotherapy in addition to that. Endocrine therapy for patients with ER and/or progesterone receptor (PR) expression of 1-9% is allowed per local/national guidelines in both cohorts.
4. Follow-up and endpoints: Patients are monitored longitudinally for invasive disease-free survival, recurrence rates, and quality of life outcomes, comparing those who received chemotherapy against those who did not.

What is the expected probability of recurrence in this patient population? What would be an unacceptable threshold?

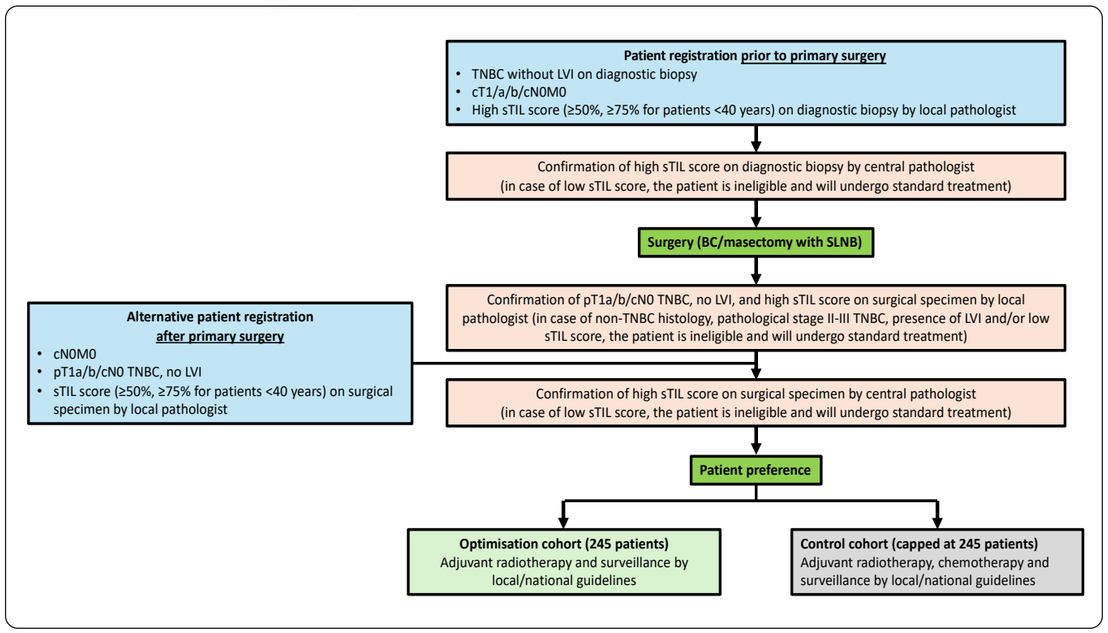
Small, node-negative TNBC patients generally have a lower risk of recurrence relative to larger or node-positive disease, particularly when sTILs are high. Retrospective and prospective observational data suggest excellent outcomes in this subgroup: patients with high TILs have reported very high survival rates, with some observational cohorts showing 10-year survival rates approaching the upper 90s without systemic therapy.

While precise recurrence rates in the fully defined eligible OPTImaL population are still unknown, expectations in the high-TIL cohort are typically single-digit percentage risk of recurrence at 3–5 years.

Ultimately, OPTImaL will define these parameters more precisely, but the study's premise rests on the assumption that, in women with very high TILs, the baseline risk of recurrence is low enough that the benefit from chemotherapy does not outweigh the relatively uncommon but severe side-effects of chemotherapy.

Contact Projectmanagement:
Kirsten Muster
optimal@gbg.de

Cooperationpartner/Sponsor:
GBG Forschungs GmbH/
Netherlands Cancer Institute



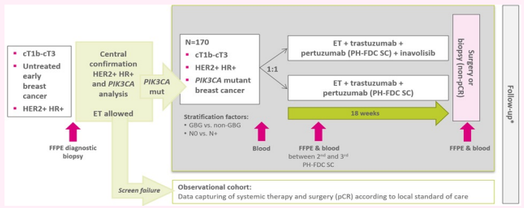
Study Design of the OPTImaL trial

GeparPiPPa

GBG 105 / EU-CT 2022-501152-28

Trial Design

neoadjuvant, multicenter, randomized, open-label, phase II study



* Outside the protocol within GBG´s registry

Recruitment

planned: 170 pts
recruited: 68 pts

Study Sites

planned : 65
active: 27 DEU
9 IT,15 ESP
4 ROU

Study Population

- Patients with early HER2+/HR+ and *PIK3CA*-mutant BC
- cT1b - cT3, any cN, M0

Endpoints

Primary Endpoint:
- pCR (ypT0/is ypN0)

Secondary Endpoints (Selection):
- other pCR definitions
- iDFS and OS
- breast conserving rate
- safety, tolerability and compliance

Cooperations

AGO-B BREAST STUDY GROUP
IBCSG International Breast Cancer Study Group
SOLTI

Sponsor

GBG GERMAN BREAST GROUP

Contact

Coordinator:
PD Dr. Mattea Reinisch

Clinical Project Manager:
Jana Roßney
geparpippa@gbg.de

BACKGROUND

PIK3CA mutations are present in approximately 20-30% of HER2+ early breast cancers (eBCs), with higher rates in HR+ compared to HR- tumors. Standard treatments yield lower pathological complete response (pCR) rates in patients with *PIK3CA*- mutant HER2+ eBC, especially if HR+ *(Loibl et al. Ann Oncol 2016)*.

The rationale for the GeparPiPPa study is based on both experimental and clinical evidence regarding alterations in the PI3K pathway. The PI3K pathway is frequently altered in HR+ breast cancer and is involved in resistance to endocrine therapies. Approximately 40% of HR+ breast cancers harbor a *PIK3CA* mutation, which can drive estrogen receptor-independent growth *(Miller et al. J Clin Invest 2010; Crowder et al. Cancer Res 2009)*. Recent studies have led to the approval of the PIK3K inhibitor inavolisib and the AKT inhibitor capivasertib in HR+/HER2- metastatic breast cancer (mBC) *(Turner et al. N Engl J Med 2024; Turner et al. N Engl J Med 2023).*

The PATINA trial investigated the addition of CDK4/6 inhibitor palbociclib to maintenance treatment with trastuzumab, pertuzumab, and endocrine therapy (ET) in HR+/HER2+ mBC, reporting an impressive improvement in median progression-free survival by 15.2 months with the addition of a fourth targeted agent *(Metzger et al. SABCS 2024). The TOUCH (IBCSG 55-17)* trial showed that dual anti-HER2 blockade with a chemotherapy-free backbone of palbociclib plus letrozole yields pCR rates similar to paclitaxel (33%), highlighting an attractive alternative approach *(Malorni et al. Ann Oncol 2025).*

Collectively, these findings support the exploration of more effective, chemotherapy-free combination therapies for HR+/HER2+ eBC.

STUDY DESIGN

Patients with *PIK3CA*-mutant, HR+/HER2+ eBC with cT1b-3 tumors are randomized 1:1 to receive neoadjuvant ET combined with dual anti-HER2 blockade (fixed-dose subcutaneous pertuzumab and trastuzumab [PH-FDC SC]), with or without inavolisib for six cycles every three weeks (18 weeks total). ET consists of tamoxifen 20mg or an aromatase inhibitor, +/- gonadotropin-releasing hormone (GnRH) analogue for premenopausal women and men.

After completion of study therapy, all patients will undergo surgery or biopsy to determine the pCR rate. If biopsy shows clinical complete remission with no tumor residuals, surgery is recommended; otherwise, further neoadjuvant treatment may be considered. Further neoadjuvant or adjuvant treatments beyond protocol are at investigator discretion per standard of care.

OBJECTIVES

The primary objective of GeparPiPPa is to compare pCR rates (ypT0/is ypN0) between both study arms.

GeparPiPPa will also address translational research questions to assess potential new biomarkers for HR+/HER2+ breast cancer and their association with response and resistance to therapies.

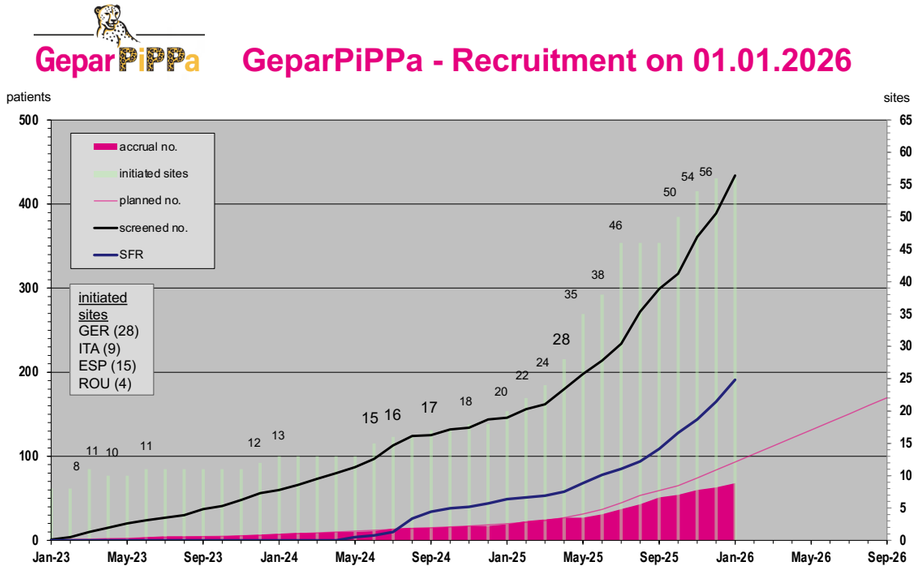
Patient health status will be collected via a patient self-reporting registry (Patientenselbstauskunft) or the GBG long-term registry of previous study participants (ETERNITY[B]). The information will be systematically collected, ensuring a comprehensive understanding of the patients' well-being.

In addition, all patients screened but found to be ineligible for trial participation may be enrolled in an observational cohort.

A current Amendment (Amendment 4) is underway with updated safety data, updated hyperglycemia management guidelines for patients in the inavolisib arm, as well as renal function assessments during screening and therapy.

STUDY RECRUITMENT

The recruitment period is 48 months, with interim safety analyses after 20 and 40 patients complete two treatment cycles. The first interim analysis for safety was performed in 2025 and yielded a manageable toxicity profile for the quadruplet combination without safety concerns.



Website link

STUDY RECRUITMENT

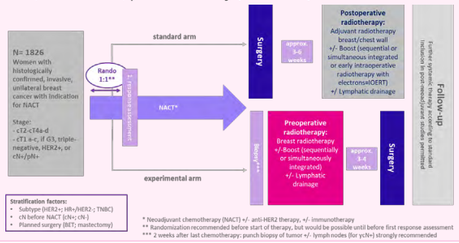
The study is recruiting internationally, aiming to enroll 170 patients across approximately 71 sites in 6 countries. As of December 31, 2025, 68 patients have been recruited globally. Currently recruiting countries include Germany, Spain, Italy, and Romania, with Slovakia and Poland starting recruitment in 2026.

NeoRad

GBG 116 / NCT04261244

Trial Design

randomized, multicenter, phase III study (non-AMG)



Recruitment

planned: 1826 pts
recruited: 204 (DEU)

Study Sites

planned : 40 DEU
active: 30 DEU

Study Population

- women with invasive, unilateral breast cancer
- indication for NACT and radiotherapy
- Hormone receptor and HER-status: no restrictions
- ECOG 0-2

Endpoints

Primary Endpoint:

- DFS

Secondary Endpoints (Selection):

- local and locoregional recurrence rate, DDFS, BCSS, OS
- pCR
- safety and QoL
- rate lymphoedema/ plexopathy

Cooperations

DKG, aro, AGO-B, Deutsche Krebshilfe, CIO Centrum für Integrierte Onkologie Aachen Bonn Köln Düsseldorf

Sponsor

UNIVERSITÄT BIELEFELD

Contact

Coordinating Investigator:
Prof. Dr. Christiane Matuschek
Co-Investigators:
Prof. Dr. W. Budach and Prof. Dr. T. Fehm

Clinical Project Manager:
Angela Kell
neorad@GBG.de

BACKGROUND

The standard of care for high-risk breast cancer regularly consists of neoadjuvant chemotherapy (NACT) and surgery followed by postoperative whole breast/chest wall irradiation, with or without an additional boost and/or irradiation of lymphatic drainage pathways. Adjuvant radiotherapy significantly reduces ipsilateral breast recurrence, breast cancer-specific mortality, and overall mortality. However, the optimal timing of radiotherapy in patients who receive NACT has not yet been addressed in a randomized controlled trial.

The NeoRad trial investigates the efficacy of preoperative versus postoperative radiotherapy in patients who have undergone NACT for high-risk early breast cancer. Administering radiotherapy preoperatively may shorten the overall treatment duration by several weeks and potentially improve locoregional control. Moreover, previous studies hinted at possible survival advantages, though these should be interpreted with caution due to the refinement of radiotherapy techniques and systemic treatments over time. Evidence from SEER database analyses and matched pair studies indicate improved disease-free survival with preoperative radiotherapy *(Wallgren et al. Cancer 1978; Poleszczuk et al. Breast Cancer Res 2017)*. Concerns regarding the potential compromise of the predictive value of pCR after preoperative radiotherapy, impacting subsequent treatment decisions in a small subgroup can be addressed by using minimally invasive biopsy to secure residual disease prior to radiotherapy.

In summary, there is sufficient evidence to postulate that preoperative radiotherapy after NACT could improve DFS compared to postoperative radiotherapy, but data from a randomized trial using modern systemic therapy and contemporary radiation techniques are lacking.

STUDY DESIGN

All participants will undergo NACT, with or without anti-HER2 therapy or other targeted therapies, in accordance with the current S3/AGO guidelines during the treatment period.

In the standard arm, patients will undergo surgery (including sentinel lymph node biopsy and/or [targeted] axillary dissection), followed by adjuvant radiotherapy and systemic treatment as per S3/AGO guidelines, including post-neoadjuvant therapies.

In the experimental arm, patients will receive whole breast irradiation (WBRT) with or without regional nodal irradiation (RNI), after completing NACT. Surgery (including sentinel lymph node biopsy and/or targeted axillary dissection) will be performed approximately three weeks (range:3 – 6 weeks) after radiotherapy. Post-surgical systemic therapies, including post-neoadjuvant treatment, will be administered according to S3/AGO guidelines.

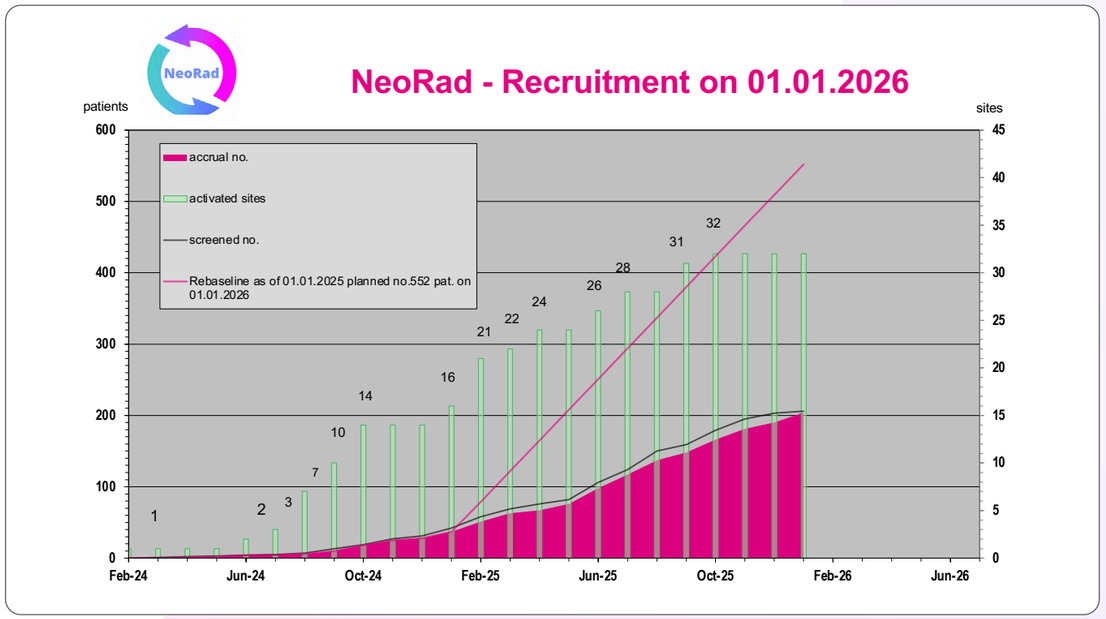
STUDY OBJECTIVES

The primary objective is to assess whether preoperative radiotherapy is superior to postoperative radiotherapy with respect to DFS, defined as the time from randomization until local recurrence, regional recurrence, contralateral breast cancer, distant recurrence, invasive second cancer, or death from any cause (whichever occurs first).
Oncologic objectives further include time to ipsilateral local recurrence as a first site of recurrence, time to regional recurrence as a first site of recurrence, distant disease-free survival (DDFS), overall survival (OS), breast cancer specific survival (BCSS), pCR defined as ypT0/is, ypN0.

