BIG
RESEARCH
IN FOCUS

November 2024 - issue n°21

FIGHTING BREAST CANCER AROUND THE GLOBE

25

25 YEARS OF PROGRESS FOR PEOPLE WITH BREAST CANCER

Co-funded by
the European Union

BIG Breast International Group

EDITORIAL

BIG'S LEGACY – CELEBRATING 25 YEARS OF PROGRESS IN BREAST CANCER RESEARCH

As 2024 marks the 25th anniversary of the Breast International Group (BIG), we are reminded of the incredible journey that began with a dinner conversation between Professor Martine Piccart and the late Professor Aron Goldhirsch, the co-founders of BIG. What started as a shared vision for a collaborative, international approach to breast cancer research has since evolved into the world's largest network solely dedicated to breast cancer research. Today, BIG, an international non-profit organisation, unites over 55 academic research groups spanning 6 continents, engages more than 10,000 breast cancer specialists, and has seen over 100,000 patients participate in approximately 60 BIG studies. Through collaboration, resilience, and a mutual commitment, we have shaped a legacy that impacts millions worldwide.

This special edition celebrates 25 years of progress and highlights BIG's pivotal role in redefining the global breast cancer research landscape. For the themed article, it was a privilege to gather first-hand insights from, naturally, Dr Martine Piccart, whose founding of BIG and visionary leadership has inspired so many, as well as Drs David Cameron, Larry Norton, Sherene Loi, Gustavo Werutsky, Carolyn Straehle, Tanja Spanic, and Matteo Lambertini. Each has contributed to BIG in unique ways, offering expertise from both its early days and more recent involvement. We are thankful for their generosity in sharing their stories and their vision for the future, captured by medical journalist Jenny Bryan in the cover article "25 years of progress for people with breast cancer".

The size of this report reflects the rich diversity of content we've gathered, covering news and activities from the BIG network and its members, in addition to updates from BIG Headquarters and *BIG against breast cancer*, BIG's philanthropic entity. It also includes the latest developments on BIG studies and conferences, as well as a comprehensive overview of BIG clinical trials, studies, and publications. A big thank you to all our member groups for their invaluable contributions!

The backbone of BIG: our member groups

Central to BIG's success are the member groups that make up our network. Each group brings distinctive expertise and perspectives, fostering an environment where international collaboration thrives. The seamless sharing of ideas and data has enabled us to scale research initiatives that single institutions could only dream of tackling alone. This collective effort has led to reduced redundancy in clinical trials, resulting in more efficient studies and a greater local and global impact.

BIG studies: shaping the future of breast cancer care

BIG's legacy is built on landmark trials such as HERA and APHINITY, which established trastuzumab as a standard therapy and helped transform HER2-positive breast cancer from one of the most aggressive types into a highly treatable condition, significantly improving disease-free survival and long-term outcomes for patients with this diagnosis. Another practice-changing trial, MINDACT, demonstrated that MammaPrint® – a 70-gene test – can identify early-stage breast cancer patients who may safely avoid chemotherapy, reducing unnecessary treatment for many patients. Further advancing the field, the AURORA programme enhances our understanding of metastatic breast cancer, the POSITIVE study offers hope to young women who aspire to motherhood after treatment, the EXPERT study explores ways to reduce or eliminate radiation therapy, the OlympiA trial shows that the PARP inhibitor olaparib significantly reduces the risk of invasive breast cancer recurrence, second cancers, or death in BRCA1/2 mutation carriers, the APPALACHES study investigates better treatment options for the elderly, and the International Male Breast Cancer Programme aims to optimise care for men with breast cancer.

These are just a few examples of BIG studies that have improved the lives of millions worldwide and that continue to set the standard for progress in breast cancer care.

To all our member groups, researchers, and partners: thank you for being an integral part of BIG's legacy. Your dedication and collaboration are what make the success of this network possible. Together, we celebrate not just 25 years of progress, but the future we will continue to build.

We are committed to expanding our research to include underrepresented populations and ensuring global inclusivity, addressing diverse breast cancer subtypes and demographic groups, as well as reaching low- and middle-income countries where breast cancer care is less accessible and mortality much higher.

Patients are at the heart of our mission

Central to BIG's philosophy is the belief that research must resonate with the people it aims to help. This belief is embodied in the BIG Patient Partnership Initiative (BIG-PPI), which integrates patient perspectives into research design and execution. By involving patient partners, BIG ensures that its studies align with the real-world needs and experiences of those living with breast cancer, making research outcomes more meaningful and impactful.

BIG's strength lies not only in its innovative research but also in the partnerships that support its mission. Alliances with the Breast Cancer Research Foundation (BCRF, US) and grants from the European Union, among others, have provided essential funding for the work involved in complex trials that push the boundaries of current knowledge. Unlike many studies driven entirely by the pharmaceutical industry, BIG's research is not guided by commercial interests but by a commitment to advancing science for the benefit of patients and the broader breast cancer community. This dedication to maintaining scientific independence, even amidst challenges, ensures that our research remains patient-focused and adheres to the highest ethical standards.

As we look to the future, the challenges are clear: rising costs, a complex funding landscape, the need for balanced partnerships with industry partners, regulatory demands, and the constantly evolving nature of breast cancer treatment. Yet, the hope remains strong. BIG's commitment to collaboration, innovation, and patient-centric research is steadfast as we strive for breakthroughs that will continue to transform lives.

We extend our deepest gratitude to our member groups, researchers, colleagues, partners, individual donors, supporters, and all other stakeholders for their tireless efforts. Most importantly, we thank the tens of thousands of patients who have volunteered to participate in our studies and, in doing so, have become our partners in developing the cures of tomorrow.

Thank you for being a part of this journey. Here's to 25 more years of progress and hope.

Enjoy the reading.

BIG's editorial team

Together, we are BIG

CONTENTS

1	EDITORIAL
2	BIG RESEARCH: 25 YEARS OF PROGRESS
12	BIG NETWORK
58	BIG STUDY UPDATES AND CONFERENCES
66	BIG STUDIES - OVERVIEW
70	ABOUT BIG

BIG's legacy

25 YEARS OF PROGRESS FOR PEOPLE WITH BREAST CANCER

In the 25 years since BIG was established, the treatment of breast cancer has been transformed and many of the clinical trials carried out through the BIG network have contributed to the advances that are benefitting today's patients. Medical journalist, Jenny Bryan, finds out how BIG has evolved into the largest global network of academic breast cancer research groups, and hears about its achievements, strengths and challenges, as well as hopes for the next 25 years of breast cancer research.

> *"We need to say a huge thank you to everyone across the globe who has made BIG what it is today. Without their knowledge, energy, commitment and enthusiasm, BIG wouldn't be the highly successful organisation it is today." David Cameron, BIG Chair*

BIG was 'born' over a dinner between its founders Professor Martine Piccart and the late Professor Aron Goldhirsch at the end of a meeting of the European Organisation for Research and Treatment of Cancer (EORTC) Breast Cancer Group in 1995. Aron already led the International Breast Cancer Study Group (IBCSG), while the North American Breast Cancer Group (NABCG) brought together multiple regional groups, but both saw the value of building a new global network to strengthen and accelerate breast cancer research, starting in Europe.

"Breast cancer research in Europe was fragmented and much less effective than in the US where groups had joined together. In Europe, there were national groups and there was EORTC and IBCSG, but even those struggled to conduct large clinical trials with enough speed," recalls Piccart, now President of *BIG against breast cancer*[1], Senior Advisor to BIG, and Research Director at Institut Jules Bordet, Brussels, Belgium. "We wanted to build a European organisation in which individual breast cancer research groups could identify questions where there was an obvious need to join forces, without losing their independence."

BIG did not stop with Europe and, for BIG Chair, Professor David Cameron, the organisation's great contribution has been to build a place of mutual respect and collaboration across all the continents of the world.

"This has enabled academic groups to share and develop study ideas, and carry out those studies on a global scale," he explains. "In Europe, for example, where each country has one or more breast cancer research groups, BIG has helped build collaboration and cooperation, leading to greater harmonisation of research with fewer studies addressing the same question than would have been the case 20 or 30 years ago."

Dr Larry Norton, Founding Scientific Director of the Breast Cancer Research Foundation (BCRF), a generous funder of many BIG projects, agrees:

> *"BIG is the epitome of international cooperation in cancer research, especially in clinical trials, and BCRF considers that such cooperation is essential for ridding the world of breast and other forms of cancer. BIG is such a potent conceptual and operational force in this arena that it would be impossible for BCRF not to support its work."*

He explains that, 25 years ago, exciting advances were starting to be made about the molecular biology of cancer, but the scientists needed to understand what questions needed answering, and the clinicians needed to understand the power of the science. It soon became apparent that, by joining forces, they could answer key questions about cancer more quickly, avoid duplication of effort, and benefit from common knowledge.

"Through BIG, there are now regular meetings and discussions between breast cancer researchers in North America and globally, including younger investigators, to decide what to study and how to conduct research," says Norton.

BIG membership has enabled breast cancer researchers in the Latin American Cooperative Oncology Group (LACOG) to participate in major international trials to which they would not previously have had access, explains LACOG Executive Director, Dr Gustavo Werutsky, who recently joined the BIG Executive Board.

"Across Latin America, there are 200,000 people with breast cancer, and they are younger and present with more locally advanced disease than in North America and Europe," he points out. "Being able to participate in BIG trials is an important opportunity for these patients to have access to new cancer therapies and to de-escalation studies that can have major benefits for healthcare systems in developing countries," he says.

"Joining the BIG Executive Board presents me with the possibility of contributing to a new era of clinical trials that will incorporate decentralised methods, digital health technologies, and increased clinical trial access and diversity," he adds.

In Australia and New Zealand, BIG has also had a significant impact on the range of research in which breast cancer specialists – and their patients – can participate, despite the countries' relatively small populations spread over large and often remote areas.

Through BIG, academic researchers in Breast Cancer Trials Australia and New Zealand (BCT-ANZ) have contributed to practice-changing studies, such as the HERA and APHINITY studies of anti-HER2 therapies in women with HER2-positive breast cancer, and the SOFT and TEXT trials of exemestane and ovarian suppression in young women with breast cancer.

"BIG has made it possible to harness the power of the breast cancer research community and enable groups such as Breast Cancer Trials to expand their research portfolio and bring more significant trials to patients in Australia and New Zealand," says Dr Sherene Loi, a member of both BIG's Executive Board and the Foundation Board of the International Breast Cancer Study Group (IBCSG).

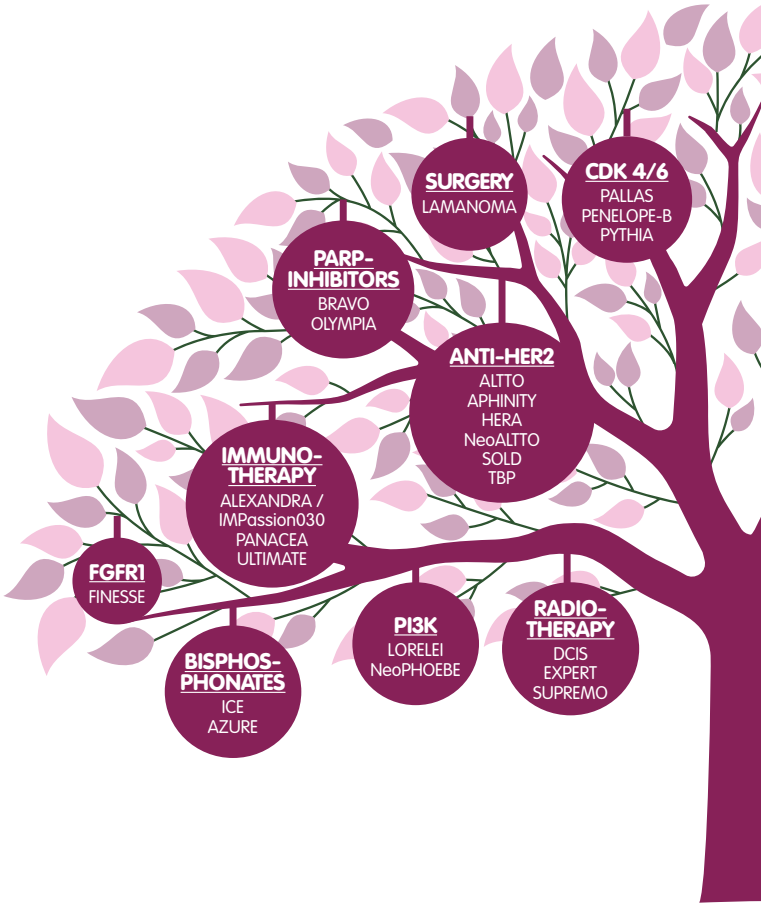
She explains that BIG and IBCSG have complementary roles in furthering breast cancer research, with great advantages in rapidly bringing new treatments to patients.

"It all comes down to scale and, by bringing together so many cooperative groups, BIG can address important questions, including about rare sub-groups of breast cancer, such as in the OlympiA study in patients with BRCA1/2 mutated breast cancer, where no individual research group would have had enough patients to get the answers," says Loi.

> *"The landscape is changing for breast cancer research and our focus is shifting to genomic subsets of patients, and to optimising, escalating or de-escalating treatment based on novel technologies for identifying tiny amounts of residual disease." Sherene Loi*

WHICH BIG TRIALS HAVE BEEN MOST IMPORTANT?

Since BIG was established as a legal entity in 1999, more than 60 studies have been carried out under the BIG umbrella, some of them landmark trials whose results have changed clinical practice, and others providing important nuggets of information that have been the building blocks for subsequent advances in patient care *(see Figure 1, BIG Trials Tree).*



In 1999, HER2-positive breast cancer was one of the hardest forms of the disease to treat. Trastuzumab (Herceptin®) had recently been approved in the US for the treatment of metastatic HER2-positive breast cancer, and EU approval was expected in 2000. However, there were still many questions about the wider use of trastuzumab.

Unsurprisingly, many at BIG consider the HERA and APHINITY trials of anti-HER2 therapies to be among the most important carried out under the BIG umbrella. HERA showed that, among patients with HER2-positive primary breast cancer who had completed (neo)adjuvant chemotherapy, one year of trastuzumab treatment reduced the risk of breast cancer recurrence and the risk of death by around 25%. Two years of treatment did not offer any additional benefit.

"HERA was a very important trial, not only for its results but because it consolidated BIG's position in breast cancer research and showed what could be achieved with our pharmaceutical partners. Our investigators were able to recruit 5,000 patients with a relatively rare subtype of breast cancer in only three years, so it was a phenomenal achievement," says Piccart.

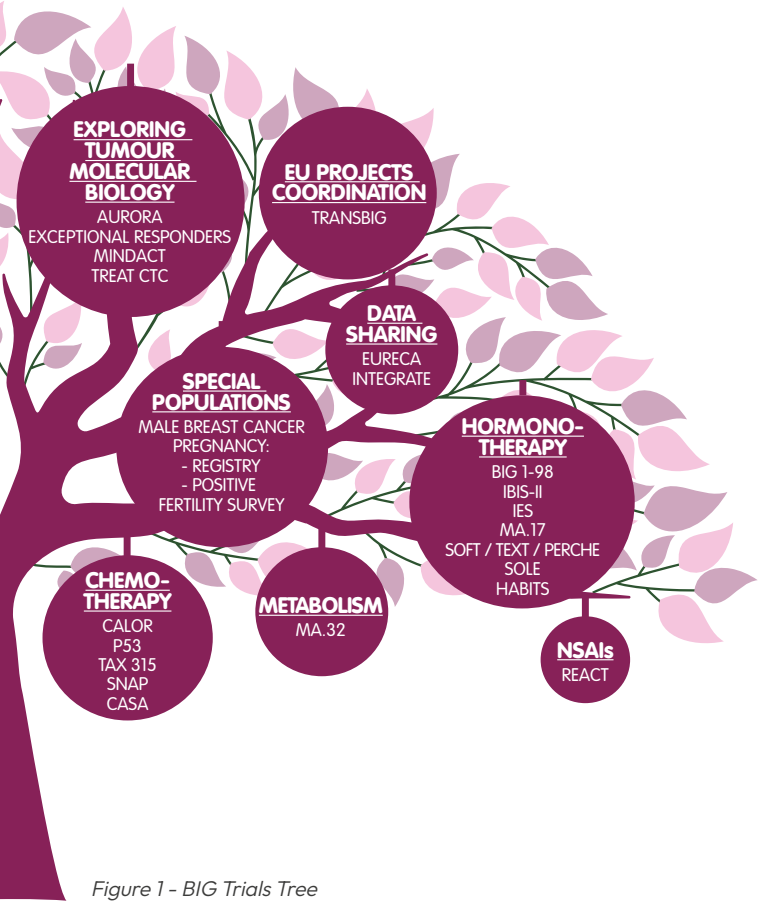


Figure 1 - BIG Trials Tree

"HERA was my first experience of setting up such a trial, and it was very exciting to establish an academic-industry partnership, with most of the BIG network's groups participating in the study," recalls BIG Deputy CEO and Research Support Director, Carolyn Straehle. "Discussions started in late 2000/early 2001 and, by 2005, the first positive results were presented at the ASCO congress!" she adds.

The APHINITY trial, in a similar group of patients, started after HERA and showed that dual anti-HER2 therapy with pertuzumab and trastuzumab, together with chemotherapy, reduced breast cancer recurrence or deaths by 19% compared to trastuzumab and chemotherapy alone.

"HERA helped put trastuzumab on the map and, together with APHINITY, has changed clinical practice. Both studies recruited at high speed across continents and showed the advantages of being able to call upon large numbers of academic breast cancer researchers within the BIG network," says Cameron.

Another practice-changing study is OlympiA, which showed that the PARP inhibitor olaparib (Lynparza®) reduces the risk of invasive breast cancer recurrence, second cancers, or death by 42% when given to patients with high-risk HER2-negative primary breast cancer who have an inherited BRCA1 or BRCA2 gene mutation and have completed all standard anti-cancer treatments.

"Logistically, OlympiA was a difficult trial because it focused on a very small population of patients who carried BRCA mutations and developed high risk breast tumours," Piccart explains. "It was a product of the relationship that BIG had built with the BCRF in the US, and it demonstrated the importance of worldwide collaboration in answering a question that would have been impossible for smaller groups because they could not have found enough patients."

For Norton, the stand-out example of such successful collaboration has been the AURORA Programme in the US and EU investigating the molecular aberrations occurring in metastatic breast cancer.

> *"AURORA could not have happened without the BIG and US leadership, and the landmark discoveries that were made were an illustration of the power of international collaboration and cooperation," says Norton.*

Norton explains that, when AURORA was conceived, research was focused on primary breast cancer, but there was a growing realisation of the need to bring together leaders in the molecular biology of metastatic breast cancer. Two separate but interrelated projects were aligned to the availability of samples in North America and Europe, with major papers subsequently published on key findings.

"The most important discoveries from this research were the significance of the microenvironment of metastatic tumours, particularly the immune system, and that cancers behave differently at the molecular level depending on the organ that they are in. This means that we need to broaden our attention from the cancer cell to its microenvironment and the tissues that metastatic cancer cells are in contact with, especially the white blood cells," says Norton.

Also on most people's list of successful (and popular) BIG trials is POSITIVE, a study of the pregnancy outcomes and safety of interrupting endocrine therapy for young women with endocrine-responsive breast cancer who want to become pregnant. In 2022, POSITIVE showed that the rates of conception and childbirth in the women who interrupted their endocrine therapy after 18-30 months were similar to, or a little higher than, rates in the general public. Just as importantly, these women had a similar risk of breast cancer recurrence to those in previous studies who did not interrupt their endocrine treatment. *(See also the themed article in BIG Research in Focus 18, April 2023)*.

> *"POSITIVE is my favourite trial and very close to my heart as it is so important to women with breast cancer who want to have children after their diagnosis. It was very difficult to get funding, and everyone had to work hard to make it happen," smiles Dr Tanja Spanic, whose own breast cancer was diagnosed when she was 26.*

"Before POSITIVE, doctors were still unsure what to tell these women with hormone-receptor positive breast cancer, but the early results of POSITIVE have been very reassuring," adds Spanic, now President of Europa Donna Slovenia and Past President of Europa Donna – the European Breast Cancer Coalition, and a member of BIG's Patient Partner Initiative (BIG-PPI).

PUTTING PATIENTS AT THE CENTRE OF BIG'S RESEARCH

When BIG wrote its first protocols, there was little role for patients in breast cancer trials, except as participants; but that is changing. In countries including the US, Canada, the UK, Australia, France, and Spain, breast cancer patient advocacy groups play an active role in advising on many aspects of study development, from initial concept and design to patient-centric endpoints, recruitment, and dissemination of results.

Even so, as Cameron points out, patient involvement in clinical trial design is evolving and there is still some way to go.

"In BIG, we want patients to participate in the research engine in an equal, respectful partnership so they are able to influence all aspects of trial development from design, oversight, and analysis right through to publication. They need to be in the 'inner circle' so that their perspective on what needs to be asked in clinical trials – and how it's asked – is taken into account," he says.

BIG has worked with patient advocates through Europa Donna since the early 2000s, but in 2019, it launched the BIG-PPI to integrate the patient perspective into all aspects of the clinical trial lifecycle, from identifying priorities in strategic planning to designing, developing, and executing clinical trials. *(See also the themed article on the BIG-PPI in BIG Research in Focus 20, April 2024)*.

Spanic, who is a member of the Steering Committees of POSITIVE, OlympiA, and the BIG-PPI, believes that it is essential that patient advocates are involved in development of breast cancer clinical trials – not just as external advisors, but integrated within a research organisation.

"It's more than 15 years since people first started talking about patient-centric trials, but in reality, we are still not there. Regulatory agencies are now asking for the patient perspective to be included in trial design, and it was very gratifying that the European Medicines Agency has adopted the Principles of Successful Patient Involvement in Cancer Research, which was developed through a European Council initiative and published in 2021," she says.

Spanic stresses the importance of involving patients at the start of the design process, not when the protocol has been drafted. This is because of the difficulty of adding more patient-relevant questions or changing logistical details, such as numbers of hospital visits or samples, further down the line.

"We know that trials need to be clinically and scientifically relevant, but they also need to be patient-relevant. For example, if you include repeated quality-of-life questionnaires with dozens of very similar questions, patients will get tired of answering them, so we need to find ways to make them more attractive to patients," says Spanic. She would also like to see future trials with longer follow-up of five or even 10 years to make them more relevant to patients' lives.

Spanic believes that the BIG-PPI is a good model for other cancer research organisations about involving and training patients, so they do not need to 'reinvent the wheel'.

"At BIG, we now receive education and training in breast cancer research and trial design, with dedicated webinars and in-person meetings, and we receive a lot of information in advance of the meetings when trials are discussed. That means we have time to become well prepared so we can give informed insights from the patient viewpoint," she explains.

BEHIND THE SCENES AT BIG

Since 1999, the team at BIG's headquarters has grown from just one to 40. Brussels was the obvious choice for the organisation's base because of its proximity to the Institut Jules Bordet where Piccart worked, and many clinicians and researchers at the institute have been involved with BIG over the years.

Straehle, who was the first BIG employee, explains that, in the early days, BIG focused on clinical trials in the adjuvant setting – treatment of primary breast cancer after tumour removal. Then, around 2013, the strategic decision was taken to extend into research on metastatic breast cancer in the light of the continuing unmet need to better understand the disease in order to develop more effective treatments. As a result, BIG started to build the strong scientific and research operations teams that are present at BIG HQ today and, in 2016-2017, an in-depth governance review led to a significant expansion of the BIG Executive Board (EB) to ensure that its member groups from around the world were better represented, as well as all the clinical and scientific disciplines involved in BIG trials.

> *"When we started in 1999, I would say that BIG was an idea that was being piloted. Twenty-five years later, we are a mature, professionally run, non-profit organisation with a strong and proud track record in practice-changing research. In some ways, little has changed but, in other ways, everything has changed," says Straehle.*

There are still the scientific meetings where BIG member groups present study concepts for discussion, improvements and decisions but, thanks to the larger EB that is representative of the entire BIG network, a much broader range of studies and projects is considered and, in many cases, approved. Keeping such a large network up to date with plans and progress is a considerable task, and advances in digital communications have, of course, been very valuable. Although Covid and funding limitations have reduced travel by BIG staff to meet member groups in their own countries in recent years, BIG recognises the value of such meetings and hopes that more can be carried out in future.

"For me, the strength of the BIG network is its members' shared passion for the best possible research that will lead to real improvements in patients' lives. Beyond that is a belief that we need to maintain our scientific independence, irrespective of who is funding our studies. Working together across borders and cultures is surely the best way to run the clinical trials to resolve the questions and challenges of breast cancer, make progress, and save lives," concludes Straehle.

ADDRESSING THE CHALLENGE OF FUNDING

Rising costs, increasingly complex clinical trials, and growing regulatory demands mean that funding for BIG's wide-ranging research programme is a constant and growing challenge for the organisation. Commercial sponsorship from pharmaceutical partners plays a valuable part in supporting some of BIG's academic research, as well as trials of new drugs. However, as Piccart explains, BIG's requirement that a trial's database is managed by one of the member groups and that the Steering Committee has responsibility for tumour samples, does not suit all companies. *(See also the themed article on Funding in BIG Research in Focus 19, November 2023).*

"We believe that the BIG model is the best one for patients, as it ensures that translational research can be carried out on tumour samples to find out, for example, whether a new treatment works in some patients but not in others. This protects patients from treatments that they don't need, and it protects society from wasting money on giving drugs to patients who won't respond," says Piccart.

