

ANNUAL
REPORT

20
20



Breast cancer research

RESILIENCE
and the strengths
of the BIG network





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*“Ballet dancers always move with such grace, elegance, beauty and softness. Yet there is so much strength, effort and discipline of character that goes on behind it. There is a continuous story of **resilience and persistence**, not unlike the research process.”*



MESSAGE FROM THE CHAIR

Dear reader,

2020 was marked by a major global public health crisis. The sudden and overwhelming COVID-19 pandemic and its global implications tested the resilience of many individuals, communities, and healthcare systems around the world. We are all indebted to the work of many people to care for those with COVID-19 infection as well as those with other conditions, and we need to remember those known to us who did not recover. We are all grateful for the amazing work done by teams of scientists to develop a vaccine in such a record time, a tribute to inventiveness, collaboration, and clinical trialists around the world.

Despite the COVID-19 pandemic and all the challenges it posed, members of the BIG network continued their efforts to advance breast cancer research, demonstrating great resilience and persistence. None of BIG's achievements would be possible without the willingness to work together.

In this annual report, we describe how and why BIG conducts large international clinical trials. Not only does this require resilience and persistence at every stage – from planning to completion –, it also entails tremendous effort to secure the necessary funding.

Research is the only way to understand breast cancer, how and why it progresses, and how it can ultimately be stopped. For over 20 years, BIG has been conducting global breast cancer clinical trials and research programmes. The BIG network and its academically driven research are crucial to conducting studies that put patients' needs first.

BIG makes it possible to rapidly enrol large numbers of patients into complex international clinical trials, to share best practices, expertise, and data in pursuit of answers to questions that really matter to patients.

BIG trials also follow patients long after the treatment ends, with the aim to detect long-term side effects, and improve treatment therapies and patients' quality of life. BIG guarantees more robust and credible research results, which leads to better treatments and cures for all patients. This requires the resilience and persistence of both patients and researchers.

The sections "**BIG Research**" and "**BIG Network**" give you a peek at BIG member groups' research and related activities around the world. It also includes a few examples of how BIG member groups adapted quickly to address the challenges of COVID-19.

In 2020, Professor Martine Piccart, BIG's co-founder, stepped down from BIG's Executive Board. She continues to be involved in the organisation as Senior Advisor to BIG and President of BIG against breast cancer.

BIG against breast cancer, BIG's dedicated philanthropy unit, conducts vital fundraising to support BIG's clinical trials and research programmes that have no commercial interest but are crucial for breast cancer patients. The funds raised provide the means for BIG member groups and their affiliated hospitals, and other partners, to finance their efforts and patient participation in a study. This is made possible by the generosity of foundations, companies, ambassadors, and individuals. The section "**BIG Philanthropy**" provides an overview of activities carried out by BIG against breast cancer.

In the years to come, the BIG network aims to continue to play an important role in international breast cancer research, allowing for the most efficient conduct of clinical trials and always keeping patients' interests at the heart of its activities. Further collaboration with research groups in countries where research is scarcer and availability of innovative trials is rarer could be a significant step towards improving treatment and care for women and men with breast cancer, wherever they live.

In name of everyone at BIG, I would like to extend our sincere gratitude and appreciation to all member groups, partners, faithful ambassadors, donors and staff for their support and collaborative spirit to help advance breast cancer research. And, just as importantly, we wish to thank and honour the thousands of patients who participate in our trials and work with us to develop tomorrow's cures.

Enjoy the reading.

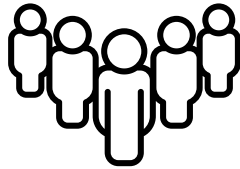
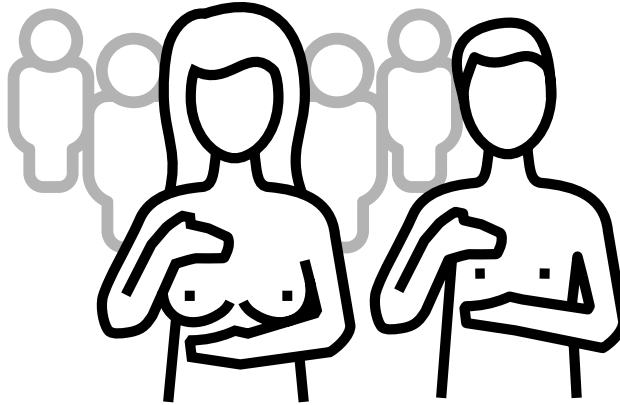
*Professor David Cameron
BIG Chair*

**TOGETHER,
WE ACHIEVE MORE**



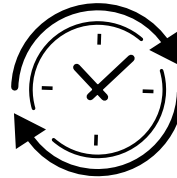
BIG PICTURE OF BIG

1 IN 8 WOMEN
and **1 IN 800 MEN**
will be diagnosed with breast cancer over the course of her/his lifetime



2,3 MILLION PEOPLE

were diagnosed with breast cancer in 2020



78 PEOPLE / HOUR

die from breast cancer



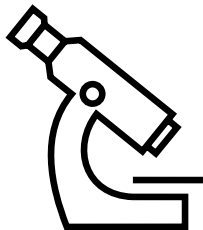
± 97 000 PATIENTS

have participated in BIG trials, thus helping to develop better breast cancer treatments



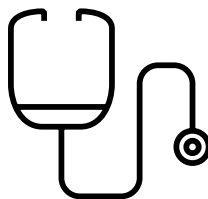
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academic research groups make up the largest international network dedicated solely to breast cancer research



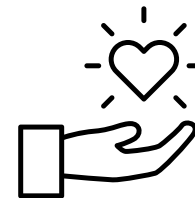
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patient-centred clinical trials and research programmes are run under the BIG umbrella at any one time



± 10 000

breast cancer specialists within the BIG network



PATIENTS ARE AT THE HEART OF BIG'S RESEARCH

The goal is to offer the best possible treatments to each patient

ABOUT BIG

For over 20 years, BIG's global network of academic research groups have been working together to find better treatments and cures for breast cancer.

The Breast International Group (BIG) is an international not-for-profit organisation that represents the largest global network of academic research groups dedicated to finding cures for breast cancer.

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, more than two decades later, BIG represents over 50 like-minded research groups from around the world and reaches across more than 70 countries on 6 continents.

Through its network of groups, BIG connects thousands of hospitals and world-class breast cancer experts who collaborate in pioneering breast cancer research. 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.

BIG's mission is to facilitate and accelerate breast cancer research at an international level. We are proud to be both global and local, helping breast cancer patients from all over the world.

Thanks to this global collaboration, BIG enrolls 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.

www.BIGagainstbreastcancer.org



HONORARY PRESIDENT

“The most common cancer in the world, breast cancer, affects both women and men. Much progress has already been made in improving patients’ quality of life and their chances of survival. Nonetheless, finding a cure is still one of the greatest challenges facing researchers everywhere. The task has not been helped by the constraints of COVID-19. However, BIG’s innovative researchers have continued their work, undaunted, throughout the pandemic.

It is crucial, therefore, that we support BIG in its efforts to find a cure and to give hope to the countless women, men and families affected by this disease.”

Her Majesty the Queen of the Belgians is the Honorary President of the Breast International Group and has been supporting BIG’s initiatives since 2015.

TOGETHER we will cure breast cancer

1 / BIG RESEARCH

RESILIENCE AND STRENGTH OF THE NETWORK TO SERVE PATIENTS' NEEDS



BIG conducts large international clinical trials and follows patients for several years after treatment ends. This requires the **resilience and persistence** of both patients and researchers. It also entails tremendous effort to secure the necessary funding.

The BIG network and its academically driven research are crucial to conducting studies that put patients' needs first. BIG member groups share the same principles of research conduct, both when working in a purely academic environment or in collaboration with pharmaceutical or biotech partners. **One of the essential elements of BIG studies is the long-term follow-up of patients** to detect side effects that may only become apparent long after treatment has ended. It also guarantees more robust and credible research results, which leads to better treatments and cures for all patients.

Three important BIG studies revealed their long-term results recently, including two in 2020: **MINDACT, NeoALTTO and IBIS II.**



“MINDACT WAS A GREAT EXAMPLE OF ACADEMIC COLLABORATION THAT LED TO PRACTICE-CHANGING RESULTS AND IMPACTED THE LIVES OF MANY PATIENTS WITH EARLY BREAST CANCER.” DR FATIMA CARDOSO, PRINCIPAL INVESTIGATOR OF MINDACT

**MINDACT (BIG 3-04)
SPARING CHEMOTHERAPY WHEN NOT NECESSARY**

In this study involving 6,693 patients and carried out by the European Organisation for Research and Treatment of Cancer (EORTC) in close collaboration with BIG in nine countries throughout Europe, researchers showed that up to **46% of high-risk patients with early stage breast cancer could avoid chemotherapy and its likely side effects** if a sophisticated tumour genomic test (MammaPrint®) showed their cancer was unlikely to come back.