Additional objectives include quality of life, acute and late toxicity as well as evaluating the cosmetic outcomes of preoperative radiotherapy, particularly in flap-based reconstructions where reduced fibrosis and shrinkage are anticipated. The impact of preoperative radiotherapy in breast-conserving surgery is less clear, and surgical morbidity after preoperative radiotherapy will be closely monitored with early interim analyses. To this end, surgical complications will be analyzed after overall 100 patients have received breast-conserving surgery or autologous flap-based reconstruction, and after overall 40 and 100 patients have undergone implant-based reconstruction.

STUDY RECRUITMENT COMPLETED

The study will be conducted at approximately 40 sites throughout Germany, with a target enrollment of 1,826 patients. As of December 31, 2025, 204 patients had been enrolled.



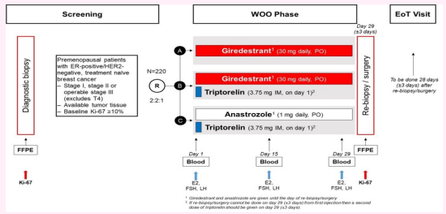
Website link

PREcoopERA

GBG 112 / EU-CT 2022-503013-32

Trial Design

randomized, international multicenter, open-label, window-of-opportunity study



Recruitment

planned: 220 /35 (DEU) pts
recruited: 232 /59 (DEU) pts

Study Sites

planned: 44/10 (DEU)
active: 10 (DEU)

Study Population

- premenopausal pts with early ER+/HER2- BC
- stage I, II or operable III (T4 excluded)
- Ki 67 ≥10% in diagnostic biopsy (local testing), tumor size must be ≥1.0 cm
- ECOG 0-1

Endpoints

Primary Endpoint:

change in Ki-67 between pre-treatment and post-treatment biopsy

Study Update: Final Analysis has been performed within Oct. – Dec.2025. Data analysis is in progress.

Secondary Endpoints (Selection): complete cell cycle arrest (CCCA), safety

Cooperations

IBCSG International Breast Cancer Study Group
SOLTI
cancer trials ireland

Sponsor

ETOP·IBCSG PARTNERS FOUNDATION
Foundation for International Cancer Research

Contact

GBG Representative:
Prof. Dr. Vesna Bjelic-Radisic

Clinical Project Manager:
Dr. Daria Vokhminova
PREcoopERA@GBG.de

BACKGROUND

The current standard of care for premenopausal women with estrogen receptor (ER)+/HER2- eBC and high risk of recurrence includes ovarian function suppression (OFS) in addition to tamoxifen or aromatase inhibitor (AI) therapy, as discovered in the SOFT and TEXT studies *(Francis et al. N Engl J Med 2018)*. While GnRH agonists for OFS are effective, these treatments can lead to significant side effects, particularly affecting personal and sexual health, which may result in lower compliance, especially among younger women. The requirement for frequent GnRH agonist injections can also be burdensome. Giredestrant, a novel oral selective ER degrader (SERD), shows promise as a potent anti-proliferative agent *(Liang et al. Journal of medicinal chemistry 2021)*. Most recently, the lidERA trial investigating adjuvant giredestrant compared to standard adjuvant endocrine treatment in HR+/HER2- eBC reported a statistically significant, and clinically meaningful benefit in invasive disease-free survival *(Bardia et al. SABCS 2025)*. However, its use in premenopausal patients has so far been investigated in combination with OFS *(Martin et al. Ann Oncol 2022*).

PREcoopERA is a biomarker-driven window-of-opportunity (WOO) study, lasting four weeks prior surgery, designed to evaluate the efficacy of giredestrant with and without OFS in premenopausal patients. The study addresses the unmet need for enhanced endocrine therapies for premenopausal women without the need for concurrent OFS. The four-week WOO framework is ideal for clinically investigating the potential of girdestrant monotherapy and could form the basis for future large-scale trials of giredestrant monotherapy in ER+ breast cancer.

STUDY DESIGN

PREcoopERA is a multicenter, open-label, randomized WOO study designed to assess the activity and safety of three different treatment arms in premenopausal patients with ER+/HER2-, operable stage I-III invasive breast cancer. A total of 220 participants were randomized in a 2:2:1 allocation to receive: giredestrant alone, giredestrant plus triptorelin, or anastrozole plus triptorelin.

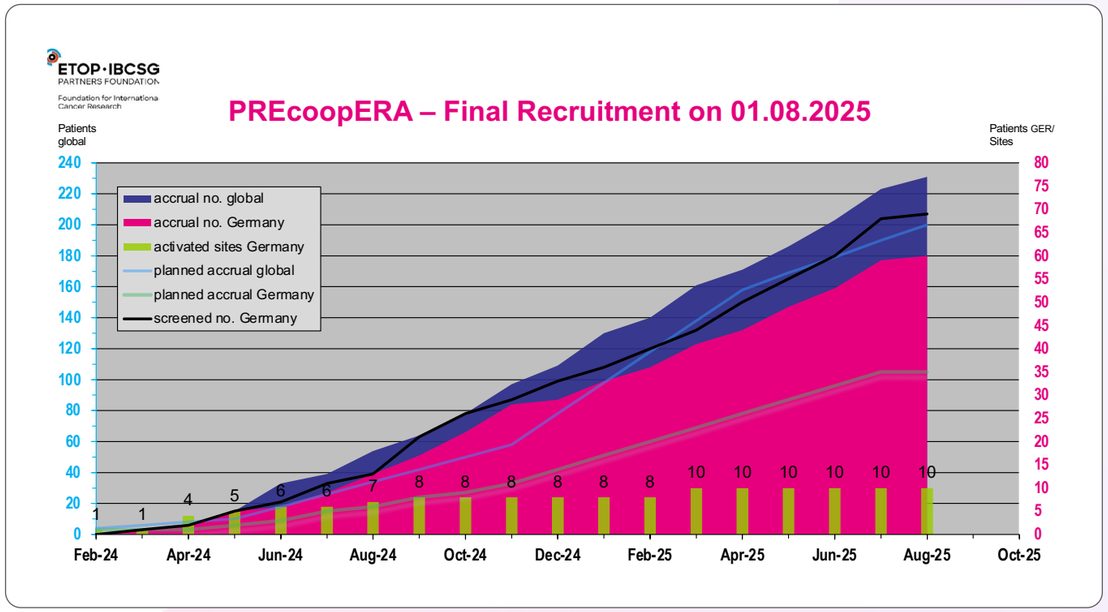
PRIMARY OBJECTIVES

The study aims to evaluate whether giredestrant plus triptorelin is superior to anastrozole plus triptorelin in reducing tumor cell proliferation (measured by the reduction in Ki67 levels between pre-treatment and post-treatment biopsies) in premenopausal patients with ER+/HER2- operable invasive breast cancer. Additionally, the study will assess whether the anti-proliferative effect of giredestrant alone is non-inferior to that of giredestrant with triptorelin.

We thank all participating sites for their dedication and continued efforts, which allowed us to nearly double GBG's enrollment goal.

STUDY RECRUITMENT

Recruitment for the PREcoopERA study was successfully completed in Q3 2025. As of August 15, 2025, a total of 231 patients had been enrolled across eight European countries over a recruitment period of 19 months. Germany contributed 59 patients, with an initial recruitment target of 35. The presentation of the study's results is anticipated in 2026, following completion of central pathology review of all tumor samples.



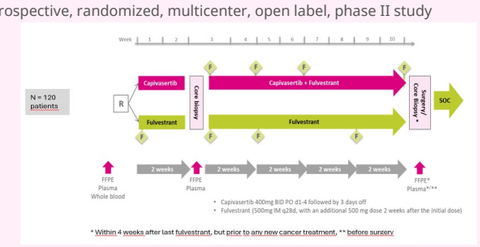
Website link

LOBSTER

GBG 118 / EU-CT 2023-509292-17

Trial Design

Prospective, randomized, multicenter, open label, phase II study



Recruitment

planned: 120 pts
recruited: 44 pts

Study Sites

planned: 34 DEU
active: 30 DEU

Study Population

- postmenopausal women, centrally confirmed untreated lobular invasive carcinoma
- HR+, HER2-, high risk of recurrence: cT1c and nodal involvement or ≥ cT2, Ki67 ≥ 8%
- no clinical evidence of metastatic disease

Endpoints

Primary Endpoint:
- CCCA rate

Secondary Endpoints (Selection):
- BCS rate
- pCR
- iDFS, OS
- Safety

Cooperations

NOGGO

Sponsor

GBG GERMAN BREAST GROUP

Contact

Coordinating Investigator :
Prof. Dr. Jens Uwe Blohmer

Clinical Project Manager:
Christina Mueller-Weisbrod
lobster@gbg.de

BACKGROUND

Although invasive lobular carcinoma (ILC) is the second most common breast cancer subtype, it remains underrepresented in clinical studies and consequently lacks clear evidence-based treatment strategies. Caution should be exercised when treating patients with ILC and low Ki67 who have a clinical tumor stage indicating a relevant risk of recurrence. The risk is likely greater than expected for patients with invasive ductal carcinoma (IDC) and similar clinical parameters *(Carbognin et al. The Breast 2017)*. ILC tends to be underestimated in size, nodal status and respond poorly to NACT, exhibiting lower pCR rates compared to IDC. Distinct metastatic patterns may contribute to observed worse OS rates *(Loibl et al. Breast Cancer Res Treat. 2014)*. Moreover, ILC shows the highest levels of AKT activation compared to IDC *(Alexander et al. Br J Cancer 2024)*, making selective inhibition of this pathway with AKT inhibitors like capivasertib an attractive therapeutic option. Studies including FAKTION and CAPItello have demonstrated improved PFS with capivasertib plus fulvestrant versus fulvestrant alone in HR+/HER2- advanced breast cancer *(Jones et al. Lancet Oncol. 2020; Oliveira et al. Lancet Oncol. 2024).*

Ki67 is strongly associated with treatment response and long-term outcomes. The POETIC study demonstrated that changes in Ki67 to below 10% after two weeks of preoperative AI therapy can effectively predict recurrence risk in patients with HR+/HER2- breast cancer independent of breast cancer subtype, yet data especially for ILC subtypes are lacking *(Smith et al. Lancet Oncol. 2020)*. Additional studies such as PALLET, NeoPalAna, and NeoMonarch have investigated the use of CDK 4/6 inhibitors in combination with AIs, achieving a complete cell cycle arrest (CCCA), with Ki67 levels reduced to 2.7% or lower *(Johnston et al. J Clin Oncol. 2019; Hurvitz et al. Clin Cancer Res. 2020).*

Given these findings and the predictive value of Ki67, the LOBSTER study hypothesizes that preoperative treatment with fulvestrant and capivasertib will result in a higher rate of a profound drop in Ki67 indicating CCCA compared to fulvestrant alone in patients with operable ILC.

STUDY DESIGN

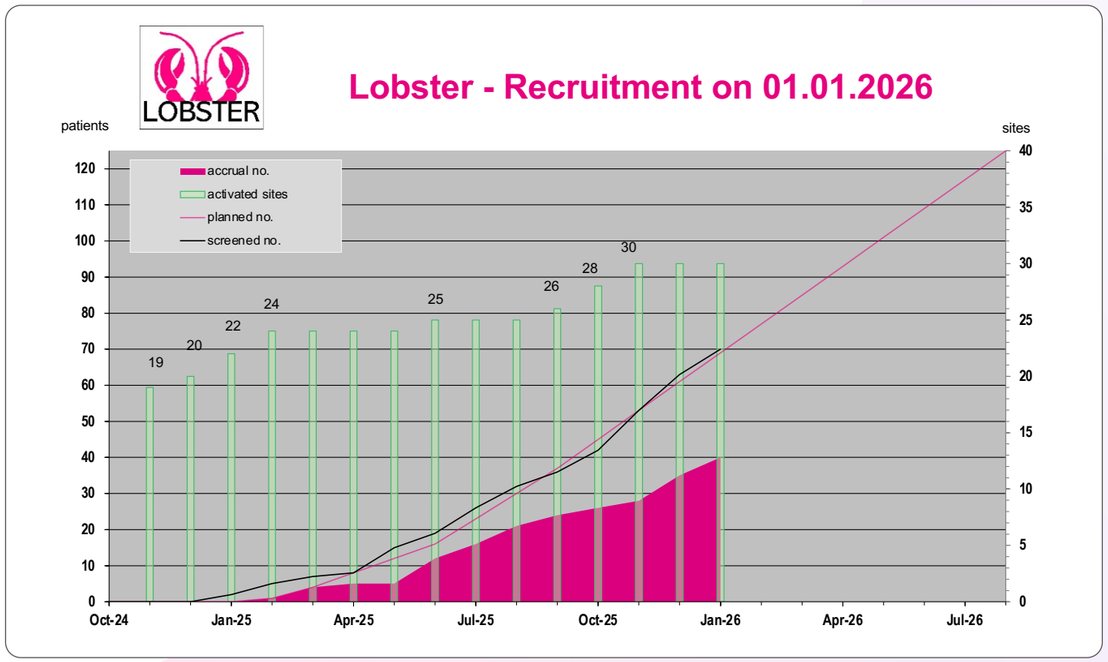
LOBSTER is a multicenter, prospective, open-label, randomized Phase II study evaluating CCCA at both week two (window of opportunity) and week 10. The study compares capivasertib plus fulvestrant versus fulvestrant alone as neoadjuvant therapy for primary high-risk ILC. In total, 120 participants will be randomized 1:1 to either capivasertib alone for the first two weeks, followed by capivasertib plus fulvestrant for an additional eight weeks, or fulvestrant alone for the full 10 weeks.

PRIMARY AND SECONDARY OBJECTIVES

The primary objective is to compare the CCCA rate, defined as a reduction in Ki67 to ≤2.7% following 10 weeks of treatment. Evaluation will be performed centrally on breast tissue samples submitted to central pathology.
Secondary objectives are designed to evaluate safety and tolerability, breast conserving surgery rate, pCR rate, invasive disease-free survival (iDFS), and OS.

STUDY RECRUITMENT

Recruitment in the LOBSTER trial started in Q4 2024. The study is conducted in approximately 35 centers in Germany, aiming to enroll 120 patients. As of December 31, 2025, 40 patients had been enrolled.