Cameron suggests that it could be easier to ensure that all relevant questions are addressed in clinical trials if BIG and other research organisations can become less dependent on single, large commercial funders and move towards joint funding by multiple sponsors.

He believes that the perfect sponsor recognises that their commercial interest is not the only reason for running a trial, and that there is mutual respect between the sponsor and the academic groups who are involved, so the trial design is influenced by all parties.

"I can think of plenty of BIG trials where we have achieved that relationship – HERA, OlympiA, and AMEERA 6 to name just a few. The problem is that, while people tend to remain in academic groups for many years, there is a rapid turnover of those in sponsoring companies, so it can be hard to maintain understanding of how a partnership can work most effectively," adds Cameron.

Commercial partnerships are not the only funding model for BIG studies, and the generous scientific grants from BCRF for more than 20 years, without which studies such as AURORA would not have been possible, and BIG's recent successes in gaining EU operating and Horizon grants, have all been important.

"The EU operating grants are significant because they co-fund activities such as meetings, communications, and our work with patient partners, activities that are generally difficult to fund. But, of course, making grant applications is very time-consuming and highly competitive, and there is no guarantee of success," Straehle points out.

It was an initial EU grant of €7 million that helped fund another practice-changing academic trial, MINDACT, which showed that the 70-gene signature test, MammaPrint®, could be used to inform decisions about whether patients with early breast cancer needed chemotherapy. However, the total cost of this practice-changing study, carried out through BIG and the study sponsor EORTC, ultimately reached €47 million – requiring multiple funding sources, including pharmaceutical contributors.

In 2012, a philanthropy team was established at BIG to raise funds for academic studies, such as AURORA, POSITIVE, and EXPERT. The latter being an investigator-initiated trial to find out whether a genomic test of breast tumour tissue can identify patients at very low risk of cancer recurrence who can safely avoid radiotherapy after breast cancer surgery. Each year, the philanthropy and communications teams at BIG HQ develop public outreach campaigns, especially during Pink October, the international Breast Cancer Awareness Month, raising awareness and funds for BIG's research.

Norton explains that, while governments may provide financial support for studies with a good chance of success based on preliminary data, philanthropic fundraising is essential for funding creative research that brings new ideas and concepts into the arena. Such research is high-risk as there is a greater chance of failure than with studies based on previous positive results. However, such failure may be important in guiding future directions for research.

Philanthropic fundraising by an organisation like BCRF is less difficult in the US than in most other countries, owing to the tax deductions received by donors to non-profit organisations. Even so, breast cancer fundraisers are, of course, competing with many other worthy causes.

"The dedication of the philanthropists who support BCRF and, indirectly BIG, is remarkable. They understand the importance of science and that many of the discoveries we make in breast cancer are relevant to other cancers and, indeed, to other illnesses such as heart disease. These sorts of messages really resonate with people, together with the importance of helping not only the people they love, but the rest of humanity," says Norton.

25 YEARS OF CHANGE FOR FEMALE RESEARCHERS

Female oncologists such as Piccart and Loi have witnessed considerable changes in the role of women in breast cancer research in the 25 years since BIG was established. When Piccart was training in the US in the mid 1980s, she was impressed to see women in

oncology gaining leadership roles – something rarely seen in Europe at that time.

"Women were chairing research groups in the US, and a few became president of the American Society of Clinical Oncology (ASCO) and the American Association for Cancer Research (AACR), while leadership roles in EORTC, the European Cancer Organisation (ECO) or the European Society of Medical Oncology (ESMO) were almost exclusively occupied by men," Piccart points out.

Although Piccart never felt discrimination as a female oncologist, and went on to become president of all three of those European research organisations, she recognised the challenges faced by many women oncologists by establishing ESMO's Women for Oncology (W4O) initiative, which addresses issues faced by female oncologists aiming for leadership roles during their careers.

Despite these successes, Piccart questions whether, as a woman, she would have been able to establish BIG on her own.

"Aron and I were a duo in persuading people of the need for BIG and getting it established, and I think it needed both of us," she says. "Subsequently, colleagues were very supportive in enabling me to reach senior positions in other organisations, but I still think Europe is probably about 20 years behind the US in enabling women to achieve leadership roles," she adds.

In the early 2000s, Loi joined Piccart at the Institut Jules Bordet in Brussels for her PhD and post-doctoral studies and is convinced of the value of young women working with and being aware of female leaders.

"I firmly believe that 'you can't be what you can't see', and if young women start off in a system where they see no female leaders or they are not aware of them, they won't see themselves as leaders of the future. Women in leadership roles need to be visible to those around them, so that other women can see what's possible," says Loi, a consultant medical oncologist who headed the newly created Translational Breast Cancer Genomics and Therapeutics laboratory at the Peter MacCallum Cancer Centre, Melbourne, when she returned to Australia.

She feels that requirements for equal representation on research groups, committees and faculties, and as lab heads, award nominees, and speakers at major conferences are helping to redress the gender balance in leadership roles.

"Fortunately, there is a history of strong female leaders in breast cancer research and that has helped to encourage the younger generation of women to move forward into leadership roles. It was certainly the biggest influence on me for reaching the position I have today, but there is still room for improvement in supporting more women to become leaders," she concludes.

> *"Doing research in addition to clinical work is challenging, and balancing work and private life isn't easy. But we need to think about succession planning, inspiring younger generations to take on leading roles in BIG." Carolyn Straehle*

BECOMING A BIG MEMBER GROUP

In June 2022, the Gruppo Italiano Mammella (GIM) became the latest member of the BIG network. GIM is the largest academic breast cancer research group in Italy, with more than 100 hospitals enrolling patients in many national trials, particularly in adjuvant endocrine therapy, dose-dense chemotherapy, and fertility preservation.

"The main drivers for joining BIG were to enable our members to participate in the very important international studies run by BIG and to meet and discuss research with the brilliant people from the other cooperative groups in the network," explains GIM representative, Dr Matteo Lambertini, from IRCCS Policlinico San Martino Hospital, University of Genoa, Italy.

GIM members will participate in the recently announced OPTIMA Young study, which will investigate whether the 50-gene signature Prosigna® test can predict the need for chemotherapy in premenopausal women with ER-positive early breast cancer.

> *"Previously, we wouldn't have been involved in such a large academic study, but not only is OPTIMA Young aligned with the specialist interests of GIM, we feel we are in a good position to recruit substantial numbers of patients and make our contribution to this important BIG study," says Lambertini.*

He advises other cooperative groups with an established record of academic breast cancer research to join BIG,

given the growing cost and complexity of doing such research for a smaller organisation.

"As well as joining BIG studies led by other members, you can bring trial ideas and plans to BIG, where you will not only have access to the BIG infrastructure but also be able to discuss and refine your design with your very knowledgeable colleagues," he points out.

THE NEXT 25 YEARS

With so much promising research into more personalised treatment for breast cancer based on molecular mutations, and rapid advances in liquid biopsy and AI-based technologies, the need for BIG's global network of academic breast cancer research groups is as great as ever.

"BIG was created at a time when there was a spirit of collaboration and I hope that, despite the current global unrest and the rise of nationalism, the collaborative culture that has been so important to BIG will continue. I don't think breast cancer will disappear in the next 25 years, but I do believe that research will enable more women to be cured and treatment to be less toxic," says Piccart.

She believes that better ways of differentiating between milder and more aggressive forms of cancer will mean shorter endocrine treatment for some patients with ER-positive disease. She also hopes that more attention will be paid to men with breast cancer, for whom BIG programmes have previously been set up for tumour collection around the world.

> *"BIG and our American colleagues agreed that we need good studies of male breast cancer as it is not acceptable that men are just treated like women. We need to pay more attention to the tumour environment of male breast cancer because it has not been fully studied but, of course, we need funding to launch specific treatment trials for men, so we need to keep trying to make that happen," says Piccart.*

In the years ahead, Cameron hopes to see member countries in South America and South East Asia leading studies within the BIG network, and representation expanding into Africa.

"Non-communicable diseases such as breast cancer are a growing problem for healthcare systems in African countries, but building infrastructure for academic cancer research would require the kind of external funding that has previously been achieved for studies of infectious diseases. My dream would be to see the emergence of a research climate in Africa with studies that address local patient needs and contribute to global understanding of breast cancer," he says.

Werutsky would like to see BIG become involved in earlier stage, Phase 2 drug trials, as well as the large Phase 3 studies involving multiple BIG groups worldwide it already carries out. He would also like to see BIG become closer to investigators in member groups to facilitate more discussion and new ideas, together with some streamlining of new study proposals, as well as further enhancement of the role of patients and patient advocacy groups in trial design. Like other BIG leaders, he believes that the discovery of new biomarkers and development of liquid biopsy techniques will have important implications for personalised treatment, and that the incorporation of AI in pathology services will have a significant impact on breast cancer diagnosis, clinical decision-making and, ultimately, patient outcomes and experience.

> *"In the future, I think we will cure more patients with early breast cancer, and we will also transform the outlook for patients with metastatic disease – turning it into a chronic disease. At the same time, BIG will need to adapt its strategies for this new future," Werutsky concludes.*

For Norton, no single aspect of breast cancer research is more important than another. However, he feels that immunotherapy, the tumour microenvironment, cancer vaccines and novel drug delivery systems, removal of senescent cancer cells, novel ways to predict treatment response, and treatment de-escalation will all be important.

"Breast cancer research has a bright future, and we need to look at the totality of research because we never know where the next advance will come from," he says. "Industry-sponsored research has brought important advances, but if we can fund investigator-initiated studies whose outcomes are commercially relevant, we can reinvest in subsequent programmes of potentially ground-breaking academic research."

[1] *At the time of this interview, Professor Martine Piccart was serving as President of BIG against breast cancer, BIG's philanthropic entity. In early November, she announced her retirement, marking the culmination of an extraordinary and inspiring career. Professor Hans Wildiers has since assumed the role of President of BIG against breast cancer. For more details, please see page 29.*

BCRF: BIG'S LIFETIME SUPPORTER

The Breast International Group (BIG) is extremely grateful for the long-standing and generous support of the Breast Cancer Research Foundation (BCRF)®, which has facilitated BIG's practice-changing research in breast cancer for over 20 years.

Founded in 1993 by Evelyn H. Lauder, BCRF is the largest private funder of breast cancer research—and metastatic breast cancer research—worldwide.

Investing in the best minds in science—from those investigating prevention, diagnosis, treatment, survivorship, and metastasis—and fostering cross-disciplinary collaboration, BCRF's approach accelerates the entire field and moves us closer to the answers we urgently need to put an end to breast cancer.

A long-standing partner of BIG, BCRF has over the years generously provided over 27 million euros in funding to support BIG's academic research. Currently, BCRF is the main funder of BIG's large AURORA research programme dedicated to metastatic breast cancer. *See also page 58.*

TOGETHER TO ADVANCE BREAST CANCER RESEARCH

BCRF has been supporting the BIG-NCTN collaboration since 2005, which has shown to be crucial in the global fight against breast cancer.

BIG and the NCI National Clinical Trials Network (NCTN) – the latter being a network of major US and Canadian-based research groups supported by the US National Cancer Institute (NCI) – meet annually, gathering about 60 world-class researchers and involving breast cancer advocates to tackle unresolved issues of the disease.

Together they identify difficult and unresolved aspects of breast cancer treatment and care, focus on research areas not supported by the pharmaceutical industry, and collaborate to set up large international research programmes that always put patients' needs first.

This collaboration was initiated by Martine Piccart and William Wood, co-chairs of the first meetings, in partnership with Larry Norton (BCRF) and JoAnne Zujewski (NCI).

Among the main achievements resulting from this collaboration, in addition to AURORA, are the POSITIVE study, which investigates the safety of pausing endocrine therapy for breast cancer to try to conceive; the MINDACT trial, which demonstrated that the MammaPrint® test could help avoid unnecessary chemotherapy for many early-stage breast cancer patients, especially postmenopausal women with low-risk disease; the International Male Breast Cancer Programme, enhancing our understanding of this rare disease and optimising treatment for men; the SOFT and TEXT studies, which showed that combining exemestane with ovarian function suppression can reduce recurrence rates by 34% in young women with breast cancer; and the DECRESCENDO trial (with its US counterpart, COMPASS HER2-pCR), aiming to de-escalate adjuvant chemotherapy in HER2-positive breast cancer.

Learn more at BCRF.org.

Celebrating 25 years

BIG'S NEW BRAND IDENTITY

BIG marks this special milestone with the introduction of its new brand identity – bold, modern, gentle, and compassionate. This fresh look for our logos, colours, and fonts captures the essence of our mission, blending collaboration, scientific excellence, and innovation; with patients at the heart of our research.

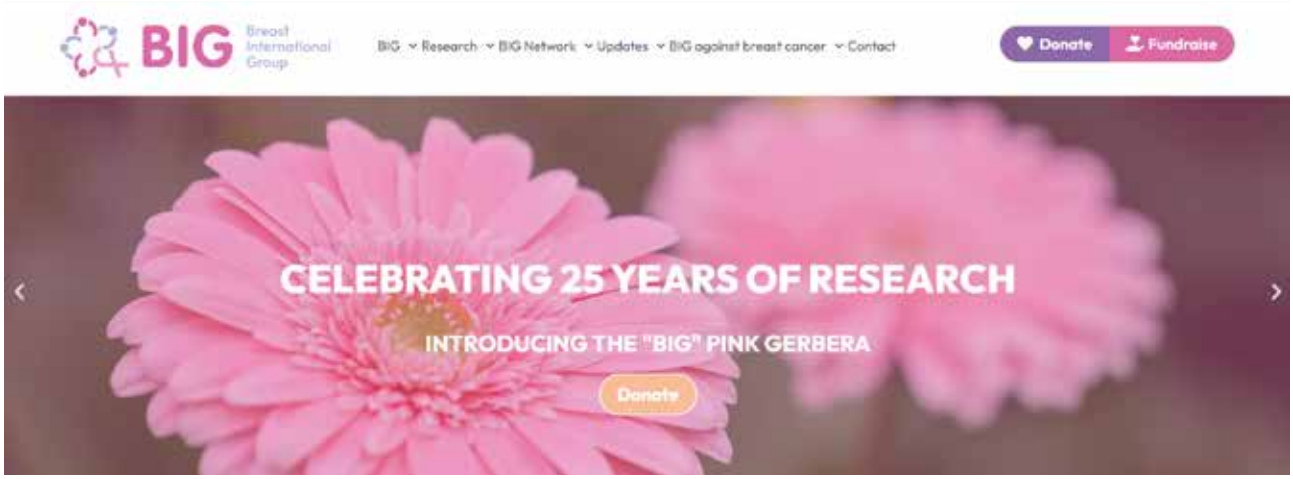
The redesigned "BIG against breast cancer" logo creates a stronger visual identity for BIG's philanthropic entity. Along with this new branding, we've also revamped our website to enhance visitors' experience and engagement.

We hope this new look resonates with everyone – from the scientific community to the general public – and builds further trust in what we stand for.

Read more on https://shorturl.at/0V3fo

BIG Breast International Group

BIG against breast cancer


BIG Breast International Group
BIG Research BIG Network Updates BIG against breast cancer Contact
Donate Fundraise
CELEBRATING 25 YEARS OF RESEARCH
INTRODUCING THE "BIG" PINK GERBERA
Donate


1%
of all breast cancers are diagnosed in men, affecting 1 in 800 men.


25%
of all cancers diagnosed in women is breast cancer, affecting 1 in 8 women.


±2,300,000
people diagnosed with breast cancer in 2022 around the world


Together we are
BIG against breast cancer
Alone we go faster, together we go further!
Patients do need us!
Donate


TOGETHER
WE WILL FIND A CURE FOR BREAST CANCER
Donate
Discover our Pink October campaign!


BIG against breast cancer
BIG against breast cancer supports the academic breast cancer research of the Breast International Group
Strengthening our position
We want people to see us, recognise us, and trust us, and this begins with a clear presentation of who we are.
Sweet and compassionate
Bold & modern
But also to convey a modern and dynamic identity, as these are the aspirations of BIG, with cutting-edge breast cancer research.

BIG Pink October 2024 campaign

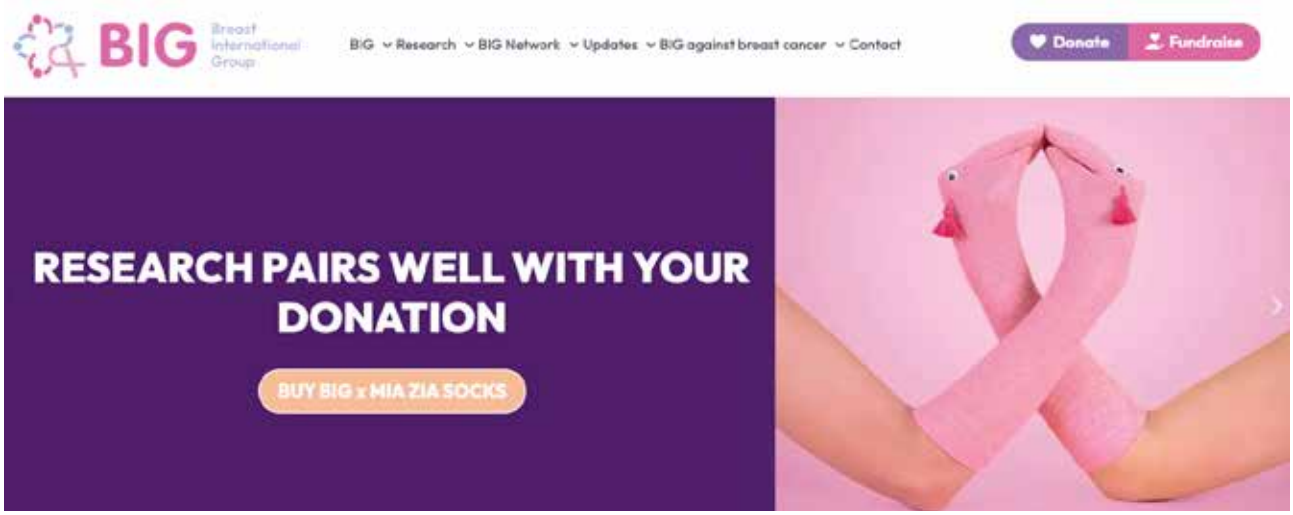
25 YEARS OF BREAST CANCER RESEARCH: RESEARCH PAIRS WELL WITH YOUR DONATION

In celebration of BIG's 25th anniversary, our 2024 Pink October awareness and fundraising campaign centred around the theme "25 years of breast cancer research: research pairs well with your donation".

With this campaign, developed by BIG's philanthropy and communications team based at BIG's Headquarters (Brussels, Belgium), we aimed to remind everyone that the global research conducted by the BIG network is essential for improving patients' survival and quality of life, yet it seriously lacks funding.

Because of the challenges of launching a truly international campaign that would resonate across the many countries and cultures represented by BIG members, and with the limited size and resources of the BIG HQ philanthropy and communications teams, we restricted our activities to Belgium. However, the hope remains that we will be able to develop activities across-countries in collaboration with BIG's member groups in the future.

Peggy De Neef (Candriam), Lara Beaupère (BIG), Natalia Cacho (BIG)



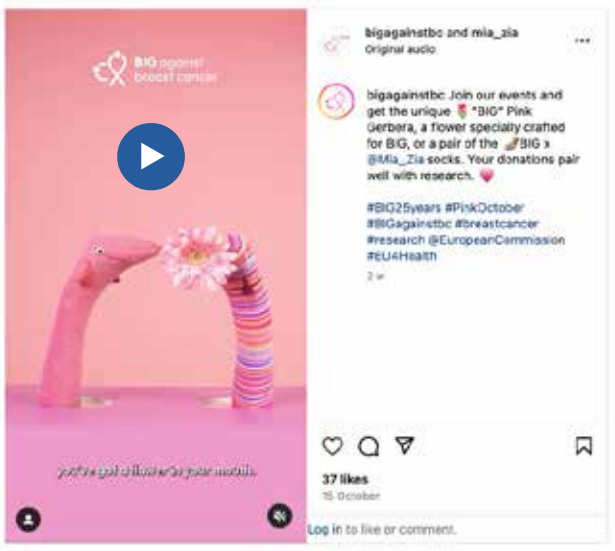
Research pairs well with your donation – BIG and Mia Zia

BIG has partnered with the Belgian brand Mia Zia to launch a unique collection in support of BIG's breast cancer research. It includes four pairs of specially designed socks, a handmade pink ribbon, and the Baraka bracelet crafted from pink spun thread – each serving as powerful symbols of hope and solidarity. They can also be purchased online.

The campaign's tagline, "Research pairs well with your donation", reminds us that academic breast cancer research greatly relies on funding. The campaign images serve as a visual pun: two hands wearing colourful BIG Mia Zia socks, resembling hand puppets, intertwine to form BIG's pink ribbon. This playful imagery captures, in a simple and catchy way, how research and donations go hand in hand to drive progress.

Additionally, we produced a series of engaging short promotional videos that feature the BIG Mia Zia socks in lively hand puppet shows, bringing an extra layer of fun to our messaging while raising awareness and funds.

Click on the image below to watch one of them.



The "BIG" Pink Gerbera

Through an additional partnership – a collaboration between Schreurs, Euroveiling, Floralco Albrecht and BeFlorist – a beautiful BIG Pink Gerbera was created exclusively to mark BIG's 25th anniversary. It is available in Belgium and will grace our events until the end of the year. Our aim is for a longer-term partnership that will lead to the BIG Pink Gerbera being available to florists in multiple countries, starting with The Netherlands and France.

With each sale of the Mia Zia items and the BIG Pink Gerbera, a portion of the profit will be donated to BIG, making every customer a contributor to breast cancer research.

Pink October calendar of events

To encourage engagement, BIG HQ's philanthropy and communications team organised a variety of activities throughout October and November, highlighting the importance of donations in supporting academic breast cancer research. An overview of these initiatives can be found on the BIG website.

BIG 25 YRS – corporate and emotional videos

As part of BIG's Pink October campaign and in celebration of our 25th anniversary, we created two short videos: one corporate and one emotional. These videos feature interviews with leading experts in breast cancer, members of BIG's global network, patient representatives, and patients.

The emotional video was unveiled at BIG's annual gala in November 2024, while the corporate video will be released in December 2024. These will be publicly available and published on the BIG website.

Campaign materials

For this campaign, BIG HQ developed press material, campaign boards (for events and as publicity in Brussels' public transportation system), videos and social media content. All communication materials can be accessed via BIG's website and the campaign's landing page: https://bigagainstbreastcancer.org/pink-october-2024/

BIG's social media platforms, where content can be found, liked, commented on, and reshared:

FOLLOW US ON

16 October 2024

ANNUAL BIG-EORTC PINK OCTOBER WEBINAR

As 2024 marks BIG's 25th anniversary, our annual BIG-EORTC Pink October webinar explored the theme *"25 years of breast cancer research: past, present, future".*

This one-hour webinar, one of the highlights of BIG's Pink October campaign 2024, was hosted by BIG and the European Organisation for Research and Treatment of Cancer (EORTC), in partnership with the European Union Health Policy Platform (EUHPP).

The webinar was open to both experts and the general public. We highlighted significant milestones and advancements over the past 25 years, current research endeavours and challenges, and offered a perspective on the future of breast cancer diagnosis and treatment, emphasising the crucial role of collaboration in driving progress. *See page 22 and 23 for the webinar's key messages.*

We welcomed 213 participants, and the feedback gathered from those who completed the post-event survey was positive: 87% rated the session as 'Good' or 'Excellent', and over 92% indicated they would be likely to attend future events.

➔ The full recording of the webinar is available on BIG's YouTube channel: https://www.youtube.com/watch?v=dAK7AfyZO0o

KEYNOTES AND PRESENTERS

Keynote 1
"BIG and 25 years of pioneering international breast cancer research: Achievements and future directions." *By Professor David Cameron*

David Cameron, MD
Chair of BIG (Breast International Group)
Professor of Oncology at Edinburgh University, UK

Professor David Cameron works at the National Health Service (NHS) Lothian's cancer centre treating breast cancer patients. He is the joint lead for the Edinburgh Experimental Cancer Medicine Centre. He also holds a part-time deputy director role in the Scottish Government-funded Innovative Health Care Delivery Programme (IHDP). This programme aims to improve access to and the use of routine cancer patient data within NHS Scotland.

> *"Over 25 years, from past breakthroughs to present advancements, BIG has been driving change in breast cancer research. With optimism and determination, we remain focused on transforming research and improving outcomes."*

BIG's leadership

Professor David Cameron, a medical oncologist, has been actively involved with BIG since 2001, making him a longstanding figure within the organisation. He joined BIG's Executive Board in 2010 and has served as its Chair since June 2019, guiding collaborative breast cancer research across a network of over 55 academic research groups worldwide. His solid background in oncology and leadership in cancer research networks are key to his work with BIG.

Professor David Cameron collaborates closely with the members of the BIG Executive Board and the BIG Patient Partnership Initiative (BIG-PPI) to advocate for innovative research initiatives and holistic cancer care. By amplifying the patient's voice from the earliest stages of clinical trial development, they ensure that BIG's research meets real-world needs. Through the BIG-PPI, they bridge the gap between researchers and patients, reinforcing their commitment to improving outcomes for breast cancer patients worldwide.

For more insights into the BIG-PPI, we invite you to read the themed article in BIG Research in Focus 20, April 2024.

Securing funding is increasingly challenging for academic organisations conducting essential research. This funding is vital, enabling organisations like BIG and the EORTC to address critical questions that matter most to those affected by the disease. However, many of these studies often lack commercial interest, as they do not involve drug development, resulting in limited or no support from the pharmaceutical industry.