Patients were followed-up for about nine years and, in 2020, **results of the longer follow-up confirmed the utility of the MammaPrint test and the possibility to substantially and safely de-escalate the use of post-surgery chemotherapy** for some groups of patients, thereby sparing many from an unpleasant treatment and its short and long-term side effects.

MINDACT: A SUCCESSFUL ACADEMIC TRIAL THAT HELPED CHANGE CLINICAL PRACTICE

- > 47 MILLION € RAISED BY ACADEMIA TO FUND THE TRIAL
- > ALMOST 9 YEARS FOLLOW-UP OF PATIENTS
- > 6,693 PATIENTS INVOLVED FROM 112 CENTRES AND HOSPITALS IN 9 COUNTRIES
- > COMPLEX AND SUCCESSFUL LOGISTICS AND DATA MANAGEMENT

The study published its first results in 2016 in the *New England Journal of Medicine*¹, and the long-term results in the *Lancet Oncology*² in March 2021.

References:
¹ Cardoso F, van't Veer LJ, Bogaerts J, et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. *N Engl J Med* 2016; 375:717-729
https://www.nejm.org/doi/full/10.1056/NEJMoa1602253?query=recirc_curatedRelated_article
² Piccart M, van't Veer LJ, Poncet C et al. 70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age. *The Lancet Oncology* 2021 March 12. doi:[https://doi.org/10.1016/S1470-2045\(21\)00007-3](https://doi.org/10.1016/S1470-2045(21)00007-3).
[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(21\)00007-3/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(21)00007-3/fulltext)
https://www.nejm.org/doi/full/10.1056/NEJMoa1602253?query=recirc_curatedRelated_article

MINDACT was supported by grants from the European Commission Framework Programme VI (FP6-LSHC-CT-2004-503426, “TRANSBIG Network of Excellence”), the Breast Cancer Research Foundation, Novartis, F. Hoffman La Roche, Sanofi-Aventis, Eli Lilly, Veridex, the U.S. National Cancer Institute, the European Breast Cancer Council-Breast Cancer Working Group (BCWG grant for the MINDACT biobank), the Jacqueline Seroussi Memorial Foundation (2006 JSMF award), Prix Mois du Cancer du Sein (2004 award), Susan G. Komen for the Cure (SG05-0922-02), Fondation Belge Contre le Cancer (SCIE 2005-27), Dutch Cancer Society (KWF), Association Le Cancer du Sein, Parlons-en!, the Brussels Breast Cancer Walk-Run and the American Women’s Club of Brussels, NIF Trust, Deutsche Krebshilfe, the Grant Simpson Trust and Cancer Research UK. This trial was also supported by the EORTC Charitable Trust. Whole genome analysis was provided in kind by Agendia.



NEOALTTO IS THE NEOADJUVANT STUDY INVESTIGATING DUAL HER2 BLOCKADE IN EARLY BREAST CANCER WITH THE LONGEST CLINICAL FOLLOW-UP (ALMOST TEN YEARS)

NEOALTTO (BIG 1-06) BENEFIT OF DUAL HER2-TARGETED THERAPY

The first results of NeoALTTO, published in *The Lancet*¹ in 2012, showed a near doubling of the pathological complete response (pCR) – meaning a disappearance of all visible signs of cancer – in patients who received a combination of trastuzumab and lapatinib (two HER2-targeted agents) rather than the single agent alone (trastuzumab or lapatinib) before surgery.

The long-term analysis, presented in 2020 after following patients for about ten years, showed that women who achieved pCR have significantly higher survival rates (i.e., event free and overall survival rates) compared to those who did not. It confirmed that pCR is likely an indicator of long-term benefit of treatment in HER2-positive breast cancer. This trend is more important in patients whose disease is hormone receptor-negative and in the population receiving the combination of lapatinib and trastuzumab.

The analysis did not report any new or long-term safety concerns.

Developed in parallel with its sister trial ALTTO (BIG 2-06), the NeoALTTO study included 455 patients and was set up to investigate whether combining trastuzumab (Herceptin®) with another drug called lapatinib (Tykerb®) – given either alone, together or one after the other – could benefit patients with HER2-positive primary breast cancer in the neoadjuvant (pre-surgical) setting.

NeoALTTO is a study co-led by SOLTI Breast Cancer Group, BIG Headquarters, Institut Jules Bordet's Clinical Trials Support Unit (IJB-CTSU) and Frontier Science & Technology Research Foundation (FSTRF).

The study was sponsored and funded by GlaxoSmithKline (GSK) until 30 November 2015, after which these responsibilities were transferred to Novartis. The study was designed and conducted following BIG's academic research principles.

Reference:

¹ Baselga J, Bradbury I, Eidtmann H, et al. Lapatinib with trastuzumab for HER-positive early breast cancer (NeoALTTO): a randomised, open-label, multicentre, phase 3 trial. *Lancet* 2012 Feb 18;379(9816):633-40

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NEOALTTO: THE STRENGTH OF INTERNATIONAL COLLABORATION

- > ALMOST 10 YEARS FOLLOW-UP OF PATIENTS
- > TOGETHER WITH ALTTO, MORE THAN 8,000 PATIENTS INVOLVED
- > A HUGE PROSPECTIVE COLLECTION OF SAMPLES FOR FUTURE RESEARCH PROJECTS
- > A TREMENDOUS INTERNATIONAL COLLABORATION BETWEEN PATIENTS, RESEARCHERS, DOCTORS AND NURSES AND PHARMA



“AN ESSENTIAL POINT IS THAT BOTH PREVENTION AND SCREENING INTERVENTIONS REQUIRE A LONG FOLLOW-UP TO GET A COMPLETE PICTURE, AND THIS NEEDS TO BE MORE WIDELY APPRECIATED AND ACCOMMODATED IN FUNDING STREAMS” PROFESSOR JACK CUZICK, PRINCIPAL INVESTIGATOR OF IBIS-II

**IBIS II (BIG 5-02)
ANASTROZOLE REDUCES BREAST
CANCER OCCURRENCE BY 49%**

The long term follow-up results of the International Breast cancer Intervention Study IBIS-II, published in *The Lancet*¹ end of 2019, indicate **a long term preventive benefit with the aromatase inhibitor anastrozole in postmenopausal women with oestrogen receptor (ER)-positive breast cancer who are identified at increased risk of developing breast cancer.**

Indeed, results have demonstrated a 49% overall reduction in breast cancer occurrence in patients receiving anastrozole compared to placebo. This was based on a 61% reduction during the 5-year treatment period and an additional 36% reduction in the 5 to 12-year post-treatment follow-up period.

No additional side effects were reported from the long-term follow-up.

It is hoped that these positive results will lead to a change in clinical practice with anastrozole being routinely prescribed as preventive medicine for post-menopausal women at high risk of breast cancer.

In total, 3,864 patients from 153 centres in 19 countries were recruited between February 2003 and January 2012.

The IBIS-II Prevention trial is run by the International Breast Cancer Intervention Study group (IBIS), with the support of the Breast International Group (BIG). The study was funded by Cancer Research UK, the National Health and Medical Research Council Australia, Breast Cancer Research Foundation, Sanofi Aventis, and AstraZeneca.

Reference:

¹ Cuzick J, Sestak I, Forbes JF et al. Use of anastrozole for breast cancer prevention (IBIS-II): long-term results of a randomised controlled trial. *The Lancet*, December 12, 2019 doi:[https://doi.org/10.1016/S0140-6736\(19\)32955-1](https://doi.org/10.1016/S0140-6736(19)32955-1) [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)32955-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32955-1/fulltext)

IBIS-II:

- > UP TO 12 YEARS FOLLOW-UP OF PATIENTS
- > 3,864 PATIENTS ENROLLED
- > A LARGE INTERNATIONAL PREVENTION TRIAL
- > A POTENTIALLY PRACTICE-CHANGING TRIAL





BIG'S RESEARCH IN 2020: TOGETHER, WE CONTINUED OUR EFFORTS TO FIND BETTER TREATMENTS AND CURES

Despite all the challenges COVID-19 posed in 2020, BIG member groups all around the world continued their efforts to advance breast cancer research and find better treatments and cures.

The year 2020 was a very good year in terms of results of BIG studies and important milestones. Here is a peek at some of them:



TARGET RECRUITMENT REACHED

The **POSITIVE trial** (IBCSG 48-14/BIG 8-13) met its target accrual, enrolling 518 patients from 203 centres from 20 countries around the world. The study expects to provide an answer to the question of whether women can interrupt their endocrine treatment to try to have a baby, without increasing the risk of cancer recurrence. Women will be followed up for 10 years after enrolment.

The **AURORA research programme** (BIG 14-01) enrolled 1,000 patients, an important milestone for this international academic study aiming to understand the biological evolution of metastatic breast cancer. This was made possible through the efforts of researchers and patients from 11 European countries, 10 BIG groups and 66 hospitals and cancer centres. The study will continue recruiting patients if sufficient funding is secured.