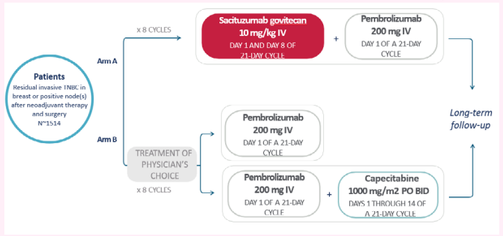
Website link

ASCENT-05

GBG 119 / EU-CT 2024-512279-10

Trial Design

international multicenter, randomized, open-label, phase III study



Recruitment

planned: 1514 pts

Study Sites

planned: 325 sites

Study Population

- TNBC defined as ER <10% PR <10% HER2-negative per ASCO/CAP
- Initial clinical stage: T1, N1-2 or T2-4, N0-2, M0
- NACT ≥ 18 weeks of a taxane and/or anthracycline-based regimen, with or without anti-PD-(L)1 agent
- Residual invasive TNBC in breast or positive node(s) after NACT and surgery

Endpoints

Primary Endpoint:
- iDFS

Secondary Endpoints:
- OS, dDFS, RFS
- Incidence of TEAEs and clinical laboratory abnormalities
- TTW of QoL

Cooperations

GBG German Breast Group, NSABP Foundation, Inc., Alliance Foundation Trials, LACOG Latin American Cooperative Oncology Group, GEICAM Spanish Breast Cancer Group, KGG 대한항암요법연구회 Korean Cancer Study Group, Cancer Trials Ireland

Sponsor

GILEAD

Contact

Coordinating Investigator:
Prof. Dr. Frederik Marmé

Clinical Project Manager:
Dr. Valerio Ketmaier
ascent-05@gbg.de

BACKGROUND

Approximately 35 to 45% of patients with early TNBC who undergo neoadjuvant polychemotherapy followed by surgery do not achieve a pCR, even with additional standard treatment using immune checkpoint inhibitor (CPI) pembrolizumab (pb). If treated with current standard of care adjuvant pb monotherapy, about one third of patients without pCR will experience recurrence and most of those will die. Currently, pb is only approved as monotherapy in the adjuvant setting and endorsed as such by major international guidelines (AGO, NCCN). However, because of the high risk of relapse among those patients without pCR there is an urgent need for more efficient treatment options *(KEYNOTE522, Schmid et al. N Engl J Med. 2024)*

The antibody-drug conjugate sacitzumab-govitecan (sg) is approved as treatment for metastatic TNBC, as well as for HR+/HER2- metastatic breast cancer, based on positive data from the ASCENT and TROPICS02 data *(Bardia et al. NEJM, 2021; Rugo et al. Future Oncol. 2020).* At ASCO 2025 convincing data from the ASCENT-04 trial investigating the combination of sg with pb in 1st line metastatic TNBC were presented *(Tolaney et al. ASCO 2025*). This study demonstrated superior efficacy for the sg/pb combination versus standard-of-care chemotherapy plus pb, with a robust safety profile and no additional toxicity from the combined treatment. Preclinical data suggest that dual therapy with sg and CPI pb may enhance CPI response via activation of the cGAS-STING pathway, leading to a synergistic effect *(Sun et al., Front Immunol. 2025)*.
Results from the CREATE-X study had demonstrated a 5-year DFS of 69.8% in the adjuvant capecitabine group versus 56.1% in control/placebo group among patients with TNBC and residual disease after neoadjuvant polychemotherapy.
These findings established the standard of care in the post-neoadjuvant setting before results from KEYNOTE522 were available *(Masuda et al. N Engl J Med, 2017)*.

ASCENT-05 is a prospective, randomized, open-label, multicenter, parallel group, phase III study assessing the efficacy and safety of sg plus pb compared to standard of care treatment with pb with or without capecitabine as decided per physician's choice (TPC) in the post-NACT-setting for patients with TNBC (ER and PR <10%, HER2- per ASCO/CAP) at high risk of relapse.

STUDY DESIGN AND OBJECTIVES

Patients with residual invasive disease and/or positive lymph nodes following NACT with or without CPI after adequate local treatment are eligible. Patients are randomized 1:1 into two treatment arms: Arm A contains 8 cycles sg 10mg/kg i.v. on day 1 and 8 plus pb 200mg i.v. on day 1 every 3 weeks. Patients in Arm B will receive TPC with either 8 cycles of capecitabine 1000mg/m2 BID p.o. day 1 through 14 plus pb 200mg i.v. day 1 every 3 weeks, or pb monotherapy. After treatment, all patients will enter a long term follow up phase.

Further eligibility criteria include initial stage cT1, cN1-2 or cT2-4, cN0-2 TNBC; negative *BRCA1/2* mutation status upon germline testing; and prior receipt of at least six cycles of neoadjuvant anthrazycline and/or taxane-based chemotherapy (with or without a PD-(L)1 or platinum agent). Patients with low HR expression (ER/PR<10%) may also be enrolled due to similar biologic characteristics and clinical risk. Stratification of participants will be according to prior ICI treatment (yes/no), prior anthracycline chemotherapy (yes/no), pathological nodal status, and geographic region (US versus East Asia versus rest of world).

The primary endpoint is invasive disease-free survival (iDFS). Key secondary endpoints include OS, DFS, incidence of treatment-emergent adverse events and quality of life.

STUDY RECRUITMENT

This study is being conducted in 272 sites across eleven countries, with a target enrollment of about 1,500 patients. As of December 31, 2025, a total of 526 patients have been recruited globally. The recruitment in Germany started in December 2024.

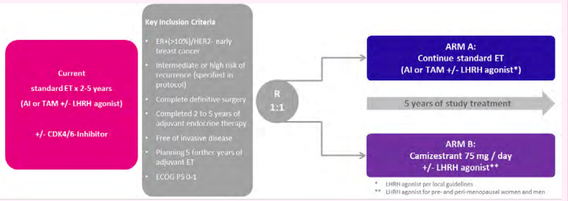
Website link

CAMBRIA-1

GBG 110 / EU-CT 2022-501024-20

Trial Design

randomized, international multicenter, open-label, phase III study



Recruitment

planned: 4300 pts

Study Sites

planned: 30 (GER)

Study Population

- women and men with early ER+/HER2- BC
- intermediate to high recurrence risk
- completion of 2 to 5 years adjuvant endocrine therapy +/- CDK4/6 inhibitor

Endpoints

Primary Endpoint:
- IBCFS

Secondary Endpoints (Selection):
- IDFS, DRFS, OS
- safety
- changes in arthralgia, hot flushes, vaginal dryness
- QoL

Cooperations

NSABP Foundation, Inc. Partners in Cancer Research
unicancer
ABCSG
GEICAM spanish breast cancer group

Sponsor

AstraZeneca

Contact

International Study Chair:
Dr. Erika Hamilton

Clinical Project Manager:
Anna Huber
cambria@gbg.de

BACKGROUND

Patients with early-stage ER+/HER+ breast cancer continue to face a substantial risk of recurrence beyond five years, prompting the exploration of extended treatment strategies. The meta-analysis by Pan et al. showed that recurrence after five years of ET remains relevant, with cumulative distant recurrence rates between years five and 20 ranging from 13% for T1N0 disease to 41% for T2N4–9 disease *(Pan et al. N Engl J Med 2017)*. Multiple trials evaluated the benefit of extended ET following five years of AI and/or tamoxifen. The ATLAS study showed that, compared with 5 years of tamoxifen, 10 years of tamoxifen provided significant further benefit for women with HR+ breast cancer in terms of reduced late disease recurrence and breast cancer mortality, with a “carry-over” benefit beyond 10 years *(Davies et al. Lancet 2013)*. The MA.17R and NSABP B-42 trials reported significant improvements in DFS with an additional five years of AI therapy *(Goss et al. N Engl J Med 2016; Mamounas et al. J Natl Cancer Inst 2023)*. Despite therapeutic advances, a risk of late recurrence persists in ER+/HER2- disease.

Camizestrant, a potent next-generation SERD and pure ER antagonist, represents a promising candidate for extended therapy, given its ability to overcome resistance mechanisms against current ETs evolving during treatment. Camizestrant is effective against *ESR1* gene mutations, providing a targeted strategy to counteract acquired resistance. Moreover, it addresses the issue of incomplete inhibition of ER signaling, offering more comprehensive suppression than traditional therapies.

Recently, the SERENA-6 phase III trial in the first line treatment setting of HR+/HER2- advanced breast cancer reported promising efficacy results *(Turner et al. ASCO 2025; Bidard et al. NEJM 2025)*. Switching the endocrine backbone of CDK4/6i therapy from AI to camizestrant in case of emerging *ESR1* mutation detected by serial ctDNA screening demonstrated a statistically significant and clinically meaningful improvement in PFS: 16.0 months for camizestrant + CDK4/6i vs 9.2 months for continuing AI + CDK4/6i. Moreover, time to deterioration in global health/quality of life and pain was significantly delayed. In addition, positive results from adjuvant phase III lidERA trial using SERD giredestrant in early breast cancer further solidifies the rationale of adjuvant SERD +/- CDK4/6i treatment *(Bardia et al. SABCS 2025).*

STUDY DESIGN

Pre- or postmenopausal female or male patients with ER+/HER2- eBC at intermediate or high risk of recurrence who have completed definitive locoregional therapy and at least two years (up to five years) of standard adjuvant ET, with or without a CDK4/6i, and who have no evidence of recurrent disease among further eligibility criteria are enrolled. Patients will be randomized 1:1 to receive either camizestrant 75 mg once daily or standard ET of physician’s choice, both for up to 60 months. Premenopausal women and men in both arms will also receive luteinizing hormone-releasing hormone (LHRH) agonists in addition to camizestrant and if required per guidelines.

CAMBRIA-1 primarily involves patients already undergoing adjuvant ET. Unlike the CAMBRIA-2 trial, patients may be enrolled only after at least two years of adjuvant ET and following completion of any indicated adjuvant CDK4/6 inhibitor therapy.

PRIMARY OBJECTIVE

The primary efficacy objective is to determine the superiority of extended therapy with camizestrant compared to standard ET, as measured by invasive breast cancer-free survival (IBCFS).

STUDY RECRUITMENT

The study will be conducted in approximately 722 sites in 39 countries aiming to enroll 4,300 patients in total globally.

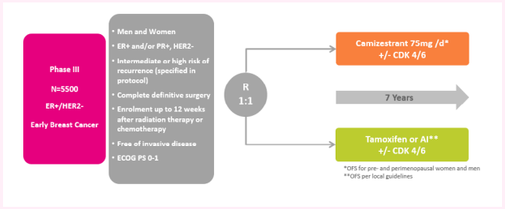
Website link

CAMBRIA-2

GBG 115 / EU-CT 2023-504031-41

Trial Design

randomized, international multicenter, open-label, phase III study



Recruitment

planned: 5500 pts

Study Sites

planned : 30 DEU

Study Population

- women and men with early ER+/HER2-BC
- intermediate to high recurrence risk
- No prior adjuvant endocrine therapy

Endpoints

Primary Endpoint:
- IBCFS

Secondary Endpoints (Selection):
- IDFS, DRFS, OS
- safety
- PROs (arthralgia, hot flushes, vaginal dryness)
- QoL

Cooperations

Sponsor

AstraZeneca

Contact

International Study Chair (in cooperation with ABCSG):
Prof. Dr. S. Loibl

Clinical Project Manager:
Angela Kell
Azcambria-2@gbg.de

BACKGROUND

Patients with early-stage HR+/HER2- breast cancer remain at persistent risk of recurrence beyond five years. Late recurrence following five years of ET is a significant concern, with cumulative distant recurrence rates for years 5 and 20 ranging from 13% for T1N0 disease to 41% for T2N>4 disease *(Pan et al. N Engl J Med 2017)*. Extended ET with additional AI or tamoxifen beyond the initial five years in one effective approach to reduce late recurrence risk *(Goss et al. N Engl J Med 2016; Mamounas et al. J Natl Cancer Inst 2023; Davies et al. Lancet 2013; Gray et al. J Clin. Oncol. 2013)*. Another approach is adjuvant CDK4/6 inhibitor therapy combined with 2-3 years of initial adjuvant ET *(Slamon et al. Ther Adv Med Oncol 2023; Paluch-Shimon et al. Ther Adv Med Oncol 2023)*. In several countries, including Germany, abemaciclib has been approved for use during the first two years of ET in high-risk patients according to the MonarchE trial, which showed maintained distant recurrence-free survival benefit, with absolute improvements of 4.2% and 6.7% at 3 and 5 years, respectively *(Baird et al. Cancer Research 2021; Oliveira et al. Lancet Oncol. 2024).* Recently, long-term follow up of the MonarchE trial reported a significant improvement in overall survival for adding adjuvant abemaciclib to ET (hazard ratio 0.842, 95% confidence interval (CI) 0.722-0.981, P = 0.027) *(Johnston et al. Ann Oncol 2026)*. Meanwhile, adjuvant ribociclib also received EMA approval, expanding eligibility to patients with lower clinical risk. The NATALEE trial reported a more modest distant disease-free survival benefit (4.0% at 5 years; *Crown et al. ESMO open 2025)*.

Camizestrant is a potent, next-generation SERD and pure ER antagonist. Its addresses two critical resistance mechanisms seen with current ET: incomplete inhibition of ER signaling and reduced effectiveness due to *ESR1* mutations acquired during standard ET.

Recently, the SERENA-6 phase III trial in the first line treatment setting of HR+/HER2- advanced breast cancer reported promising efficacy results *(Turner et al. ASCO 2025; Bidard et al. NEJM 2025*). Switching the endocrine backbone of CDK4/6i therapy from AI to camizestrant in case of emerging *ESR1* mutation detected by serial ctDNA screening demonstrated a statistically significant and clinically meaningful improvement in PFS: 16.0 months for camizestrant + CDK4/6i vs 9.2 months for continuing AI + CDK4/6i. Moreover, time to deterioration in global health/quality of life and pain was significantly delayed. In addition, positive results from adjuvant phase III lidERA trial using SERD giredestrant in early breast cancer further solidifies the rationale of adjuvant SERD +/- CDK4/6i treatment *(Bardia et al. SABCS 2025)*.

STUDY DESIGN

Key eligibility criteria include pre- or postmenopausal female or male patients with ER+/HER2- eBC with intermediate or high risk of recurrence, who have completed definitive locoregional therapy and have no evidence of disease. Patients may have received up to a total of 12 weeks of ET in the neoadjuvant or adjuvant setting before randomization. Participants will be randomized 1:1 to receive either 75mg camizestrant once daily with or without abemaciclib (as approved by local/institutional guidelines), or standard ET of physician's choice with or without abemaciclib (as approved by local/institutional guidelines), each for a duration of up to 84 months. Pre- and peri-menopausal women and men will receive concurrent luteinizing hormone-releasing hormone (LHRH) agonists, except males receiving tamoxifen.

CAMBRIA-2 mainly targets a treatment-naive cohort. In contrast to CAMBRIA-1, patients may be included at the onset of adjuvant ET and may receive concurrent abemaciclib as per standard of care, offering targeted therapy alongside optimal standard CDK4/6 inhibitor-containing treatment.

PRIMARY OBJECTIVE

To demonstrate the superiority of camizestrant ± abemaciclib compared to standard ET ± abemaciclib, as measured by invasive breast cancer-free survival (IBCFS).

STUDY RECRUITMENT

The study will be conducted in approximately 735 sites across 43 countries, aiming to enroll 5,500 patients globally.

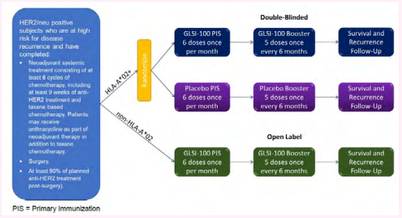
Website link

FLAMINGO-01

GBG 111 / EU-CT 2023-504323-25

Trial Design

randomized, international multicenter, double-blinded, phase III study



Recruitment

planned: 750 pts
recruited: 38 (DEU)

Study Sites

planned : 40 DEU
active: 27 DEU

Study Population

- early HER2+ BC HLA-A*02 + (exception: non-HLA-A*02 arm)
- stage I-III at initial diagnosis & non-PCR OR stage III with pCR after NACT
- neoadjuvant, surgical and adjuvant standard therapy completed

Endpoints

Primary Endpoint:
- IDFS

Secondary Endpoints (Selection):
- OS, DDFS, IDFS
- safety
- QoL

Cooperations

GEICAM investigación en cáncer de mama
unicancer

Sponsor

Greenwich LifeSciences

Contact

GBG Representative :
Prof. Dr. Marcus Schmidt

Clinical Project Manager:
Viktoria Tierbach
Flamingo01@gbg.de

BACKGROUND

One promising approach in cancer treatment is leveraging the body's own immune mechanisms to target and eliminate tumor cells. The introduction of trastuzumab, a monoclonal antibody targeting the HER2 receptor, 20 years ago marked a turning point in the management of patients with HER2+ eBC *(Piccart-Gebhart et al. N Engl J Med 2005; Romond et al. N Engl J Med 2005)*. Initially approved as adjuvant therapy, trastuzumab is often given in combination with pertuzumab during NACT as treatment of choice for high-risk, HER2+ eBC. Exchanging post-neoadjuvant trastuzumab with trastuzumab-emtansine (T-DM1) in patients with invasive residual disease after NACT in the KATHERINE study has demonstrated clinically meaningful improvements in iDFS and, more recently, also in OS *(von Minckwitz G et al. N Engl J Med 2019; Geyer et al. N Engl J Med 2025)*. A remarkable improvement of an absolute 13.7% in 7-year iDFS, from 67.1% with trastuzumab to 80.8% with T-DM1 was reported. However, nearly 20% of these high-risk patients still experience relapse despite optimal anti-HER2 targeted therapies, highlighting an unmet clinical need.
Immunizations targeting specific tumor antigens, such as HER2, have gained attention for their potential to induce long-lasting immune modulation. The immunogenic cytotoxic T lymphocyte (CTL) epitope GP2, derived from HER2, is currently under investigation as a peptide vaccine in HLA-A*02 subjects *(Fisk et al. J Exp Med 1995; Peoples et al. Proc Natl Acad Sci U S A 1995)*. The development of such immunization strategies holds promise as novel adjuvant therapies for high-risk breast cancer patients, potentially providing lasting immune responses without the need for ongoing treatments.