BIG continues to seek ways to diversify its funding sources, securing grants, forming corporate partnerships, and other new avenues for support of its patient-centric breast cancer research. *We recently explored how leading cancer groups and funders are addressing their fundraising challenges. For those seeking grants, their insights and advice have been gathered in the* BIG Research in Focus 19, November 2023.

Keynote 2
"Reflecting on the past and embracing the future: The evolution of liquid biopsies in breast cancer diagnosis and treatment."
By Professor Michail Ignatiadis

Michail Ignatiadis, MD, PhD
Chair of EORTC BCG - Director of Breast medical oncology clinic, Institut Bordet, H.U.B, BE
Associate professor at the Université Libre de Bruxelles, Belgium

Leading the Academic Trials Promoting Team, Professor Ignatiadis has served on the IJB Executive and Research Boards since October 2016, contributing to the institute's research strategy and promoting high-quality, innovative academic research.

> *"With 2.3 million new breast cancer cases in 2022, integrating liquid biopsies into daily practice offers immense promise for advancing care and improving the lives of all those affected by the disease. By using a simple blood sample, liquid biopsies can complement or sometimes replace invasive procedures such as biopsies of metastases. They can offer more accurate, real-time insights and facilitate personalised treatments based on each patient's molecular profile. It holds immense promise for daily oncology practice."*

The TREAT CTC and TREAT ctDNA trials

The clinical trials TREAT CTC (EORTC 90091-10093 / BIG 1-12) and TREAT ctDNA (EORTC 2129-BCG / BIG 22-01), led by the EORTC and conducted under the BIG umbrella, are part of a broader effort to personalise cancer treatment. By using advanced biomarkers, these trials aim to detect and treat cancer more effectively at earlier stages.

The TREAT CTC study that Professor Michail Ignatiadis led was the first trial to use circulating tumour cell (CTC) detection. CTCs are cancer cells that break away from a primary tumour and circulate in the bloodstream, potentially leading to the formation of metastases. The TREAT CTC trial examined the effectiveness of treatments that aim to eliminate these cells and prevent the spread of cancer.

TREAT ctDNA is a recent phase III clinical trial also led by Prof Ignatiadis. It was launched in December 2023 and will enrol approximately 1,900 patients across over 120 sites in 12 European countries. It aims to assess the efficacy of the drug elacestrant (Orserdu®, by the Menarini Group) in delaying or preventing metastasis in early-stage, ER+/HER2- breast cancer patients who show molecular relapse indicated by circulating tumour DNA (ctDNA) but without clinical or radiographic evidence of recurrence. In addition to assessing the efficacy of elacestrant, the hope is to be able to demonstrate the utility of using ctDNA as a biomarker of early relapse.

Keynote 3
"The EU Cancer Mission: Collaborative vision, driving research and patient care, raising awareness."
By Dr Jan-Willem van de Loo

Jan-Willem van de Loo, PhD
Senior expert cancer research and innovation, EU Cancer Mission - Science and stakeholders, European Commission

Jan-Willem van de Loo, Cancer Theme Lead since 2019, has been a Policy and Scientific Officer at the European Commission in charge of cancer research since 2003. He led a team co-creating the Horizon Europe Mission on Cancer. Other policy initiatives include contributions to the Europe's Beating Cancer Plan, public-public and public private research and innovation partnerships. He has been involved with BIG since the early 2000s, when he was the EU project officer for TRANSBIG, an international research network established by BIG.

> *"Europe needs more patient-centric research approaches that strengthen cooperation across sectors and disciplines, reduce inequalities, and improve health outcomes for all. Hosting the annual BIG-EORTC Pink October webinar on the EU Health Policy Platform ensures that insightful information reaches a broad and diverse audience, further reinforcing the EU's efforts in cross-border research collaboration and reducing the burden of cancer."*

The EU Cancer Mission

Launched in 2021, the Horizon Europe Cancer Mission and Europe's Beating Cancer Plan – among the pillars of the European Health Union – outline an EU strategy for cancer prevention, treatment, and care, emphasising the use of advanced technologies, research, and innovation. The plan aims to enhance our understanding of cancer development and improve diagnostic, treatment and care methods by integrating tools such as molecular biomarkers, genomic data, and liquid biopsy. This approach will advance the prevention and early detection of cancer as well as patient care, improving outcomes for all.

TRANSBIG and MINDACT

Funded in part by the EU, the TRANSBIG project aimed to enhance personalised breast cancer treatment through translational research that connects laboratory findings with clinical practice. MINDACT, its landmark study, demonstrated that MammaPrint® – a 70-gene test – could identify early-stage breast cancer patients who may safely avoid chemotherapy, reducing unnecessary treatment for nearly 46% of patients.

This impactful trial, a collaboration between TRANSBIG, the EORTC, the EU and other institutions, highlighted how genomic data can guide treatment decisions, offering safer and more effective care for breast cancer patients.

For more information, please refer to the project descriptions on BIG's website: "TRANSBIG, an EU-funded consortium to promote collaboration in translational breast cancer research" and MINDACT .

Keynote 4:
"Incorporating patient perspectives from trial inception: The importance of the patient's voice."
By Dr Tanja Spanic

Tanja Spanic, PhD
President of Europa Donna Slovenia and the European Breast Cancer Coalition
Member of the BIG-PPI (BIG Patient Partnership Initiative)

Dr Tanja Spanic was diagnosed with breast cancer at a young age, just 26. Although breast cancer is most commonly diagnosed in individuals aged 55-60, younger women are also significantly affected. In 2022, 29% of the 2.3 million new breast cancer cases globally were in women under 50 *(source: Globocan 2022)*.

> *"After my breast cancer diagnosis at 26, I shifted from a researcher with a background in veterinary medicine and a PhD in molecular and behavioural neuroscience to become a patient advocate. My journey through chemo-therapy, surgery, radiation therapy, and a decade of hormonal treatment profoundly*

shaped my commitment to amplifying the voices of those affected by breast cancer. Becoming a mother in 2020 was a blessing I cherish, especially knowing that not all women with breast cancer are so fortunate. Through my work with Europa Donna and the European Breast Cancer Coalition, I am dedicated to ensuring that patient needs are central in clinical studies and trials. Given that 1 in 8 women and 1 in 800 men will face a breast cancer diagnosis in their lifetime, such advocacy is crucial for improving the lives of millions. As a member of the BIG-PPI contributing to the development of BIG's research agenda, I am more than ever committed to this mission.

From 2010 to 2014, Dr Tanja Spanic led the young breast cancer patients group within Europa Donna Slovenia, one of the few such groups in Europe at the time. Her leadership continued to grow, and in April 2017, she became the president of Europa Donna Slovenia after serving as its secretary general. Her commitment to breast cancer advocacy was further recognised when she joined the Executive Board of the European Breast Cancer Coalition, Europa Donna, in 2018, eventually becoming its president in April 2020.

Today, her influence extends across national and international borders. As a member of the BIG-PPI, she plays a crucial role in ensuring that patient perspectives shape research and decision-making within BIG. For instance, she serves on the steering committee of the POSITIVE study, an international academic study conducted under the BIG umbrella. The first results show that young patients can safely interrupt hormone therapy in order to conceive without increasing the risk of relapse in the short term. Tanja is also a member of the steering committee of the OlympiA clinical trial conducted under the BIG umbrella. This study demonstrated how treatment with olaparib reduces the mortality risk for hereditary breast cancer by 32%.

Key messages of the webinar

IN BRIEF: 25 YEARS OF BREAST CANCER RESEARCH: PAST, PRESENT, FUTURE

At this year's Pink October webinar, hosted by BIG and the EORTC, in partnership with the EUHPP, presenters looked back at the achievements of breast cancer studies over the last 25 years, current research, and future opportunities and challenges for patients and researchers.

BIG successes

> BIG was set up in 1999 to bring together breast cancer research groups, initially in Europe and now worldwide, to reduce clinical trial duplication, strengthen and accelerate research, and address questions that matter most to patients

> More than 60 clinical trials of breast cancer treatments have been carried out under the BIG umbrella, including rapidly recruited, practice-changing trials of anti-HER2 therapies (HERA and APHINITY), PARP inhibition (OlympiA) and ovarian suppression (SOFT/TEXT)

> BIG trials have also investigated predictive tests to reduce the need for chemotherapy (TRANSBIG-MINDACT) and radiotherapy (EXPERT), and OPTIMA Young will evaluate a predictive test for chemotherapy need in younger women

> In metastatic breast cancer, AURORA involves ground-breaking research to better understand the biology of breast cancer that has spread to other parts of the body

> For younger women with breast cancer, early results from POSITIVE are reassuring about the safety of interrupting endocrine therapy to try to have a baby

Novel technologies

> Liquid biopsy is an exciting new technology to detect cancer cell DNA (ctDNA) in the blood with potential for earlier breast cancer diagnosis, more targeted treatment selection, and better surveillance of micrometastatic disease

> In metastatic breast cancer, ctDNA testing has been shown to identify some treatable cancer mutations more successfully than with tissue biopsy alone[1]

> In women with early breast cancer, ctDNA monitoring has been shown to detect relapse approximately 12 months before clinical signs appear[2]

> An EORTC Phase III trial is underway under the BIG umbrella to compare the effects of endocrine therapies on development of distant metastasis or death in patients with breast cancer who have rising ctDNA levels but no sign of progression on conventional scans

EU funding for breast cancer research

> EU Mission Cancer funds research and innovation for cancer prevention and cure, and to enable those affected by cancer to live longer and better. Funding to date has exceeded €375 million, and projects have included:

- Collaborative Oncological Gene-environment Study (COGS) which identified more than 80 novel genomic areas linked to breast, ovarian or prostate cancer risk and led to development of the CanRisk Tool that calculates breast and ovarian cancer risk based on genetic, hormonal, lifestyle and other risk factors

- MINDACT – this impactful trial, developed with the EORTC and other institutions as part of the TRANSBIG network, highlighted how genomic data can guide treatment decisions, offering safer and more effective care for breast cancer patients

- Rational Therapy for Breast Cancer (RATHER) which focused on identification of novel targets, assays and treatment for triple negative breast cancer (TNBC) and invasive lobular carcinoma

- Mutanome Engineered RNA Immuno-therapy (MERIT) – a Phase 1/2 trial of RNA vaccines against tumour antigens and tumour-specific mutations in TNBC

> Ongoing activities include:

- MyPeBS – an EU-funded study enrolling more than 70,000 women aged 40-74 to compare the effectiveness of risk-stratified and standard breast cancer screening
- MONITOR-RCT to compare scanning methods for advanced breast cancer so that second line therapies can start earlier and potentially prolong survival and improve quality of life

The Patient Voice

> Patient involvement in breast cancer research is increasing, especially in BIG and EORTC studies, and those supported by the EU

> Best practice is to involve patients from the start – to ensure that a study asks questions that are patient relevant as well as clinically and scientifically relevant

> Patient input into the practical aspects of study design can also ensure that a study will attract and retain patients

> In 2021, the European Council published *Principles of Successful Patient Involvement in Cancer Research,* developed by more than 160 patient organisations, medical experts, and policymakers, to guide research planners

> Education and training platforms, such as the BIG-PPI, are ensuring that patient advocates have the knowledge and understanding of breast cancer to enable them to participate equally with medical experts in discussions about clinical trial design

> Such initiatives have become a valuable source of patient experts for future clinical trial development in many countries

Future opportunities and challenges

> The future is bright for breast cancer research, with many trials on potentially curative treatments and innovative approaches to enable patients to live longer and better with advanced disease

> Personalised treatment strategies will aim to adapt treatment intensity and duration according to individual needs and what matters most to each patient

> Fundraising for larger academic studies and patient-led research is a major challenge owing to the rising cost and complexity of research

References

1. Iams WT, Mackay M, Ben-Shachar R, et al . Concurrent Tissue and Circulating Tumor DNA Molecular Profiling to Detect Guideline-Based Targeted Mutations in a Multicancer Cohort. JAMA Netw Open. 2024 Jan 2;7(1):e2351700.

2. Garcia-Murillas I, Cutts RJ, Walsh-Crestani G, et al. Longitudinal monitoring of circulating tumor DNA to detect relapse early and predict outcome in early breast cancer. Breast Cancer Res Treat. 2024 Oct 18.

6 November 2024

EXCLUSIVE ROUNDTABLE WITH HER MAJESTY THE QUEEN OF THE BELGIANS

Professor Hans Wildiers, Professor Martine Piccart, Her Majesty the Queen of the Belgians, Professor David Cameron

Professors Martine Piccart, co-founder of BIG, and David Cameron, Chair of BIG, had the great honour of welcoming Her Majesty the Queen of the Belgians, Honorary President of BIG, to an exclusive roundtable session in Brussels. The event, hosted by BIG and inspired by an idea from Her Majesty herself, underscored her ongoing commitment to breast cancer research and her support for BIG's initiatives.

Her Majesty, accompanied by Professor Martine Piccart, participated in roundtable discussions with influential figures from various sectors, discussing the latest developments in breast cancer research. The event brought together prominent breast cancer experts and researchers, patient advocates, loyal partners, stakeholders, as well as members of BIG's Executive Board and BIG HQ, offering a platform for insights on new treatments and research directions.

The guests were seated at seven different tables, each dedicated to a specific topic, with an expert present at each table to provide detailed explanations, answer questions, and offer their professional perspective.

1. Breast cancer treatment in special populations, chaired by Dr Ines Vaz-Luis
2. BIG-Patient Partnership Initiative, chaired by Professor Judith Bliss
3. Advances in immunotherapy, new drugs and treatments on the horizon, chaired by Dr Philippe Bedard
4. Clinical research and climate change, chaired by Professor Seamus O'Reilly
5. Metastatic breast cancer to the brain, chaired by Dr Evangelia Razis
6. Treatment de-escalation, chaired by Professor Hans Wildiers
7. Prognostic genetic tests and reimbursement in Belgium, chaired by Dr Philippe Aftimos

Her Majesty and Professor Piccart spent equal time at each of the tables, with a maximum of eight guests per table. This closed-door session provided both Her Majesty and the guests with the opportunity to engage thoughtfully with one another, ensuring balanced and meaningful discussions at each table.

This event was a perfect opportunity to mark the end of BIG's Pink October campaign and to celebrate the organisation's 25-year history of impactful breast cancer research, honouring past achievements and embracing a hopeful vision for the future.

Since 2010, Her Majesty has been supporting BIG's research, helping expand its collaborative network and fostering healthcare innovation, both in Belgium and internationally. We are sincerely grateful for her long-standing commitment to our mission and her enduring endorsement of our work.

Royal recognition: BIG in the spotlights

Thanks to Her Majesty's attendance, the event received significant media attention, with press coverage in Belgian, French, Dutch, Spanish, and UK media, including leading daily newspapers, news websites, social media, royalty magazines, and prominent medical and scientific publications. For an overview, please visit the press room on our website.














ET LA RECHERCHE
FONT LA FORCE







Photos by © Gabriel Lelièvre, 2024

NEW PRESIDENCY FOR *BIG AGAINST BREAST CANCER*

Honouring Professor Martine Piccart's legacy

Celebrating 25 years of BIG is not only about marking the organisation's milestone but also honouring the exceptional career of Professor Martine Piccart, who co-founded BIG with Professor Aron Goldhirsch in 1999. For two decades, she led BIG as its Chair, guiding the organisation with vision and dedication.

In 2019, Professor Piccart passed the torch to Professor David Cameron, who has held the position of BIG's Chair since then. Even after stepping down from the role of Chair, Professor Piccart continued to contribute to BIG. She took on the role of President of *BIG against breast cancer*, BIG's philanthropic unit, and also served as a Senior Adviser to BIG. Her tireless work has played a key role in BIG's growth and development, ensuring its ongoing impact in the fight against breast cancer.

Professor Piccart's influence extends beyond the countless lives saved. Her pioneering and groundbreaking work has earned her the highest respect from her peers around the globe and opened doors for innovation in breast cancer research, opportunities for young researchers to thrive, and the development of key partnerships. She has played a pivotal role in advancing fundraising efforts, securing vital support for numerous studies and trials. Through her leadership, BIG has not only gained international recognition but also expanded its global reach, fostering a more collaborative and impactful approach to breast cancer research.

A new chapter for *BIG against breast cancer*

After decades of commitment to BIG and the broader breast cancer research community, it is with deep gratitude and a heavy heart that we announce Professor Piccart's decision to step down as President of *BIG against breast cancer* and take an additional step towards a well-deserved retirement. Her legacy within BIG is indelible, and she will always be a key figure in the organisation's history, particularly for those of us who have had the privilege of working closely with her, including the team at BIG HQ in Brussels.

Welcome, Professor Hans Wildiers

As we look forward to the future, we are excited to welcome Professor Hans Wildiers as the new President of *BIG against breast cancer*. Professor Wildiers is a

well-known medical oncologist dedicated to breast cancer research and geriatric oncology at the University Hospitals Leuven, Belgium. He is the past Chairman of the Cancer in the Elderly task force of the EORTC and a member of the EORTC Breast Cancer Group. He has served as President and is currently a board member of SIOG (International Society of Geriatric Oncology). He has been involved with BIG for many years, and his expertise and commitment to advancing research and improving patient outcomes will be critical as we continue our mission.

From all of us at BIG, we extend our heartfelt thanks to both Professors Piccart and Wildiers for their dedication and leadership.

Looking ahead: securing BIG's future

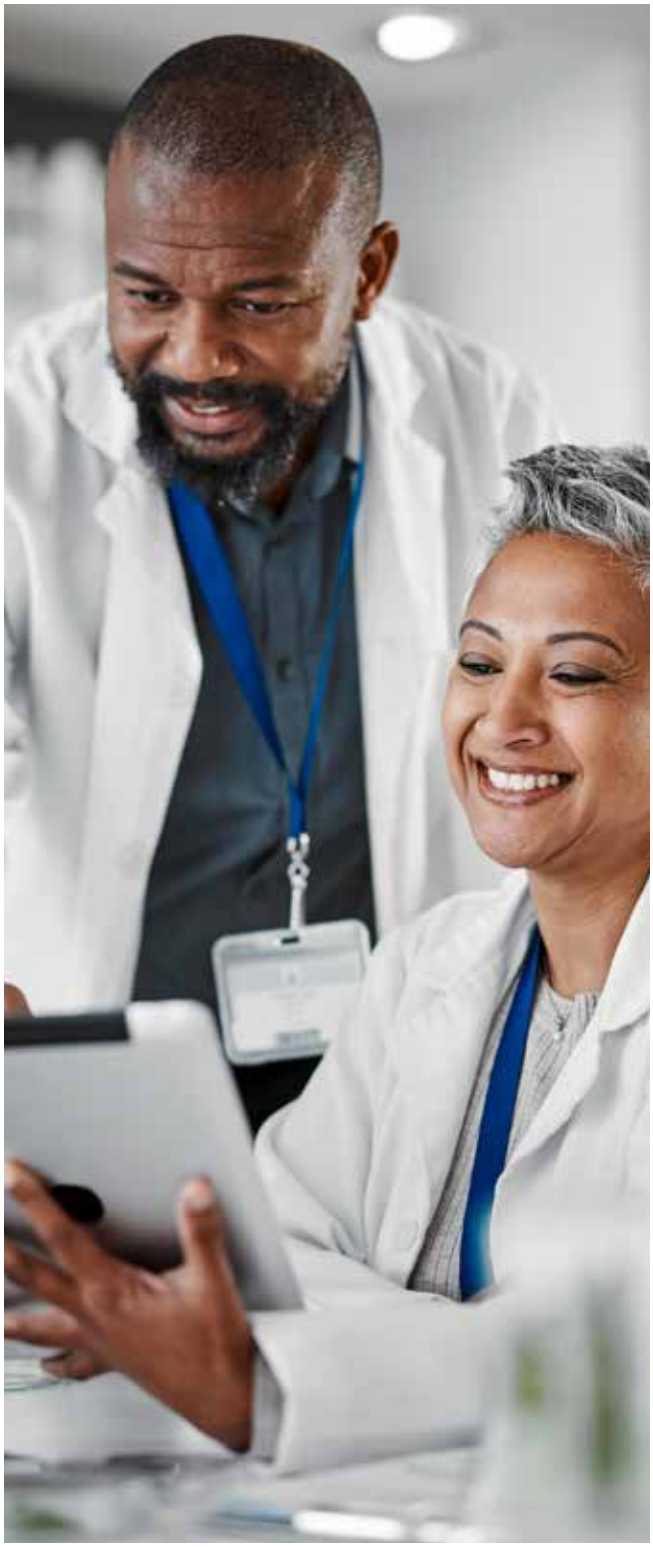
This news was officially announced just before the closure of this edition of *BIG Research in Focus*, and we didn't want to wait until our next edition in April 2024 to share it. In our upcoming issue, we will pay tribute to Professor Piccart and her lasting legacy, while also offering a closer look at our on-going mission. This includes a strong focus on securing funding and exploring new ways to finance our studies and trials, such as through EU funding, new partnerships, recurrent financial support from foundations, governmental bodies, corporate partners, and fundraising events.

Throughout it all, we remain steadfast in our commitment to putting patients at the heart of our research. We continue to prioritise patient-centric research and advocacy, recognising the vital role of BIG's patient partners and the many other breast cancer patients who have participated in BIG studies and otherwise supported and endorsed our work.

Securing funding

Co-funded by the European Union

EU GRANTS ACTIVITIES



HORIZON EUROPE PATH4YOUNG PROJECT TARGETS PERSONALISED BREAST CANCER CARE FOR YOUNG WOMEN

BIG, in collaboration with the project coordinator UNICANCER, Warwick University, Institut Gustave Roussy, and 22 other esteemed partners, will soon sign a grant agreement with the European Commission for the Horizon Europe-supported project Path4Young. Led by Dr Ines Vaz-Luis from Institut Gustave Roussy, this ambitious initiative, based on the ongoing international multicentre clinical trial OPTIMA (@OPTIMAbstudy), seeks to redefine the care standards for premenopausal women considered at high risk of recurrence.

Funded by the European Union, the Path4Young project aims to reshape care standards with the following objectives:

> Safely reduce chemotherapy for premenopausal patients through a multiparametric test, focusing on minimising side effects without compromising treatment effectiveness.

> Enhance quality of life by providing ongoing support to patients throughout treatment and recovery, leveraging digital tools and increasing patient engagement in the project's implementation.

The trial's multidisciplinary consortium brings together leading experts from Europe, Latin America, and Oceania, integrating a wide range of perspectives from clinicians, supportive care specialists, patient advocates, digital technology providers, and social science experts. Through a comprehensive approach, the project seeks to transform the treatment of breast cancer in young women, offering more personalised care and improving long-term outcomes.

BIG-SUPPORT

BIG awarded EU4Health Framework Partnership Agreement

BIG has signed an EU4Health Framework Partnership Agreement for its project BIG-SUPPORT: "Sustainability for patient-focused breast cancer research, philanthropy, outreach, and networking". This agreement makes BIG eligible for operating grants of up to 1M Euro each in 2025 and 2026. Among other elements, BIG-SUPPORT was selected for its commitment to advancing breast cancer research across Europe and beyond, with a strong emphasis on patient needs.

With this opportunity for co-funding to build on the progress already achieved with the operating grants BIG-SCOPE (2023) and BIG-SPARK (2024), BIG can further enhance patient-focused breast cancer research by expanding capacity building, improving health literacy, and increasing patient involvement in the development of its studies. The activities foreseen under BIG-SUPPORT also allows BIG to extend its public outreach efforts, ensuring that both scientific progress and the patient voice remain central to breast cancer care.

This agreement marks a significant milestone for BIG, celebrating 25 years of leadership in breast cancer research and treatment. It holds the potential for BIG to make an even greater impact on the health and well-being of millions of women and men across Europe and beyond in the years to come, aligning with the EU's broader health policy goals.

BIG-SPARK

Advancing collaboration and patient-centric breast cancer research in 2024

With support from the EU4Health 2024 operating grant, providing up to 1M Euro in co-funding, BIG-SPARK has, since its launch in February 2024, bolstered BIG's research by fostering greater collaboration among breast cancer experts, expanding public awareness, and increasing patient involvement in the research process. This crucial support has enabled BIG to build on the work it started in 2023 with the BIG-SCOPE operating grant, especially regarding its work with patient partners.

Strengthening expert collaboration and patient engagement

One of the key achievements of BIG-SPARK has been to enhance collaboration between BIG's breast cancer researchers and patient partners. Through events such as the bi-annual BIG Scientific Meetings held in March and September, and the strategic Executive Board retreat in November, experts shared new clinical trial ideas and discussed ongoing studies. Most importantly, they reflected on how to best leverage the strengths of BIG's vast network of collaborative research groups and relationship with patient partners to meet the challenges of academic research in the coming years.

BIG's patient partners, members of the BIG-PPI (BIG Patient Partnership Initiative), played an active role in these discussions. Through a patient-focused "landscape analysis" conducted jointly with the scientific team at BIG Headquarters, they identified unmet needs where research would be most useful for patients, as well as niches where international collaboration is needed and BIG's resources could be most impactful. Additionally, a patient-focused checklist for investigators preparing trial proposals for presentation at BIG meetings has been developed. This will help ensure that patient perspectives are considered from the start.

Public outreach and advocacy

BIG-SPARK has significantly strengthened BIG's public outreach efforts, increasing awareness of breast cancer research and its impact on treatment. In 2024, BIG extended its reach through its website, social media channels, newsletters, and press articles. We also reached a wide audience through public events such as the 20KM of Brussels and BIG's Pink October awareness campaign, which included a series of events and fundraising activities (*see also page 14-28*).