FIRST ENCOURAGING RESULTS

PYTHIA (IBCSG 53-14/BIG 14-04), a downstream trial of the AURORA programme, revealed its first results and showed that serum thymidine kinase activity (TKa) may be an independent prognostic biomarker in patients with luminal metastatic breast cancer treated with palbociclib and fulvestrant, helping doctors to identify those patients who will develop primary resistance to the treatment.

The **DCIS study** (TROG 07.01/BIG 3-07) demonstrated the importance of tailoring radiation treatment of patients with DCIS according to their risks of recurrence to avoid over- or under-treatment. It showed that, after breast conserving surgery, higher radiation doses to the part of the breast where the DCIS was found, in addition

to radiotherapy of the whole breast, significantly reduced its risk of returning in patients with higher-risk DCIS. Compared to 5 weeks of whole breast radiotherapy, the study also showed that the shorter, more convenient 3 weeks of radiotherapy did not increase recurrence.

The DCIS results will likely have a significant impact on how patients with DCIS are best managed worldwide

INVESTIGATING THE BENEFITS OF PALBOCICLIB IN EARLY BREAST CANCER

The results of **PALLAS** (BIG 14-03), presented in September 2020, showed that the addition of two years of palbociclib to endocrine therapy had no effect on invasive disease-free survival (iDFS) compared to standard of care (endocrine therapy alone) in patients with hormone receptor-positive (HR+), HER2-negative, early-stage breast cancer.

Despite the unexpected negative results, PALLAS is a great example of worldwide collaboration between academia and industry to run a huge pivotal clinical trial and advance breast cancer research.

The 5,796 patients enrolled in PALLAS will be followed for at least 10 years, and both clinical data and collected biomaterial build a huge treasure for future translational research

Later in 2020, these results were corroborated by the findings of **PENELOPE-B** (GBG 78 / BIG 1-13), which showed that the CDK4/6 inhibitor palbociclib did not improve iDFS when given in addition to standard endocrine therapy for a period of one year to patients with HR+, HER2-negative primary breast cancer who are at high risk of recurrence following neoadjuvant chemotherapy.



WHAT DRIVES BIG RESEARCHERS?

BIG designs and conducts research through its member groups and their extended network of hospitals and investigators.

The shared vision of BIG members and their expertise, combined with that of the pharmaceutical and other partners, make it possible to conduct highly credible research.

PROTECTING PATIENTS AND GENERATING CREDIBLE RESULTS

Research groups within the BIG network share the same principles of research conduct*, including strict rules about scientific integrity in trial design and governance. These principles aim to eliminate bias from the research process, and maintain integrity vis à vis patients, both when working with the pharmaceutical partners or when working alone. A key principle is that data collected are handled and analysed independently from industry. BIG trials also follow patients long after treatment, with the aim to detect long-term side effects. All BIG studies are governed by committees and policies to ensure that patients' best interests stay in focus at every step of the way. Finally, BIG trials anticipate the future, collecting biospecimens for translational research to help us identify the treatments most suited to each individual patient.

SUCH LARGE-SCALE COOPERATION IS CRUCIAL TO MAKE SIGNIFICANT ADVANCES AND REQUIRES LONG-TERM RESILIENCE AND PERSISTENCE

** Consult BIG's Mission and Principles of Research Conduct on www.BIGagainstbreastcancer.org*

BIG asked Professor Boon Chua, Professor Ander Urruticoechea and Professor Carlos Barrios, members of BIG's Executive Board, what drives them to carry out academic breast cancer research.



Professor Boon Chua, MB, BS, PhD, radiation oncologist (Australia)

“The evolving regulatory environment is such that the conduct of clinical trials is increasingly complex and costly. This should not become a disincentive and barrier, particularly for the next generation of researchers. Our singular focus must be on our patients who depend on us to continue this critical work.”



Professor Ander Urruticoechea, MD, PhD, oncologist (Spain)

“What primarily drives BIG researchers, as most cancer researchers around the world, is rage. Rage from seeing our patients in pain, suffering from a too frequently deadly disease; rage from seeing how long it takes to translate our deep knowledge of cancer biology into effective actions. Rage from seeing the lack of global collaboration impeding a faster access to results; rage from seeing how some secondary or commercial needs take over the most urgent questions in some non-academic clinical trial designs. What drives our interest in a global research network is the need to provide our patients with effective solutions as soon as possible. The need is urgent and an academic worldwide network of researchers such as BIG is a privileged tool to get solutions faster.”

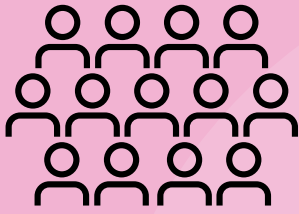


Professor Carlos Barrios, MD, oncologist (Brazil)

“BIG is a unique organisation with very clear objectives. Over the years and through careful and competent research, it has achieved unparalleled success in the advancement of the care of patients with breast cancer all over the world. Of the many different aspects of BIG as a research network, its ability to congregate and to engage researchers and patients from all continents is one of its most important and vital characteristics. The challenge of curing more and more women with breast cancer wherever they may be diagnosed is what brought us so far; it keeps us together and will continue driving BIG’s future collaborative research.”

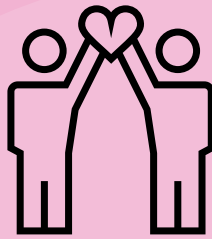
2 / BIG PHILANTROPY

BIG PICTURE OF BIG AGAINST BREAST CANCER



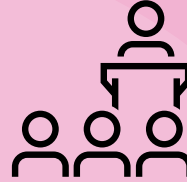
3 500

community members



6

grants from foundations



21

influential
ambassadors



1 500

attendees at our
fundraising events



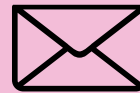
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corporate and event partners



± 15 600

emails sent



± 8 000

letters sent



± 5 015

followers on Facebook
and Instagram



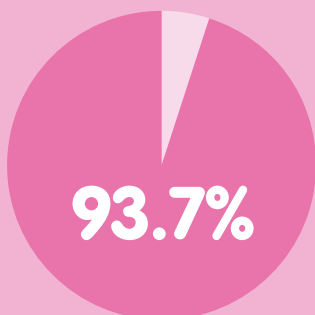
114 926

people reached
via Facebook and Instagram



14

Facebook Fundraisers by
you, our community



OF ALL FUNDS BIG RECEIVED IN 2020,
INCLUDING FROM *BIG AGAINST BREAST
CANCER'S* PHILANTHROPIC ACTIVITY,
WERE SPENT DIRECTLY ON BIG'S RESEARCH



BIG'S PHILANTHROPIC COMMUNITY

BIG's dedicated philanthropy unit - *BIG against breast cancer* - conducts vital fundraising to help finance academic clinical trials and research programmes that have no commercial interest but are crucial for patients with breast cancer. These collaborative efforts have led to practice-changing achievements in the field of breast cancer care. The funds raised help BIG's member groups (made up of breast cancer experts across the globe), their affiliated hospitals, and research staff at BIG Headquarters to finance their efforts and patients' participation in one or more BIG studies.

“THERE ARE MANY EXCELLENT PROPOSALS FOR CLINICAL TRIALS ASKING QUESTIONS WITH NO COMMERCIAL INTEREST, BUT FOR WHICH ANSWERS COULD LEAD TO SIGNIFICANT IMPROVEMENTS FOR PATIENTS AND SOCIETY. HOWEVER, THESE TRIALS OFTEN DO NOT TAKE OFF FOR LACK OF FUNDING. I HOPE THAT IN THE FUTURE, OUR SOCIETY WILL RECOGNISE THE IMPORTANCE OF THESE TRIALS AND WORK WITH US TO SUPPORT THEM.”

BOON CHUA,
BIG EXECUTIVE BOARD MEMBER.





ACADEMIC TRIALS YOU CAN SUPPORT

THANKS TO BIG'S UNIQUE POSITION IN THE FIELD OF BREAST CANCER RESEARCH, ACADEMIC CLINICAL TRIALS WITHOUT COMMERCIAL INTEREST CAN BE DEVELOPED BY BIG RESEARCHERS AND FINANCED IN-PART THROUGH OUR PHILANTHROPIC COMMUNITY.

The Metastatic Breast Cancer GPS is an innovative, international research programme that aims to understand why breast cancer spreads by mapping the routes that cancer cells take to invade other organs as well as understand why some patients respond poorly to standard treatment while others respond very well.

BIG METASTATIC BREAST CANCER GPS (SCIENTIFIC NAME: AURORA)

Today, it is thought that approximately one in three or four breast cancers will spread to other organs, or metastasise. This form of the disease is treatable but remains incurable. Metastatic breast cancer still represents the leading cause of death among patients with this disease.