One such agent, GLSI-100, combines the GP2 peptide with granulocyte-macrophage colony-stimulating factor (GM-CSF). The phase I study established the safety profile and optimal dose (500 mcg GP2 and 125 mcg GM-CSF) of GLSI-100. Subsequent phase II trials, including a randomized 5-year follow-up study, have shown a significant DFS benefit in HER2+ patients receiving GLSI-100 compared to controls. Local and systemic toxicities were minimal, and GLSI-100 induced robust immune responses, including GP2-specific CTL expansion *(Patel et al. SABCS 2020; Patel et al. AACR 2021; Patel et al. ASCO 2021)*.

These findings support the potential of GLSI-100 as an adjuvant therapy for preventing HER2+ breast cancer recurrence in HLA-A*02-positive patients. Further research aims to clarify its role in combination therapies and its efficacy across diverse patient populations, contributing to the evolving landscape of cancer immunotherapy.

STUDY DESIGN

FLAMINGO-01 is a prospective, randomized, double-blind, placebo-controlled, multicenter, phase III study. Eligible patients must be diagnosed with HER2+ breast cancer at high risk of recurrence, defined as stage III disease with pCR at surgery, or stage I, II, or III disease with pathological evidence of residual invasive disease at surgery. HLA-A*02 positive subjects are randomized 1:1 to receive either GLSI-100 or placebo (N=600). At selected sites, non-HLA-A*02-positive patients may receive open-label GLSI-100 therapy (N=250).
HLA type screening may be performed after surgery, up to one year prior to enrolment, as treatment begins after completion of adjuvant trastuzumab-based therapy. Subjects will receive 11 intradermal injections over three years and will be followed for an additional year, for a total study duration of four years.

Participation in this trial offers an additional treatment option for patients who remain at high risk after completion of all standard therapies.

PRIMARY OBJECTIVES

The primary objective is to evaluate the efficacy of GLSI-100 compared to placebo in HLA-A*02-positive patients with HER2+ eBC at high risk of disease recurrence.

STUDY RECRUITMENT

Recruitment in Germany started in QII 2024. The study is being conducted across six countries, aiming to enroll a total of 750 patients. As of December 31, 2025, 38 patients had been enrolled in Germany.

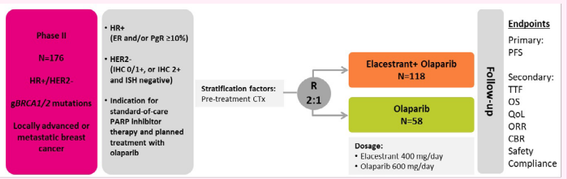
Website link

ELEMENT

GBG 114 / EU-CT 2023-504925-38

Trial Design

Prospective, randomized, multicenter, open label, phase II study



Recruitment

planned: 176 pts
recruited: 15 pts

Study Sites

planned: 40 DEU
active: 35 DEU

Study Population

- HR+, HER2- locally advanced or metastatic BC
- g*BRCA1/2* mutation
- Prior palliative chemo-/endocrine therapy (or adjuvant CDK4/6 inhibition)

Endpoints

Primary Endpoint:
- PFS

Secondary Endpoints (Selection):
- TTF, OS, ORR, CBR
- Safety
- QoL/PROs

Cooperations

Sponsor

GBG GERMAN BREAST GROUP

Contact

Coordinating Investigator :
Prof. Dr. Thomas Decker

Clinical Project Manager:
Laura Steinmann
element@gbg.de

BACKGROUND

Endocrine therapy (ET) is an important cornerstone in the treatment of HR+ mBC *(Cardoso et al. Ann Oncol 2020)*. Until 2023, fulvestrant was the only SERD approved in Europe *(Howell et al. J Clin Oncol. 2002; Osborne et al. J Clin Oncol. 2002; Di Leo et al. J Clin Oncol. 2010)*. It requires intramuscular administration, and resistance to therapy can occur *(O'Leary et al. Cancer Discov. 2018)*. Introduction of the oral SERD elacestrant in the EMERALD trial showed a statistically significant improvement in PFS compared to other ETs (including fulvestrant) in patients with second- and third-line HR+/HER2- mBC after prior CDK4/6 inhibitor therapy *(Bardia et al. J Clin Oncol. 2021; Bidard et al. J Clin Oncol. 2022*). As a result, elacestrant was approved by both the FDA and EMA for patients with ER+/HER2-, *ESR1*-mutated advanced or mBC who have progressed following at least one line of ET.

The PARP inhibitor Olaparib has demonstrated efficacy and safety as monotherapy in patients with HER2- germline *(g)BRCA1/2* mutated mBC *(Robson et al. N Engl J Med. 2017)*. The phase III OlympiAD study showed improved median PFS, higher response rates, and reduced toxicity with olaparib compared to standard therapy. Additionally, one year of olaparib with concurrent ET proved safe and effective in patients with early HR+ BC and *gBRCA1/2* mutations *(Tutt et al. N Engl J Med. 2021)*. However, despite these benefits, the median PFS with PARP inhibitor monotherapy in the metastatic setting remains low, emphasizing the need for new therapeutic approaches to preserve response to the well tolerable treatment *(Robson et al. N Engl J Med. 2017; Gelmon et al. Eur J Cancer. 2021)*.
The ELEMENT trial aims to evaluate whether the addition of the oral SERD elacestrant as ET to olaparib standard PARP inhibitor therapy can improve PFS compared to olaparib alone in patients with HR+/HER2- locally advanced or mBC and *gBRCA1/2* mutations.

STUDY DESIGN AND OBJECTIVES

Eligible patients have HR+/HER2- locally advanced or mBC with *gBRCA1/2* mutations and are candidates for PARP inhibitor therapy. Participants will be randomized in a 2:1 ratio to receive elacestrant plus olaparib versus olaparib alone. Premenopausal women and men assigned to elacestrant will also receive GnRH analogues.

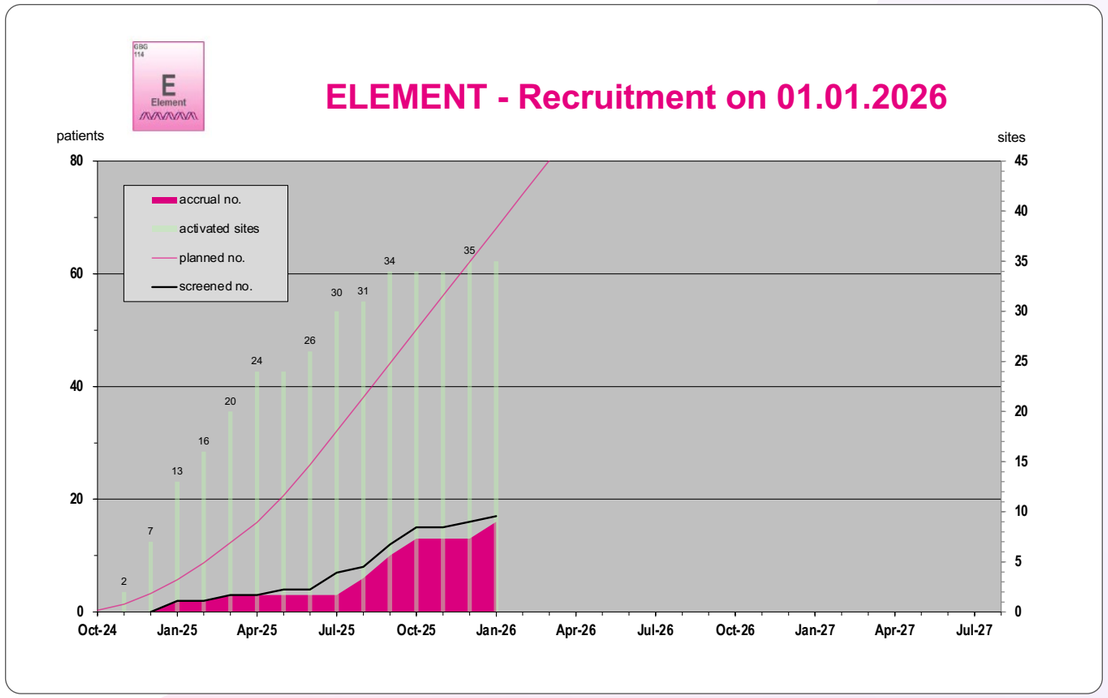
Local confirmation of HR and HER2 status as well as *gBRCA1/2* mutations is required. Additional eligibility criteria include ECOG performance status of 0-2 and a life expectancy greater than six months. Key exclusions include acute life-threatening visceral metastases, previous PARP inhibitor therapy, and uncontrolled significant infections.

PRIMARY OBJECTIVE

The primary objective is to compare PFS between treatment arms. Secondary objectives include time to treatment failure (TTF), OS, quality of life and patient-reported outcomes, overall response rate (ORR), clinical benefit rate (CBR), safety, and compliance. Translational research objectives include biomarker analyses for both efficacy and toxicity.

STUDY RECRUITMENT

The recruitment period is 36 months, with an interim safety analysis planned after the first 15 patients per arm have completed two cycles (or two months) of treatment. The study will be conducted in approximately 40 sites in Germany with a target enrollment of 176 patients. As of December 31, 2025, 16 patients were enrolled.



Website link

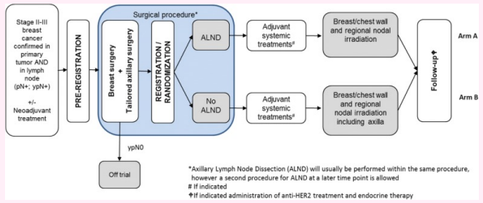
TAXIS

GBG 101/ NCT03513614

Universitätsspital Basel

Trial Design

randomized, multicenter, phase III study (non-AMG)



Recruitment

planned: 1500 pts
recruited: 1545 / 126 (DEU)

Study Sites

planned: 5 DEU
active: 5 DEU

Study Population

- operable node positive BC, detected by palpation or imaging (most suspicious lymph node clipped)
- stage II-III
- eligible for primary axillary lymph node dissection or sentinel lymph node biopsy procedure

Endpoints

Primary Endpoint:

- DFS

Secondary Endpoints (Selection):

- OS, BCSS, TTLR, TTRR, TTDR
- lymphedema, range of shoulder motion
- surgical site infections
- safety and QoL

Cooperations

SAKK
IBCSG International Breast Cancer Study Group
ABCSG

Sponsor

Universitätsspital Basel

Contact

Coordinating Investigator:
Prof. Dr. Walter Weber

Clinical Project Manager:
Jan Steffen
taxis@gbg.de

BACKGROUND

Axillary lymph node dissection (ALND) was the standard treatment for breast cancer for nearly a century, until the introduction of sentinel lymph node biopsy (SLNB). Conventional ALND remains the standard procedure in cases with extensive nodal involvement or persistent lymph node metastases after NACT. However, ALND is associated with substantial morbidity, including lymphedema, impaired shoulder mobility, sensory disorders, and chronic pain in up to one-third of patients.

The TAXIS trial aims to determine the optimal management for patients with breast cancer and confirmed node-positive disease at diagnosis, specifically regarding surgical and radiotherapeutic strategies. It investigates the value of tailored axillary surgery (TAS), a minimally invasive technique focusing on the selective removal of positive lymph nodes (clinically suspected or known), which may significantly reduce morbidity by avoiding unnecessary surgery. This trial may help establish a new treatment standard with fewer side effects and improved quality of life, while preserving the oncologic efficacy of conventional ALND.

STUDY DESIGN AND OBJECTIVES

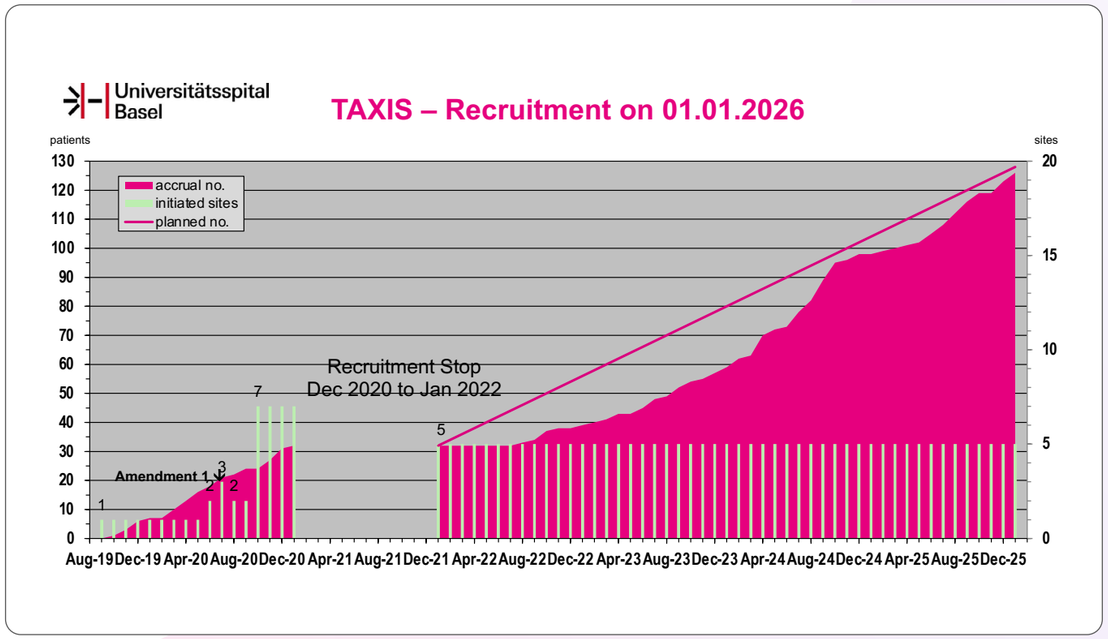
Eligible participants are women or men aged ≥18 years with node-positive breast cancer (confirmed histologically or cytologically in both the primary tumor and lymph node) at AJCC/UICC stage II-III, across all molecular subtypes. Participants are randomized 1:1 to TAS (SLNB plus removal of clipped positive nodes and palpably suspicious nodes), followed by ALND and regional nodal irradiation excluding the dissected axilla (arm A) or TAS, followed by regional nodal irradiation including the full axilla (arm B). All patients receive adjuvant whole-breast irradiation after breast conserving surgery and chest wall irradiation following mastectomy. Neoadjuvant therapy may be administered prior to TAS, and adjuvant systemic treatment may be given after TAS and before radiotherapy, if indicated.

The trial seeks to enroll 1,500 patients (750 per arm). Radiation therapy should begin within eight weeks post-surgery (no later than 12 weeks), and within six weeks after the final chemotherapy cycle (no later than eight weeks). Standard radiotherapy doses are 50 Gy in 25 fractions of 2 Gy or 50.4 Gy in 28 fractions of 1.8 Gy; hypo-fractionated schedules are permitted. Each patient is followed for 10 years after randomization.

The primary objective of TAXIS is to demonstrate that TAS plus axillary irradiation is non-inferior to ALND in terms of disease-free survival (DFS). Secondary endpoints include quality of life (QoL), OS, breast cancer-specific survival (BCSS), time to local recurrence (TTLR), time to regional recurrence (TTRR), time to distant recurrence (TTDR), reported morbidity outcomes (lymphedema and decreased range of shoulder motion), adverse events, late radiotherapy-related adverse events, and surgical site infections (SSI).

STUDY RECRUITMENT

TAXIS recruitment began in August 2019 in Germany, with a temporary pause at the end of 2020. Recruitment resumed in January 2022 in collaboration with a new sponsor (Universitätsspital Basel). The recruitment ended December 31, 2025. Patient follow-up will continue for up to 10 years. As of December 31, 2025, a total of 1,545 patients were included, 126 of which were enrolled in Germany.