To mark its 25th anniversary, BIG organised a distinguished roundtable event attended by Her Majesty the Queen of the Belgians. As Honorary President of BIG, Her Majesty has graced BIG's initiatives since 2010, supporting BIG's ability to raise awareness, expand research-driven partnerships, and encourage health innovation both in Belgium and internationally (*see also page 24-28*).

Looking ahead

Thanks to the co-funding provided by the EU4Health 2024 grant for BIG-SPARK, BIG has strengthened its research and collaboration efforts, contributing to the EU's broader health policy goals. With several initiatives in progress, BIG remains dedicated to ensuring that patients are at the heart of its breast cancer research, shaping studies that address their most pressing concerns.

Updates

BIG MEMBER GROUPS

ABCSG
AUSTRIAN BREAST AND COLORECTAL CANCER STUDY GROUP

Advancing personalised breast cancer treatment: new ABCSG studies

At the forefront of clinical and translational breast cancer research, the Austrian Breast & Colorectal Cancer Study Group (ABCSG) continues to push the boundaries of treatment options by developing new clinical trials that focus on tailoring therapies based on individual patient and tumour molecular profiles. These efforts are critical to ensuring that patients receive the most appropriate treatments, minimising unnecessary interventions and improving outcomes. In the background of this scientific setting, new ABCSG trials are about to start, two of which anticipate enrolling patients from early 2025.

ABCSG 61 / TEODOR (Neoadjuvant **T**r**E**atment **O**ptimization driven by ct**D**NA and end**O**crine **R**esponsiveness) is a prospective, randomised, controlled, open-label, multicentre phase II study. The trial will focus on patients with HR-positive, HER2-negative, early and locally advanced breast cancer who are ctDNA-negative and endocrine-responsive. Using baseline (negative) ctDNA status and endocrine sensitivity (measured by Ki67 dynamics) for selection, patients will be randomised to receive either neoadjuvant chemotherapy or endocrine therapy. With the larger goal of optimising treatment selection and minimising overtreatment in patients who may not need pre-operative chemotherapy, this protocol aims to determine the efficacy of endocrine therapy compared to chemotherapy in these selected patients. Efficacy will be measured using the modified Preoperative Endocrine Prognostic Index (PEPI) score and pCR.

"The growing precision of breast cancer treatment, guided by biomarkers and molecular profiles, allows us to better tailor therapies to each patient's individual tumour biology and, in certain subpopulations, to avoid chemotherapy and its associated side effects. De-escalation strategies, such as focusing on endocrine therapy when appropriate, are crucial to reducing treatment burden while maintaining excellent outcomes," emphasises ABCSG President Professor Michael Gnant. With 256 patients participating across 15 sites in Austria, ABCSG 61 / TEODOR aims to improve personalised treatment strategies for women with early-stage breast cancer.

Professor Michael Gnant at NIFA 2024
© Oreste Schaller

ABCSG 63 / ERIKA (**E**lacestrant and **RI**bociclib in **K**i67-tested endocrine responsive bre**A**st cancer) takes a similarly personalised approach, focusing on endocrine-responsive, HER2-negative early breast cancer. In this open-label, two-arm, randomised neoadjuvant phase II trial, patients will receive either elacestrant plus ribociclib or an aromatase inhibitor

(AI) plus ribociclib, with the addition of a GnRH agonist in pre-/perimenopausal women. By incorporating the dynamics of tumour proliferation marker Ki67 as a determining factor is assessing whether patients are endocrine-sensitive, this study aims to provide deeper insights into the efficacy of targeted endocrine therapies in the neoadjuvant setting. The primary objective is to evaluate the superiority of elacestrant plus ribociclib compared to AI (and GnRH agonist) plus ribociclib in endocrine-responsive early breast cancer, measured by the modified Preoperative Endocrine Prognostic Index (PEPI) score at the time of surgery.

"We are in a position of having more and more access to a wide range of potent agents in the early breast cancer setting, with substances such as oral SERDs. One of our important tasks is to test these against standards, also by determining who will likely benefit most from the addition of these novel drugs," says study PI and ABCSG vice president Professor Christian Singer. With 18 sites planned across Austria and Germany, ABCSG 63 / ERIKA will enrol 120 patients, with the first randomisations scheduled for early 2025.

These two trials represent the latest in ABCSG's commitment to expanding personalised breast cancer care in partnership with biotech and pharma companies in the field of molecular testing/ctDNA assays, focusing on tailored treatment plans based on cutting-edge molecular profiling and biomarker-driven approaches.

Professor Christian Singer at NIFA 2024
© Oreste Schaller

25 Years of BIG: congratulations for a legacy of global collaboration

Global collaboration is an essential cornerstone of cancer research, particularly in large (adjuvant) phase III trials that have ambitious timelines and require the commitment of multiple partners with the operational and scientific quality necessary to conduct successful research. For 25 years, the Breast International Group (BIG) has played a pivotal role in advancing breast cancer trials, enabling key clinical questions to be addressed through a network of strong academic and industrial partners.

ABCSG has proudly contributed to BIG-led and co-led studies and held leadership positions on the BIG Executive Board for over 10 years. In this context, it is crucial to maintain effective collaborative models that allow for academic independence while working closely with industry. *"We must continue to develop new strategies and approaches to ensure that academic research retains its strong, independent presence while working closely with pharmaceutical companies, even as we navigate an increasingly complex regulatory environment,"* says ABCSG President Professor Michael Gnant.

As we celebrate 25 years of the Breast International Group, we reflect on a remarkable journey that has transformed breast cancer research. Over the past two decades, the BIG network has fostered collaboration among diverse institutions and researchers, paving the way for significant advances in clinical practice and treatment options. Together, we have tackled pressing questions and challenged established paradigms.

As we look to the future, our vision is to continue to strengthen our network by embracing innovative approaches to research and fostering new collaborations between academic and industry partners. Our goal is to remain at the forefront of breast cancer research and ensure that our collective efforts translate into improved care for patients worldwide.

The importance of the BIG network serves as a testament to the power of collaboration in tackling the complexities of breast cancer and achieving meaningful progress. Together, we have built a legacy of excellence that will undoubtedly shape the future of breast cancer research for many years to come.

Happy 25th anniversary, BIG, and here's to many more years of fruitful collaboration!

Contribution by Professor Michael Gnant, President of ABCSG, past member of the BIG Executive Board.

BCT-ANZ
BREAST CANCER TRIALS – AUSTRALIA AND NEW ZEALAND

We congratulate the Breast International Group (BIG) on 25 years of breast cancer clinical trials research, which has advanced our scientific knowledge in the treatment and prevention of this disease.

Breast Cancer Trials (ANZ) has a long history of collaboration with our European colleagues, from the day that BIG was founded by Professors Martine Piccart and Aron Goldhirsch.

Studies such as HERA, SOFT and TEXT, and OlympiA are just a few of the examples of international trials that have changed practice, improved treatments, and saved lives. They have provided opportunities for leading researchers and clinical trial participants from around the world, so that we can combine resources and multi-disciplinary expertise, for the benefit of all those diagnosed with breast cancer.

This network of researchers remains just as vital today as it did 25 years ago, as we look to the future of research with more personalised treatments, improving survival and improving patient quality of life.

We look forward to the next 25 years of collaboration!

Retirement of our CEO – Soozy Smith

After 13 years of dedicated service, our CEO, Soozy Smith, has decided to retire, effective November 2024. Soozy has been instrumental in guiding the success of Breast Cancer Trials ANZ, and her leadership has played a significant role in our growth over the years.

Her vision, dedication, and strategic guidance have been invaluable to our organisation and relationships with so many organisations internationally, including the BIG network.

Recruitment milestones

The BCT-ANZ and BIG co-led EXPERT clinical trial has reached a significant recruitment milestone, with 1,000 trial participants from Australia, New Zealand, Argentina, Chile, Ireland, Italy, Spain, Switzerland, and Taiwan. Our target for recruitment is 1,170.

We produced a recruitment video for EXPERT that was translated into Spanish, Italian and Mandarin, which

CEO Soozy Smith

was provided to participating institutions. Additionally, a guide for surgeons is being prepared to assist with enhancing recruitment.

OPTIMA is also recruiting well in Australia and New Zealand, reaching a milestone of 100 trial participants with a local target of 300 patients.

New trials

CAMBRIA-2 has opened to recruitment in Australia and aims to find out if giving a new endocrine therapy treatment known as a 'selective estrogen receptor degrader' (SERD) is better at stopping cancer from coming back compared with the usual endocrine (hormone) treatments such as letrozole, anastrozole, exemestane or tamoxifen. BCT-ANZ aims to recruit 225 patients at 25 sites in Australia and 3 in New Zealand.

The OLIO clinical trial has also opened in Australia and aims to find out if adding olaparib, or olaparib combined with durvalumab, to standard chemotherapy given to pre-menopausal (18-44 year old) women

with HR-positive, HER2-negative, HRD-positive breast cancer before surgery will do a better job of controlling the cancer. BCT-ANZ is trialling a remote telehealth pre-screening process to broaden clinical trials access to regional and remote patients and improve clinical trial recruitment. OLIO aims to recruit 56 patients and involves 21 sites in Australia.

BCT-ANZ awards

Winners of the 2024 Breast Cancer Trials Awards were presented at the 45th Annual Scientific Meeting in Cairns, Queensland, Australia.

The 2024 recipients were:

> The BCT Gold Medal – Dr Soozy Smith. During her 13 years at BCT, Soozy has made an enormous contribution to our organisation and to improved outcomes for women with breast cancer. Soozy has had many achievements during this time, and BCT is in a stronger position than ever before, thanks to her leadership.

> The Alan Coates Award for Excellence in Clinical Trials Research - Ms Leslie Gilham. Leslie is the Chair of the Breast Cancer Trials Consumer Advisory Panel, is a passionate advocate for clinical trials, and was a participant in the TEXT clinical trial. She is a member of the BIG 3-07 / TROG 07.01 DCIS Steering Committee, a member of the Breast International Group Patient Partnership Initiative (BIG-PPI), the Roche Global Breast Cancer Council, and an advisor to the TILs International Working Group.

> The Robert Sutherland Award for Excellence in Translational Research - Professor Andrew Tutt. Andrew is a Consultant Oncologist and a member of the multidisciplinary Breast Units at Guy's and St Thomas' and Royal Marsden NHS Foundation Trusts. He is Professor of Breast Oncology and Director of the Breast Cancer Now Toby Robins Research Centre at The Institute of Cancer Research, London. He is a member of the St Gallen Early Breast Cancer International Consensus Panel, the Oxford Early Breast Cancer Trialists Cooperative Group (EBCTCG), and is Chair of the CRUK Experimental Medicine Expert Review Panel.

CTC-H.U.B.
CLINICAL TRIALS CENTER – HÔPITAL UNIVERSITAIRE DE BRUXELLES (BELGIUM)

Institut Jules Bordet and BIG: a long-term collaboration

For more than two decades, the Clinical Trials Support Unit (CTSU) of Institut Jules Bordet (IJB) – now the Clinical Trials Center (CTC) of the Hôpital Universitaire de Bruxelles (H.U.B) – has maintained a close partnership with the Breast International Group (BIG) since its foundation to conduct large-scale international clinical trials, significantly impacting oncological research.

Some of the most notable studies born from this collaboration include TAX 315, HERA, ALTTO, APHINITY, FINESSE, ALEXANDRA/IMpassion030, and AURORA; each contributing to expanding the boundaries of scientific knowledge and improving breast cancer treatments.

Since TAX 315, the first of these studies, the Breast European Adjuvant Study Team (BrEAST), has been closely linked to BIG and was instrumental in establishing the CTSU later. Through continuous innovation, the CTSU eventually evolved into the current CTC, now recognised internationally as a major player in the coordination and execution of oncology clinical trials.

What is the Clinical Trials Center (CTC) and what is its purpose?

The CTC is a cornerstone department within the H.U.B, a network of three major hospitals in Brussels founded in 2022: Institut Jules Bordet, Hôpital Erasme (HE), and Hôpital Universitaire des Enfants Reine Fabiola (HUDERF).

The CTC serves as a pivotal support structure for both commercial and academic clinical research conducted by H.U.B researchers. Its primary mission is to offer comprehensive and professional assistance in managing clinical research by streamlining and harmonising the administrative, operational (e.g., data management, monitoring, regulatory affairs), contractual, and financial aspects of clinical studies.

A collaborative ecosystem for advancing clinical research

The success of clinical trials relies heavily on the close collaboration of multidisciplinary teams, including medical, scientific, and operational experts. With over 20 years of experience, the CTC has developed a broad spectrum of services for clinical study management, ranging from contractual support to full operational oversight. These services help researchers navigate the entire research process. Moreover, the CTC fosters an environment of research and innovation, encouraging synergies between academic partners, pharmaceutical companies, and other stakeholders in the healthcare sector.

Tailored contractual and operational expertise for clinical studies

Within the CTC, support is categorised into two primary areas:

1. Contractual support for promotion and investigation

This centralised management unit facilitates the work of researchers and investigators across all three H.U.B hospitals, providing a comprehensive framework for the legal and financial administration of clinical studies, translational research, and European-funded projects. A dedicated team of legal and financial experts ensures that all contractual, legal and financial matters directly or indirectly linked to research are properly addressed. Whether managing clinical study contracts or handling the financial intricacies of research projects, the team is committed to supporting successful collaborations with internal and external stakeholders, including pharmaceutical and biotech companies, academic institutions, and foundations.

"Investigation" refers to the contract support offered to clinical studies conducted at participating sites, while "Promotion" focuses on the operational backing for clinical study sponsorship activities.

2. Operational support for promotion

Operating within the CTC, this area oversees the operational aspects of clinical studies sponsored by any of the H.U.B hospitals. Working in close collaboration with the medical and scientific teams, it offers a professional operational infrastructure that nurtures scientific innovation and creativity. The team's expertise is not limited to internal projects but is also extended to external collaborations with both academic institutions and private industry partners, such as pharmaceutical and biotechnology firms.

Empowering researchers with essential tools and training for clinical trials

In addition to its core services, the CTC also provides a range of tools and resources to enhance research efficiency and capacity, including:

> **"Introduction to Clinical Trials – Academic Sponsor Perspectives" training:** This training module is designed to offer researchers, particularly those initiating hospital-sponsored clinical trials, a clear understanding of the processes, roles, and responsibilities involved in clinical studies. It offers a detailed overview of the sponsor's responsibilities.

> **GCP eLearning:** In collaboration with other Belgian University Clinical Trials Centres, the CTC offers an eLearning programme on Good Clinical Practice (GCP) based on the R2 version of ICH-GCP E6. Upon successful completion, participants receive a GCP certificate recognised internationally by TransCelerate Biopharma Inc.

> **Other templates, protocols, and processes:** The CTC also provides various standardised templates, protocols, and processes designed to ensure that all clinical trials adhere to the highest standards of quality and compliance.

Conclusion: a support service for clinical research and patients

By offering these specialised services and fostering collaborations, the H.U.B's CTC plays a crucial role in advancing clinical research that has a tangible impact on patients' lives, while also contributing to the overall scientific and medical excellence of the H.U.B.

EORTC BCG
EUROPEAN ORGANISATION FOR RESEARCH AND TREATMENT OF CANCER – BREAST CANCER GROUP

The EORTC Breast Cancer Group (BCG) comprises a network of 681 investigators from numerous hospitals in Europe. Our mission is to challenge, redefine, and develop standards of care in all areas of breast cancer diagnosis and therapy. The focus of our research is the evaluation of innovative treatments and multidisciplinary approaches to increase survival and improve quality of life of all breast cancer patients.

Collaboration has been in our DNA since the creation of the BCG. That is why we highly value the solid long-standing partnership with BIG, and we congratulate them on their 25 anniversary!

Additionally, we are proud to have co-organised, for the sixth consecutive year, a Pink October webinar with BIG. This year's theme was "25 years of breast cancer research: yesterday, today, tomorrow". The webinar, organised in partnership with the EU Health Policy Platform, took place on 16 October and highlighted the significant milestones and advancements in breast cancer research over the past quarter-century. It also offered a forward-looking perspective on future innovations and breakthroughs. Invited speakers included David Cameron, Michail Ignatiadis, Jan-Willem van de Loo, and Tanja Spanic. *For more details, please see page 18-23.*

Actively recruiting studies

EORTC-2129-BCG / BIG 22-01 TREAT ctDNA: Elacestrant for ctDNA-positive ER+/HER2- breast cancer (NCT05512364)
Principal Investigator: Michail Ignatiadis
EORTC study co-coordinators: Emmanouil Saloustros and Wolfgang Janni

This phase III study aims to evaluate whether elacestrant can delay occurrence of distant metastasis or death when compared to standard endocrine therapy in ER+/HER2- breast cancer patients with ctDNA-relapse, treated with adjuvant endocrine therapy. Patients are randomised after a positive ctDNA test during the screening period and after confirmation by imaging of the absence of distant metastasis or locoregional recurrence.

Elacestrant is provided by Menarini Group (Berlin-Chemie AG), and the SignateraTM assay is performed by Natera, Inc. This trial is being conducted in collaboration with different groups, including from within the BIG network (as a BIG supporter model trial). More than 120 sites will participate in total. The first sites have been activated, and the study has been open for recruitment in Belgium, Germany, France, Cyprus, Italy, Ireland, The Netherlands, Spain and Switzerland since December 2023.

A trial-in-progress poster was presented at ESMO 2024:

From left to right: Orsolya Birta, Medical Advisor at BIG; Ana Joaquim, Clinical Research Physician at EORTC; Jose Casas, Translational Research Scientist at EORTC; Michail Ignatiadis, Chair of the EORTC Breast Cancer Group, Director of the Breast Medical Oncology Clinic & Program at the Jules Bordet Institute, Associate Professor at the Université Libre de Bruxelles, and Study Coordinator of the TREAT ctDNA trial; and Carmela Caballero, Sr. Medical Advisor at BIG.

EORTC-1408-BCG / BIG 14-01 (AURORA): Aiming to Understand the MOlecular Aberrations in Metastatic Breast Cancer (NCT02102165).
Principal Investigators: Philippe Aftimos, Angel Guerrero Zotano, Matteo Benelli
EORTC study coordinator: Fatima Cardoso

This is an intergroup study led by BIG. Recruitment to the first phase of the AURORA programme closed on 1 March 2021, and an extension of the study (AURORA 2.0) is taking place at some of the sites, including five from the EORTC

EORTC-1811 (E²-RADIatE) (NCT03818503)
(Homepage - E2-RADIatE (eortc.org) is an EORTC-ESTRO radiotherapy registry/platform that was launched on 25 June 2019. This multi-cohort platform aims to collect real-world data of cancer patients treated with radiotherapy. Currently it includes two cohorts:

> **RP_1822 OligoCare cohort:** This observational cohort evaluates radical radiotherapy for patients with oligometastatic lung, breast, prostate or colorectal cancer. As of 30 September 2024, 3023 patients had been enrolled, including 438 (13%) patients with oligometastases from their breast cancer.

> **RP_2011 ReCare cohort:** The objective of this cohort is to evaluate patients treated with high-dose re-irradiation. As of 30 September 2024, 18 sites (out of a selected total of 25) had been authorised for recruitment, and 307 patients had already been enrolled.

RP-1828 (IMMUcan) is a downstream project of 1553-SPECTA (NCT02834884). The goal is to generate broad molecular (WES and RNAseq) and cellular profiling data (multiplex IF and IMC) of the tumour and its microenvironment, integrated with clinical data from cancer patients, to understand how the immune system and tumours interact, as well as the impact of current therapeutic interventions. A molecular report with all clinically targetable molecular alterations will be returned to clinicians.

Enrolment opened for recruitment on 27 May 2019 and was closed on 30 August 2024. Of the 1,469 patients enrolled for IMMUcan, 776 were enrolled in the three breast cohorts.

Access to IMMUcan human biological material for further research can be requested via the website: IMMUcan - How to Collaborate?

EORTC-1841-QLG-BCG: Adaption of the EORTC QLQ-Breast Cancer Module for male BC
Study coordinators: Vesna Bjelic-Radisic and Fatima Cardoso

Recruitment for phase 1 of the module development has been completed. Phase 2 will start after the approval of the related protocol amendment.

Trial in advanced stage of development phase

EORTC 2237-BCG-QLG: Improvement of Quality of Life through supportive treatments for Endocrine Therapy – related symptoms in patients with early Breast Cancer: A pragmatic randomized Controlled Trial (QOL-ET-BC) (NCT06407401)
Study coordinator: Galina Velikova
Study co-coordinator: Katarzyna Pogoda

This is a pragmatic international, multi-centre, randomised, open label, 3-arm trial for patients with ER+/HER2- early breast cancer suffering from endocrine therapy-related musculoskeletal pain. Patients will be randomised between standard care versus six months of duloxetine or furosemide.

The plan is to open in 17 sites in Cyprus, France, Poland, Slovenia, Spain, the United Kingdom, and countries from Middle East via the MECO intergroup. Regulatory submissions are ongoing.

Recent publications

- Kaidar-Person O, Boersma LJ, De Brouwer P, et al. ERTC Radiation Oncology and Breast Cancer Groups. The EORTC 22922/10925 trial investigating regional nodal irradiation in stage I-III breast cancer: Outcomes according to locoregional and systemic therapies. *Radiother Oncol.* 2024 Sep 26;201:110563. doi: 10.1016/j.radonc.2024.110563. Online ahead of print. PMID: 39341505

- Siman-Tov M, Ostrovski A, Mast M, et al. Dosimetric Analyses of the Three Radiation Techniques Used in the EORTC 22922/10925 IM-MS Breast Cancer Trial. *Clin Oncol* (R Coll Radiol). 2024 Aug 24:S0936-6555(24)00369-8. doi: 10.1016/j.clon.2024.08.012. Online ahead of print.

- Alongi F, Nicosia L, Ricardi U, et al. Acute toxicity in patients with oligometastatic cancer following metastasis-directed stereotactic body radiotherapy: An interim analysis of the E2-RADIatE OligoCare cohort. *Radiother Oncol.* 2024 Oct;199:110466. doi: 10.1016/j.radonc.2024.110466. Epub 2024 Jul 31.PMID: 39094630

- Christ SM, Alongi F, Ricardi U, et al. Cancer-specific dose and fractionation schedules in stereotactic body radiotherapy for oligometastatic disease: An interim analysis of the EORTC-ESTRO E(2)-RADIatE OligoCare study. *Radiother Oncol.* 2024 Jun;195:110235. doi: 10.1016/j.radonc.2024.110235. Epub 2024 Mar 19.PMID: 38508239

Upcoming events

> EORTC BCG Spring Group Meeting: date to be confirmed

> 14-20 June 2025: 25th Workshop on Methods in Clinical Cancer Research (MCCR) (Sint-Michielsgestel, Netherlands). More information is available on the EBCC website: https://event.eortc.org/mccr2025/

> 25-27 March 2026: EBCC-15 (Barcelona, Spain)

See also page 64.

The BCG Group at the Group Meeting in Bordeaux, September 2023.

Left to right: Michail Ignatiadis (Chair EBCC-14), Stella Kyriakides (European Commissioner for Health and Food Safety), Fiorita Poulakaki (Co-Chair), Alberto Costa (ESO CEO) attending EBCC-14

EUBREAST
EUROPEAN BREAST CANCER RESEARCH ASSOCIATION OF SURGICAL TRIALISTS

Contributions in the new era of breast cancer surgery

The following experts, representing diverse regions across Europe, including Switzerland, Germany, Italy, and Portugal, and bringing a wealth of expertise in breast cancer care and research, are the Executive Team of the EUBREAST.

- Professor Maria Luisa Gasparri, MD, PhD: Department of Gynecology and Obstetrics, Ente Ospedaliero Cantonale, Centro di Senologia della Svizzera Italiana, and Faculty of Biomedical Science, University of Italian Switzerland, Lugano, Switzerland
- Professor Maggie Banys-Paluchowski, MD, PhD: Department of Gynecology and Obstetrics, University Hospital Schleswig-Holstein Campus Lübeck, Lübeck, Germany
- Dr Rosa Di Micco, MD, PhD: Breast Surgery Unit, San Raffaele University Hospital, Milan, Italy
- Professor Nina Ditsch, MD, PhD: Breast Cancer Center, University Hospital Augsburg, Augsburg, Germany
- Dr Eduard-Alexandru Bonci, MD: Breast Unit, Champalimaud Clinical Centre, Champalimaud Foundation, Lisbon, Portugal
- Ms Sarah Jennie Goldman, MBA: EUBREAST Network Coordinator, Parma, Italy
- Professor Oreste D. Gentilini, MD, PhD: Breast Surgery Unit, San Raffaele University Hospital, Milan, Italy
- Professor Thorsten Kuehn, MD, PhD: Department of Gynecology and Obstetrics, University of Ulm, Ulm, Germany; and Department of Gynecology and Obstetrics, Die Filderklinik, Filderstadt, Germany

A physician who follows guidelines is not just an executor, but also a custodian of medical science, while a physician who generates guidelines is an architect of care, shaping the future of medicine with evidence-based recommendations.

The EUropean Breast Cancer REsearch Association of Surgical Trialists (EUBREAST) is a non-profit organisation founded with a dual objective: to develop and promote clinical trials that contribute to the evolution and standardisation of international guidelines ("architects of care") and to help keep international experts in the breast cancer field up to date about the most recent scientific achievements ("custodians of medical science"). Both of these goals have the same aim: to accelerate scientific progress for the direct benefit of breast cancer patients.