The Metastatic Breast Cancer GPS is an innovative, international research programme that aims to understand why breast cancer spreads by mapping the routes that cancer cells take to invade other organs as well as understand why some patients respond poorly to standard treatment while others respond very well.

This academic research programme, launched in 2014, involves more than 60 hospitals in 12 European countries. At the end of December 2020, its milestone of 1,000 patients included had been achieved.

In 2019, the initial results of the programme reported on the first 381 patients included. BIG's researchers identified genetic abnormalities that may be correlated with the spread of cancer and increased resistance to

standard treatments. In addition, researchers estimate that in almost 50% of cases, the genetic abnormalities identified could provide treating oncologists with additional useful information.

The Metastatic Breast Cancer GPS is made possible in part by generous grants from the Breast Cancer Research Foundation® (BCRF), Fondation Cancer (Luxembourg), National Lottery (Belgium), NIF Foundation, Barrie and Deena Webb, Candriam, Fondation Futur 21, Sogerim, Think Pink Belgium (SMART Fund) and many individual donors. AURORA has also been supported by the Fund Friends of BIG, managed by the King Baudouin Foundation.

“THE HOPE OF SCIENTISTS AND RESEARCHERS IS THAT, BY LEARNING MORE ABOUT THE EVOLUTION AND CHARACTERISTICS OF METASTATIC BREAST CANCER, WE WILL BE ABLE TO BLOCK AND TREAT THE DISEASE MORE EFFECTIVELY IN THE FUTURE.”

**PROFESSOR MARTINE PICCART, PRESIDENT
OF *BIG AGAINST BREAST CANCER*.**

BIG TIME FOR BABY (SCIENTIFIC NAME: POSITIVE)

About 15% of patients with breast cancer are diagnosed during their reproductive years.

BIG Time for Baby represents a unique opportunity to allow young women who have had breast cancer to plan and try to become pregnant without waiting many years after completing their endocrine treatment. This study will evaluate the safety of interrupting endocrine therapy for young women with hormone-sensitive breast cancer who wish to become pregnant, as well as the pregnancy outcomes.

518 women are participating in the study, which includes questionnaires designed to help us learn about their concerns and psychological well-being. As of 31 December 2020, 246 healthy babies were born within the context of the BIG Time for Baby study.



BIG RADIO TUNING (SCIENTIFIC NAME: EXPERT)

Which women could be spared radiotherapy following breast conserving surgery? Generally, after surgically removing the tumour, radiation therapy will be administered to patients to limit the risk of relapse. However, not all patients benefit from this therapy.

Like adjusting your radio to find the right frequency, the BIG Radio Tuning study aims to personalise radiation therapy to each individual patient, even going as far as to avoid it altogether. To do this, the tumours of patients potentially interested in the study are analysed for risk of recurrence using a test of 50 genes.

The societal impact of this academic study on breast cancer could be substantial, influencing how 2 in 5 women with breast cancer are treated in the future. The BIG Radio Tuning study follows other efforts by BIG to optimise treatment to individual tumour characteristics, such as the MINDACT study, which demonstrated that as many as 46% of patients who definitely would have received chemotherapy in the past, could safely avoid it.

As of December 2020, 350 out of a total of 1,170 patients had already been included.



OUR AMBASSADORS

COMMITTEE OF AMBASSADORS

Strategic Committee

Made up of a group of people who – one way or another – each has a stake in the fight against breast cancer, the Committee of Ambassadors supports the work of the *BIG against breast cancer* philanthropy team.

Overseen by a Strategic Committee, each member contributes in their own way through their networks of contacts, generosity, participation in events, creative ideas and search for new donors and partners.

During a particularly dramatic and intense 2020, it became clear that nothing can be taken for granted and that, in the future, our ambassadors will have to work even harder to be able to secure the necessary resources to support *BIG against breast cancer*.

Chaired by Princess Nathalie de Merode, the members of the Strategic Committee are Patsy Israël, Mathy Kandiyoti, Nathalie Misson, and Jessica Parser.



Nathalie de Merode

“As time goes by, as an ambassador, you become increasingly aware of the exceptional impact of BIG’s work on the world around us. The progress made in recent years has been extraordinary, bringing so much hope in the face of what remains one of the most devastating cancers. I am very proud and happy to be able to make a modest contribution to BIG.”

Nathalie de Merode



Patsy Israël

“I am so honoured to be part of the BIG Ambassadors’ Committee. We need to support research and facilitate collaboration between medical experts around the world. This is the only way to eradicate disease and give life a chance.”

Patsy Israel



Mathy Kandiyoti

“It is with conviction that I adhere to this organisation. It’s hard not to be concerned by this evil that affects so many women. This kind of initiative really gives hope to recover, and the assurance of not feeling lonely in front of adversity. It is so important to feel supported and understood. In fact, this is a real part of the therapy. I consider BIG as truly essential.”

Mathy Kandiyoti



Nathalie Misson

“A couple of years ago, the sky was falling down on my head: breast cancer. I was going to leave my loved ones forever. Thanks to Martine Piccart, her team, and the administered treatments, today I can say that ‘I survived’. Armed with this experience, I’m convinced that bringing experts together to work on international trials – just the way BIG does – is the key to finding a cure for breast cancer.”

Nathalie Misson



Jessica Parser

“The year 2020 was a challenging time for everyone as the entire world focused on COVID-19 and its devastating consequences. But it’s essential not to forget the continuing importance of BIG’s research programmes and studies and the enormous positive impact they have had – and continue to have – in saving lives. I am proud to be part of the group of Ambassadors whose role is to keep BIG against breast cancer in the public’s mind.”

Jessica Parser

Extended committee:

Julia Carakéhian, Vladimir Cardon de Lichtbuer, Sylvia Chiche, Anne-Françoise Decrop, Evelyn Gessler, Anne-Marie Gillion Crowet, Eleonora de Ligne, Léontine Prat Y Coll, Matilde de’ Medici di Toscana di Ottajano, Bernadette Reynders, Edith Roland, Brigitte de Roquemaurel, Frédéric Van der Schueren, Catherine Vaxelaire and Marc de Villenfagne de Vogelsanck.

“RESEARCH CANNOT WAIT. BIG’S RESEARCH REMAINS VITAL BECAUSE OF THE HOPE IT BRINGS AND THE LIVES IT SAVES.”

SAD PASSING OF AN EXTRAORDINARY FIGURE AND A WONDERFUL BIG AMBASSADOR

Evelyn Gessler passed away on Easter Sunday 2020, having fought a brave and determined battle against metastatic breast cancer. A Brussels native and key figure in Belgium’s social and cultural life, she founded the company Decitime (now Decider’s) in 1982 in addition to many other successful professional endeavours. Beyond her impressive career, she was a remarkable figure, a refreshingly candid creative thinker who was as likeable as she was capable. Good natured and generous, she was always happy to lend

a helping hand to anyone who asked. She joined BIG’s Extended Committee of Ambassadors in 2017, helping us immeasurably and opening so many doors in a relatively short space of time. BIG has lost an incredible ambassador.



OUR PHILANTHROPY EVENTS

2020 – a year that proved how essential medical research is!

When 2020 started, we could hardly have imagined how quickly COVID-19 would have the entire globe in its grip. But the research world did not sit still, and by the end of 2020 several anti-COVID-19 vaccines had been developed, tested, and approved for use. This achievement is a great testament to how international scientific collaboration, financial support from multiple sources, and the resilience and persistence of a great many people to move things forward fast, proved that research is essential for saving lives.

2020 – an impactful year despite being a challenging one!

As every year, 2020 promised a fantastic line-up of *BIG against breast cancer* events organised by our Philanthropy Team. These are fundamental to maintaining contact with our donors and forging new networks to enable BIG to promote its work and raise funds for its research. Unfortunately, the COVID-19 pandemic and the lockdown forced us to cancel almost all of them. Having to innovate rapidly, we set up several online events to replace many of the usual in-person ones. So, despite COVID-19's challenges, we persisted, as did our donors, who remained loyal to BIG's vital cause.

“TOGETHER, WE WILL MAKE A DIFFERENCE IN THE FIGHT AGAINST BREAST CANCER – BIG'S RESEARCH MAKES A DIFFERENCE!”

NEW YEAR RECEPTION

An informal cocktail reception, organised on 19 February at the BIG headquarters, enabled our ambassadors to meet the entire BIG team, who are responsible for fulfilling our goals and promoting the values we hold dear. The evening was a great success and featured a talk given by Professor Martine Piccart, which attracted the full attention of the guests.