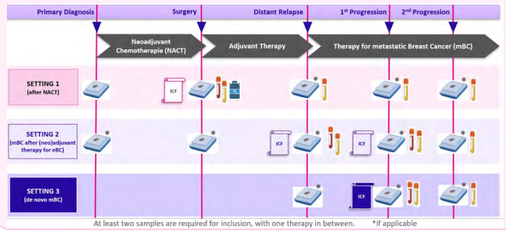
Website link

MOMENTUM

GBG 108 / DRKS00033761

Trial Design

multicenter, prospective, translational, non-interventional study (registry)



Recruitment

planned: 2000 pts
recruited: 39 pts

Study Sites

planned : 50
active: 14

Study Population

- patients with eBC, clinically gross residual tumor after NACT
- distant recurrence of BC during/after (N)ACT
- mBC with progression after at least one line of therapy for mBC

Endpoints

Primary Endpoint:

- assess tumor heterogeneity by analyzing longitudinal tumor samples

Secondary Endpoints (Selection):

- biomarker identification to predict resistance in systemic therapy
- change in BC subtype after systemic therapy
- identification of new therapy targets

Cooperations

Sponsor

GBG GERMAN BREAST GROUP

Contact

Principal Investigator:
Prof. Dr. Sibylle Loibl

Clinical Project Manager:
Jan Steffen
momentum@gbg.de

BACKGROUND

Patients with eBC who do not achieve a pCR to NACT, particularly those with TNBC and/or high-risk clinical or biological features, face an increased risk of relapse. While multiple lines of treatment are available for mBC, successive lines tend to become less effective as resistance mechanisms evolve and most potent agents have already been utilized.

Next-generation sequencing has significantly enhanced our understanding of breast cancer tumor heterogeneity, which is closely linked to treatment resistance and clinical outcomes. Several key gene mutations have been identified as drivers of disease progression *(Arnedos et al. Nat Rev Clin Oncol 2015; Cancer Genome Atlas N. Nature 2012; Curtis et al. Nature 2012; Stephens et al. Nature 2012).* Recently, innovative therapies targeting tumor-specific genetic alterations and acquired resistance mechanisms have been approved *(Turner et al. N Engl J Med 2024; Jhaveri et al. N Engl J Med 2024; Bidard et al. J Clin Oncol 2024; Turner et al. N Engl J Med 2023).*

Further research is critical for characterizing breast cancer heterogeneity, especially the molecular changes that occur under therapeutic pressure. Unraveling drug resistance mechanisms is essential for identifying new treatment targets and developing effective strategies to improve survival. Acquired resistance to endocrine therapy, such as through *ESR1* mutations, is an exemplary for tumor heterogeneity in longitudinal samples and can inform adaptive treatment approaches. Tumors evolve in response to the selection pressure exerted by therapies, enabling disease escape; however, these changes may also represent effective therapeutic targets *(Chaudhary et al. NPJ Breast Cancer 2024; Bidard et al. NEJM 2025).*

Examining residual tumors after NACT in eBC and comparing them to corresponding metastases in mBC is crucial for understanding mechanisms of resistance and sensitivity, and for identifying new potential treatment targets. Therefore, MOMENTUM is a prospective registry focusing on the follow-up of eBC patients with residual disease after NACT and following up patients with mBC.

STUDY DESIGN AND OBJECTIVES

MOMENTUM aims to document all administered (neo) adjuvant, post-neoadjuvant, and palliative therapies, and to collect longitudinal biomaterial samples (tissue and blood) obtained during routine care. These samples will facilitate systematic assessment of tumor heterogeneity through molecular profiling and biomarker analyses over time.

Eligible participants include female and male patients with eBC and clinically evident residual tumor following NACT, those with distant recurrence of breast cancer during or after (neo)adjuvant therapy, or mBC patients who have progressed after at least one line of therapy. Participation is independent of breast cancer histology (ductal, lobular, others) and subtype (luminal A, luminal B, HER2+, triple-negative).

Retrospective inclusion of deceased patients in MOMENTUM is possible for those who had distant progression following initial neoadjuvant and/or adjuvant and/or metastatic therapy, if archived biomaterial and clinical data are available.

All patients must provide a pair of longitudinal tissue samples:

- one sample before NACT and one after NACT for patients with eBC
- one sample before and one after disease progression for patients with mBC

For detailed eligibility criteria, please refer to the MOMENTUM trial protocol.

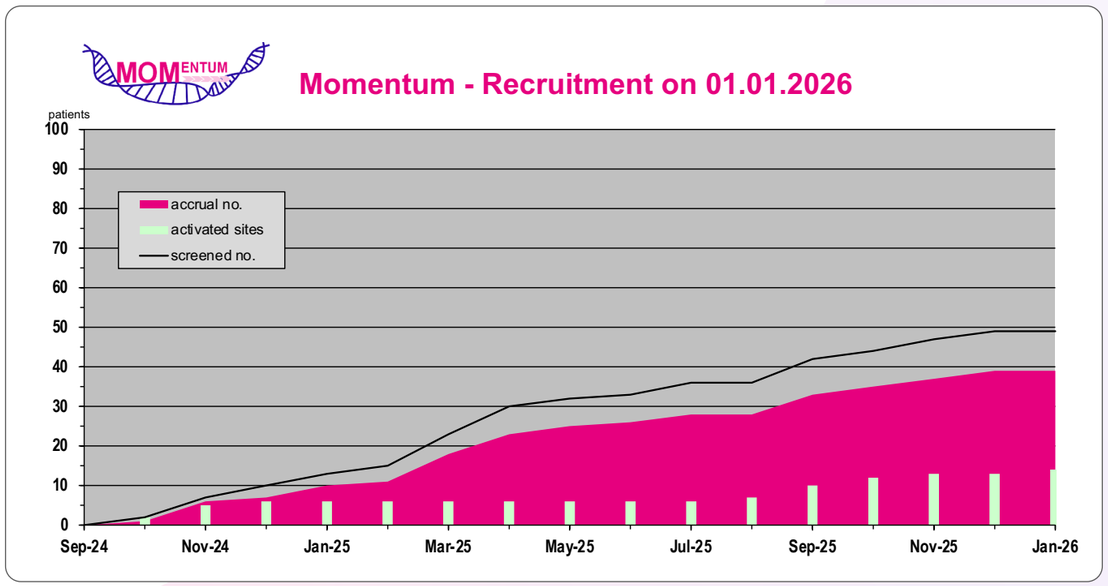
MOLECULAR PRE-SCREENING FOR THERAPY-STUDY COGNITION-GUIDE

While MOMENTUM's primary goal is translational research, it also offers direct potential benefit for eBC patients. Tumor tissue from eBC patients with residual invasive disease after NACT for TNBC or HER2+ will undergo sequencing to identify actionable mutations, enabling referral to the COGNITION-GUIDE therapy trial for further treatment after standard post-NACT treatment in case required alterations are detected. COGNITION-GUIDE is a multicenter, open-label, umbrella phase II study implementing genomics-guided, targeted post-neoadjuvant therapy for early breast cancer patients sponsored by the German Cancer Research Center (DKFZ) and managed by the National Center for Tumor Diseases (NCT) in Heidelberg.

Further information on COGNITION-GUIDE is available at the NCT website Link

STUDY RECRUITMENT

As of December 31, 2025, 39 of total 2,000 patients had been enrolled.



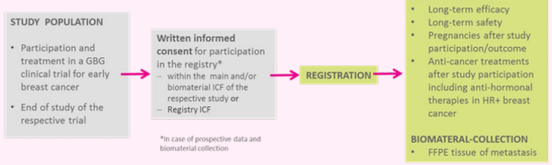
Website link

ETERNITY[B]

GBG 107 / NCT05739591

Trial Design

international, multicenter, prospective/retrospective, non-interventional observational study (registry)



Recruitment

planned: n.a.
recruited: 144pts

Study Sites

planned : n.a.
active: 25

Study Population

- participation and treatment in a GBG clinical trial for early breast cancer outside Germany
- prospective registration: written informed consent

Objectives

Primary Objective:
- to evaluate long-term-survival

Secondary Objectives (Selection):
- to determine long-term toxicity
- to determine further anti-cancer therapies after study participation
- to determine pregnancies after study participation and their outcome

Cooperations

GEICAM investigación en cáncer de mama
IBCSG International Breast Cancer Study Group
Japan Breast Cancer Research Group
ABCSG Austrian Breast & Colorectal Cancer Study Group
Cancer Trials Ireland
unicancer
KBCG 대한항암요법연구회

Sponsor

GBG German Breast Group

Contact

Coordinator:
Prof. Dr. Sibylle Loibl

Clinical Project Manager:
Dr. Thomas Ballhausen
eternity@gbg.de

BACKGROUND

Although long-term patient survival and safety are critical for determining the risk-benefit ratio of investigational treatment strategies, recommendations for early and advanced breast cancer are typically based on the primary results of randomized clinical trials, which often have relatively short follow-up periods at the time of primary analysis.

Extended collection of survival and safety data is essential to a comprehensive understanding of the efficacy of investigational treatments, to identifying late-onset toxicities, and to evaluating long-term quality of life outcomes.

To address this gap, we established a patient self-reported outcome (PSRO) registry (GBG 71) in Germany. However, since GBG 71 is not accessible to our European and non-European partner sites, we initiated the international registry study ETERNITY[B] to gather a similar long-term outcome data set worldwide.

STUDY DESIGN AND OBJECTIVES

Eligible participants for ETERNITY[B] are patients who were previously enrolled in a GBG clinical trial for eBC. Inclusion in ETERNITY[B] requires written informed consent. Data collection and follow-up documentation begin after the regular conclusion of the corresponding GBG trial or at the start of the post-study follow-up phase, as specified in the respective study protocol.

The registry is linked to individual study databases via participant identification numbers, enabling analysis of long-term therapy effects and correlation of effectiveness with late side effects. Post-study long-term follow-up aligns with local and national guidelines and allows at least annual documentation. Relapse assessments, safety evaluations, and collection of survival status are performed for all registered patients and may be performed during routine follow-up visits or by alternative means, such as telephone or written correspondence.

If disease recurrence is confirmed, histological examination is recommended. While the submission of a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block from any metastatic lesion to GBG is encouraged, biomaterial submission is not a requirement for participation in ETERNITY[B].

STUDY DURATION AND PLANNED UPGRADE

ETERNITY[B] is currently scheduled to run through 2030. A comprehensive study amendment is planned for 2026, aiming to enhance digitalization.

STUDY RECRUITMENT

Recruitment for ETERNITY[B] began in September 2022. As of December 31, 2025, a total of 144 patients have been enrolled. Additional participants from the GeparPiPPa study are anticipated to join ETERNITY[B] in early 2026.

Website link

Brain Metastases in Breast Cancer (BMBC)

GBG 79

Trial Design

international, multicenter, prospective/retrospective, non-interventional observational study (registry)

Recruitment

planned: n.a.
recruited: 4745 pts

Study Sites

planned : n.a.
active: 155 DEU
5 INT

Study Population

- brain metastases and history of breast cancer or metastatic breast cancer (diagnosed since the year 2000)
- patients with leptomeningeal disease without brain metastases are eligible

Objectives

Objectives (Selection):

- To assess the incidence of brain metastases
- To assess number/size and location of brain metastases
- To assess histopathological characteristics
- To assess the influence of treatment strategies on prognosis
- Collection of tissue samples

Cooperations

AGO-B BREAST STUDY GROUP
UKE HAMBURG

Sponsor

GBG GERMAN BREAST GROUP

Contact

Coordinator:
Prof. Dr. Volkmar Müller

Clinical Project Manager:
Dr. Cora Strobel
brainmet@gbg.de

BACKGROUND

The occurrence of brain metastases significantly reduces both quality of life and survival rates in patients with breast cancer. Over the past decades, an increasing incidence of brain metastases has been observed *(Fisk et al. 1995)*. Approximately 10-40% of patients with mBC will develop brain metastases, varying according to the biological subtype of the primary tumor. The overall prognosis for patients with brain metastases is poor; however, factors such as good performance status and a limited number of brain metastases are associated with prolonged survival *(Ogawa et al. 2008)*. Current treatment options include surgery, radiotherapy, systemic chemotherapy, or a combination of these.

Despite advancements, gaps remain in our understanding of the risk factors for developing brain metastases and the impact of early detection, mainly due to insufficient analysis in small and heterogeneous patient cohorts. As the incidence of brain metastases is predicted to rise, particularly with better control of systemic disease outside the nervous system, there is an increasing need for improved intracranial treatment strategies. A comprehensive, multidisciplinary approach that rapidly integrates novel therapies is crucial for patients with brain metastases, aiming to extend survival, preserve neurological function, and enhance quality of life.

The Brain Metastases in Breast Cancer (BMBC) registry was established to systematically include breast cancer patients diagnosed with brain metastases from the year 2000 onwards. Prospective registration of patient data requires informed consent, while retrospective entries of anonymized data without further follow-up are permitted without individual consent. The registry is conducted in collaboration with the University Hospital Hamburg-Eppendorf [1-4].

Amendment 1 enabled the inclusion of patients with meningeosis carcinomatosa. For registry participants, tumor samples from the primary tumor, metastatic lesions, or brain metastases, as well as blood and cerebrospinal fluid samples, when available, are centrally collected in the GBG biobank following patient consent.

STUDY OBJECTIVES

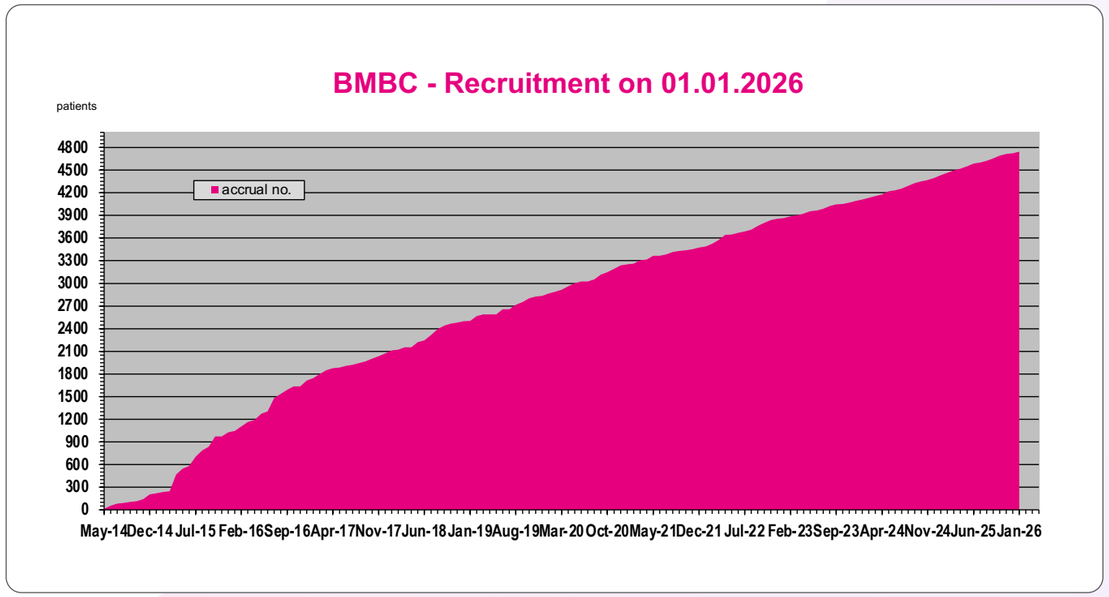
The BMBC registry aims to collect comprehensive data on the incidence and characteristics of brain metastases, including their number, size, location, histopathology, diagnostic sensitivity, performance status, prognosis, and the impact of treatments on patient outcomes and neurological function. The registry also facilitates translational research analyzing specimens from primary and metastatic tumors. Planned analyses will examine treatment patterns, patient outcomes, evolving therapeutic context, and the validation of prognostic scoring systems. Translational research projects will investigate the effects of glycosylation, resistance mechanisms to HER2-targeted therapies, the role of the blood-brain barrier, and markers of radio-resistance and genomic alterations associated with breast cancer cell brain tropism.

PUBLICATIONS

1. Riecke K, Muller V, Weide R et al. Predicting Prognosis of Breast Cancer Patients with Brain Metastases in the BMBC Registry-Comparison of Three Different GPA Prognostic Scores. Cancers (Basel) 2021; 13 (4).
2. Laakmann E, Witzel I, Neunhoffer T et al. Characteristics of patients with brain metastases from human epidermal growth factor receptor 2-positive breast cancer: subanalysis of Brain Metastases in Breast Cancer Registry. ESMO Open 2022; 7 (3): 100495.
3. Riecke K, Muller V, Neunhoffer T et al. Long-term survival of breast cancer patients with brain metastases: subanalysis of the BMBC registry. ESMO Open 2023; 8 (3): 101213.
4. Laakmann E, Schmidt M, Lübbe K et al. Clinical characteristics and prognostic factors in patients with breast cancer and leptomeningeal metastases from a large registry of BMBC. Breast. 2025 Jun;81:104433.