EUBREAST has been working to achieve these objectives in the following manner:

-Creating important opportunities for collaboration amongst international surgical researchers to enhance the quality and impact of surgical trials;

-Offering educational opportunities for surgeons and researchers to improve their skills in conducting clinical trials and stimulate the scientific curiosity;

-Promoting best-practice standards for surgical trials, ensuring that research is conducted ethically and effectively, using methodological principles and facilitating the collection and sharing of data amongst participating institutions to better understand treatment outcomes and patient experiences;

- Networking amongst professionals in the field of surgical research, in order to share knowledge, resources, and best practices;

- Advocating for the importance of surgical research in improving patient care and outcomes.

Since its creation in 2018, the EUBREAST scientific community has been active in over 35 countries and has promoted or supported several trials, including landmark studies that today represent practice-changing studies, such as the SOUND[1] and SENOMAC[2] trials.

Prof Thorsten Kuehn, Prof Maggie Banys-Paluchowsky, Prof Nina Ditsch, Dr Eduard A. Bonci, Prof Oreste D. Gentilini, Dr Rosa Di Micco, Prof Maria Luisa Gasparri

EUBREAST has also launched international registries that are currently amongst the largest in each specific area of study. Since 2020, AXSANA/EUBREAST[3], a prospective multicentre registry on axillary surgical techniques after neoadjuvant chemotherapy, has recruited over 5,000 patients[3]. The target accrual for MELODY/EUBREAST[4], a multicentre cohort study to evaluate different imaging-guided methods for localisation of malignant breast lesions, is over 7,000 patients 4 within a relatively short timeframe. This accrual rate and the development of such an important international network not only confirm the needs of breast surgeons in answering these questions, but also emphasise that our vision, coordinated planning, and international cooperation are key to moving forward [5].

The Network is also facilitated by its relationships with other international organisations in the field, such as the OPBC, SENATURK, Ibra-Net (*full list in the Acknowledgement section*) which contribute, for example, by circulating surveys amongst their members, with the scope of identifying, defining, and filling in the knowledge gaps. This approach offers an international snapshot of the real life of a breast surgeon, particularly when there is not a clear evidence-based supported position yet, such as during the adaptation of medical practice in the COVID pandemic [6], which was one of the most cited publications on breast cancer and COVID during the pandemic. Additionally, there are significant challenges, such as the international discrepancies of specialist training across Europe (UEMS MJC project, submitted for publication), the heterogeneity and lack of international consensus on surgical axillary management[7], and the differing approaches to regional nodal irradiation after primary systemic treatment (paper accepted for publication in Radiation Oncology Journal). The results of these investigations amongst breast care specialists helped identify the grey zones, while ongoing EUBREAST trials are trying to fill the knowledge gaps and form consensus.

Last but not least, EUBREAST eV and EUBREAST ETS (the two network associations) are grateful to the BIG network for its valuable support in promoting news related to the group's research programmes and activities. After all, scientific progress is never the result of the work of a single individual, but rather the product of cooperation among many. When this cooperation meets scientific curiosity, methodology, and perseverance, individual motivation becomes a community's raging torrent, where innovation and advancement become unstoppable processes.

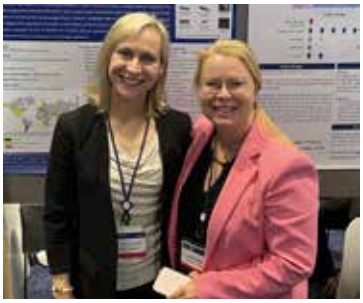
Contribution by Professor Maria Luisa Gasparri, MD, PhD
Executive Board Member of the EUBREAST ETS
EUBREAST Ambassador in Switzerland
marialuisa.gasparri@eoc.ch

For more information: www.eubreast.org

Acknowledgements

American Society of Breast Surgeons; Arbeitsgemeinschaft für gynäkologische Onkologie; Associazione Nazionale Italiana Senologi Chirurghi; Collegio Italiano dei Senologi; Deutsche Gesellschaft für Radioonkologie; Deutsche Gesellschaft für Senologie; Die Schweizerische Gesellschaft fuer Plastische, Rekonkstruktive und Aesthetische Chirurgie; European Union of Medical Specialists; Global Breast Cancer Leaders & Innovators | BIG; IbraNet; Israel Breast Surgeons Society; Israel Radiation Therapy society; Italian Society of Plastic and Reconstructive Surgery; Oncoplastic Breast Consortium; Swiss Society of Senology; Scuola Italiana di Senologia; SENATURK; Società Polispecialistica Italiana Giovani Chirurghi; Swiss Society of Pathology.

Dr Eduard A. Bonci, Dr Rosa Di Micco, Prof Thorsten Kuehn, Prof Maria Luisa Gasparri, Prof Oreste D. Gentilini



Prof Maggie Banys-Paluchowsky, Prof Nina Ditsch

References

1. Gentilini OD, Botteri E, Sangalli C, et al. Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes: The SOUND Randomized Clinical Trial. *JAMA Oncol* 2023. doi: 10.1001/jamaoncol.2023.3759.

2. de Boniface J, Appelgren M, Szulkin R, et al. Completion axillary lymph node dissection for the identification of pN2-3 status as an indication for adjuvant CDK4/6 inhibitor treatment: a post-hoc analysis of the randomised, phase 3 SENOMAC trial. *Lancet Oncol* 2024. doi: 10.1016/S1470-2045(24)00350-4

3. Banys-Paluchowski M, Gasparri ML, de Boniface J, et al. Surgical Management of the Axilla in Clinically Node-Positive Breast Cancer Patients Converting to Clinical Node Negativity through Neoadjuvant Chemotherapy: Current Status, Knowledge Gaps, and Rationale for the EUBREAST-03 AXSANA Study. *Cancers (Basel)* 2021. doi: 10.3390/cancers13071565

4. Banys-Paluchowski M, Kühn T, Masannat Y, et al. Localization Techniques for Non-Palpable Breast Lesions: Current Status, Knowledge Gaps, and Rationale for the MELODY Study (EUBREAST-4/iBRA-NET, NCT 05559411). *Cancers (Basel)* 2023. doi: 10.3390/cancers15041173

5. O. Gentilini, Lessons from the SOUND trial and future perspectives on axillary staging in breast cancer. *Br J Surg* 2024. doi: 10.1093/bjs/znad391

6. Gasparri ML, Gentilini O, Lueftner D, et al. Changes in breast cancer management during the Corona Virus Disease 19 pandemic: An international survey of the European Breast Cancer Research Association of Surgical Trialists (EUBREAST). *Breast* 2020. doi: 10.1016/j.breast.2020.05.006

7. Gasparri ML, de Boniface J, Poortmans P, et al. Axillary surgery after neoadjuvant therapy in initially node-positive breast cancer: international EUBREAST survey. *Br J Surg* 2022. doi:10.1093/bjs/znac217

GEICAM
SPANISH BREAST CANCER GROUP

GEICAM's experience and view on being part of BIG

From the broad perspective provided by our nearly 30 years of history, at GEICAM we are aware that we are immersed in a shift in the paradigm of academic breast cancer research.

A quick analysis of the clinical research landscape clearly demonstrates that the dominance of trials designed and conducted by the pharmaceutical industry is steadily becoming the majority, while academically inspired research is progressively diminishing.

In this context, it is more necessary than ever to design and carry out clinical trials that address unanswered questions and provide direct benefits to our patients. In the era of personalised medicine, identifying patient subgroups that benefit most from innovations, minimising side effects, and tailoring treatments to patient preferences are aspects that remain largely unaddressed in many industry-defined clinical trials, especially when done without prior dialogue with the academic world.

At GEICAM, we continue to face the challenge of generating academic evidence, relying on the foundations that have allowed us to get this far: a broad implantation base with a deeply rooted cooperative approach among peers, a great capacity for recruitment in clinical research projects, and a professionalised structure with internationally recognised quality. With these tools, we will continue to develop new projects, including not only academically designed clinical trials but also real-world data registries, translational research projects to address the need for new biomarkers, and innovative healthcare projects in areas with limited funding.

This effort would have little impact if done alone. That is why global collaboration – particularly through our partnership with BIG, a network with which we share goals, enthusiasm, and a common approach – is an essential condition for success.

In recent years, we have made a particular effort to renew our generation by incorporating young researchers into the leadership of our group. They are highly trained and deeply motivated for this work that excites us so much.

We remain more motivated than ever, better prepared than ever, and with the goal of definitive breast cancer control closer than ever.

Contribution by Dr Ander Urruticoechea, GEICAM Vice President, member of the BIG Executive Board

Highlights from GEICAM Translational Research in 2024

In 2024, GEICAM presented findings from several important translational research projects at international scientific meetings, including the ASCO Annual Meeting and ESMO Congress, reflecting advances in molecular biomarkers in breast cancer treatment and precision medicine.

Below are some key studies that were shared.

> Comprehensive Clinical Characteristics and ctDNA Mutational Profile Analysis of Endocrine Resistance in HR+ Breast Cancer (GEICAM/2014-03 RegistEM Registry).

In an oral presentation, Dr Ángel Guerrero showed results from the ctDNA (circulating tumour DNA) analysis in patients with luminal (HR+) metastatic breast cancer who experienced recurrence after adjuvant endocrine therapy (ET). This study aimed to better understand the mechanisms of ET resistance, a major challenge in the treatment of HR+ breast cancer.

The study revealed that patients with primary resistance to adjuvant ET had significantly worse overall survival and a poorer response to first-line treatment compared to those with secondary resistance or those sensitive to ET. Moreover, ctDNA analysis identified specific genomic alterations associated with poor outcomes in patients with endocrine-resistant breast cancer. The study found that both primary and secondary resistance were linked to treatable mutations, including those in the ESR1 (oestrogen receptor) and EGFR genes.

ASCO 2024: Oral communication. Comprehensive Clinical Characteristics and ctDNA Mutational Profile Analysis of Endocrine Resistance in HR+ Breast Cancer (GEICAM/2014-03 RegistEM Registry). doi: 10.1200/JCO.2024.42.16_suppl.1011.

Dr Ángel Guerrero at ASCO 2024

Dr Federico Rojo at ASCO 2024

> Non-basal Subtype Defined by FOXC1 Expression as a Predictor of Capecitabine Efficacy in TNBC (GEICAM/2003-11_CIBOMA/2004-01 Trial).

In another high-impact presentation, Dr Federico Rojo shared new data from the Phase III GEICAM/CIBOMA trial, focused on patients with triple-negative breast cancer (TNBC). The study, led by Dr Miguel Martín, evaluated the role of FOXC1 expression in predicting patient response to extended adjuvant capecitabine therapy. The GEICAM study highlighted that patients with a non-basal TNBC subtype, defined by the absence of FOXC1 expression, experienced significant clinical benefits in terms of disease-free survival from extended adjuvant capecitabine therapy.

Patients with non-basal TNBC were identified through an IHC-based (immunohistochemistry) test for FOXC1 expression (the VERESCA test). Dr Miguel Martín emphasised the simplicity and feasibility of incorporating FOXC1 IHC evaluation into routine clinical practice, potentially improving the standard of care for this specific subgroup of patients. FOXC1 pathological evaluation details were presented by Dr Rojo in an additional poster presentation during the 36th European Congress of Pathology (September 2024).

ASCO 2024: Rapid Oral Abstract Session. Non-basal Subtype Defined by FOXC1 Expression as a Predictor of Capecitabine Efficacy in TNBC (GEICAM/2003-11_CIBOMA/2004-01 Trial). doi: 10.1200/JCO.2024.42.16_suppl.516

> Ki67 and Oncotype DX Recurrence Score as Predictive Biomarkers in the CARABELA Trial (GEICAM/2019-01).

The GEICAM CARABELA trial investigated the role of abemaciclib, a CDK4/6 inhibitor, combined with letrozole (an aromatase inhibitor) as neoadjuvant therapy in patients with highly proliferative HR+/HER2- breast cancer. Dr Guerrero presented biomarker analysis focusing on Ki67 and the Oncotype DX Recurrence Score.

The study found that for patients with high proliferation rates (Ki67 ≥20%), 12 months of neoadjuvant hormone therapy with abemaciclib did not achieve the same residual cancer burden (RCB) 0-I rates as standard chemotherapy. However, patients with lower proliferative tumours (Ki67 <40%) and those with a low Oncotype DX score (RS <26) showed similar pathological response rates to chemotherapy. This suggests that chemotherapy might not be necessary for patients with lower tumour proliferation or an RS below 26, regardless of tumour stage.

Rojo F et al, 36th European Congress of Pathology – Abstracts. *Virchows Archiv* 2024 Volume 485 Page 69 Abstract PS-02-025. doi: 10.1007/s00428-024-03880-y.

ASCO 2024: Poster presentation: Ki67 and Oncotype DX Recurrence Score as Predictive Biomarkers in the CARABELA Trial (GEICAM/2019-01). Plasma mutational burden in PIK3CA and TP53 independently predicts early progression in HR+/HER2- metastatic breast cancer patients enrolled in the GEICAM/2014-12 FLIPPER trial. doi: 10.1200/JCO.2024.42.16_suppl.1029

> Plasma Mutational Burden in PIK3CA and TP53 as Predictors of Early Progression in HR+/HER2- Metastatic Breast Cancer (GEICAM/2014-12 FLIPPER Trial).

Dr Rojo also presented results from the GEICAM/2014-12 FLIPPER trial, which investigated biomarkers associated with resistance to palbociclib and fulvestrant in HR+/HER2- metastatic breast cancer. The study employed a highly sensitive NGS

(Next-Generation Sequencing) panel, Plasma Seq-Sensei BC, to analyse plasma samples for common breast cancer gene mutations. The study revealed that patients with two or more mutations in PIK3CA and TP53 had significantly poorer progression-free survival, overall survival, and clinical response. These patients progressed within 12 months despite treatment with palbociclib and fulvestrant, highlighting the importance of genomic profiling in predicting treatment outcomes.

This biomarker-driven approach could help identify patients at high risk of rapid progression, enabling more aggressive or alternative treatment strategies for those unlikely to respond to standard palbociclib-fulvestrant therapy.

ASCO 2024: Plasma mutational burden in PIK3CA and TP53 independently predicts early progression in HR+/HER2- metastatic breast cancer patients enrolled in the GEICAM/2014-12 FLIPPER trial. doi: 10.1200/JCO.2024.42.16_suppl.1029

> Thymidine Kinase Activity (TKa) as a Predictor of Progression in the FLIPPER Trial

In a related analysis from the FLIPPER trial, researchers evaluated the prognostic value of thymidine kinase activity (TKa) using the DiviTum assay as a liquid biomarker for tumour proliferation.

The study found that patients with elevated TKa levels at baseline or after 12 weeks of treatment were more likely to experience early progression (within 12 months). TKa levels were linked to both progression-free survival and overall survival, suggesting that this biomarker could be used to identify patients who would benefit most from adding palbociclib to their treatment regimen.

ASCO 2024: The Liquid Biomarker Thymidine Kinase Activity (TKa) Independently Predicts Outcome and Progression in Metastatic Breast Cancer Patients in the GEICAM/2014-12 FLIPPER Trial. doi: 10.1200/JCO.2024.42.16_suppl.1028

> Ki67 as a Prognostic Factor in Male Breast Cancer (GEICAM/2016_04 MaBC Registry)

The GEICAM Male Breast Cancer Registry (MaBC) is the largest collection of data on male breast cancer patients in Spain. First results from the full cohort of 773 patients were presented, including information on tumour characteristics, treatment patterns, and outcomes in early or localised disease. The analysis showed that HR+/HER2- is the most common subtype in male breast cancer, similar to female breast cancer, with high ER and PR positivity. However, unlike in female breast cancer, Ki67 (a marker of tumour proliferation) was not found to be a prognostic marker in men, as no statistically significant survival differences were observed based on Ki67 levels. Additionally, male breast cancer tended to present at more advanced stages, and local treatments were more aggressive, highlighting a need for improved neoadjuvant treatment strategies for men.

ASCO 2024: Poster presentation: Ki67 as a prognostic factor in male breast cancer (male bc): results from a large GEICAM Spanish cohort of male BC. doi: 10.1200/JCO.2024.42.16_suppl.556

> Prevalence of HER2-low Breast Cancer in the GEICAM/2011-06 Trial

Dr Rojo examined the prevalence of HER2-low breast cancer. The study compared results from standardised immunohistochemistry (IHC) assays, including an improved version of the HercepTest, to evaluate concordance between local and central HER2-low determinations. The findings showed that concordance for HER2-low classification was moderate and significantly lower than for traditional HER2-positive/negative determination. This discrepancy underscores the need for updated methodologies for HER2-low assessment, which is critical for selecting patients eligible for new ADC therapies.

ESMO 2024: Poster presentation: Prevalence of HER2-low breast cancer in the GEICAM/2011-06 trial: agreement in HER2-low classification between standardized immunohistochemistry assays. Poster presentation. doi: 10.1016/j.annonc.2024.08.222

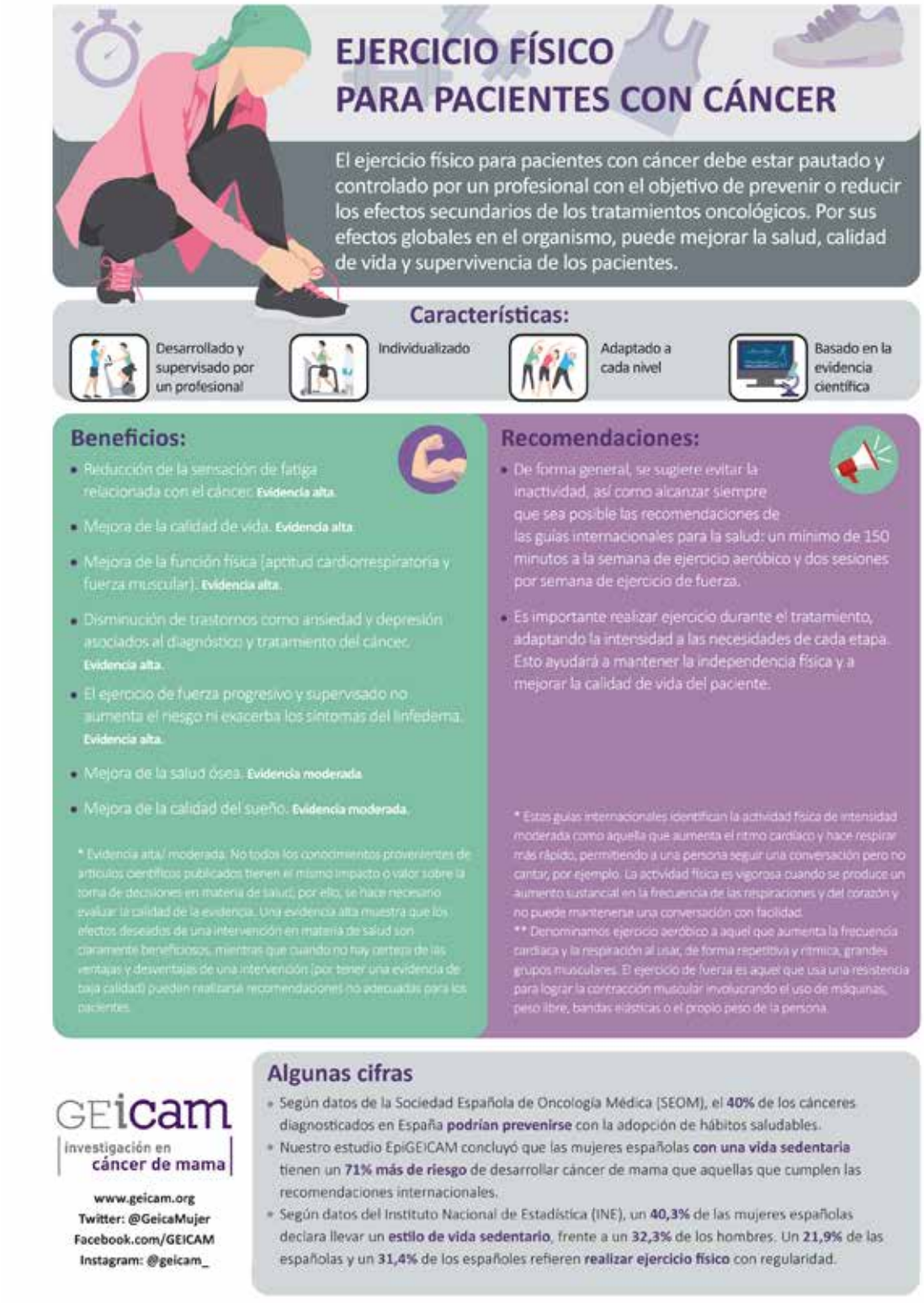
Physical exercise and breast cancer

We are thrilled to share some exciting developments from our ongoing research projects focused on physical exercise for breast cancer patients: GYMNOS and EVAL-ACTIVA.

On the one hand, GYMNOS is dedicated to understanding the daily physical activity levels of Spanish breast cancer patients, including their preferences for exercise programmes. We are proud to collaborate with patient associations to ensure the maximum number of participants complete a survey that reflects their reality as accurately as possible. We are eager to gather insights that can enhance the quality of life for breast cancer patients through tailored exercise interventions.

On the other hand, EVAL-ACTIVA focuses on validating internationally recognised questionnaires for the general population related to physical activity, specifically for breast cancer patients. The objective is to validate those questionnaires with different cohorts of patients at various stages of breast cancer progression. Having a validated tool is crucial for clinical research, as it allows us to accurately assess the physical activity levels and needs of this population. Notably, our first cohort comprised patients with metastatic breast cancer, and we successfully recruited participants in under three months!

We believe that these projects will significantly contribute to the understanding and enhancement of physical activity among breast cancer patients, ultimately leading to better health outcomes.



IBCSG
INTERNATIONAL BREAST CANCER STUDY GROUP

The International Breast Cancer Study Group IBCSG, a division of the ETOP IBCSG Partners Foundation.

Focusing on young patients: past, present, future

The International Breast Cancer Study Group (IBCSG) is one of the three original founding entities of the Breast international Group (BIG) established as a legal entity in 1999. At that time, Professor Aron Goldhirsch, IBCSG Scientific Director (Bern, Switzerland), and Professor Martine Piccart, a medical oncologist at Institut Jules Bordet (Brussels, Belgium) and affiliated with the European Organisation for the Research and Treatment of Cancer (EORTC), clearly saw the need for academically-based, international breast cancer cooperative groups to work together with pharmaceutical companies. Their goal was to design and conduct the randomised phase III trials that would be most impactful to improve breast cancer patient care. The emphasis of such trials would be on developing the safest and most effective approaches to treating the disease while considering all aspects of the patient experience throughout the process.

In 1978, the role of menopausal status as a modifier of treatment effectiveness and the importance of accurate and consistent assessment of the oestrogen receptor status of the tumour were gaining traction worldwide. In that year, the Ludwig Breast Cancer Study Group, the precursor to IBCSG, launched four trials directed towards premenopausal women (two cohorts defined based on recurrence risk) and postmenopausal women (two cohorts defined by age). Menopausal status was defined by biological parameters, not only by age. As Professor Elwood Jensen was a member of the Ludwig Institute for Cancer Research Board, pathologists from each of the group's institutions were active participants in group meetings and conducted in-person workshops to standardise oestrogen receptor and progesterone receptor assessments within each of the participating centres worldwide. These two founding features – biological definition of menopausal status and quality-controlled central pathology review – enabled IBCSG to design and conduct pivotal clinical trials directed towards targeted patient populations based on menopausal and steroid hormone receptor status.

Richard Gelber, Professor in the Department of Biostatistics at Harvard University and the Dana-Farber Cancer Institute in Boston, is a key figure in the IBCSG and has played a pivotal role in the development and analysis of clinical trials related to breast cancer treatment. As a biostatistician, he has contributed significantly to the statistical design and development of various studies under IBCSG and BIG, including POSITVE. His expertise lies in integrating interdisciplinary perspectives into trial design, ensuring that studies are comprehensive and relevant across various healthcare settings.

Professors Aron Goldhirsch and Martine Piccart – founders of BIG

Professors Richard Gelber and Aron Goldhirsch – Fathers of the spirit of our academic trials

Given this solid background, it is not surprising that IBCSG has contributed substantially to improving treatment and care for premenopausal women with endocrine-responsive early breast cancer. Secondary analyses of IBCSG trials, with confirmation in other cooperative group trials, observed that premenopausal women who maintained or regained premenopausal status after chemotherapy had poorer prognosis than those who became postmenopausal.

SOFT (IBCSG 24-02 / BIG 2-02) and TEXT (IBCSG 25-02 / BIG 3-02)

In 2003, the IBCSG launched the Suppression of Ovarian Function Trial (SOFT) and the Trial of EXemestane and Tamoxifen (TEXT) studies under the BIG umbrella, with SOFT specifically testing the hypothesis that use of ovarian function suppression (OFS) with tamoxifen would improve outcomes for patients who were premenopausal after chemotherapy. Both BIG Groups and the United States NCI-sponsored (NCTN) cooperative groups contributed to SOFT-TEXT to enrol almost 6,000 premenopausal patients worldwide. A third trial launched concurrently, the Premenopausal Endocrine Responsive Chemotherapy Trial (PERCHE), aimed to understand the value of using adjuvant chemotherapy when OFS plus oral endocrine therapy was given, closed early because of low enrolment. The results from the SOFT-TEXT trials have contributed substantially to clinical care guidelines for this patient population.[1-4]

In 2024, the SOFT and TEXT databases are completing long-term follow-up with a maximum of 21 years and median follow-up of 15 years. Such long-term follow-up took extraordinary efforts on behalf of collaborating BIG and North American cooperative groups. However, as the risk of recurrence persists for many years in this premenopausal, hormone receptor-positive cohort, such follow-up is essential to fully inform patients and providers regarding the sustained effectiveness of the tested therapeutic approaches. Updated main results are anticipated in 2025, and clinical and translational research will continue to inform and generate new hypotheses for the care of these patients.