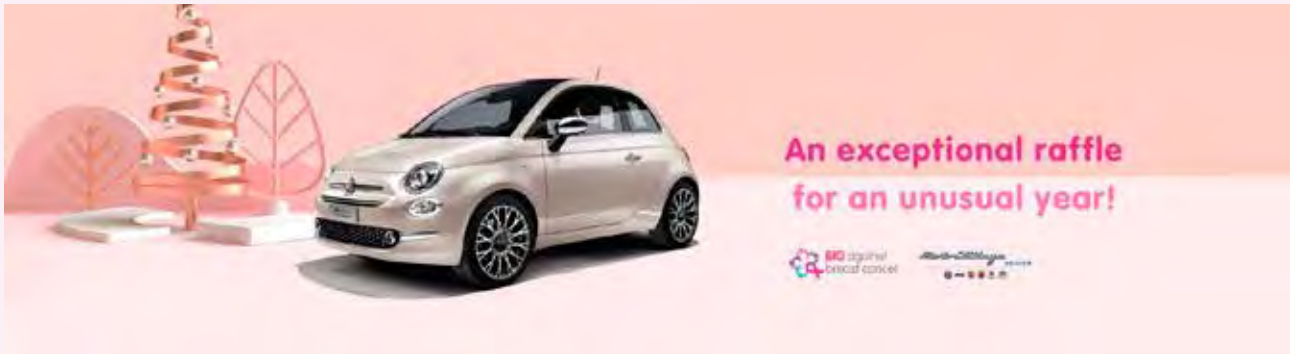
MOVE FOR BIG RESEARCH VIRTUAL CHALLENGE

Together against metastatic breast cancer!

Organised at the height of the lockdown in Belgium, during this first ever BIG virtual challenge, our community was invited to run, walk, garden, do yoga or cycle at home, all with the goal of reaching 28,800 steps each. This number was symbolic of the EUR 28,800 cost of involving one patient in the Metastatic Breast Cancer GPS study (scientific name: AURORA) for up to 10 years.

In just 26 days, 38 participants reached a total of 2,755,905 steps, equal to 2,100 km, altogether!





CHRISTMAS RAFFLE

Between 23 November and 27 December 2020, *BIG against breast cancer* organised an exceptional raffle, with the prize being a hybrid Fiat 500.

Thanks to the enthusiasm of our community, we were able to raise **EUR 28,052**. These funds will be used to cover the participation of **9 patients** in the Metastatic Breast Cancer GPS (scientific name: AURORA) programme for one year.

This research is crucial, as this advanced form of the disease is more difficult to treat and remains incurable.



Olivier La Porta, Tamara Lintermans, Patricia Decraemer, Nathalie de Merode and Nathalie Misson

“1 NOTE, 1 DONATION” CROWDFUNDING CAMPAIGN IN COLLABORATION WITH FANNY LEEB

4,860 notes, for one song of hope for women and men with breast cancer

From September till the end of October, a crowdfunding campaign was launched in collaboration with French singer Fanny Leeb. For each donation of EUR 11, a note of her song “Show them how it goes”, which she specifically produced for BIG, was revealed.

In total, **EUR 9,513** was raised via social media and e-newsletters.

About Fanny Leeb and her most recent album called *The Awakening*

For several months in 2018, Fanny Leeb led a fierce fight against breast cancer. She was able to turn her illness into a real strength, and this daily battle against her illness inspired her album “The Awakening”, composed with the help of her friend Keni Arifi and her brother Tom Leeb, and produced by Remark records (Vanessa Paradis, Raphaël, Christine and the Queens, ...). She decided to expose herself without



taboo, to try with humility to be the voice of all those who are fighting the disease and to speak about it openly and without fear within her networks and in the media. 11 songs that express her full sincerity about the perils of love or sickness.

“The Awakening” is her tribute to life.



“IT WAS OBVIOUS FOR ME TO DONATE MY COPYRIGHT SALES TO THE CRUCIAL SCIENTIFIC RESEARCH THAT SAVES OUR LIVES. I MYSELF RECEIVED A GENETIC TEST THAT WOULD NEVER HAVE SEEN THE LIGHT OF DAY WITHOUT RESEARCH AND THAT HELPED DETERMINE WHAT WAS THE BEST TREATMENT COURSE FOR ME. IT WAS EXTREMELY IMPORTANT FOR ME TO CONTRIBUTE TO THIS CAUSE. WITHOUT THIS SUPPORT FOR BIG MY BOOK WOULD NOT HAVE MADE AS MUCH SENSE. I AM HAPPY TO CONTRIBUTE TO BIG.”

“DELPHINE REMY, AUTHOR OF “CANCER? JE GÈRE!”

CONFERENCE BY DELPHINE REMY

On 28 September, during a conference attended by 100 people, Delphine Remy gave a talk about her journey from being diagnosed with breast cancer, through treatment, and to remission. During her treatment, Delphine wrote a blog (cancer-je-gere.blog) chronicling this chapter of her life, which she then turned into a book titled “Cancer? Je gère!” (Cancer? I’ve got this!). Doctor Martine Piccart, who wrote the preface of Delphine’s book, gave a brief introduction during the conference. The event concluded with a question-and-answer session, where participants could ask questions to both Delphine and Dr Piccart.

Delphine Remy has pledged to give the proceeds from the copyright sales of her book to support BIG’s research. It may be purchased via Amazon, or in bookstores in Belgium, France, Quebec, Switzerland, and Luxembourg.



HOW YOU CAN MAKE A DIFFERENCE

Why support BIG?

By doing so, you help the millions of patients around the world and thousands of researchers who – thanks to your support and donations – work tirelessly to develop new treatments and therapies that improve the quality of life of women and men with breast cancer.

Your donations represent hope – your donations represent LIFE!

Please let us know if you wish to support all research conducted under the BIG umbrella, or if you would prefer to focus on one particular study.

MoveForBIG

MoveforBIG.org is a user-friendly online crowdfunding platform that allows you to launch your own fundraising campaigns to support BIG's research.

Taking on a new personal sports challenge?
Celebrating a birthday or an anniversary?

You can create your own [MoveforBIG.org fundraising page](#) that you can easily share with your friends and family and encourage them to support this important cause.

A personal fundraising page gives extra hope and support to many women and men who are confronted with breast cancer.



Every act of support contributes to BIG's research, crucial for finding cures for breast cancer. Giving is also contagious; help us spread the word.

How you can make a difference

- Join our community and stay in touch with news from the ***BIG against breast cancer*** team
- Introduce BIG to your professional network
- Donate for any occasion. Think BIG for birthdays, Mother's Day, anniversaries or make a gift as a tribute to a family member or friend who has had breast cancer. You can do this by making donation via bank transfer, our donation platform or with the MoveforBIG.org crowdfunding platform
- Attend an event
- Give in-kind (e.g., artwork from your own collection or an exceptional experience) for auction to benefit BIG
- Set up a legacy fund to support BIG's research against breast cancer long into the future
- Create a Facebook birthday fundraiser @ [BIGagainstbreastcancer](#)



BIG ACKNOWLEDGEMENTS

A SPECIAL THANK YOU TO OUR SUPPORTERS WHO "THOUGHT BIG" IN 2020

Mr and Mrs Bernard Amory
Mrs Marianne Anciaux
Countess Amelie d'Archot Schoonhoven
Countess Catherine d'Aspremont Lynden
Mrs Violette Audiffret
Mrs Véronique Barbier
Mrs Chantal Beinex-Gillion
Mr and Mrs Berko
Mr and Mrs Patrice Bourg
Mrs Priscillia de Brabander
Mr Patrick Callewaert
Mr and Mrs Yves Carakéhian
Mr and Mrs Cardon de Lichtbuer
Mrs Sylvia Chiche
Prince and Princess Philippe de Chimay et de Caraman
Mr and Mrs Marcel Croes
Mr and Mrs Marc Decorte
Mrs Patricia Decraemer
Mr and Mrs Marc-Henri Decrop
Mr and Mrs Alain De Pauw
Mrs Nicole De Smet
Mr Marc Filipson
Mr François Gérard and Mrs Jessica Parser
Baron and Baroness Gillion Crowet
Mrs Vanessa Greindl
Mrs Ariane Hourdeau
Mr and Mrs Nissim Israël
Mrs Laurence Isralson
Baroness Jonet
Mr and Mrs Philippe Jungers
Mr and Mrs Adnan Kandiyoti
Mr and Mrs Erol Kandiyoti
Mr Olivier Laporta
Countess Fournier Laroque de Saint Côme
Mrs Diane de Lasteyries du Saillant
Mr Arnaud Lefebvre
Prince and Princess de Ligne
Their Royal Highnesses Prince Guillaume and Princess Sibilla de Luxembourg
Family Luyckx
Donna Matilde de' Medici di Toscana di Ottajano
Mrs de Menthon de Horne
Prince and Princess Amaury de Merode
Mrs Alexandra Mikolajczak
Mr and Mrs Thierry Misson
Mrs Jan Hein van de Mortel
Mr Michel Moortgat
Mrs Martine Nolet de Brauwere
Mr and Mrs Cedric Olbrechts
H.E. Ambassador and Mrs Juan Prat Y Coll
Mrs Delphine Remy
Mr the European Commissioner and Mrs Didier Reynders
Mr and Mrs Xavier Roland
Mr and Mrs Frederic Van der Schueren
Mrs Michèle Sioen
Mr and Mrs Thomas Spiller
Viscountess Sibylle de Spoelberch
Mr and Mrs Olivier Israël
Mr and Mrs Jean-Philippe Thierry
Baron and Baroness Guy de Vaucleroy
Baron and Baroness Raymond Vaxelaire
Mrs Virginie Vaxelaire
Baron and Baroness Marc de Villenfagne de Vogelsanck
Mr and Mrs Andy Wyckmans-Vaxelaire



CORPORATE PARTNERS

COMPANIES THAT CARE

In a year marked by the devastating effects of COVID-19, many businesses were also confronted by the crisis. Despite the remarkably difficult economic climate, we were thankful to be able to rely on the loyalty of our existing partners.