STUDY RECRUITMENT

The registry began documentation in April 2014 and now includes more than 160 participating centers. As of December 31, 2025, a total of 4,745 patients have been registered, with 802 tissue samples received. Patient registration is ongoing. The study has expanded its international reach, recruiting over 136 patients from Belgium, Portugal, Switzerland, and Spain. The clinical database and biobank have also grown significantly. Registration of more than 800 patients from the Netherlands is expected to additionally increase total numbers in 2026.



Website link

Patient Self-Reported Outcome Registry (PSRO)

GBG 71 / DRKS00038176

Trial Design

- non-interventional observational study (registry)
- collection of long-term safety and efficacy parameters of former German GBG study participants from prospective clinical trials
- data reporting by the patient via questionnaire

Recruitment

planned: n.a.
recruited: 13549 pts

Study Sites

277 sites
26 trials

Study Population

- participation and treatment in a GBG clinical trial for breast cancer in Germany

Objectives

- to determine long-term outcome
- to determine long-term toxicity

Cooperations

ZKS Köln – Zentrum für Klinische Studien

Sponsor

GBG – German Breast Group

Contact

Clinical Project Manager:
Jan Steffen
follow.up@gbg.de

BACKGROUND

Long-term follow-up in early breast cancer trials is essential for a comprehensive understanding of treatment efficacy and the emergence of late or chronic toxicities. Extended observation enables reassessment of the overall patient benefit, which may differ from initial results based on the primary endpoints. Nevertheless, logistical and financial constraints often limit the ability of study sites and sponsors to collect long-term data.

To address this challenge, we established a patient self-reported outcome (PSRO) registry in 2010, enabling patient consent and ongoing written correspondence to collect vital health status information beyond standard study timelines.

METHODS

Patients are invited to participate in the PSRO registry by the site investigator. Upon providing consent, patients' name, contact details, and unique study identifier are collected; participants agree to receive regular health status questionnaires. In accordance with German privacy laws and Good Clinical Practice (GCP) guidelines, the sponsor does not have access to patient-identifying data. To ensure compliance, the registry utilizes a strict separation of identifying information and pseudonymized medical data via an independent data trustee. This trustee, who is financially and organizationally independent from the GBG, maintains patient names and addresses in a secure database inaccessible to GBG staff.

On notification from GBG, the trustee sends health status questionnaires to patients, collecting information on recurrence, secondary malignancies, and date of death. If a participant has passed away, a designated third party may complete the questionnaire. All forms sent to GBG contain only the unique study identifier as a pseudonym, maintaining privacy. Address changes and withdrawals of consent are handled through to the original study databases and GBG informs respective study sites about relevant patient status changes.

STUDY RECRUITMENT

Enrollment in the PSRO registry is open to participants from multiple GBG breast cancer trials, with over 13,000 patients from 20 trials and 450 sites currently participating.

Breast cancer in Pregnancy (BCP)

GBG 29 / NCT00196833

Trial Design

international, multicenter, prospective/retrospective, non-interventional observational study (registry)

STUDIES POPULATION
- Patients with breast cancer (BC) during pregnancy
- Non-pregnant women with BC ≤ 40 years
- M1 possible
- Prospective and retrospective data collection

→ Informed Consent* → REGISTRATION →

*for prospective data collection

- Oncological treatment according to local standards

DATA COLLECTION
- Tumor characteristics
- Treatment data
- Fetal outcome
- Maternal outcome (delivery and BC)
- Side effects
- Further pregnancies

BIOMATERAL
- FFPE tissue tumor
- FFPE tissue placenta

Recruitment

planned: n.a.
recruited: 4529 pts

Study Sites

planned : n.a.
active: 303

Study Population

- patients with breast cancer during pregnancy
- non-pregnant women with breast cancer ≤ 40 years
- M1 possible

Endpoints

Primary Endpoint:
- fetal outcome 4 weeks after delivery

Secondary Endpoints (Selection):
- maternal outcome of pregnancy
- breast cancer characteristics and
- treatment
- safety
- other outcome parameters

Cooperations

INCIP ESGO International Network of Cancer, Infertility and Pregnancy

BIG Breast International Group

Sponsor

GBG German Breast Group

Contact

Coordinator:
Prof. Dr. Sibylle Loibl

Clinical Project Manager:
Dr. Ioannis Gkantiragas
bcp@gbg.de

BACKGROUND

Breast cancer is the most common cancer among women and remains one of the leading causes of cancer-related deaths worldwide *(Sung et al. CA Cancer J Clin 2021).* It is also one of the most frequently diagnosed cancers during pregnancy, with an incidence of 2.4 to 7.3 cases per 100,000 pregnancies *(Andersson et al. Obstet Gynecol 2009; Eibye et al. Obstet Gynecol 2013; Lee et al. BJOG 2012)*. Data from Sweden and Australia show a rising number of pregnancy-related breast cancer cases, supporting a theory that postponing childbirth to an older maternal age may contribute to this trend *(Andersson et al. Obstet Gynecol 2009; Lee et al. BJOG 2012*). However, specific incidence rates of breast cancer during pregnancy in Germany and Western Europe remain unclear.

In 2003, the GBG initiated a registry study, later expanded globally through the Breast International Group, to systematically evaluate breast cancer during pregnancy and provide evidence for treatment strategies. A protocol amendment allows the inclusion of a non-pregnant control group, consisting of women diagnosed with breast cancer at 40 years of age or younger.

All women with histologically confirmed breast cancer who are pregnant, and/or aged 40 years or younger, can be included in the registry upon providing informed consent for data and biomaterial collection. Prospective enrolment by obtaining formal informed consent allows the collection of valuable long-term follow-up data, which is therefore preferred. Still, participants, that e.g. cannot be reached by trials sites, may be added anonymously for the collection of retrospective data only without individual consent.

STUDY OBJECTIVES

The primary goal of the BCP study is to evaluate the fetal outcome four weeks post-delivery. Secondary endpoints include maternal outcomes during pregnancy, tumor stage at presentation, biological characteristics, breast cancer therapy, type of surgery, mode of delivery (vaginal versus caesarean), and the breast cancer outcome after diagnosis. Moreover, the registry supports translational research using tumor and placental tissue from individuals with breast cancer during pregnancy. A joint analysis with INCIP registry, destined for several publications, is currently in preparation.

STUDY REPORT

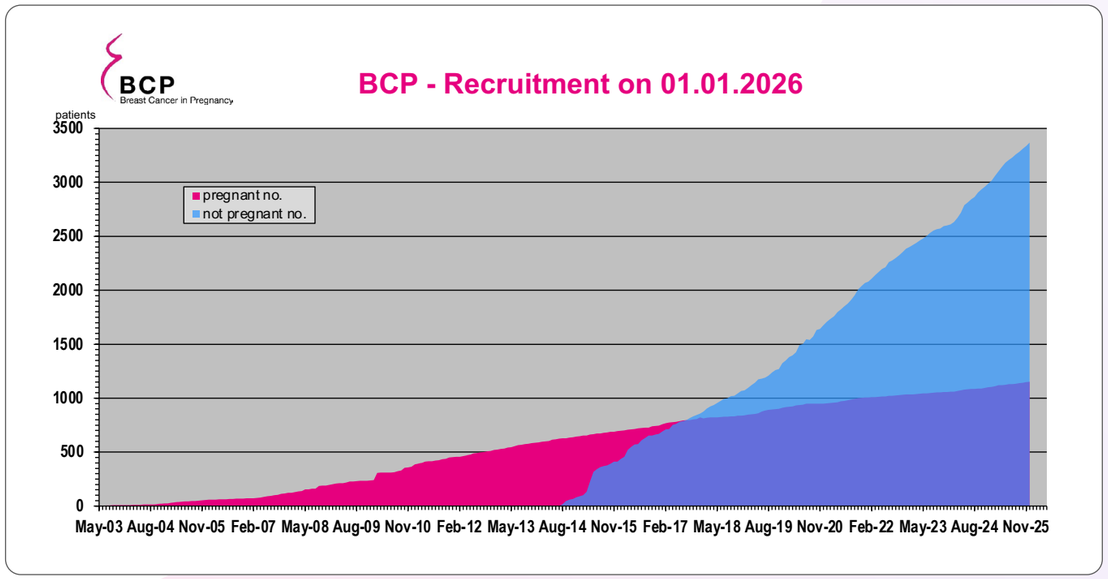
Recent analyses indicate that outcomes of women with breast cancer treated with chemotherapy during pregnancy are comparable to those of young non-pregnant patients. After a median follow-up of 66 months, disease-free survival and overall survival were similar in both groups *(Amant et al. Eur J Cancer 2022)* [1]. These results support the use of chemotherapy during pregnancy when indicated, in accordance with clinical guidelines *(Amant et al. Lancet Oncol 2021)* [2].

PUBLICATIONS:

1. Amant F, Nekljudova V, Maggen C et al. Outcome of breast cancer patients treated with chemotherapy during pregnancy compared with non-pregnant controls. *Eur J Cancer 2022; 170: 54-63.*
2. Amant F, Lefrère H, Borges VF, Cardonick E, Lambertini M, Loibl S, Peccatori F, Partridge A, Schedin P. The definition of pregnancy-associated breast cancer is outdated and should no longer be used. *Lancet Oncol. 2021 Jun;22(6):753-754.*

STUDY RECRUITMENT

As of December 31, 2025, a total of 4,529 patients has been registered, 4,128 in Germany (816 pregnant and 3,312 non pregnant women).



Website link

The following studies are currently in the follow-up phase. We kindly encourage all participating sites to continue providing follow-up data for their patients.

Preventive studies

BRCA-P
(GBG 106 / NCT04711109)

This prospective, randomized, double-blind, placebo-controlled, multicenter, international Phase III prevention trial evaluated denosumab 120 mg versus placebo, administered subcutaneously every six months for five years. Daily supplementation with calcium and vitamin D was strongly recommended throughout the study. Due to slow accrual, the recruitment period was extended by one year, ending on December 31, 2024. Ultimately, 364 of the planned 2,918 patients were recruited globally, including 33 of the planned 500 in Germany. Participants are currently under treatment and will be followed up every 12 months for five years after their last dose.

Neoadjuvant studies

GeparOLA
(GBG 90, NCT02789332)

A multicenter, prospective, randomized open-label phase II study enrolling 107 patients with HER2- early breast cancer and homologous recombination deficiency (HRD). The trial compared neoadjuvant paclitaxel plus olaparib versus paclitaxel plus carboplatin, both followed by epirubicin/cyclophosphamide (EC). Long-term data showed inferior outcomes with olaparib (instead of carboplatin) in patients without *BRCA1/2* tumor or germline mutations, while survival difference was observed in patients with these mutations. The study is currently in long-term follow-up.

Manuscript published in Clinical Cancer Research entitled
"Neoadjuvant paclitaxel/olaparib in comparison to paclitaxel/carboplatin in patients with HER2- BC and HRD –long-term survival of the GeparOLA study" IF 10.2
Link manuscript

Manuscript published in Clinical Cancer Research entitled
"RAD51 testing in patients with early HER2- breast cancer and homologous recombination deficiency: post-hoc analysis of the GeparOla trial" IF 10.2
Link manuscript

GeparNuevo
(GBG 89, NCT02685059)

A multicenter, prospective, randomized, double-blinded, placebo-controlled phase II study enrolling 174 patients. The trial compared pathological complete response (pCR) rates of nab-paclitaxel plus durvalumab followed by epirubicin/cyclophosphamide plus durvalumab versus the same regimen with placebo. The study is in long-term follow-up.

Manuscript accepted by Journal of Clinical Oncology entitled
"Durvalumab in Combination with Neoadjuvant Chemotherapy in Early Triple-Negative Breast Cancer (TNBC) – Long-Term Analysis from the GeparNuevo Trial" IF 41.9

Oral presentation at ESMO 2025 by Prof. Dr. Sibylle Loibl entitled
"Durvalumab in combination with neoadjuvant chemotherapy in early triple-negative breast cancer (TNBC): Long-term analysis from the GeparNuevo trial"

GeparX
(GBG 88, NCT02682693)

A multicenter, prospective, 2x2 randomized, open-label, phase IIb study with 780 patients. The trial evaluated the addition of denosumab to anthracycline/taxane-based neoadjuvant chemotherapy and compared weekly versus 2-out-of-3-week nab-paclitaxel schedules in primary breast cancer. The study is in long-term follow-up.

Manuscript published in ESMO Open entitled
"Long-term effect of neoadjuvant denosumab treatment in high-risk early breast cancer (GeparX)" IF 8.3
Link presentation

Manuscript in preparation on manual vs automated Ki67 assessment from GeparX study.

Poster presentation at SABCS 2025 by Prof. Dr. Marion van Mackelenbergh entitled
"Evaluation of stable calcium isotope ratios in women undergoing neoadjuvant chemotherapy (NACT) with and without denosumab (GeparX)"
Link presentation

Post-neoadjuvant studies

Penelope[B]
(GBG 78, NCT01864746)

A prospective, international, multicenter, randomized, double-blind, placebo-controlled, post-neoadjuvant phase III study evaluating the addition of the CDK4/6 inhibitor palbociclib in HER2-, HR+ patients at high risk of relapse after NACT. 1,250 patients were enrolled, including 434 from Germany.

Manuscript published in Cancer Cell entitled
"Dynamics of molecular heterogeneity in high-risk luminal breast cancer-From intrinsic to adaptive subtyping" IF 44.5
Link manuscript

Manuscript published in Annals of Oncology
"Final survival results from the PENELOPE-B trial investigating palbociclib versus placebo for patients with high-risk HR+/HER2- breast cancer and residual disease after neoadjuvant chemotherapy" IF 65.4
Link manuscript

Manuscript published in JCO Precision Oncology entitled
"*BRCA1/2* and Other Predisposition Genes in High-Risk Hormone Receptor+/Human Epidermal Growth Factor Receptor 2- Breast Cancer Treated With Endocrine Therapy With or Without Palbociclib: A Secondary PENELOPE-B Study Analysis" IF 5.6
Link manuscript

Manuscript in preparation on immunohistochemical markers and transitional investigation in the Penelope-B trial.

DESTINY-Breast05/TruDy
(GBG 103, NCT04622319)

A global, multicenter, randomized, open-label, phase III study comparing trastuzumab deruxtecan (T-DXd) with trastuzumab emtansine (T-DM1) in patients with high-risk, HER2+ primary breast cancer and residual invasive disease after neoadjuvant chemotherapy. Conducted in collaboration with Daiichi-Sankyo, AGO-B, and SOLTI, the study enrolled 1,635 patients worldwide, including 69 from Germany. Recruitment was completed on February 12, 2024. The first interim efficacy analysis (database cut-off July 2, 2025) showed statistically significant and clinically meaningful improved iDFS with adjuvant T-DXd versus T-DM1, with a 3-year invasive disease-free survival of 92.4% vs. 83.7% (HR = 0.47, 95% CI: 0.34–0.66; p < 0.0001), representing a 53% reduction in the risk of invasive disease recurrence or death. T-DXd demonstrated superior efficacy and a manageable safety profile, positioning it as a potential new standard of care for high-risk HER2+ early breast cancer with residual invasive disease after neoadjuvant therapy. Results were published in the *New England Journal of Medicine* and led to breakthrough therapy designation by the FDA on December 22, 2025.

Manuscript published in The New English Journal of Medicine entitled
"Trastuzumab Deruxtecan in Residual HER2+ Early Breast Cancer" IF 78.5
Link manuscript

Oral presentation at ESMO 2025 by Prof. Dr. Charles E. Geyer entitled
"Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients (pts) with high-risk human epidermal growth factor receptor 2–positive (HER2+) primary breast cancer (BC) with residual invasive disease after neoadjuvant therapy (tx): Interim analysis of DESTINY-Breast05"

Oral presentation at SABCS 2025 by Prof. Dr. Sibylle Loibl entitled
"Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients with high-risk human epidermal growth factor receptor 2-positive (HER2+) primary breast cancer (BC) with residual invasive disease after neoadjuvant therapy: Interim analysis of DESTINY-Breast05"

SASCIA
(GBG 102, NCT04595565)

A global, multicenter, randomized, open-label, phase III study of sacituzumab govitecan (SG) versus treatment of physician's choice (capecitabine, platinum-based chemotherapy, observation/endocrine therapy, or pembrolizumab for patients with triple-negative breast cancer (TNBC) in patients with high-risk, HER2- primary breast cancer who and residual invasive disease in breast or regional lymph nodes after neoadjuvant chemotherapy. In collaboration with Germany, Spain, France, Austria, Ireland, Belgium, and Switzerland, the study enrolled 1,391 patients worldwide, including 760 from Germany.