Supported by funding from the Breast Cancer Research Foundation (BCRF), the BIG-NCTN collaboration was initiated in 2005. Participants formed Working Groups to propose and develop research strategies to advance the field. Larissa Korde and Aron Goldhirsch co-chaired the Endocrine Therapy Working Group. The group recognised that one of the most complex patient-oriented issues faced in the clinic was the prospect of informing a young woman with hormone receptor-positive early breast cancer that the endocrine therapy she would need to take for the next 5-10 years would harm a foetus, and therefore that she could not become pregnant during the treatment period. Every investigator had seen a few patients like this, for whom the diagnosis of breast cancer interrupted family planning. Could a clinical trial be designed to provide data to help these patients?

POSITIVE (IBCSG 48-14 / BIG 8-13 /A221405)

The POSITIVE (Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer) trial was launched in late 2014 and accrued 516 evaluable patients through the end of 2019. Women with hormone receptor-positive early breast cancer who had received primary treatment and between 18 to 30 months of prior endocrine therapy, were 42 years old or younger, and who desired pregnancy could interrupt their endocrine therapy, undergo a 3-month wash-out period, and then attempt to become pregnant. Resumption of endocrine therapy was planned after pregnancy attempts ended and not longer than two years after interruption. The primary results, published in May 2023 in the *New England Journal of Medicine*, showed that in the short term (41-month median follow-up), the risk of breast cancer recurrence was below the pre-specified safety threshold and similar to that observed in an external control cohort of SOFT-TEXT patients who would have been eligible for enrolment in POSITIVE.[5]

At the time of the primary analysis of POSITIVE, of the 497 women who were followed for pregnancy status, 368 (74.0%) had at least one pregnancy and 317 (63.8%) had at least one live birth. A total of 365 babies were born. Secondary analyses were performed and recently presented, highlighting the frequency, efficacy, and safety of assisted reproductive technologies (ART)[6] and of breastfeeding.[7] Analyses of translational endpoints and patient-reported outcomes are ongoing.

The next POSITIVE database lock is planned for early 2025, with updated results to be analysed and presented in 2025. Follow-up of the women enrolled in POSITIVE is planned to continue until the end of 2029, 10 years after the enrolment of the last patient.

HOHO (IBCSG 43-09)

In addition to concerns about infertility and pregnancy after breast cancer, there are other unique medical and psychosocial issues that younger women with breast cancer face as a result of their diagnosis and treatment. In particular, sexual dysfunction, body image, economic impact and employment discrimination, and challenges related to children and family caregiving are major concerns for these patients and may contribute to the greater distress observed in this population.

The IBCSG 43-09 HOHO (Helping Ourselves Helping Others) study aims to characterise this population at diagnosis and during follow-up with respect to disease and psychosocial outcomes, providing healthcare professionals with information to better understand and manage their unique needs. The study – a companion to the original project developed by researchers at the Dana-Farber Cancer Institute in the US – is a longitudinal cohort study of women diagnosed with early/advanced breast cancer at age 40 years or younger, who were enrolled at 18 centres in Italy and Switzerland between July 2009 and January 2016. Participating women completed a comprehensive survey at baseline, every 6 months for 3 years, and then annually for a total of 10 years. Medical data on disease outcome, treatment, and comorbidities were collected by the investigators at annual follow-up visits.

The most recent analysis of the IBCSG HOHO cohort, published in *The Breast* in July 2024,[8] aimed to assess factors associated with non-persistence to endocrine treatment and to investigate the association between quality of life and symptom trajectories with non-persistence over a 5-year period in young survivors.

The results showed that many women continue with endocrine therapy despite experiencing side effects. In particular, partnered, childless women are more likely to discontinue endocrine therapy, highlighting the importance of addressing pregnancy desire and timing when discussing treatment. The initial results of the POSITIVE study are encouraging and, if confirmed in the long term, a pause in endocrine treatment for pregnancy could improve adherence among young women who want to become mothers. In addition, fostering good communication and relationships with healthcare providers may encourage these patients to persist with their prescribed therapies.[8]

Research and collaboration

Conducting prospective clinical trials in this area is challenging due to the relatively small population of young women with breast cancer and the complex emotional and personal preferences at play. Achieving meaningful results requires a strong commitment from both patients and investigators, as collaboration is essential to address these unique issues. Involving patients in the research process and ensuring that their voices are heard can help address their needs and improve trial participation.

Continued collaboration of BIG groups with NCTN and other academic groups worldwide is necessary to tailor adjuvant treatment for this premenopausal patient population. An ongoing NCTN-led trial (OFSET; NCT05879926) is revisiting the question of the value of chemotherapy when OFS with oral endocrine therapy is used. Trials for the adjuvant use of novel therapeutics, such as CDK4/6 inhibitors, enrolled premenopausal patients, but greater attention to the concomitant use of OFS and oral endocrine therapy is needed in future studies to better understand the relative contributions of novel therapies when tailoring treatment. While we know that OFS is necessary for premenopausal patients to be treated with an aromatase inhibitor, whether it remains necessary with novel endocrine therapies, such as oral selective oestrogen receptor degraders (SERDs), is uncertain. This question is being addressed in the IBCSG-sponsored PREcoopERA study (NCT05896566). Such research, focused on improving the ability to balance the efficacy and side effects of adjuvant therapies, is the core of providing the best care for each individual patient.

Contributions by Richard Gelber PhD, Meredith Regan ScD, Monica Ruggeri, Anita Hiltbrunner and Heidi Roschitzki-Voser PhD.

References

1. Francis PA, Pagani O, Fleming GF, et al. Tailoring Adjuvant Endocrine Therapy for Premenopausal Breast Cancer. *New England Journal of Medicine* 2018;379:122-37. doi: 10.1056/NEJMoa1803164

2. Francis PA, Regan MM, Fleming GF, et al. Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. *New England Journal of Medicine* 2015;372:436-46. doi: 10.1056/NEJMoa1412379

3. Pagani O, Regan MM, Walley BA, et al. Adjuvant Exemestane with Ovarian Suppression in Premenopausal Breast Cancer. *New England Journal of Medicine* 2014;371:107-18. doi: 10.1056/NEJMoa1404037

4. Pagani O, Walley BA, Fleming GF, et al. Adjuvant Exemestane With Ovarian Suppression in Premenopausal Breast Cancer: Long-Term Follow-Up of the Combined TEXT and SOFT Trials. *Journal of Clinical Oncology:* official journal of the American Society of Clinical Oncology 2023;41:1376-82. doi: 10.1200/JCO.22.01064

5. Partridge AH, Niman SM, Ruggeri M, et al. Interrupting endocrine therapy to attempt pregnancy after breast cancer. N*ew England Journal of Medicine* 2023;388:1645-56. doi: 10.1056/NEJMoa2212856

6. Azim HA, Jr., Niman SM, Partridge AH, et al. Fertility Preservation and Assisted Reproduction in Patients With Breast Cancer Interrupting Adjuvant Endocrine Therapy to Attempt Pregnancy. *Journal of Clinical Oncology* : official journal of the American Society of Clinical Oncology 2024;42:2822-32. doi: 10.1200/JCO.23.02292

7. Azim HA, Jr., Niman S, Partridge AH, et al. 1814O Breastfeeding in women with hormone receptor-positive breast cancer who conceived after temporary interruption of endocrine therapy: Results from the POSITIVE trial. *Annals of Oncology* 2024;35:S1076. doi: 10.1016/j.annonc.2024.08.1910

8. Pagan E, Ruggeri M, Bianco N, et al. Factors influencing 5-year persistence to adjuvant endocrine therapy in young women with breast cancer. *Breast* (Edinburgh, Scotland) 2024;77:103765. doi: 10.1016/j.breast.2024.103765

JBCRG
JAPAN BREAST CANCER RESEARCH GROUP

JBCRG is a Japanese clinical trial group that has been conducting exploratory and challenging studies for over 20 years. To address various questions in daily clinical practice, we will continue conducting high-quality, practice-changing clinical trials, collaborating with BIG to shape the future of breast cancer treatment. Through these efforts, we hope to contribute to society and improve the lives of breast cancer patients worldwide.

Ongoing clinical trials and publications

JBCRG is running the following clinical trials:

- **JBCRG-ABCD project:** the Advanced Breast Cancer Database (ABCD) project.
- **JBCRG-M08 (AMBER):** innovation of the 1st line strategy optimised as abemaciclib with endocrine therapy based on the ESR1 mutation of ctDNA for HR-positive HER2-negative advanced metastatic breast cancer patients (JBCRG-M08) – a multi-institutional phase II trial.
- **JBCRG-C11 (CREA):** A multicentre prospective observational study in patients with HER2-positive advanced or metastatic breast cancer who achieved a Complete REsponse to trAstuzumab deruxtecan (CREA)

Congress presentations

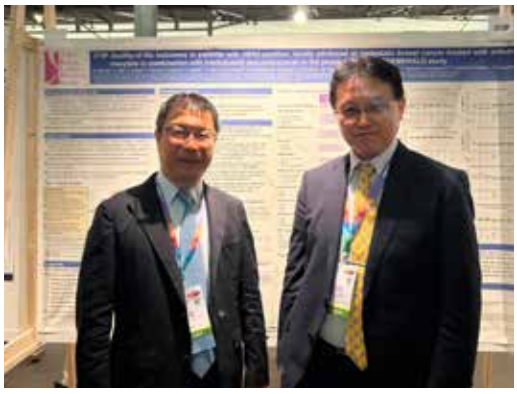
1) ESMO 2024 (13-17 September 2024): JBCRG-M06 Poster presentation by Dr Norikazu Masuda: Quality-of-life outcomes in patients with HER2-positive, locally advanced or metastatic breast cancer treated with eribulin mesylate in combination with trastuzumab and pertuzumab in the phase 3 JBCRG-M06/EMERALD study.

2) ESMO 2024 (13-17 September 2024): JBCRG-C07 Poster presentation by Dr Hiroko Masuda: Interim analysis of prospective observational study to evaluate the impact of cancer gene panel tests on treatment decision making in metastatic or recurrent breast cancer in Japan: JBCRG-C07 REIWA Study.

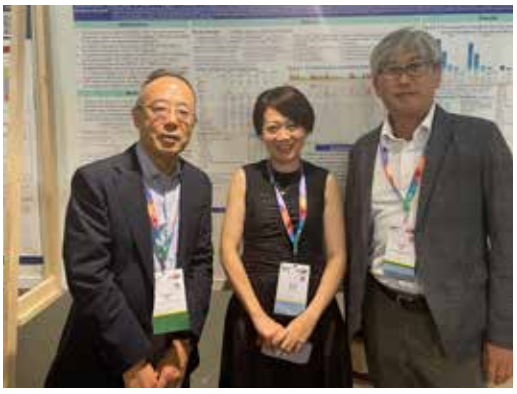
3) ASCO 2024 (31 May-4 June 2024): JBCRG-M06 Oral presentation by Dr Toshinari Yamashita: Trastuzumab and pertuzumab in combination with eribulin mesylate or a taxane as first-line chemotherapeutic treatment for HER2-positive, locally advanced or metastatic breast cancer: Results of a multicentre, randomised, non-inferiority phase 3 trial in Japan (JBCRG-M06/EMERALD).

4) ASCO 2024 (31 May-4 June 2024): JBCRG-M08 Poster presentation by Dr Tetsuhiro Yoshinami: Innovation of the first-line strategy optimised as abemaciclib with endocrine therapy based on the ESR1 mutation of ctDNA for patients with HR-positive HER2-negative advanced metastatic breast cancer (JBCRG-M08; AMBER study).

5) AACR 2024 (5-10 April 2024): JBCRG-M07TR Poster presentation by Dr Takashi Takeshita: Identification of prognostic and predictive biomarkers for palbociclib add-on therapy using cancer panel sequencing of cell-free DNA in patients with HR-positive/HER2-negative advanced and metastatic breast cancer with fulvestrant resistance.



Dr Norikazu Masuda, Dr Toshinari Yamashita



Dr Shigehira Saji, Dr Hiroko Masuda, Dr Hiroshi Tada

Dr Hiroji Iwata, Dr Norikazu Masuda, Yamashita, Dr Shigehira Saji

6) SABCS 2024 (10-14 December 2023): JBCRG-26 Poster presentation by Dr Hiroko Bando: Health-Related QOL and physical activity collected via wearable device in patients With HR+/HER2- advanced breast cancer in Japan treated with palbociclib+endocrine therapy (ET) or ET alone: 6-month longitudinal study (JBCRG-26).

Recent publications

1) JBCRG-M07TR in *Breast Cancer Research and Treatment,* 2024
Iwamoto T, Niikura N, Watanabe K, et al. Prognostic value of the 21-Gene Breast Recurrence Score® assay for hormone receptor-positive/human epidermal growth factor 2-negative advanced breast cancer: subanalysis from Japan Breast Cancer Research Group-M07 (FUTURE trial). *Breast Cancer Research and Treatment,* 2024 June. doi: 10.1007/s10549-024-07414-7

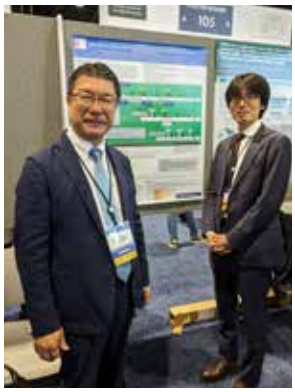
2) JBCRG-20 Follow in *Breast Cancer Research and Treatment*, 2024.
Takano T, Masuda N, Ito M, et al. Long-term outcomes of neoadjuvant trastuzumab emtansine + pertuzumab (T-DM1+P) and docetaxel + carboplatin + trastuzumab + pertuzumab (TCbHP) for HER2-positive primary breast cancer: results of the randomised phase 2 JBCRG20 study (Neo-peaks). *Breast Cancer Research and Treatment*, 2024 May. doi: 10.1007/s10549-024-07333-7.

3) JBCRG-M07TR in *ESMO Open*, 2024.
Takeshita T, Iwamoto T, Niikura N, et al. Identifying prognostic biomarkers for palbociclib add-on therapy in fulvestrant-resistant breast cancer using cell-free DNA sequencing. *ESMO Open,* 2024 April. doi: 10.1016/j.esmoop.2024.102385.

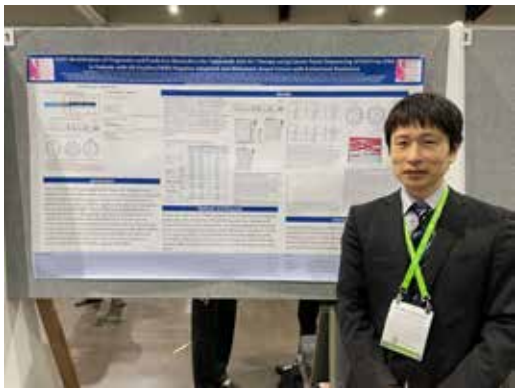
Participation in global BIG trials

JBCRG is involved in the following studies run under the BIG umbrella: ALEXANDRA/IMpassion030 (BIG 16-05), OlympiA (BIG 6-13), POSITIVE (BIG 8-13), Penelope-B (BIG 1-13) and PALLAS (BIG 14-03). *For details about the trial leadership, please refer to the overview of BIG trials on page 66-69.*

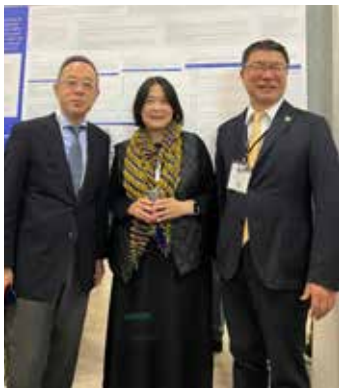
, Dr Toshinari



Dr Norikazu Masuda, Dr Tetsuhiro Yoshinami



Dr Takashi Takeshita



Dr Shigehira Saji, Dr Hiroko Bando, Dr Norikazu Masuda

KCSG
KOREAN CANCER STUDY GROUP

The Korean Cancer Study Group (KCSG) is a nation's leader in multi-institutional cancer clinical trials in Korea. Since our establishment in 1998, KCSG has been dedicated to the advancement of clinical and translational cancer research and joined BIG as a full member in 2017.

The KCSG breast cancer committee is currently recruiting patients for the following studies and would like to introduce two clinical trials presented at ASCO 2024.

Studies

- **BR23-18:** Comparison of clinical efficacy between trastuzumab-deruxtecan vs. physician's choice in HER2 low, hormone receptor-positive metastatic breast cancer: a randomised, phase II study.
- **BR22-20:** Comparison of clinical efficacy between letrozole + ribociclib vs. fulvestrant + letrozole + ribociclib in hormone receptor-positive, HER2-negative metastatic breast cancer: a randomised, phase II study.
- **BR21-10:** A randomised phase II clinical trial of talazoparib maintenance therapy in TNBC patients who showed platinum-sensitivity on first- or second-line platinum-based chemotherapy.
- **BR21-09 / Young-PALETTA:** PALbociclib endocrine therapy followed by Talazo vs. Talazo-Atezo (Young-PALETTA) study: a randomised phase II trial
- **BR20-16:** Phase II trial of pembrolizumab in combination with paclitaxel in hormone receptor-positive metastatic breast cancer with high tumour mutational burden selected by whole exome sequencing: a Korean Cancer Study Group trial.
- **BR19-03 / ESPERO:** A randomised, open label, multicentre, phase II trial of eribulin with or without SB3 (trastuzumab-biosimilar) in patients with HER2-overexpressed recurrent or stage IV breast cancer who have received at least 2 prior HER2-directed regimens.
- **BR19-13 / HIPEx:** A single-arm phase II study of palbociclib plus endocrine therapy in patients with high risk ER(+) / HER2(-) T1-2N0-1 early breast cancer incorporating GenesWell® BCT.
- **KM-16:** A phase II study of abemaciclib plus trastuzumab biosimilar (Herzuma®) ± fulvestrant in patients with HER2-positive metastatic breast cancer in brain who progressed after HER2 directed chemotherapy.
- **BR18-10/MINI:** A phase IB & II study of ribociclib with trastuzumab plus letrozole (+/- GnRHa) in premenopausal women in premenopausal/ postmenopausal HR+, HER2+ advanced breast cancer patients.
- **BR18-21 / MIRINAE:** A randomised, phase II trial to evaluate the efficacy and safety of atezolizumab plus capecitabine adjuvant therapy compared to capecitabine monotherapy for triple receptor-negative breast cancer with residual invasive cancer after neoadjuvant chemotherapy.

Two clinical trials presented at ASCO 2024

A pivotal role for premenopausal hormone receptor-positive breast cancer

Young-PEARL (KCSG BR15-10) is a randomised, phase II study of palbociclib plus exemestane with GnRH agonist versus capecitabine in premenopausal women with HR-

Professor Yeon Hee Park, MD. PhD.
Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
Young-PEARL (KCSG BR15-10). Presentation at ASCO 2024

Professor Joohyuk Sohn, MD, PhD
Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea
PEARLY (BR15-01, BIG supporter trial). Presentation at ASCO 2024

positive metastatic breast cancer. In Asia, about half of breast cancer patients are under 50, with a peak onset at 45-49 years, unlike in Western countries where the peak is around 70. Premenopausal breast cancers in younger women tend to be more aggressive and less responsive to hormonal treatment. In this study, a total of 189 patients previously treated with 0 or 1 line of chemotherapy for metastatic breast cancer were enrolled from 14 KCSG institutions. The primary endpoint, median progression-free survival (mPFS) showed superiority for endocrine therapy plus palbociclib over capecitabine [20.1 vs. 14.4 months, P=0.02 by log-rank test; HR 0.65 (0.43–0.99)]. The result for this primary endpoint was previously presented at the 2019 ASCO meeting 3,4.

This is the first study to compare treatment with the CDK4/6 inhibitor palbociclib plus endocrine therapy with single agent capecitabine chemotherapy exclusively in premenopausal women. These results contributed to expansion of the palbociclib plus aromatase inhibitor (AI) label to include premenopausal patients by the US FDA in September 2022. The updated results of overall survival (OS) at a median follow-up of 54.0 months were selected as an oral presentation at ASCO 2024, in Chicago, IL5. The median PFS was 19.5 vs. 14.0 months (P=0.035; HR 0.74 (0.56–0.97)), and the median OS was 54.8 vs. 57.8 months (P=0.91; HR 1.02 (0.68–1.51)). PFS benefit in palbociclib + endocrine arm did not lead to OS benefit, however use of CDK4/6 inhibitor after progression was associated with longer overall survival in multivariable analysis.

Phase III trial to assess the role of carboplatin in early triple-negative breast cancer

PEARLY (BR15-01, BIG supporter trial) is a randomised, multicentre, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo)adjuvant therapy in patients with early triple-negative breast cancer (TNBC). TNBC is a challenging subtype of breast cancer with high relapse rates and poor prognosis.

This study aimed to determine whether carboplatin improves event-free survival (EFS) and overall survival (OS) when used in a (neo)adjuvant setting. Between January 2016 and June 2020, 868 patients across 22 KCSG institutions were enrolled. At a median follow-up of 51.1 months, carboplatin significantly improved EFS compared to the control arm (5-year EFS rate: 82.3% vs 75.1%, HR 0.67 (95% CI 0.49–0.92), P=0.012). The 5-year OS rate was 90.7% vs 87.0% (HR 0.65 (95% CI 0.42–1.02), P=0.057), showing a trend towards improved survival but not statistically significant.

In conclusion, the addition of carboplatin to standard anthracycline followed by taxane therapy significantly improved EFS in patients with early-stage TNBC. This work was selected as an oral presentation at the annual meeting of ASCO 2024[6].

BIG 25 YRS

"Congratulations to BIG on 25 years of impactful breast cancer research. KCSG is confident that, together with BIG, we will continue to play a vital role in advancing knowledge in this field and improving outcomes for breast cancer patients worldwide."

KCSG Breast Cancer committee members at ESMO-PAGA Korean Workshop

References

1. Yap YS, Lu YS, Tamura K, et al. Insights Into Breast Cancer in the East vs the West: A Review. *JAMA Oncol.* 2019;5(10):1489–1496. doi:10.1001/jamaoncol.2019.0620

2. Lin CH, Yap YS., Lee KH, et al. Contrasting Epidemiology and Clinicopathology of Female Breast Cancer in Asians vs the US Population. *J Natl Cancer Inst.* 2019 Dec 1;111(12):1298-1306. doi: 10.1093/jnci/djz090

3. Park YH, Kim, TY, Kim GM, et al. A randomized phase II study of palbociclib plus exemestane with GNRH agonist versus capecitabine in premenopausal women with hormone receptor-positive metastatic breast cancer (KCSG-BR 15-10, NCT02592746). *J Clinl Oncol.* 2019 May, 37, no. 15_ suppl:1007-1007. doi: 10.1200/JCO.2019.37.15_suppl.1007

4. Park YH, Kim TY, Kim GM, et al. Palbociclib plus exemestane with gonadotropin-releasing hormone agonist versus capecitabine in premenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer (KCSG-BR15-10): a multicentre, open-label, randomised, phase 2 trial. *Lancet Oncol.* 2019 Dec;20(12):1750-1759. doi: 10.1016/S1470-2045(19)30565-0

5. Park YH, Lee KH, Kim GM, et al. Palbociclib plus exemestane with GnRH agonist vs capecitabine in premenopausal patients with HR+/HER2- metastatic breast cancer: Updated survival results of the randomized phase 2 study Young-PEARL. *JCO* 2024 June, 42, LBA1002-LBA1002(2024). doi: 10.1200/JCO.2024.42.17_suppl.LBA1002

6. Sohn J, Kim GM, Jung KH, et al. A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial. *JCO* 42, LBA502-LBA502(2024). doi: 10.1200/JCO.2024.42.17_suppl.LBA502

LACOG
LATIN AMERICAN COOPERATIVE ONCOLOGY GROUP

Celebrating 25 years of BIG: a journey of innovation and collaboration in the fight against breast cancer

It is with great enthusiasm that we celebrate the 25th anniversary of the Breast International Group (BIG). Over the past quarter-century, BIG has distinguished itself as a cornerstone in breast cancer clinical research and scientific advances, not only in Europe but across the globe. On behalf of the Latin American Cooperative Oncology Group (LACOG), BIG's Latin American partner, I express my respect and admiration for BIG's leadership role in this field and extend congratulations to all collaborators in the network for their exemplary journey. The organisation's dedication through numerous contributions have transformed how we approach breast cancer research and treatment, providing hope to millions of patients worldwide.

Since its inception, BIG has been at the forefront of breast cancer clinical research in Europe, quickly attracting academic collaborative groups working in other parts of the world. The partnership between BIG and LACOG has been fundamental in advancing clinical research in Latin America, whereas the synergy from this relationship enables the sharing of knowledge and experiences that benefit both patients and healthcare professionals.

In the past decade, LACOG has participated in several BIG clinical trials, such as ALEXANDRA/Impassion030, PALLAS, LORELEI, NeoALTTO, and Male Breast Cancer, among others. These studies are relevant within this region as they encompass the Latin American population, promoting an inclusive and diverse approach to research and ensuring that progress translates into better clinical outcomes in practice.

As an Executive Board member and partner, I have had the opportunity to work alongside BIG to enhance and strengthen the group's organisation and capabilities, preparing us for a new era of clinical trials in breast cancer.

BIG's 25 anniversary is a milestone that symbolises not only the success of the organisation but also the hope for a future filled with new discoveries and developments in the fight against breast cancer. The path taken thus far is a reason for celebration and reflection. Together, we can turn challenges into opportunities and make a meaningful difference in the lives of thousands of breast cancer patients and their families worldwide, maintaining hope for a healthier future.