We have also been able to count on the commitment and generosity of new partners for whom breast cancer research is essential.

Online sales saw a boom, and we benefited from a number of initiatives.

Finally, we saw the development of partnerships internationally, which are key to reflecting BIG's global alliance.

All these initiatives have enabled us to support a significant number of patients in our flagship studies.

TO ALL OUR PARTNERS, WE WOULD LIKE TO SAY A HEARTFELT "THANK YOU!"

You have helped us in our efforts by involving your staff in our activities, by inviting them to raise funds, or by asking your clients and partners to support breast cancer research.

AG INSURANCES

As a socially responsible insurance company with a stake in a happy and productive Belgian society, AG Insurances attaches particular importance to the prevention of disease but also of suffering.

This translates into AG's support for BIG, in order to support them in the research aimed at minimising suffering and providing a better recovery path for people with breast cancer.

BAOBAB COLLECTION

The "Woman" and "Gentleman" candles were created by Corinne Bensahel, artistic director at Baobab Collection. Baobab Collection wishes to show its love for women and its commitment to a cause that concerns us all in one way or another: breast cancer research. The "Woman" and "Gentleman" candles will illuminate everyone's conscience with their little flame, because without research we will not be able to overcome this disease that takes away our loved ones.





CANDRIAM

Candriam is a European multi-specialist asset manager, pioneer, and leader in sustainable investing with a broad and innovative range covering all asset classes.

Sustainability and social impact are core to Candriam's DNA. Two years ago, Candriam launched the industry's first oncology fund aimed at investing in listed companies that research and develop products for the treatment of cancer. In keeping with Candriam's commitment to social impact and in order to support the fight against cancer, the firm also donates part of the fund's net management fees to European institutions involved in cancer research, diagnosis, medicine and technology.

It is in this respect that the Candriam Institute for Sustainable Investment – Candriam's philanthropic body – supports the high-quality research projects that BIG facilitates.

MY BOB

"MY BOB wants to be responsible towards its stakeholders and community. We are happy to support a great organisation such as BIG with a great cause. Let's embellish the life of people." **Geoffroy Moreels**

SOGERIM

A few years ago, Laurent Delgouffre, Managing Director of Sogerim, was confronted with the breast cancer of his then 35-year-old wife.

He remembers his reaction on hearing the news: "The world was slipping out from under us, and we felt overwhelmed by the thought of a year's worth of treatments ahead of us."

On the anniversary of the end of treatment, he wanted to partner with BIG to celebrate her recovery and to support research.

"Our support for BIG is a mark of gratitude to the entire medical profession and all those fighting on behalf of patients." **Laurent Delgouffre**

ZAG BIJOUX

"Supporting research to cure breast cancer was a no-brainer for us and we were honoured to get involved. Women are the ambassadors of our brand, they wear our jewellery with pride, so it was important for us to get involved in a cause that mainly affects women, to dedicate a piece of jewellery to them and to deliver our designer's message: Stay strong, you are strong." **Michelle Zhang**



A BIG THANK YOU TO 2020 EVENT SPONSORS AND PARTNERS:

AG Insurances • Art's BIG • Atlas Go • B19 • Baobab Collection • Benoît Colette Photography • Buy Way • Cacaoon • Candriam • Delphine Remy • Elle & Cousine • Le Soir • L'Eventail • market@home • Motor Village • My Bob • Nexus • Olivier Strelli • Peter & Clark • Prune BVBA • Rothschild & Co Wealth Management Belgium • Sablon d'art • Stronger • Sogerim • Sotheby's • Stay Young Clinic • Vlan • Worldline • ZAG bijoux



BIG IMPACT

HOW YOUR COMPANY CAN MAKE A DIFFERENCE

Supporting BIG is supporting researchers who work hard to find cures for patients with breast cancer all over the world! During the last four years, BIG has expanded the number and types of impactful collaborations with the corporate world, and we are very proud to be able to count on the loyalty of our partners!

As a company, you can partner with BIG to help make research progress.

Not only can companies become part of the solution but, by doing so, they can engage their employees and sensitise their customers to an important cause, in turn adding value to their brand.

Be involved, be creative ... With different packages, your company can support breast cancer research, for example:

PATRONAGE PACKAGES

Having your company associated with a leading international organisation in breast cancer research can only be positive. Such a partnership helps refine your corporate identity and your Corporate Social Responsibility (CSR) commitments. This package entails a long-term, stable engagement between your company and BIG, through a donation or a global partnership.

MY-EMPLOYEES-COUNT PACKAGES

With such a high incidence rate, breast cancer greatly impacts employees and their family members confronted with the disease, and

ultimately business life. You can choose among various attractive packages, including information sessions, sports activities (MoveforBIG.org), corporate events, sponsoring private concerts, gala evenings, among others.

CORPORATE CHARITY CHALLENGE

Directly involve your employees in a company-wide fundraising challenge via the MoveforBIG.org platform. Not only is this a great opportunity to foster team spirit, it's also a fun way of raising funds for BIG and help push forward research against breast cancer.

Do not hesitate to contact BIG's philanthropy team, who would be happy to help you develop a corporate charity challenge that's right for your organisation!

"BIG TOGETHER" MARKETING PACKAGES

What about taking the opportunity to engage your customers through your brand? Simply allocate a percentage of your total turnover, or a percentage of the sales of a specific product or service, to breast cancer research. It's the opportunity to communicate your support for a cause that touches many women and men in our communities.

PREFERENTIAL PARTNER

As a sponsor of one of our philanthropic activities, by providing financial support (covering part of our communications, venue, or catering costs) or by giving in-kind, your company can become a preferential partner.

BIG CAN ALSO PROPOSE DIFFERENT SPONSORSHIP PACKAGES TAILORED TO YOU.

BE CREATIVE ... IF YOU HAVE AN IDEA, A SUGGESTION ... OUR PHILANTHROPY TEAM IS HERE FOR YOU!

Together we can find actions to support breast cancer research
Philanthropy@BIGagainstbreastcancer.org



FOUNDATIONS SUPPORTING BIG

It is mainly thanks to the precious support of foundations that we were able to maintain the financing of the participation of patients in BIG's trials.

BCRF

The Breast Cancer Research Foundation® (BCRF) is a not-for-profit organisation committed to achieving prevention and a cure for breast cancer. The BCRF provides financial support for clinical and translational cancer research projects worldwide, to fuel advances in tumour biology, genetics, prevention, treatment, metastasis and survivorship. It is one of the highest-rated breast cancer organisations in the US.

A loyal partner of BIG, BCRF has, over many years, provided generous funding to support the **BIG Metastatic Breast Cancer GPS programme (scientific name: AURORA)**, as well as many other other projects.

www.bcrf.org

BELGIAN NATIONAL LOTTERY

Diversity is a key element in the successful core strategy of the Belgian National Lottery. We are aiming to reach a large and diverse audience through different channels in retail and online, offering a wide range of appealing draw and scratch games. We want our players to feel connected to the Good Causes we can support thanks to them. Because our players are very diverse, we choose to support a very large variety of causes in our society, going from culture over civil society projects to extensive scientific research.

Since 2018, BIG has been receiving support for the **BIG Radio Tuning study (scientific name: EXPERT)**. "BIG against breast cancer is one of those Good Causes which is dear to the hearts of many Belgians, including myself. The fact is that we all know someone in our surroundings that has been directly or indirectly affected by breast cancer or any other kind of cancer. It goes without saying that we will not hesitate to contribute to improving patient survival, quality of life and finding the most appropriate treatment for every patient. Thanks to all our players the Belgian National Lottery can offer much more than just games. Together we can make a difference" – **Jannie Haek, CEO of Belgian National Lottery**

#muchmorethanjustgames #nationallottery #proudpartner

www.loterie-nationale.be

www.nationale-loterij.be

FONDS BAILLET-LATOUR

For the fourth consecutive year, BIG was blessed with the support of the Baillet-Latour Fund, specifically for the BIG Time for Baby study (scientific name: POSITIVE). This charitable trust was created to encourage, promote, and foster human excellence in Belgium, with a diligent but open approach to social development. Over the years, and through the allocation of grants, prizes and scholarships, the organisation has increased its scope of action focusing on four pillars: health, culture, education, and sports. All the projects and initiatives supported in each field have a Belgian dimension and international vocation.

www.fondsbailletlatour.com



FONDATION CANCER, LUXEMBOURG

The foundation's objective is to raise awareness about cancer prevention and the fight against cancer, as well as to encourage all sort of initiatives, scientific research and information campaigns that contribute more generally to fighting cancer. For several years now, Fondation Cancer, Luxembourg has been a strong supporter of BIG's research, providing funds to support the **BIG Metastatic Breast Cancer GPS programme (scientific name: AURORA)**.