Adjuvant studies

PALLAS
(GBG 87, NCT02513394)

A multicenter, prospective, international, randomized, open-label, adjuvant phase III study evaluating the addition of two years of palbociclib to standard adjuvant endocrine therapy for patients with HR+/HER2- early breast cancer. In collaboration with ABCSG, NSABP Foundation Inc., PrECOG, LLC., and BIG, 5,796 patients were enrolled worldwide.

Manuscript published in Breast Cancer Research entitled
"Clinical characterization, prognostic, and predictive values of HER2-low in patients with early breast cancer in the PALLAS trial (ABCSG-42/AFT-05/BIG-14-13/PrE0109)"
IF 6.1
Link manuscript

Manuscript published in ESMO Open entitled
"Quality of Life and Symptom Severity in the Randomized Trial of Palbociclib with Adjuvant Endocrine Therapy in Early Breast Cancer (AFT-05, ABCSG-42, BIG-14-13, PrE0109)"
IF 8.3
Link manuscript

Manuscript published in ESMO Open entitled
"Drug-drug interactions between palbociclib and proton pump inhibitors in early breast cancer: an exploratory analysis of PALLAS (ABCSG-42/AFT-05/BIG-14-13/PrE0109)"
IF 8.3
Link manuscript

Manuscript published in Breast Cancer Research entitled
"Outcomes in stage IIA versus stage IIB/III in the PALLAS trial (ABCSG-42/AFT-05/PrE0109/BIG-14-13)"
IF 5.6
Link manuscript

Manuscript published in Breast Cancer Research and Treatment entitled
"Impact of adding palbociclib on treatment adherence to ongoing adjuvant endocrine treatment in the global randomized PALLAS randomized trial in patients with early breast cancer"
IF 3.0
Link manuscript

Manuscript published in Annaly of Oncology entitled
"Palbociclib with adjuvant endocrine therapy in early breast cancer: 5-year follow-up analysis of the global multicenter, open-label, randomized phase III PALLAS trial (ABCSG-42/AFT-05/PrE0109/BIG-14-13)"
IF 65.4
Link manuscript

Poster presentation at ASCO 2025 by Dr. Kristina Fanucci entitled
"Treatment-related neutropenia as a predictor of response to adjuvant palbociclib in the PALLAS trial (ABCSG-42/AFT-05/BIG-14-13/PrE0109)"

Oral presentation at SABCS 2025 by Dr. Heather A. Parsons entitled
"Tumor-informed circulating tumor DNA analysis to assess molecular residual disease for prognosis and prediction of benefit from palbociclib in the PALLAS trial"

Oral presentation at SABCS 2025 by Dr. Angela DeMichele entitled
"Adjuvant palbociclib for ER+ breast cancer in the PALLAS Trial (ABCSG-42/AFT-05/PrE0109/BIG-14-13): post-recurrence treatment and overall survival"

Poster presentation at SABCS 2025 by Dr. Luca Malorni entitled
"Prognostic and predictive role of RBsig and CCNE1/RB1 gene-expression signatures for patients with early breast cancer treated with endocrine therapy with or without palbociclib in the PALLAS trial (ABCSG-42, AFT-05, BIG 14-13)"

Poster presentation at SABCS 2025 by Dr. Marcus Vetter entitled
"Predictors of early discontinuation of adjuvant palbociclib in early HR+/HER2- breast cancer: final analysis of the PALLAS trial integrating patient-reported outcomes"

Poster presentation at SABCS 2025 by Dr. Otto Metzger entitled
"Exploratory analysis of palbociclib benefit in the PALLAS trial by SETERPR index and prior chemotherapy regimens (ABCSG-42/AFT-05/BIG-14-13)"

Poster presentation at SABCS 2025 by Dr. Guilherme Nader-Marter entitled
"Long-term prognostic and predictive value of lobular histology in the PALLAS trial"

OLYMPIA
(GBG 82, NCT02032823)

A multicenter, double-blind, parallel-group, placebo-controlled, randomized phase III trial evaluating the efficacy of olaparib versus placebo in the adjuvant/post-neoadjuvant setting for patients with germline *BRCA1/2* mutations and high-risk, HER2- early breast cancer. A total of 1,836 patients were enrolled.

APHINITY
(GBG 67, NCT01358877)

An adjuvant, prospective, two-arm, randomized, multicenter, international, double-blind, placebo-controlled phase III adjuvant trial comparing the safety and efficacy of trastuzumab and pertuzumab plus chemotherapy versus chemotherapy with trastuzumab alone for HER2+ early breast cancer. In collaboration with Genentech, Inc., and BIG, 4,805 patients were enrolled.

Manuscript published in European Journal of Cancer entitled
"Body Mass Index and Weight Changes in Patients with HER2+ Early Breast Cancer: a sub-analysis of APHINITY trial"
IF 7.1
Link manuscript

Oral presentation at ESMO BC 2025 by Prof. Dr. Sibylle Loibl
"Adjuvant pertuzumab or placebo + trastuzumab + chemotherapy (P or Pla + T + CT) in patients (pts) with early HER2+ operable breast cancer in APHINITY: Final analysis at 11.3 years' median follow-up"

Oral presentation at SABCS 2025 by Dr. Roberto Salgado entitled
"Prognostic and predictive associations of manual, digital and AI-derived tumor infiltrating lymphocytes-scoring: A retrospective analysis from the Phase III APHINITY trial"

APPALACHES
(GBG 100, NCT03609047)

A randomized, international, phase II study for patients aged ≥70 with stage II/III early invasive breast cancer. Patients were randomized 2:1 to receive either adjuvant endocrine therapy (≥5 years) plus palbociclib (up to 2 years) or adjuvant chemotherapy followed by endocrine therapy. Primary objective: efficacy comparison of endocrine therapy plus palbociclib versus standard chemotherapy in older patients with ER+/HER2- disease. Secondary objectives include time-to-event endpoints, toxicity, discontinuation rates, completion of oral therapy, health-related quality of life (HRQoL), and geriatric assessments. Translational research focuses on aging biomarkers, with samples collected at baseline, 6 months, and 3 years. The study ended in November 2025 after protocol amendment discontinued long-term follow-up.

Metastatic studies

PATINA
(GBG 94, AFT-38, NCT02947685)

An international, multicenter, randomized, open-label, phase III trial evaluating palbociclib plus anti-HER2 therapy plus endocrine therapy versus anti-HER2 therapy and endocrine therapy alone after induction treatment for HR+/HER2+ metastatic breast cancer. In collaboration with Alliance Foundation Trials (AFT), LLC, 496 patients were enrolled worldwide, including 34 in Germany. Follow-up is scheduled to conclude in October 2026.

Oral presentation at SABCS 2025 by Dr. Otto Metzger
"Central nervous system outcomes from the phase III PATINA trial (AFT-38)"

AURORA
(GBG 85, NCT02102165)

An exploratory, multinational, collaborative molecular screening program designed to better understand the genetic aberrations in metastatic breast cancer, elucidate mechanisms of response or resistance, and identify optimal therapies for individual patients.

Poster presentation at SABCS 2025 by Prof. Matteo Benelli
"Multi-omics characteristics of ER+/HER2- breast cancer switching to metastatic non-luminal subtype: findings from the AURORA study (BIG14-01)"

Locoregional

EUBREAST-01
(GBG104, NCT 04101851)

A multicenter, single arm study that enrolled 393 patients with triple-negative or HER2+ invasive breast cancer (cT1c-cT3 tumor, initial cN0/iN0 status before neoadjuvant systemic therapy, and pCR of the breast tumor). The primary objective is to assess 3-year axillary recurrence-free survival (ARFS) after breast-conserving surgery without axillary therapy. Secondary endpoints include survival outcomes and the diagnostic accuracy of imaging for breast pCR. Screening ended in December 2024; the last patient was enrolled in September 2025.

Follow-up

META-ANALYSES ON FOLLOW-UP TRIALS

Manuscript published in Journal of Clinical Oncology entitled
“Surrogate End Points for Overall Survival in Neoadjuvant Randomized Clinical Trials for Early Breast Cancer” IF 41.9
Link manuscript

Manuscript published in Lancet Oncology entitled
“Distant disease-free survival as a surrogate endpoint for overall survival in randomised trials of neoadjuvant therapy for early breast cancer: a pooled analysis of GBG and AGO-B Study Group trials“ IF 35.9
Link manuscript

Oral presentation at SABCS 2025 by Dr. Johannes Holtschmidt entitled
“Prognostic Markers in Residual Tumors after neoadjuvant chemotherapy (NACT) for Early Triple-negative Breast Cancer (TNBC) - a Pooled Analysis from nine Neoadjuvant GBG/AGO-B Trials”
Link presentation

Poster presentation at SABCS 2025 by Prof. Dr. Carsten Denkert entitled
“Predicting response and survival after neoadjuvant systemic treatment with on-treatment biopsies)“
Link presentation

Translational Research & Biobanking

Longitudinal Transcriptomic and Spatial Omics Analyses at the Institute of Pathology, University Hospital Marburg

In 2025, the Institute of Pathology at the University Hospital Marburg expanded its expertise in longitudinal molecular profiling and spatial omics, deepening our understanding of tumor evolution, therapeutic adaptation and intratumoral heterogeneity across major breast cancer subtypes.

A primary focus was longitudinal bulk RNA expression profiling in large, well-annotated clinical trial cohorts. By analyzing pre-treatment biopsies, post-neoadjuvant residual tumors and, where available, distant metastatic lesions, the institute investigated dynamic changes in gene expression under therapeutic pressure. Within the Penelope-B trial, pronounced molecular heterogeneity and dynamic gene expression patterns were demonstrated in high-risk luminal B breast cancer. This research identified gene expression–based adaptive clusters with strong prognostic impact, going beyond classical intrinsic subtypes and highlighting their potential relevance for refined risk stratification and treatment guidance [1].

In the triple-negative breast cancer (TNBC) setting, longitudinal tumor samples were analyzed to characterize molecular adaptation under standard chemotherapy, as well as under combined chemotherapy and immune checkpoint inhibition with durvalumab. These analyses provided insights into therapy-induced transcriptional reprogramming and mechanisms of response and resistance in TNBC [2].

Beyond bulk transcriptomics, the institute further strengthened its capabilities in spatial transcriptomics and proteomics. By integrating multiplex immunofluorescence imaging (CellDIVE) with spatial gene expression platforms such as GeoMx and Visium, both stromal and immune components of the tumor microenvironment were analyzed in situ. Particular emphasis was placed on TNBC treated with immune checkpoint inhibitors and on invasive lobular breast cancer, enabling a spatially resolved characterization of tumor–microenvironment interactions.

To support these efforts, new high-throughput targeted and whole-exome RNA sequencing technologies were implemented in 2025, enabling large-scale transcriptomic analyses and advanced multi-omics integration. This technological expansion lays a robust foundation for future translational research linking genomic, transcriptomic, and spatial data to clinical outcomes.

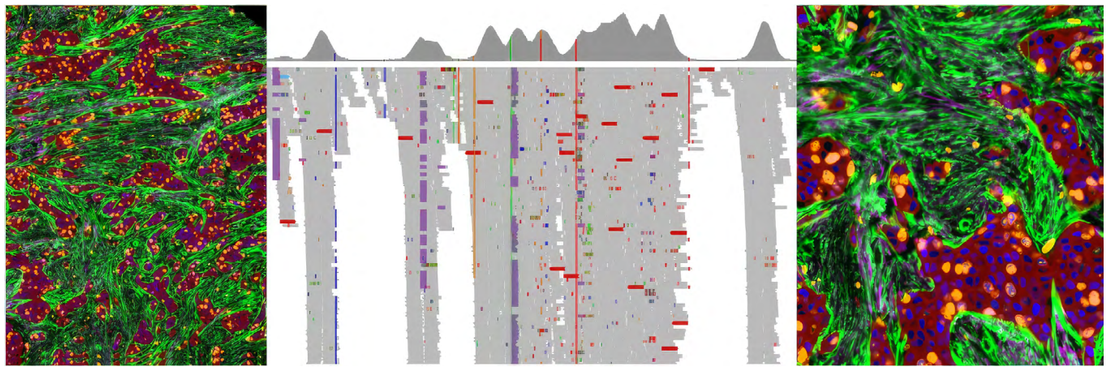


Figure 5: Mutlicolor immunofluorescence and whole-exome analysis of breast cancer

NSABP-B59/GeparDouze: Heterogeneity of TNBC

In the NSABP-B59/GeparDouze translational substudy, 494 pre treatment biopsies from early TNBC were profiled (2,549 genes; HTG EdgeSeq), and tumors were assigned to AIMS and TNBC gene expression subtypes.

A predefined 126 gene panel (covering immune, proliferation, and stromal genes) confirmed that immune and proliferation signals were associated with pathological complete response (pCR) in both arms. However, for EFS, a subset of immune genes (e.g., HLA A, HLA B, IL6R) was significant only in patients treated with atezolizumab (IL6R interaction p=0.017). These signatures are consistent with prior GeparNuevo results and formed the basis of the current assay approach.

Gene expression subtyping underscored marked biological heterogeneity in early TNBC: immune rich tumors achieved the highest pCR rates and better EFS, while stromal high tumors had lower response rates and poorer outcomes. Although the overall NSABP-B59/GeparDouze result was negative for EFS, biomarker analyses identified candidate niches (notably BL2 and LAR), where atezolizumab may numerically enhance pCR rates. Immune genes (HLA A, HLA B, IL6R) emerged as promising predictors of long term benefit with checkpoint inhibitors and merit prospective validation. Together with GeparNuevo derived signatures, these data support immune based stratification and biomarker enriched trial designs for neoadjuvant immunochemotherapy in early TNBC.

NSABP-B59/GeparDouze: Oncobiome

The EU-funded Oncobiome project, launched in 2019, was completed in June 2025. The consortium comprised 17 partner teams from nine European countries and Canada **Link .** The aim was to identify and validate specific microbial signatures (Gut OncoMicrobiome Signatures, GOMS) associated with cancer development, prognosis, and therapy response focusing on breast, colon, lung cancer, and melanoma. In total, 5,339 cancer patients and 4,535 healthy controls participated, with up to 12,059 stool specimens sequenced within the ONCOBIOME network. In the NSABP-B59/GeparDouze study, GBG facilitated the collection of stool samples from over 400 patients. RNA-based evaluations were performed in parallel on core biopsies.

ONCOBIOME generated three main translational outputs: (i) **diagnostic tools for gut dysbiosis** (e.g., an omics based scoring framework using GOMS and circulating markers), (ii) **candidate biomarker panels** classifying microorganisms by their putative impact on antitumor immunosurveillance, and (iii) **microbiota modulating interventions** (dietary strategies, live biotherapeutics, fecal microbiota transplantation) under clinical evaluation to enhance therapy efficacy or mitigate toxicity [3-5].

AI Meets Research

Artificial Intelligence (AI) is increasingly emerging as a valuable tool in cancer research, with promising but still evolving applications. In pathology, AI-based image analysis aids in tumor detection, grading, and biomarker quantification, potentially improving consistency and efficiency. Machine learning applied to clinical data, including electronic health records and genomic profiles, can reveal patterns that support patient stratification and inform treatment decisions. While these tools offer potential to advance precision oncology, their integration into routine clinical practice remains in early stages - challenges related to data quality, standardization, and model interpretability must be addressed prior to widespread adoption.

Nevertheless, AI is increasingly complementing established methods and is poised to play a decisive role in the future of cancer research.

Notably, AI is already indispensable in researchactivities: for example, in 2023, histological tissue sections in the INSEMA study were evaluated using AI.

GBG continuously engaged in multiple ongoing AI-related projects, dedicated to exploring novel approaches and driving progress in AI-driven cancer solutions.

New project proposals are welcome, including from groups currently not represented in any GBG subboard.