Contribution by Gustavo Werutsky, medical oncologist, Executive Director of LACOG, and member of the BIG Executive Board.

The Brazilian Breast Cancer Conference 2024 – LACOG-GBECAM – Best of SABCS

On 15 and 16 March 2024, the Brazilian Breast Cancer Conference 2024 - LACOG-GBECAM - Best of SABCS, was held at the Intercontinental Hotel in São Paulo.

Developments in breast cancer diagnosis and treatment, as well as the latest evidence on tumour markers, new drugs and therapies, were presented and discussed. Additionally, experts from across Brazil gathered to share insights and review the key studies from the oral sessions of the San Antonio Breast Cancer Symposium 2023.

Around 650 in-person participants, including radio-oncologists, surgeons, clinical oncologists, and other specialists, attended the event.

LACOG Scientific Meeting at ASCO 2024

The LACOG Scientific Meeting was held on 31 May, during the ASCO Annual Meeting 2024. The meeting took place at the Hyatt Regency Chicago Hotel and was attended by approximately 60 members of the group from Latin America. During the meeting, ongoing LACOG studies were presented, and new research projects for the upcoming year were discussed.

Active studies, recruiting

Classifying for HER2 dependence to de-escalate neoadjuvant chemotherapy in patients with HER2+ early breast cancer undergoing HER2 double-blockade – CHERRY-PICK TRIAL (LACOG 0721)

The CHERRY-PICK clinical trial is a single-arm phase 2 trial aimed at evaluating an anti-HER2 chemo-free neoadjuvant regimen using a fixed-dose combination of pertuzumab and trastuzumab (PHESGO). It targets a HER2 enriched population selected by standard biomarkers (hormone receptor status and HER2 score) and uses a PET/CT response-based strategy to assess pathological complete response (pCR).

This study opened for recruitment in Brazil in June 2024 and will enrol 70 participants across 10 research sites.

Evaluation of sequencing of anthracyclines and taxanes for locally advanced HER2-negative breast cancer – NEOSAMBA (GBECAM/LACOG 0419) trial

The NEOSAMBA trial is a randomised phase 3 trial investigating the sequencing of anthracyclines and taxanes for locally advanced HER2-negative breast cancer. This trial will assess invasive disease-free survival and pathological complete response between an anthracycline-initiated neoadjuvant chemotherapy regimen (AC-T) versus a taxane-initiated regimen (T-AC) in patients with locally advanced HER2- breast cancer. From January 2021 to October 2024, 409 patients have been enrolled, with a total of 444 patients expected to be included. The first results are anticipated in 2025.

A study to observe patient characteristics, treatment patterns and outcomes in patients with newly diagnosed breast cancer in Latin America – LATINA Breast (LACOG 0615)

LATINA Breast is a prospective breast cancer registry that recruited over 3,300 patients from 2020 to 2022 across more than 30 sites in 10 countries throughout Latin America. The first results were presented in 2023, showing that a third of patients diagnosed with breast cancer are < 50 years, with most cases being diagnosed through symptoms rather than screening. The majority of patients had stage II and III disease. Follow-up is ongoing, and new data will be presented at upcoming major conferences.

LACOG Scientific Meeting at ASCO 2024, Chicago, US

INSTITUTO PROJETO CURA – BRAZIL (PROJECT CURA INSTITUTE)

Projeto Cura: sparked by BIG's vision

In 2012, I had the privilege of meeting Dr Martine Piccart, professor of oncology at the Université Libre de Bruxelles (Belgium), medical oncologist, and scientific director at the Institut Jules Bordet in Brussels, and co-founder of BIG. That meeting truly opened my eyes to the necessity of conducting research across all regions of the world. Our diverse backgrounds and experiences underscore the importance of exploring our unique characteristics, such as culture, cuisine, genetics, and more.

In 2014, Dr Piccart introduced me to Dr Carlos Barrios, co-founder and director of the Latin American Clinical Oncology Research Group (LACOG). In 2016, this led to the creation of Instituto Projeto Cura, dedicated to promoting research in Latin America.

Fernanda Schwyter and Professor Martine Piccart

I firmly believe that effective global results require global research and that we must unite in our dedication to saving lives through science, innovation and collaboration.

Contribution by Fernanda Schwyter, President Instituto Projeto Cura (São Paulo, Brazil).

Since its founding, the Instituto Projeto Cura (Project Cura Institute) has made significant and important strides. Here we highlight some initiatives and achievements, as well as their impacts that have shaped our work.

To raise awareness in society and improve the regulatory environment, the Instituto Projeto Cura has been carrying out actions with patients and the government, along with fundraising campaigns and public and private calls for proposals.

Webinar at ONE (Ocean Network Express): raising awareness

In November 2023, the Instituto Projeto Cura, in partnership with our sponsor ONE (Ocean Network Express), held a webinar entitled "Where does the cancer cure begin?". This event was part of the company's efforts in Latin America to raise awareness about Pink October.

The live event was broadcast from ONE's office in São Paulo, reaching Brazil, Chile, Uruguay, Mexico, Peru, and Colombia, reflecting Cura and ONE's commitment to raising awareness about breast cancer and all types of cancer across Latin America. We were honoured by the participation of oncologists Dr Cynthia Villarreal Garza and Dr Denise Bretel, representatives from Mexico and Peru, respectively, as well as oncologists Dr Abna Vieira and Dr Max Mano, both from Brazil.

Fernanda Schwyter, Dr Max Mano, Dr Abna Vieira, Fabiana Amorim

The Magal Way campaign: cycling to support cancer research

The Magal Way's mission is powerful: cycling to support cancer research. #TheMagalWay | Projeto Cura. Marcos Magalhães is a Brazilian living in the United States who is committed to raising funds for a worthy cause: the Instituto Projeto Cura. Through his cycling challenge, he combines passion and energy to support those affected by this devastating disease and to help in the search for a cure.

The NeoSamba trial

The Instituto Projeto Cura launched the crowdfunding campaign "Together we can be stronger than cancer" to raise funds to support one year of data processing for the NeoSamba study. This 100% Brazilian, randomised phase 3 clinical trial is investigating a new treatment sequence of neoadjuvant chemotherapy for HER2-negative breast cancer and covers the treatment of almost 500 women over three years.

The approval of the NeoSamba trial by Pronon (Programa Nacional de Apoio à Atenção Oncológica), a Brazilian public grant, allowed companies from various sectors to allocate up to 1% of their income tax to finance the research.

SOLTI
SPANISH BREAST CANCER GROUP

Cyclibtool
SOLTI launches AI-based tool to avoid toxicities in the treatment of patients with hormonal breast cancer

SOLTI, a leading group in clinical cancer research in Spain, has launched the renewed version of Cyclibtool (www.cyclibtool.org), a freely accessible digital tool for professionals based on artificial intelligence (AI) technology. It is designed for patients with hormonal breast cancer (HR+) to help avoid serious or unnecessary toxicities resulting from the combination of drugs during cancer treatment.

Thanks to the incorporation of AI, in addition to evaluating the drug interactions of the most common treatments in combination with each of the different approved CDK 4/6 inhibitor-specific treatments for hormonal breast cancer, Cyclibtool offers positive lists, which means alternative drugs that the oncologist can safely administer, avoiding a toxic combination for the patient.

Hormonal breast cancer affects approximately 70% of all breast cancer patients. Recently, the approval of CDK 4/6 inhibitors (ribociclib, palbociblib and abemaciclib) has revolutionised the approach to this cancer pathology, both in the early and metastatic settings. However, this treatment, based on oral drugs, often lasts for more than two years, a period during which patients may need parallel drugs in case of the appearance of other pathologies in addition to the oncological pathology.

According to Dr Meritxell Bellet (Vall d'Hebron Hospital and VHIO), member of SOLTI's Executive Board and promoter of Cyclibtool: "Since the revolution brought about by the approval of CDK 4/6 inhibitors in the approach to hormonal breast cancer, we have found ourselves in a new situation where two factors converge. On the one hand, patients, during the time that this oncological treatment lasts, are receiving other medications due to the appearance of new comorbid processes. On the other hand, and along these lines, other medical specialties outside oncology prescribe their drugs without considering that the interaction between their prescription and the CDK 4/6 inhibitors that the patient is already taking may be toxic, as they do not consider this oncological treatment as aggressive as chemotherapy. This puts us in a very challenging scenario for the oncologist to ensure that, with the medication they are administering, they are not putting the patient at risk".

Dr Bellet concludes: "Until Cyclibtool came out, there were tools that simply told us whether or not there were drug interactions; that is, whether the toxicity from the combination of certain drugs could be dangerous for patients. However, they did not specify how much, for what reason and what safe alternatives we could give them. Thus, the oncologist was faced with the additional work of looking for alternatives".

Dr Mafalda Oliveira, President of SOLTI and medical oncologist at Vall d'Hebron and VHIO, adds: "For us it is essential to create instruments and tools that, through the integration of new technologies such as artificial intelligence, expand the knowledge base that professionals can receive in less time and in a more appropriate way to optimise clinical practice. This update of Cyclibtool stems from this ongoing effort to promote not only research but also care in routine clinical practice in accordance with one of SOLTI's strategic lines: medical education and training for professionals involved in cancer management".

The updated Cyclibtool

Following the excellent reception of Cyclibtool in its four years of life by oncologists, pharmacists, and other healthcare professionals in many countries around the world, with an average of 1,600 monthly queries, SOLTI has devised a new version that has quadrupled the number of active ingredients included, is dynamic, multilingual, and incorporates AI for the first time and for prescriptive purposes.

The first version of the platform that SOLTI presented in 2020 was based on the SOLTI manuscript *"Palbociclib and ribociclib in breast cancer: consensus workshop on the management of concomitant medication"*, published in May 2019.

SOLTI has recently created a working group led by Dr Meritxell Bellet and composed of five pharmacists with extensive experience in the management of these drugs to re-evaluate and add the active ingredients to the tool's database. This update has been possible thanks to the sponsorship of the three pharmaceutical companies that own the three cyclin inhibitors: Novartis, Pfizer, and Lilly.

STUDY UPDATES

For the past 25 years, BIG has been at the forefront of international breast cancer research, conducting groundbreaking studies that lead to practice-changing results and make a significant difference in the lives of countless women and men.

With continued commitment to advancing knowledge and improving patient care, BIG remains focused on studies with the potential to drive meaningful change. Below are two examples of recent research initiatives that demonstrate this ongoing impact and promise to reshape future breast cancer treatment approaches.

OPTIMA Young to pave the way for personalised breast cancer treatment for young women

The OPTIMA Young clinical trial, part of the focus of the EU-supported Path4Young project, is set to redefine breast cancer care for young women with hormone receptor-positive (HR+), HER2-negative breast cancer. This ambitious international initiative aims to establish a new standard of care that focuses on safely de-escalating chemotherapy and improving long-term quality of life for patients.

OPTIMA Young will leverage the ongoing OPTIMA-UK randomised controlled trial (RCT), expanding it into a global study with participants from Europe, Latin America, and Oceania. The goal is to identify personalised treatment routes, minimising the use of chemotherapy while ensuring continued support throughout the cancer-care journey.

By embracing the principles of P5 Health Management – predictive, personalised, preventive, participatory, and psycho-cognitive – this trial promises to provide innovative, holistic care that puts patients' quality of life first. The trial is supported by a multidisciplinary team of clinicians, epidemiologists, social scientists, and patient advocates, working together to improve treatment outcomes for young women around the world.

AURORA secures renewed funding from BCRF for research on metastatic breast cancer

AURORA is a crucial research initiative led by BIG. This programme focuses on analysing tumour and blood samples from patients with metastatic breast cancer to better understand the disease's progression and how it responds to various treatments. In August, BIG received thrilling news from the Breast Cancer Research Foundation (BCRF): the application for the project "Exploring advanced research opportunities through the analytical study of plasma samples in the AURORA Program: A comprehensive feasibility study" was approved for funding. This grant of $225,000 will support the project from 1 October 2024 to 30 September 2025. With this renewed funding, the AURORA team is ready to continue its important work in metastatic breast cancer research, aiming to improve the lives of patients worldwide.

BIG CONFERENCE NEWS

Over the years, BIG and its members have leveraged a robust network of dedicated academic breast cancer research groups from around the world to introduce, present, and discuss innovative clinical trials and academic research programmes at leading conferences.

This section of the report provides a comprehensive overview of BIG studies and trials presented in 2024 at several key conferences, including the Global Breast Cancer Conference (GBCC), the American Society of Clinical Oncology (ASCO) Annual Meeting, the European Society for Medical Oncology (ESMO) Congress, the European Society of Surgical Oncology (ESSO) Congress, and the San Antonio Breast Cancer Symposium (SABCS).

These presentations highlight innovative approaches and new insights that will advance breast cancer research.

GLOBAL BREAST CANCER CONFERENCE (GBCC 2024)

25 – 27 April 2024, Seoul, South Korea

BIG participated in a special session hosted by the Korean Breast Cancer Society, entitled "Exploring the significance of BIG in Asia and opportunities for collaboration". It focused on how BIG is working with Asian partners to expand research efforts and patient involvement. Presentations by Dr David Cameron, Dr Sung-Bae Kim, Dr Giuseppe Curigliano, Dr Carmela Caballero, and Dr Janice Tsang addressed topics such as the BIG-Asia collaboration, Women for Oncology through BIG Asia, and the BIG Patient Partnership Initiative (BIG-PPI). Furthermore, other members of the BIG Executive Board, including Dr Etienne Brain and Dr Shigehira Saji, also delivered insightful presentations.

By fostering these partnerships, BIG aims to facilitate a bi-directional understanding of the opportunities and challenges of breast cancer research in Asia.

GBCC 2025 will take place from Thursday 17 April to Saturday 19 April 2025, at the Grand Walkerhill in Seoul, South Korea.

AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO 2024)

31 May – 4 June, Chicago, US

THE BIG-NCTN ANNUAL MEETING

The BIG-NCTN Annual Meeting took place during ASCO, with researchers from BIG and the US National Clinical Trials Network (NCTN) convening to discuss the latest advances in breast cancer research. Since 2005, and thanks to the support of The Breast Cancer Research Foundation, experts from the BIG network and the National Clinical Trials Network (NCTN) have been collaborating to spearhead research activities focused on specific issues in breast cancer. This collaboration has concentrated on addressing the most pressing issues relevant to patients and the academic research networks of BIG and the US.

This year's meeting featured approximately 60 top researchers with patient advocates from the US and BIG's Patient Partnership Initiative (BIG-PPI). The 2024 Chairs were Dr Boon Chua and Dr Nancy Lin. The keynote talks focused on "How can academic research

Dr Janice Tsang, Dr Carmela Caballero, Dr Yoon Sim Yap, Dr Shigehira Saji, Dr Sung-Bae Kim

Dr Janice Tsang, Dr Giuseppe Curigliano, Dr Sung-Bae Kim, Dr Carmela Caballero Dr Janice Tsang, Dr Carmela Caballero,

Dr David Cameron (Zoom), Dr Giuseppe Curigliano, Dr Sung-Bae Kim

thrive in a world dominated by pharmaceutical industry studies?" and "Molecular Imaging Biomarkers for Breast Cancer". The role of the patient-partners in these discussions is essential for ensuring that clinical trials reflect the real-world concerns of those affected by breast cancer, emphasising the importance of integrating patient perspectives into research – especially in areas that may be overlooked by the pharmaceutical industry.

Video patient advocates of BIG's Patient Partnership Initiative such as Lydie Meheus, managing director at the Anticancer Fund

Professor Boon Chua, co-chair of the BIG-NCTN 2024 Annual Meeting

BIG EXECUTIVE BOARD MEETING IN CHICAGO

Members of the BIG Executive Board and BIG Headquarters

PALLAS (BIG 14-03) STUDY

During a poster presentation, researchers presented the "Analysis of the sensitivity to endocrine therapy (SET) assay in the PALLAS adjuvant trial of palbociclib in HR+/HER2- breast cancer (ABCSG-42/AFT-05/BIG-14-13)", an analysis from the PALLAS trial. It studied the impact of adding the drug palbociclib to standard hormone therapy for patients with hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer. The study used a test called the SET2,3 index, which measures how sensitive the cancer might be to hormone therapy by looking at specific genes and tumour characteristics. Researchers analysed tumour samples from over 3,000 patients and found that patients with a high SET2,3 index had significantly better 5-year disease-free survival rates (91.4%) compared to those with low scores (78.5%). However, they did not find evidence that the SET2,3 index could predict who would benefit from adding palbociclib to their treatment. This suggests that while the SET2,3 index is useful for understanding prognosis, it does not help identify patients who would benefit from palbociclib.

Clinical trial information: NCT02513394.

EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY (ESMO 2024)

13 – 17 September, Barcelona, Spain

BIG's Scientific Meeting held at ESMO featured a keynote talk by Dr Fabrice Andre on "The need for pragmatic, affordable, and practice-changing real-life clinical trials in oncology". Additionally, Dr Dario Trapani, representing Common Sense Oncology, led a session on conducting research based on endpoints that matter to patients. He was joined in a panel discussion by Dr Tanja Spanic, president of Europa Donna (Slovenia), and Judy Needham from the Canadian Cancer Trials Group (CCTG), both members of the BIG-PPI.

Dr Dario Trapani

Members from BIG HQ

BIG EXECUTIVE BOARD MEETING AT ESMO

Drs Ander Urruticoechea, Gustavo Werutsky, Etienne Brain, Ines Vaz-Luis, Seamus O'Reilly, Barbro Linderholm, Evangelia Razis, Sherene Loi, Shigehira Saji, Eva Carrasco

BIG-PPI WORKSHOP

Representatives from BIG's Executive Board, Headquarters, and the BIG-PPI came together for a workshop focused on new trials, an analysis of the breast cancer research landscape presented at ESMO, and the development of a patient-focused checklist for new trials ideas to be presented by investigators. New collaborations with Frontier Science Scotland and Grasp Cancer were also discussed with the patient partners. This workshop was made possible through EU funding from BIG-SPARK.

CELEBRATING ACHIEVEMENTS

Several distinguished researchers were honoured for their contributions to breast cancer research and care. Dr Ann Partridge received the ESMO award for her contribution to breast cancer. She delivered a keynote talk focused on disparities for younger patients surviving cancer. Other awardees included Dr Myung-Ju Ahn, who was honoured with the Women for Oncology Award, and Dr Serena Nik-Zainal, who received the Translational Research Award. Additionally, Dr John Haanen was recognised with the Lifetime Achievement Award for his outstanding career contributions, specifically in immunology, and his research on "Empowering T cells to fight cancer".

AURORA (BIG 14-01)

On 15 September, Dr Gabriele Zoppoli from the University of Geneva presented new findings from the AURORA study: "Impact of aging on the genetic and transcriptional landscape of advanced breast cancer: an AURORA program (BIG 14-01) sub-analysis."

This study investigated how aging affects breast cancer at a genetic level, providing valuable insights that could improve treatment options for older patients.

The study analysed 830 patients with advanced breast cancer, specifically looking at how the disease changes in people over the age of 60. The research revealed that older patients tend to have breast tumours that grow more slowly, with many presenting invasive lobular carcinoma (ILC). One key finding was that older patients had certain genetic mutations, such as PIK3CA, EPHB1, and ESR1, which can potentially be targeted with new treatments. Additionally, the Hedgehog signalling pathway, which helps cells grow, was found to be less active in older patients, providing a clue about how their cancer behaves differently from that in younger patients. The researchers also found that older patients had more frequent mutations in genes like CARD11, MYH11, and BRCA2, while younger patients had different mutations, such as those in PTCH1 and ERCC4. These findings show that as patients age, breast cancer develops distinct genetic features that can influence how the disease

progresses. Understanding these changes opens the door to more personalised treatment strategies that consider a patient's age and specific genetic profile, potentially leading to more effective therapies for older individuals with advanced breast cancer.

Clinical trial information AURORA: NCT02102165.

HERA (BIG 1-01)

Dr Sung Gwe Ahn from the Yonsei University Health System (YUHS, Seoul, South Korea), presented the results of an exploratory analysis of HERA, one of BIG's first trials: "Ovarian function suppression in HR-positive, HER2-positive breast cancer: An exploratory analysis from the HERA trial".
Citation: Annals of Oncology (2024) 35 (suppl_2): S309-S348. 10.1016/annonc/annonc1577

The research showed that adding ovarian function suppression (OFS) to hormone therapy significantly improves survival rates for premenopausal women with HR-positive, HER2-positive breast cancer. The study, which included 965 patients, found that those who received OFS had better 10-year disease-free survival and overall survival compared to those who did not. Women treated with an aromatase inhibitor alongside OFS saw the greatest benefits. These results highlight the importance of refining personalised endocrine therapies, ensuring that treatment plans are tailored to the unique needs of each patient.

Clinical trial information HERA: NCT00045032.

POSITIVE (BIG 8-13)

The results of the POSITIVE trial, shared by Dr Fedro A. Peccatori from ETOP-IBCSG (European Thoracic Oncology Platform – International Breast Cancer Research Group), provided encouraging data on breastfeeding after breast cancer treatment. The findings suggest that it is safe for many women with HR+ early-stage breast cancer who have undergone treatment. These results help address a critical concern for younger patients who wish to start a family after their treatment.

Clinical trial information POSITIVE: VNCT02308085.

TREAT ctDNA (BIG 22-01)

On 16 September, a poster was presented on the new TREAT ctDNA trial, led by EORTC and BIG, which tests elacestrant in patients with ER+/HER2- breast cancer who have experienced a relapse detected by the ctDNA, a type of blood test that identifies cancer DNA. The trial is still recruiting patients and will involve 12 countries.

Clinical trial information: NCT05512364.

From left to right: Orsolya Birta, Medical Advisor at BIG; Ana Joaquim, Clinical Research Physician at EORTC; Jose Casas, Translational Research Scientist at EORTC; Michail Ignatiadis, Chair of the EORTC Breast Cancer Group, Director of the Breast Medical Oncology Clinic & Program at the Jules Bordet Institute, Associate Professor at the Université Libre de Bruxelles, and Study Coordinator of the TREAT ctDNA trial; and Carmela Caballero, Sr. Medical Advisor at BIG.

EUROPEAN SOCIETY FOR SURGICAL ONCOLOGY (ESSO 2024)

02 – 04 October, Antwerp, Belgium

The 43rd annual ESSO congress featured a Research Methodology session focused on "Engaging with surgeons and patients for high-quality surgical oncology research". The speakers included Dr Wim Ceelen, who spoke about the "Basics of surgical research methodology and ethical aspects of surgical trials"; Dr Giuseppe Catanuto, who talked about "Current difficulties in setting up trials in surgery and new trial designs"; and Dr Lydie Meheus, a member of the BIG-PPI who delivered an insightful talk on "How can we work together with patients to improve cancer research development and implementation?", highlighting the importance of meaningful patient involvement within the BIG-PPI.

Professor Lydie Meheus (Managing Director of the Anticancer Fund and member of the BIG-PPI) presenting at ESSO congress and showing a picture of the BIG-PPI meeting at the BIG-NCTN 2024 Annual Meeting.

SAN ANTONIO BREAST CANCER SYMPOSIUM (SABCS 2024)

10 – 13 December, Texas, US

OLYMPIA (BIG 6-13)

On Wednesday 11 December, the oral presentation (GS1-09) by Judy Garber, Dana-Farber Cancer institute, is scheduled: "OlympiA: A phase 3, multicentre, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1 and/or BRCA2 pathogenic variants and high-risk HER2-negative primary breast cancer: longer term follow-up".

Clinical trial information OLYMPIA: NCT02032823.

DECRESCENDO (BIG 19-02)

On Thursday 12 December (12:00 PM - 2:00 PM CST), the following abstract (P3-11-03) has been accepted for a poster presentation: "De-escalation of chemotherapy in patients with HER2-positive, hormone receptor-negative, node-negative early breast cancer: Primary results of the phase II DECRESCENDO trial".

Clinical trial information DECRESCENDO: NCT04675827.

SUPREMO (BIG 2-04)

On Thursday 12 December, the oral presentation (GS2-03) by Ian Kunkler, Edinburgh Cancer Centre, University of Edinburgh, is scheduled during the General Session 2: "Does postmastectomy radiotherapy in 'intermediate-risk' breast cancer impact overall survival? 10 year results of the BIG 2-04 MRC SUPREMO randomised trial: on behalf of the SUPREMO trial investigators."

Clinical trial information SUPREMO: NCT00966888

To lean more, visit also https://www.supremo-trial.com/

We invite you to join us to attend the SABCS sessions when the findings from these studies are shared.

19TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE 2025

Primary Therapy of Patients with Early Breast Cancer. Evidence, Controversies, Consensus

12 – 15 March 2025, Vienna / Austria

WWW.SG-BCC.ORG

RECENTLY PUBLISHED MANUSCRIPTS ABOUT BIG TRIALS

ALEXANDRA/Impassion030 (BIG 16-05)

McArthur H, Bailey A, Saji S, et al. Adjuvant chemotherapy with or without atezolizumab for stage II and III triple-negative breast cancer: final analysis of the ALEXANDRA/IMpassion030 phase 3 trial. *European Journal of Cancer*. 2024;200. doi:10.1016/j.ejca.2024.113952

ALTTO (BIG 2-06)

de Azambuja E, Piccart-Gebhart M, Fielding S, et al. Final analysis of the ALTTO trial: adjuvant trastuzumab in sequence or in combination with lapatinib in patients with HER2-positive early breast cancer [BIG 2-06/NCCTG N063D (Alliance)]. *ESMO Open*. 2024;9(11):103938. doi:10.1016/j.esmoop.2024.103938

APHINITY (BIG 4-11)

Loibl S, Jassem J, Sonnenblick A, et al. Adjuvant Pertuzumab and Trastuzumab in Early Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer in the APHINITY Trial: Third Interim Overall Survival Analysis With Efficacy Update. *JCO*. 2024;0(0):JCO.23.02505. doi:10.1200/JCO.23.02505

de Azambuja E, Agostinetto E, Samy F, et al. Abstract PS09-04: The benefit of adjuvant pertuzumab and trastuzumab according to estrogen receptor and HER2 expression: sub-analysis of the APHINITY trial. *Cancer Research*. 2024;84(9_Supplement):PS09-04. doi:10.1158/1538-7445.SABCS23-PS09-04

NeoALTTO (BIG 1-06)

Fernandez-Martinez A, Rediti M, Tang G, et al. Tumor Intrinsic Subtypes and Gene Expression Signatures in Early-Stage ERBB2/HER2-Positive Breast Cancer: A Pooled Analysis of CALGB 40601, NeoALTTO, and NSABP B-41 Trials. *JAMA Oncology*. Published online March 28, 2024. doi:10.1001/jamaoncol.2023.7304

PALLAS (BIG 14-03)

Metzger O, Ballman KV, Gnant M, et al. Analysis of the sensitivity to endocrine therapy (SET) assay in the PALLAS adjuvant trial of palbociclib in HR+/HER2- breast cancer (ABCSG-42/AFT-05/BIG-14-13). *JCO*. 2024;42(16_suppl):538-538. doi:10.1200/JCO.2024.42.16_suppl.538

PENELOPE-B (BIG 1-13)

Denkert C, Rachakonda K, Filipits M, et al. Relationship of adaptive subtyping and tumour heterogeneity of treatment response to neoadjuvant therapy in hormone receptor–positive HER2-negative early breast cancer: PENELOPE-B. *JCO*. 2024;42(16_suppl):566-566. doi:10.1200/JCO.2024.42.16_suppl.566

García-Sáenz JA, Marmé F, Untch M, et al. Patient-reported outcomes in high-risk HR+ /HER2- early breast cancer patients treated with endocrine therapy with or without palbociclib within the randomized PENELOPEB study. *European Journal of Cancer*. 2024;196. doi:10.1016/j.ejca.2023.113420

Marmé F, Martin M, Untch M, et al. Palbociclib combined with endocrine treatment in hormone receptor-positive, HER2-negative breast cancer patients with high relapse risk after neoadjuvant chemotherapy: subgroup analyses of premenopausal patients in PENELOPE-B★. *ESMO Open*. 2024;9(6). doi:10.1016/j.esmoop.2024.103466

POSITIVE (BIG 8-13)

Azim HA, Niman SM, Partridge AH, et al. Fertility Preservation and Assisted Reproduction in Patients With Breast Cancer Interrupting Adjuvant Endocrine Therapy to Attempt Pregnancy. *JCO*. 2024;42(23):2822-2832. doi: 10.1200/JCO.23.02292

BIG GENERAL

A new publication lead by Dr Carmela Caballero: Caballero C, Lundon DJ, Vasileva-Slaveva M, et al. A multidisciplinary team and patient perspective on omission of surgery after neoadjuvant systemic therapy for early breast cancer: A European Society of Surgical Oncology (ESSO) Research Academy survey. *European Journal of Surgical Oncology*. 2024;50(10):108585. doi:10.1016/j.ejso.2024.108585

Coles CE, Earl H, Anderson BO, et al. The Lancet Breast Cancer Commission. *The Lancet*. 2024;403(10439):1895-1950. doi:10.1016/S0140-6736(24)00747-5

Overview

CURRENT STUDIES RUN WITHIN THE BIG NETWORK

Open trials / research programmes

Study name	BIG number	Short description	Principal Investigator(s)	Trial model & partners
AURORA (Metastatic Breast Cancer GPS)	BIG 14-01	The AURORA programme: aiming to understand the molecular aberrations in metastatic breast cancer - NCT02102165	P. Aftimos M. Benelli A. Guerrero Zotano	BIG-sponsored programme (Co)-Leading partners: BIG (sponsor) / IJB-CTSU / FSS Pharma partner: N/A Funding: Breast Cancer Research Foundation® (BCRF) as the main funder, Fondation Cancer (Luxembourg), Pfizer grant for non-drug research, Fondation contre le Cancer (Belgium), National Lottery (Belgium), NIF Foundation, Rhone Trust, Barrie and Dena Webb, Candriam, Fondation Futur 21, Sogerim, Think Pink Belgium (SMART Fund), Cognizant Foundation, Eurofins Foundation and many individual donors. AURORA has also been supported by the Fund Friends of BIG, managed by the King Baudouin Foundation.
Breast Cancer in Pregnancy	BIG 2-03	Prospective registry of women treated for breast cancer while pregnant - NCT00196833	S. Loibl G. von Minckwitz	Supporter trial (Co)-Leading partner: GBG (sponsor) Pharma partner: N/A Funding: GBG, Deutsches Konsortium für Translationale Krebsforschung
DIANER	BIG 18-03	A Randomized Phase II Study to Evaluate the Incidence of Discontinuations due to Diarrhoea at 3 Cycles in patients with Early-stage HER2-positive (HER2+), Hormone Receptor-positive (HR+) Breast Cancer treated with Neratinib plus Loperamide prophylaxis versus Neratinib with Initial Dose Escalation plus PRN Loperamide prophylaxis versus Neratinib plus Loperamide plus Colesevelam prophylaxis. - NCT 05252988	M.Martin M. Gil	Supporter trial (Co)-Leading partner: GEICAM Pharma partner: Puma Biotechnology
EXPERT (BIG Radio Tuning)	BIG 16-02	A randomised phase III trial of adjuvant radiation therapy vs observation after breast conserving surgery for patients with molecularly characterised low-risk luminal A early breast cancer - NCT02889874	B. Chua G. Gruber	Co-lead trial (Co)-Leading partners: BCT-ANZ (sponsor) and BIG HQ Pharma partner: N/A Funding: BCT-ANZ, the National Health and Medical Research Council of Australia, National Lottery (Belgium), and BIG HQ fundraising initiatives
OPTIMA	BIG 22-02	Optimal personalised treatment of early breast cancer using multi-parameter analysis	R. Stein A. Makris J. Dunn	Supporter trial Coördinating group: ICR Foundation (sponsor): University College London Pharma partner:/ Funding: UK National Institute for Health Research (NIHR) Health Technology Assessment Programme
POLAR	BIG 18-02	Palbociclib for HR+ isolated local or regional recurrence of breast cancer - NCT03820830	E. Munzone S. Aebi	Supporter trial Coordinating group: ETOP IBCSG Partners Foundation (sponsor) Pharma partner: Pfizer Funding: Pfizer

RIBOLARIS	BIG 21-02	Neoadjuvant and Adjuvant Ribociclib and ET for Clinically High-risk ER+ and HER2- Breast Cancer - NCT05296746	A. Prat P. Cottu J. Gavilá T. de La Motte Rouge	Supporter trial Coordinating group: SOLTI (sponsor) Pharma partner: Novartis Pharma AG Funding: Novartis Pharma AG
TREAT ctDNA Elacestrant	BIG 22-01	Elacestrant for treating ER+/HER2- breast cancer patients with ctDNA relapse - NCT05512364	M. Ignatiadis E. Saloustros W. Janni	Supporter trial Coördinating group: EORTC Foundation (sponsor): EORTC Pharma partner: Menarini Ricerche (collaborator for ctDNA analysis: Inivata)

Follow-up or post-study activities, recently closed studies

Study name	BIG number	Short description	Principal Investigator(s)	Trial model & partners
ALEXANDRA / IMpassion 030	BIG 16-05	A randomised phase III trial comparing atezolizumab (anti-PD-L1 inhibitor), given in combination with standard chemotherapy vs. chemotherapy alone as adjuvant treatment in patients with operable TNBC - NCT03498716	M. Ignatiadis H. McArthur S. Saji	Lead trial (Co)-Leading partners: BIG HQ / IJB-CTSU / FSTRF and AFT Pharma partner: Roche/Genentech (sponsor) Funding: Roche / Genentech
ALPHABET	BIG 18-04	A randomised phase III trial of trastuzumab + ALpelisib +/- fulvestrant vs. trastuzumab + chemotherapy in patients with PIK3CA mutated previously treated HER2+ Advanced BrEasT cancer - NCT05063786	A. Pérez-Fidalgo C. Criscitiello P. Bedard	Co-lead trial (Co)-Leading partners: GEICAM (sponsor) / ETOP IBCSG Partners Foundation and BIG HQ Pharma partner: Novartis Funding: Novartis
ALTTO	BIG 2-06	Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation: sequence and combination for patients with HER2/ErbB2 positive primary breast cancer - NCT00490139	M. Piccart A. Moreno-Aspitia	Lead trial (Co)-Leading partners: BIG HQ / IJB-CTSU / FSTRF / Alliance (former NCCTG, sponsor for the US) Pharma partner: Novartis (global sponsor for all countries with the exception of US) Funding: GSK (past) / Novartis
APHINITY	BIG 4-11	Comparison of single-versus-dual anti-HER2 therapy (trastuzumab, pertuzumab) for patients with HER2-positive primary breast cancer - NCT01358877	M. Piccart S. Loibl J. Bines	Lead trial (Co)-Leading partners: BIG HQ / IJB-CTSU / FSTRF Pharma partner: Roche (sponsor) Funding: Roche
APPALACHES	BIG 18-01	A Phase II study of Adjuvant PALbociclib as an Alternative to CHemotherapy in Elderly patients with high-risk ER+/HER2- early breast cancer - NCT03609047	H. Wildiers E. Brain K. Punie	Supporter trial Coordinating group: EORTC (sponsor) Pharma partner: Pfizer Funding: Pfizer
BRAVO	BIG 5-13	Niraparib for patients with HER2-negative, germline BRCA mutation-positive, locally advanced or metastatic breast cancer - NCT01905592	N. Turner J. Balmaña D. Cameron J. Erban	Co-lead trial (Co)-Leading partners: EORTC / BIG HQ Pharma partner: Tesaro (sponsor) Funding: Tesaro
DCIS	BIG 3-07	Radiation doses and fractionation schedules for women with DCIS - NCT00470236	B. Chua	Supporter trial (Co)-Leading partner: TROG (sponsor) Pharma partner: N/A Funding: National Health & Medical Research Council Project Grant, Susan G. Komen
DECRESCENDO	BIG 19-02	De-escalation of adjuvant chemotherapy in HER2-positive, HR-negative breast cancer - NCT04675827	M. Piccart G. Zoppoli	Co-lead trial (Co)-Leading partners: IJB-CTSU (sponsor) and BIG HQ Pharma partner: Roche Funding: Roche (grant)
Exceptional Responders	BIG 16-04	A global hunt for exceptional responders in the BIG network: aiming to identify breast cancer patients with a truly remarkable clinical response to anticancer treatments, and to characterise their tumours molecularly	A. Irrthum (coordinator)	BIG-sponsored programme (Co)-Leading partner: BIG HQ Pharma partner: N/A Funding: Breast Cancer Research Foundation

IBIS-II	BIG 5-02	Prevention study of anastrozole for postmenopausal women at increased risk of breast cancer; and of effects of tamoxifen vs. anastrozole in postmenopausal women with DCIS -NCT00072462	J. Cuzick	Supporter trial (Co)-Leading partner: IBIS Pharma partner: AstraZeneca Sponsor: Queen Mary University of London Funding: Cancer Research UK, Queen Mary University of London
INTERNATIONAL MALE BREAST CANCER PROGRAMME	BIG 2-07	Registration and biologic characterisation programme of breast cancer in men - NCT01101425	F. Cardoso S. Giordano	Supporter programme (Co)-Leading partners: EORTC (sponsor) / NABCG NCTN / TBCRC (US) Pharma partner: N/A Funding: Breast Cancer Research Foundation
LORELEI	BIG 3-13	Neoadjuvant letrozole plus taselisib versus letrozole plus placebo in postmenopausal women with ER+, HER2-negative, early-stage breast cancer - NCT02273973	C. Saura E. de Azambuja	Co-lead trial (Co)-Leading partners: ABCSG, SOLTI and BIG HQ Pharma partner: Genentech (sponsor) Funding: Genentech
MA.32 Metformin	BIG 5-11	Effect of metformin on recurrence and survival in early stage breast cancer - NCT01101438	P. J. Goodwin	Supporter trial (Co)-Leading partner: CCTG (sponsor) Pharma partner: Apotex Funding: NCI/NIH grants, Cancer Research UK, the Canadian Cancer Society, the Breast Cancer Research Foundation® (BCRF) and the Canadian Breast Cancer Foundation.
MINDACT	BIG 3-04	Can addition of 70-gene signature to common clinical-pathological criteria safely spare patients with 0 to 3 node positive breast cancer from adjuvant chemotherapy? - NCT00433589	E. Rutgers F. Cardoso M. Piccart	Co-lead trial (Co)-Leading partners: EORTC (sponsor) / BIG HQ Commercial partners: Roche, Sanofi, Novartis and Agendia Funding: European Commission, Roche, Sanofi and Novartis grants, BCRF, Susan G. Komen for the Cure, Cancer Research UK, EORTC Charitable Trust, numerous national cancer societies and many other charitable grants*
NEO-ALTTO	BIG 1-06	Comparison of dual HER2 inhibition (lapatinib, trastuzumab) plus chemotherapy before surgery versus single HER2-targeted therapy - NCT00553358	S. Di Cosimo J. Huober	Co-lead trial (Co)-Leading partners: IJB-CTSU / FSS / SOLTI / BIG HQ Pharma partner: Novartis (global sponsor for all countries with the exception of US, where Alliance is the sponsor) Funding: GSK (past) / Novartis
OLYMPIA	BIG 6-13	Olaparib vs. placebo for patients with BRCA- mutated, high-risk HER2-negative breast cancer, having completed local treatment and (neo)adjuvant chemotherapy - NCT02032823	A. Tutt D. Cameron B. Kaufman J. Garber C. Geyer	Lead trial (Co)-Leading partners: NRG Oncology (sponsor in US), BIG HQ and FSTRF Pharma partner: AstraZeneca (global sponsor for all countries excluding the US) and Merck (co-developer of the drug) Funding: AstraZeneca
PALLAS	BIG 14-03	PALbociclib CoLlaborative Adjuvant Study: palbociclib with standard adjuvant encodcrine therapy versus standard adjuvant endocrine therapy alone for HR+ / HER2-negative early breast cancer - NCT02513394	E. Mayer M. Gnant A. DeMichele	Co-Lead trial (Co)-Leading partners: ABCSG, Alliance for Clinical Trials in Oncology Foundation (sponsors for Rest of the World and the US respectively) and BIG HQ Pharma partner: Pfizer Funding: Pfizer grant
PENELOPE-B	BIG 1-13	Post-neoadjuvant palbociclib for patients with HR+, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy - NCT01864746	S. Loibl	Supporter trial (Co)-Leading partner: GBG (sponsor) Pharma partner: Pfizer Funding: Pfizer grant

* full information available on the BIG website.
Legend: AFT: Alliance Foundation Trials, LLC; BCRF: Breast Cancer Research Foundation; FSS: Frontier Science Scotland, LTD; FSTRF: Frontier Science and Technology Research Foundation, Inc; N/A: not applicable; NCTN: National Clinical Trials Network; NCCTG: North Central Cancer Treatment Group; NCI: US National Cancer Institute; SCTBG: Scottish Cancer Trials Breast Group; TBCRC: Translational Breast Cancer Research Consortium

POSITIVE (BIG time for Baby)	BIG 8-13	Endocrine therapy interruption to enable conception for young women with ER+ breast cancer - NCT02308085	O. Pagani	Supporter trial (Co)-Leading partner: ETOP IBCSG Partners Foundation (sponsor) Pharma partner: N/A Funding: ETOP IBCSG Partners Foundation, Fonds Baillet-Latour, BIG HQ, national and local funding bodies, individual donors
PYTHIA	BIG 14-04	Palbociclib plus fulvestrant for pretreated patients with ER+/HER2- metastatic breast cancer - NCT02536742	L. Malorni	Co-lead trial (Co)-Leading partners: ETOP IBCSG Partners Foundation (sponsor) and BIG HQ Pharma partner: Pfizer Funding: research grants and drugs from Pfizer and AstraZeneca. BIOVICA supplied support for sample handling and thymidine kinase assays.
SOFT	BIG 2-02	Evaluation of ovarian suppression and of exemestane as adjuvant therapy for premenopausal women with endocrine responsive breast cancer - NCT00066690	P. Francis G. Fleming	Supporter trial (Co)-Leading partner: ETOP IBCSG Partners Foundation (sponsor) Pharma partner: Pfizer Funding: grants from BCRF, Cancer Research CH, Pfizer, Ipsen, Debiopharm, TerSera Therapeutics, US NCI, IBCSG and many participating collaborative academic groups, as well as various charities. Pfizer and Ipsen provided the drugs for these studies.
SOLE	BIG 1-07	A phase III trial evaluating the role of continuous letrozole versus intermittent letrozole following 4 to 6 years of prior adjuvant endocrine therapy for postmenopausal women with hormone-receptor positive, node positive early stage breast cancer (SOLE - Study Of Letrozole Extension) - NCT00553410	M. Colleoni P. Karlsson S. Aebi J. Chirgwin	Supporter trial Coordinating group: ETOP IBCSG Partners Foundation Sponsor: ETOP IBCSG Partners Foundation Pharma partner: Novartis Funding: Novartis
SUPREMO	BIG 2-04	Selective Use of Postoperative Radiotherapy AftEr MastectOmy: adjuvant chest wall irradiation for 'intermediate risk' breast cancer following mastectomy - NCT00966888	I. Kunkler P. Canney	Supporter trial (Co)-Leading partner: SCTBG Sponsor: UK Medical Research Council Pharma partner: N/A Funding: UK Medical Research Council, EORTC, Cancer Australia, William and Elizabeth Davies Charitable Trust, Peter Chan Jee Yat Foundation, Yeung Ying Yin and May Yeung Foundation.
TEXT	BIG 3-02	Tamoxifen and Exemestane Trial: evaluation of exemestane plus GnRH analogue for premenopausal women with endocrine responsive breast cancer - NCT00066703	O. Pagani B. Walley	Supporter trial (Co)-Leading partner: ETOP IBCSG Partners Foundation (sponsor) Pharma partner: Pfizer Funding: grants from BCRF, Cancer Research CH, Pfizer, Ipsen, Debiopharm, TerSera Therapeutics, US NCI, IBCSG and many participating collaborative academic groups, as well as various charities. Pfizer and Ipsen provided the drugs for these studies.
TREAT-CTC	BIG 1-12	TRastuzumab in HER2-negative Early breast cancer as Adjuvant Treatment for Circulating Tumor Cells (CTC) - NCT01548677	M. Ignatiadis M. Piccart J.-Y. Pierga B. Rack C. Sotiriou	Supporter trial (Co)-Leading partners: EORTC BCG, SUCCESS, UNICANCER Sponsor: EORTC Pharma partner: Roche, Janssen Diagnostics Funding: Roche educational grant/ medication; Janssen test kits

NB: This table does not include the studies in development and all closed trials. For more information, please visit: www.BIGagainstbreastcancer.org.

THE BIG NETWORK: GLOBAL RESEARCH COLLABORATION TO CURE BREAST CANCER

2024 marks BIG's 25th anniversary! For the past quarter-century, BIG's academic research groups have relentlessly been working together to find better treatments and cures for breast cancer.

The Breast International Group (BIG) is an international non-profit organisation that represents the largest global network of academic research groups dedicated to finding cures for breast cancer. Its mission is to facilitate and accelerate breast cancer research at an international level.

In 1999, BIG was founded with the aim to address fragmentation in European breast cancer research. Research groups from other parts of the world rapidly expressed interest in joining BIG and, 25 years later, BIG represents over 55 like-minded research groups from around the world and reaches across approximately 70 countries on 6 continents.

Through its network of groups, BIG connects several thousand specialised hospitals, research centres and world-class breast cancer experts who collaborate to design and conduct pioneering breast cancer research. Each BIG group plays a crucial role. The combined expertise, collaborative spirit, dedication and hard work are essential to improving the lives of patients confronted with breast cancer. BIG is thus global and local.

More than 30 clinical trials are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute and the North American Breast Cancer Group, to act as a strong integrating force in the field of breast cancer research. Thanks to this global collaboration, BIG enrols large numbers of patients from around the world into clinical trials quickly, which in turn leads to faster results.

BIG's research is supported in part by its philanthropy unit, known as ***BIG against breast cancer.*** This denomination is used to interact with the general public and donors, and to raise funds for BIG's purely academic breast cancer trials and research programmes.

www.bigagainstbreastcancer.org

AFRICA

BGICS Breast Gynaecological International Cancer Society

ASIA

BDPCC Breast Disease Professional Committee of CMEA

BIEI Breast Intergroup of Eastern India

CTRG Cancer Therapeutics Research Group

HKBOG Hong Kong Breast Oncology Group

ICON ARO Indian Co-operative Oncology Network

IOSG Indian Oncology Study Group

JBCRG Japan Breast Cancer Research Group

KCSG Korean Cancer Study Group

SKMCH & RC Shaukat Khanum Memorial Cancer Hospital & Research Centre

TCOG Taiwan Cooperative Oncology Group

TSCO Thai Society of Clinical Oncology

AUSTRALASIA

BCT-ANZ Breast Cancer Trials Australia and New Zealand

TROG Trans-Tasman Radiation Oncology Group

EUROPE

ABCSG Austrian Breast & Colorectal Cancer Study Group

AGO-B Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group

BOOG Borstkanker Onderzoek Groep

CEEOG Central and East European Oncology Group

CT-IRE Cancer Trials Ireland

DBCG Danish Breast Cancer Cooperative Group

EORTC BCG European Organisation for Research and Treatment of Cancer Breast Cancer Group

EUBREAST The European Breast Cancer Research Association of Surgical Trialists Network (EUBREAST e.V./Germany and EUBREAST ETS./Italy)

FBCG Finnish Breast Cancer Group

FSS Frontier Science Scotland

GCSG Georgian Cancer Study Group

GEICAM Spanish Breast Cancer Group

GIM Gruppo Italiano Mammella

GOIRC Gruppo Oncologico Italiano di Ricerca Clinica

HSBS Hellenic Society of Breast Surgeons

HeCOG Hellenic Cooperative Oncology Group

HORG Hellenic Oncology Research Group

IBCG Icelandic Breast Cancer Group

IBCSG International Breast Cancer Study Group

IBIS International Breast Cancer Intervention Studies

ICCG International Collaborative Cancer Group

ICR-CTSU Institute of Cancer Research - Clinical Trials & Statistics Unit

IJB-CTSU Institut Jules Bordet Clinical Trials Support Unit

ITMO Italian Trials in Medical Oncology

MICHELANGELO Fondazione Michelangelo

NBCG Norwegian Breast Cancer Group

NCRI-BCSG National Cancer Research Institute - Breast Cancer Clinical Studies Group

SABO Swedish Association of Breast Oncologists

SAKK Swiss Group for Clinical Cancer Research

SLO Société Luxembourgeoise d'Oncologie

SOLTI Breast Cancer Research Group

SUCCESS Study Group

SweBCG Swedish Breast Cancer Group

UCBG Unicancer Breast Group

WSG Westdeutsche Studiengruppe

LATIN AMERICA

GAICO Grupo Argentino de Investigación Clínica en Oncología

GECO PERU Grupo de Estudios Clinicos Oncologicos Peruano

GOCCHI Chilean Cooperative Group for Oncologic Research

GOCUR Grupo Oncológico Cooperativo Uruguayo

LACOG Latin American Cooperative Oncology Group

MIDDLE EAST

IBG Israeli Breast Group

ICRC Iranian Cancer Research Center

SBCG Sheba Breast Collaborative Group

NORTH AMERICA

CCTG Canadian Cancer Trials Group

TOGETHER, WE ARE BIG

Use this space to express your gratitude – write a thank-you message to a researcher, doctor, patient, family member, friend, colleague, or supporter who has made a difference in your breast cancer journey or that of someone you love.

Share what they mean to you or what you would want them to see. With your consent, we'll feature it on our socials, in our newsletters, or annual report, and more! Inspire others, strengthen our community, and help us in the fight to find the cures of tomorrow. Research saves lives.

We'd love to hear your story!

Email us at communications@bigagainstbc.org and join the celebration of progress.

Thank you for your support!

COLOPHON

Print
VCP Graphics BV
IZ 'Blauwe Toren'
Hoge Hul 49
8000 Brugge
Belgium

BIG Research in Focus is published by Breast International Group (BIG)-aisbl. The opinions or conclusions stated or implied in the articles herein are those of the authors and do not necessarily reflect those of the publisher.

BIG Breast International Group

BIG Headquarters' contact address:
Breast International Group (BIG)-aisbl
Rue de Bretagne 20 Bretagnestraat
1200 Brussels
Belgium
Tel: +32 2 486 16 00
VAT: BE 0468 176 240
E-mail: info@BIGagainstbc.org
www.BIGagainstbreastcancer.org

Récolte de fonds Ethique asbl
Ethische Fondsenwerving vzw

Kruidtuinstraat 75 Rue Botanique
1210 Brussels
Belgium
Tel: 02 225 43 29
info@re-ef.be - www.re-ef.be

Co-funded by the European Union under an operating grant from the European Union's EU4Health programme under grant agreement No 101124555. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HaDEA). Neither the European Union nor the granting authority can be held responsible for them.