“Research is vital in oncology, it provides hope. I am regularly asked by patients in my consultations about whether there are any new advances and what drugs are coming onto the market. It is only by promoting research that we can move forward. This is one of the Belgian Cancer Foundation's main aims. Supporting *BIG against breast cancer* (BIG) goes without saying.” **Doctor Carole Bauer, President of Fondation Cancer**

www.cancer.lu

FONDATION NIF

The NIF Foundation supports initiatives that increase the well-being of all men and women, irrespective of their age, origin, nationality, philosophical and religious views. It seeks to address needs that are felt in the social fabric in areas where public institutions are unable, not yet able or can no longer intervene. It contributes financially, in accord with its *raison d'être* and within its means, to humanitarian projects that are in-line with its mission statement. A generous supporter of many years, the NIF Foundation currently contributes to the **BIG Metastatic Breast Cancer GPS programme (scientific name: AURORA)**.

www.fondation-nif.com





BIG

Breast International Group

OUR MISSION

BIG's mission is to facilitate and accelerate breast cancer research at the international level.

OUR VISION

Together we will find a cure for breast cancer through global research and collaboration.





GLOBAL AND LOCAL

BIG is the largest global network of breast cancer research groups and their affiliated experts. Their work benefits patients locally.

TRUSTED

We have been recognised for over 20 years to generate credible scientific results and safeguard patients' interests.

IMPACTFUL

Our research changes practice in the treatment of women and men with breast cancer. We have a real impact on patients' lives.



3 / BIG NETWORK

NEWS AND ACTIVITIES FROM BIG'S HEADQUARTERS

FAREWELL TO PROFESSOR ARON GOLDHIRSCH (1946 – 2020), 'FATHER' OF THE BREAST INTERNATIONAL GROUP (BIG)



In February 2020, the world of oncology lost one of its most brilliant medical doctors and breast cancer researchers. **Professor Aron Goldhirsch**, the 'father' of BIG and a founder of the **International Breast Cancer Study Group (IBCSG)**, passed away at the age of 73 on 26 February 2020.

Professor Goldhirsch was much more than a brilliant medical oncologist. He was a truly remarkable person known for his very high sense of ethics, humanity, and openness. He will be profoundly missed, not only by his family, friends, and patients, but also by the scientific world and his extended BIG family.

Throughout his career, Prof Goldhirsch made significant contributions to breast cancer medicine and education and, besides his many

national duties, he worked tirelessly to foster international collaboration and preserve academic independence in cancer research.

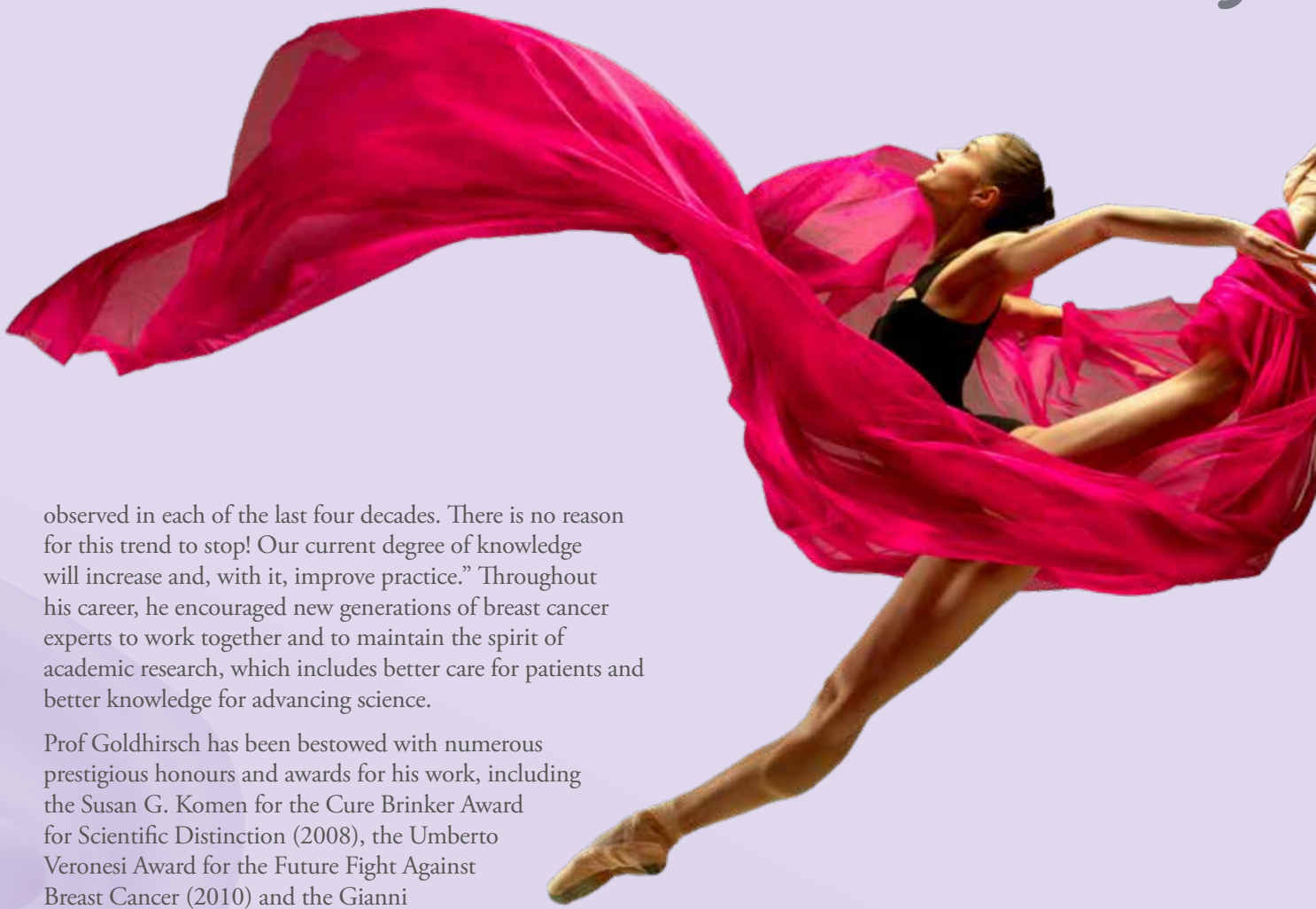
Over the years, his humanity and openness inspired people with different backgrounds and expertise to join efforts and build a genuine collaboration. As he often said: "A multidisciplinary approach across groups and institutions, working together with the spirit of 'all for one, one for all', is the most powerful attitude to improve results in breast cancer research".

In the early 1990s, while breast cancer research was highly fragmented, with academic groups running many similar trials and consequently duplicating efforts, wasting time and resources, Prof Goldhirsch, together with **Professor Martine Piccart**, shared a different vision of the future: groups debating the latest research findings, sharing ideas for new clinical trials and working in harmony to conduct these trials together. He strongly believed that this was the only way forward to make significant advances in breast cancer research and answer pertinent therapeutic questions more rapidly and efficiently.

In 1996, Professors Goldhirsch and Piccart created the **Breast International Group (BIG)** with the aim of bringing together academic research groups. More than 20 years later, more than 60 trials have been run under the BIG umbrella, many of them landmark, having a real impact on patients' lives.

Prof Goldhirsch was one of the main drivers behind the St Gallen International Expert Consensus Conference, which gives practicing oncologists recommendations on how to optimise treatment for patients with early breast cancer.

When asked about the future, Prof Goldhirsch was an optimistic: "Improvement of patient care has been



observed in each of the last four decades. There is no reason for this trend to stop! Our current degree of knowledge will increase and, with it, improve practice.” Throughout his career, he encouraged new generations of breast cancer experts to work together and to maintain the spirit of academic research, which includes better care for patients and better knowledge for advancing science.

Prof Goldhirsch has been bestowed with numerous prestigious honours and awards for his work, including the Susan G. Komen for the Cure Brinker Award for Scientific Distinction (2008), the Umberto Veronesi Award for the Future Fight Against Breast Cancer (2010) and the Gianni Bonadonna ASCO Breast Cancer Award & Lecture (2014).

But his impact extends well beyond these prizes and the over 700 peer-reviewed articles he authored. **Prof Goldhirsch’s greatest legacy is his vision: provide the best care for each individual patient through collaboration, academically independent research, and education.**

He will continue to live and inspire future generations of cancer scientists, and everyone else who had the privilege to know him.