For more information please visit our website

1. Denkert, C., et al., Dynamics of molecular heterogeneity in high-risk luminal breast cancer-From intrinsic to adaptive subtyping. Cancer Cell, 2025. 43(2): p. 232-247.e4.
2. Denkert, C., et al., Molecular adaptation to neoadjuvant immunotherapy in triple-negative breast cancer. Cell Reports Medicine, 2024. 5(11).
3. Zitvogel, L., et al., Impact of the ONCOBIOME network in cancer microbiome research. Nat Med, 2025. 31(4): p. 1085-1098.
4. Fidelle, M., et al., A microbiota-modulated checkpoint directs immunosuppressive intestinal T cells into cancers. Science, 2023. 380(6649): p. eabo2296.
5. Thomas, A.M., et al., Gut OncoMicrobiome Signatures (GOMS) as next-generation biomarkers for cancer immunotherapy. Nat Rev Clin Oncol, 2023. 20(9): p. 583-603.

New proposals may also be submitted by groups that are currently not represented in any GBG subboard.

gbg.de/translationale-forschung

Further Information:
Dr. Bärbel Felder
Head of Translational Research

Phone: +49 6102 / 7480-217
Fax: +49 6102 / 7480-440
baerbel.felder@GBG.de

Workshops 2025
“GBG Brustkrebs kompakt erklärt”

Introduced in 2025, the “GBG Brustkrebs kompakt erklärt” workshop series is designed to support gynecologists and oncologists involved in the clinical care and research of breast cancer patients. The workshops address current therapeutic challenges, emerging treatment options and biomarkers, as well as new trial concepts. Led by renowned breast cancer specialists from major academic breast centres in Germany, the program integrates the latest evidence from international conferences with real-world clinical experience. Topics range from novel adjuvant and post-neoadjuvant treatment strategies and personalized therapy approaches in HER2+ and triple-negative disease, to practical aspects of implementing molecular and genetic testing, as well as toxicity management for new oral therapies. The initiative aims to improve patient outcomes by providing relevant, up-to-date knowledge for informed clinical decision-making and by promoting clinical trial participation as a cornerstone of progress in breast cancer care.

For more information, please visit the GBG library

Rrecordings of our workshops on our youtube channel

Molekulare Testungen bei Brustkrebs kompakt erklärt – endlich Klarheit
Molecular testing for breast cancer explained in a nutshell – clarity at last
06.05.2025 and 24.09.2025

Prof. Dr. Thomas Decker, Prof. Dr. Kerstin Rhiem, Prof. Dr. Carsten Denkert
Molecular and genetic testing are playing an increasingly important role in breast cancer therapy. However, such testing is still too often omitted or performed too late to impact clinical management. This workshop focused on the rationale for comprehensive molecular testing, ideally performed at the time of metastatic disease diagnosis, especially in HER2- cases. Indication, reimbursement, and documentation are less complex than they may initially seem.


Prof. Dr. Thomas Decker


Prof. Dr. Kerstin Rhiem


Prof. Dr. Carsten Denkert

Brustkrebs ist nicht gleich Brustkrebs: Fokus auf das lobuläre Karzinom
Not all breast cancer is the same: Focus on lobular breast cancer
19.05.2025 and 07.10.2025

Prof. Dr. Carsten Denkert, Prof. Dr. Maria Margarete Karsten, Prof. Dr. Sibylle Loibl and Dr. Johannes Holtschmidt
Invasive lobular carcinoma (ILC) presents unique challenges in diagnosis, treatment planning, and clinical study designs. The risk of relapse is often be underestimated in routine practice, as clinical decisions for invasive ductal carcinoma may not be appropriate for ILC. In this practice-oriented online workshop, experts from pathology, clinical care, and research provided an up-to-date overview of the biological and clinical aspects of ILC, with a special focus on the LOBSTER study.


Prof. Dr. Carsten Denkert


Prof. Dr. Maria Margarete Karsten


Prof. Dr. Sibylle Loibl


Dr. Johannes Holtschmidt

KN522 und keine pCR? Optimierte postneoadjuvante Therapie beim TNBC – Was können wir aus der metastasierten Situation lernen?
KN522 and no pCR? Optimized post-neoadjuvant therapy for TNBC - what can we learn from the metastatic situation?
24.06.2025 and 17.11.2025

Prof. Dr. Frederik Marmé, Dr. Johannes Holtschmidt
While adjuvant pembrolizumab monotherapy aligns with current international guidelines, the risk of relapse and death remains high for patients without pathological complete response (pC) after neoadjuvant therapy for triple-negative breast cancer (TNBC). Current treatment options including pembrolizumab, capecitabine, olaparib, and antibody-drug conjugates (ADCs), may be given individually or in combination, ideally within clinical trials. This workshop provided guidance on optimal treatment selection, with a focus on emerging data from ADC therapies in metastatic settings.


Prof. Dr. Frederik Marmé


Dr. Johannes Holtschmidt

Adjuvante endokrine Therapie – Neues vom ASCO 2025: adjuvant SERD und/oder CDK4/6-Inhibitoren?
Adjuvant endocrine therapy – News from ASCO 2025: adjuvant SERDs and/or CDK4/6 inhibitors?
01.07.2025

PD Dr. Laura Michel, Prof. Dr. Frederik Marmé
This workshop addressed the latest developments in adjuvant endocrine therapy for HR+ breast cancer, with a particular emphasis on new data regarding selective estrogen receptor degraders (SERDs) and CDK4/6 inhibitors. The discussion focused on potential benefits and drawbacks of adjuvant CDK4/6 inhibitor therapy, stressing the importance of individualized treatment decisions based on patient risk profiles, preferences regarding side effects, and the need for therapy monitoring.


PD Dr. Laura Michel


Prof. Dr. Frederik Marmé

Weg frei für die personalisierte Therapie beim HER2+ Mammakarziom: Erst Testen, dann gezielt therapieren!
Paving the way for personalized therapy for HER2+ breast cancer: test first, then treat specifically!
08.07.2025

Prof. Dr. Marion van Mackelenbergh, PD Dr. Mattea Reinisch, Dr. Theresa Link
This workshop focused on personalized therapy for HER2+ breast cancer, emphasizing the role of chemotherapy-free regimens guided by *PIK3CA* mutation status and recent clinical trial data. The rationale for combining the PI3K inhibitor inavolisib with endocrine therapy and trastuzumab/pertuzumab as a chemotherapy-free neoadjuvant regimen in the GeparPiPPa trial was discussed, based on observed reduced sensitivity to neoadjuvant anti-HER2 therapy with chemotherapy in *PIK3CA*-mutant, HR+/HER2+ breast cancer.


Prof. Dr. Marion van Mackelenbergh


PD Dr. Mattea Reinisch


Dr. Theresa Link

Nebenwirkungsmanagement und Therapiebegleitung: Praxiswissen für orale Tumortherapien
Side effect management and therapy support:
Practical knowledge on treatment with oral tumor therapies
09.09.2025

Dr. Athina Kostara, PD Dr. Laura Michel, Dr. Theresa Link
This workshop provided practical strategies for managing uncommon side effects associated with new targeted oral anti-tumor therapies. Oral administration of these agents presents unique challenges for both patients and healthcare teams, particularly in the outpatient setting.


Dr. Athina Kostara


PD Dr. Laura Michel


Dr. Theresa Link

Statistische Methoden in der Brustkrebsforschung
Statistical methods in breast cancer research
18.09.2025

Vanessa Schaser, Dr. Natalie Filmann
Statistical analysis is a fundamental component of high-quality breast cancer research. Selecting the appropriate statistical methods for specific research questions is crucial, as is the correct interpretation of results and awareness of potential pitfalls.


Vanessa Schaser


Dr. Natalie Filmann

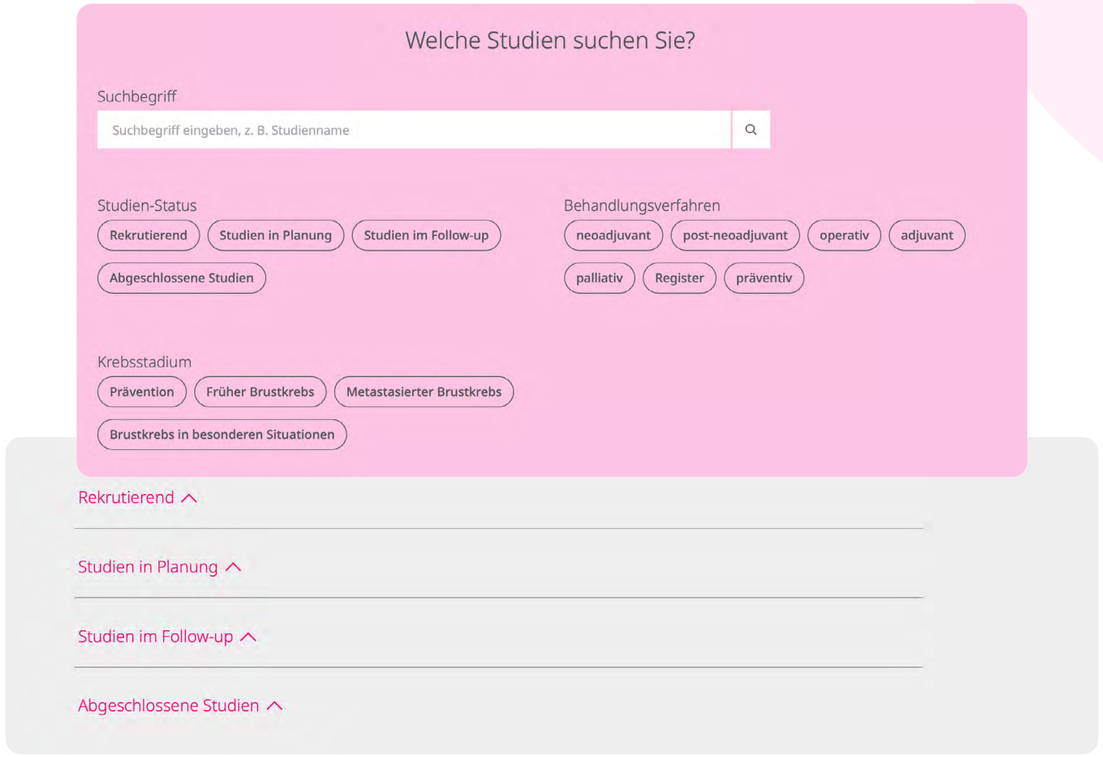
Immunisierung in der Onkologie – Zukunftsstrategie bei Brustkrebs?
Immunization in oncology – a future strategy for breast cancer?
02.12.2025

Prof. Dr. Marcus Schmidt, Prof. Dr. Marion van Mackelenbergh
Can targeted immunization become an integral part of breast cancer treatment in the future? This workshop provided a structured overview of current developments and study concepts in cancer vaccination, including the FLAMINGO-01 study. Opportunities and limitations of adjuvant vaccination therapy in HER2+ breast cancer were discussed.


Prof. Dr. Marcus Schmidt


Prof. Dr. Marion van Mackelenbergh

How to use our new Study Finder on GBG website



The well-known Study Finder at the end of the Annual Scientific Report has been replaced by a digital and optimized version on our website.

The user interface offers a range of search parameters: among other things, you can search for relevant studies directly using a search term such as the study name or a drug name. You can also refine your search by selecting the study status (recruitment, planned, follow-up, completed), the cancer stage (screening, early breast cancer, metastatic breast cancer, breast cancer in special situations), and the treatment modality (neoadjuvant, post-neoadjuvant, surgical, adjuvant, palliative, preventive, registry).

If your search is successful, you will see tiles below the Study Finder with study suggestions that match the search criteria. This tile view contains all the necessary information to give you a brief overview of the studies. If you are interested in the details of the study, you can click through to study page with just one click.

Click here for more info

New feature on our website: Easily find participating study centers

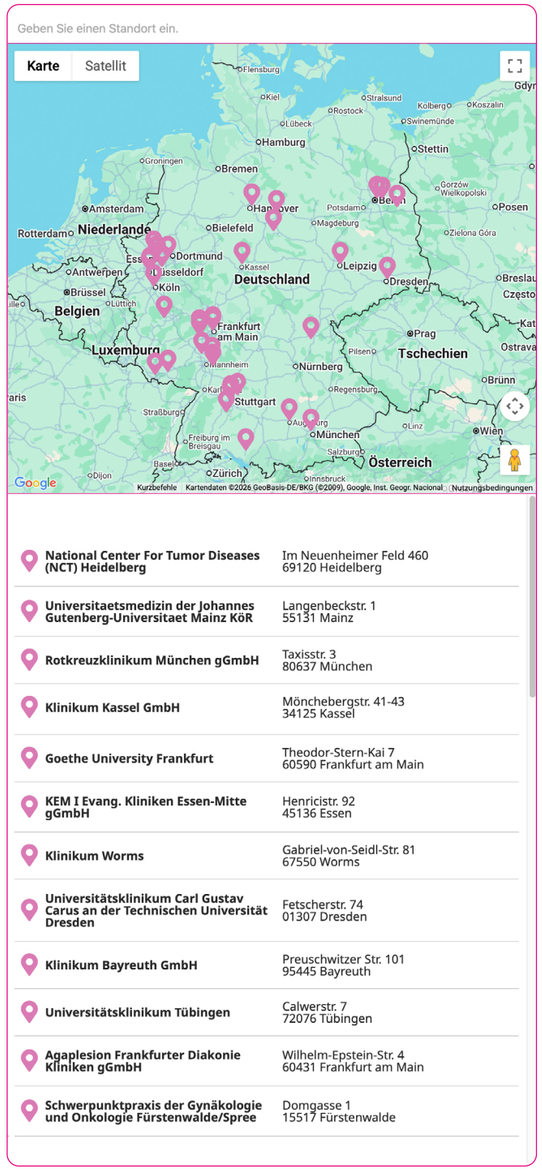
In addition to our new digital Study Finder, we have introduced another helpful feature on our website to further simplify access to our clinical trials.

Physicians and patients seeking a participating study center – following an initial medical consultation and referral - can now easily locate suitable centers directly on our website. An interactive map displays all participating centers for each study, including address details and direct contact options to schedule an on-site appointment. This makes the pathway to study centers faster and more convenient for patients.

Additionally, by using the standard search field, users can display the distance to nearby centers from a selected location, allowing for a quick preselection of study sites in close proximity.

Currently, this new feature is available for the ELEMENT trial. Expansion to additional studies is already underway and will continue throughout 2026.

Test the new function



National Center For Tumor Diseases (NCT) Heidelberg	Im Neuenheimer Feld 460 69120 Heidelberg
Universitaetsmedizin der Johannes Gutenberg-Universitaet Mainz KöR	Langenbeckstr. 1 55131 Mainz
Rotkreuzklinikum München gGmbH	Taxisstr. 3 80637 München
Klinikum Kassel GmbH	Mönchebergstr. 41-43 34125 Kassel
Goethe University Frankfurt	Theodor-Stern-Kai 7 60590 Frankfurt am Main
KEM I Evang. Kliniken Essen-Mitte gGmbH	Henricistr. 92 45136 Essen
Klinikum Worms	Gabriel-von-Seidl-Str. 81 67550 Worms
Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden	Fetscherstr. 74 01307 Dresden
Klinikum Bayreuth GmbH	Preuschwitzer Str. 101 95445 Bayreuth
Universitätsklinikum Tübingen	Calwerstr. 7 72076 Tübingen
Agaplesion Frankfurter Diakonie Kliniken gGmbH	Wilhelm-Epstein-Str. 4 60431 Frankfurt am Main
Schwerpunktpraxis der Gynäkologie und Onkologie Fürstenwalde/Spree	Domgasse 1 15517 Fürstenwalde

Thank you ...

... **to all patients** who have participated or are still participating in our trials. Without you, our clinical studies would be worthless.

... **to all our Study Chairs,** our investigators and all their team members at participating centers for their commitment and efforts so far.

... **to all our partner organizations,** collaborating study groups, Independent Data Monitoring Committees (IDMC), Ethics Committees and competent authorities for their great support.

... **to all members of our Subboard and Scientific Board members** for their ideas, knowledge, and tireless ambition to advance clinical research.

... **to all our pharmaceutical partners** for providing drugs and study budget to realize our clinical research projects.

SOME IMPORTANT LINKS

GBG

GERMAN
BREAST
GROUP

Leading in Breast Cancer Research

Impressum:
GBG Forschungs GmbH
Dornhofstraße 10
63263 Neu-Isenburg
GERMANY
www.GBG.de