“ALL FOR ONE,
ONE FOR ALL.”

To honour Professor Aron Goldhirsch’s legacy, BIG dedicated the following publication to him:
“The Legacy of Professor Aron Goldhirsch - 40 years of advances in breast cancer research”

Over the years, many of Aron’s collaborators have become firm friends and, in this special publication dedicated to him, some of them have come together to talk about his legacy to the breast cancer community – as a researcher, an educator and a mentor – and about some of the key BIG trials in which he played such an essential role.

The publication can be found on BIG’s website: https://research.bigagainstbreastcancer.org/sites/default/files/tribute_to_aron_goldhirsch.pdf





TRIBUTE TO ARON

By Martine Piccart, co-founder of BIG



Sadly, on 26 February 2020, my dear friend, colleague and mentor, Professor Aron Goldhirsch, passed away. Aron, who was like a brother to me, was 73.

BIG was ‘born’ over a dinner I had with Aron at the end of a meeting of the **European Organisation for Research and Treatment of Cancer - Breast Cancer Group (EORTC BCG)** in 1995, at which he was an invited speaker. He was immediately enthusiastic about the idea of a new global network to strengthen and accelerate breast cancer research, starting in Europe. Aron already led the successful **International Breast Cancer Study Group (IBCSG)**, but he saw the value of a larger collaboration to perform important clinical trials on a scale that no single organisation could do alone.

It was Aron who chose the name, **BIG**, when we were still a very small, fragile network of academic breast cancer research groups. This was not a random choice; Aron firmly believed in collaboration, cooperation, loyalty, and friendship, and he was confident that **BIG** would grow into its name and become successful.

It wasn’t all plain sailing. At the start, some research groups were concerned about being ‘swallowed up’, but that was never our aim. We knew there was a place for studies done by individual partners within the network and those performed together under the **BIG** umbrella. We also had the example of the **North American Breast Cancer Group (NABCG)**, which successfully brought together a number of regional groups that still retained their independence.

Aron himself had a remarkable capacity for assessing whether a proposed trial would be best done by **IBCSG** or by **BIG**. At the heart of all his decisions was what was best for the patient. Whether he was in his clinic, planning a trial, or supporting his colleagues, the

patient always came first. His presence – calm, thoughtful, and patient – was key to finding solutions and moving forward. Whenever I was discouraged, his energy, optimism and steadfastness took us through.

At quite an early stage in the history of **BIG**, the threatened withdrawal of funding for an important planned trial became the unlikely catalyst for uniting all our member organisations firmly behind **BIG**. On hearing of the looming disaster, Aron insisted we contact all the research groups that were members of **BIG** – as well as academic groups outside our network – and everyone agreed to boycott the trial unless it was led by **BIG**. As a result, the decision was reversed, **BIG** carried out the trial, and patient recruitment was so rapid that we were able to present the results alongside those of similar North American studies that had started well before ours.

This was a turning point for **BIG** because it gave our members confidence in the value of the network and what could be achieved if we all worked together. In the years that followed, Aron’s input played an essential part in making **BIG** the organisation it is today – extending our presence across continents, bringing on board some of the finest breast cancer researchers, and completing multiple practice-changing clinical trials.

We all miss Aron’s wisdom, his generosity, and the unique brightness in his eyes whenever a brilliant idea came to him. And there were many! During his working life, Aron dedicated himself to moving breast cancer care from the generalised to the personalised, so that every patient received treatment tailored to their cancer, their needs, and their priorities. He and his collaborators made much exciting progress towards those goals. We continue that journey while always remembering Aron’s extraordinary contribution and remaining true to his mantra: **‘All for One, One for All’**.

Martine J. Piccart

*Professor of Oncology at the Université Libre de Bruxelles
and Scientific Director at the Jules Bordet Institute in*

Brussels, Belgium

Co-founder of BIG

Senior Advisor to BIG

President of BIG against breast cancer

(BIG’s philanthropy unit)

PROFESSOR MARTINE PICCART RETIRED FROM BIG'S EXECUTIVE BOARD



After having dedicated more than 20 years to BIG, **Professor Martine Piccart**, co-founder of BIG, stepped down from BIG's Executive Board. In recognition of the fact that BIG would not have evolved as it did without her vision and drive, and given her tremendous experience and skills, Prof Piccart has been designated "Senior Advisor to BIG". In this capacity, she will contribute to the training of patient advocates for BIG and be called upon to provide scientific and other more general advice on issues of strategic importance such as governance, collaborations with pharmaceutical partners, and various other partnerships. She is also President of *BIG against breast cancer*, the philanthropy unit of BIG dedicated entirely to raising funds to support BIG's research.

A strong advocate for and leader of international research collaborations, Prof Piccart remains unfailingly committed

and motivated to move breast cancer research forward. With the ultimate goal to offer more personalised treatments, and hopefully a cure, for each patient.

Prof Piccart is a professor of oncology at the Université Libre de Bruxelles (ULB) and scientific director at the Jules Bordet Institute (Brussels/Belgium). Earning her medical degrees at ULB and oncology qualifications in New York and London, she is also a member of the Belgian Royal Academy of Medicine. Prof Piccart is a past president of the European CanCer Organisation (ECCO, 2014-2015). She has also held presidencies of the European Organisation for the Research and Treatment of Cancer (EORTC) and the European Society for Medical Oncology (ESMO), and has served on the American Society of Clinical Oncology Board (ASCO).

PROFESSOR MARTINE PICCART RECEIVED THE 2020 GIANTS OF CANCER CARE® AWARD

On 5 November 2020, during a virtual ceremony, Prof Martine Piccart was honoured with the **2020 Giants of Cancer Care® Award for Breast Cancer** for her contribution to advancing breast cancer research and the crucial impact she has had in oncology.

The Giants of Cancer Care® recognition programme honours researchers and scientists who have realised ground-breaking achievements in the global field of oncology.



PINK OCTOBER: EORTC & BIG WEBINAR ON DE-ESCALATION OF BREAST CANCER TREATMENTS

The month of October is international breast cancer awareness month. In this context, on Wednesday 14 October 2020, the **European Organisation for Research and Treatment of Cancer (EORTC)** and the **Breast International Group (BIG)** organised a webinar on breast cancer addressed to the general public.

The purpose of the webinar, which counted 169 participants from different countries, was to raise awareness about breast cancer and the importance of international academic research.

The main topic of the session focused on the growing importance of **treatment de-escalation to improve breast cancer patients' quality of life by avoiding unnecessary overtreatment.**

Breast cancer experts from the **EORTC** and **BIG** networks gave examples of de-escalation clinical trials and explained how they may help breast cancer patients by safely reducing treatment burden. A patient advocate from **Europa Donna** also gave her perspective on this topic.

The session included the following presentations:

- Brief introduction on global breast cancer research and de-escalation of breast cancer treatments – *By Professor Etienne Brain, EORTC Breast Cancer Group Chair & BIG Executive Board member (Brussels, Belgium)*

- Brief presentation of DESCRESCENDO study and introduction of the speakers – *By Professor David Cameron, BIG Chair and EORTC Breast Cancer Group member (Edinburgh, UK)*

- Tailoring radio therapy after surgery to an individual patient's risk of recurrence (EXPERT study – BIG Radio Tuning). Tailoring radiation dose escalation after surgery: cosmetic results and patient reported outcomes informing treatment decision-making (DCIS study) – *By Professor Boon Chua, BIG Executive Board member & Study Principal Investigator of EXPERT and DCIS (Sydney, Australia)*

- Using the biological characteristics of a tumour and novel diagnostic tests to help safely exclude chemotherapy (MINDACT study) – *By Professor Fatima Cardoso, EORTC Breast Cancer Group and BIG member & Study Principal Investigator of MINDACT*

- Getting the patient's perspective: importance of giving patients the right information about de-escalation risks – *By Ms Elizabeth Bergsten Nordstrom, EUROPA DONNA Executive Board member*

During the session, participants – who were a mix of breast cancer patients, advocates, family members, students, researchers and breast cancer specialists – were also invited to ask the speakers any questions they had, allowing for a true learning and sharing experience.

BIG THANK YOU

Recently, we said good-bye to five research groups. Because of mergers with other BIG member groups, retirement or changes in structure or research orientation, **ARCAGY-GINECO**, the **Francilian Breast Intergroup (FBI)**, the **German Breast Group (GBG)**, **GONO (Grupo Oncologico Nord-Ouest)**, and **ITMO (Italian Trials in Medical Oncology)** left BIG during 2020.

The expertise, collaborative spirit, dedication, and hard work of these groups over the years has been essential to improving the lives of patients confronted with breast cancer. We would like to thank them for the commitment and support they have shown and wish them and their representatives all the best for the future.

Today, BIG represents over 50 like-minded breast cancer research groups from around the world and reaches across approximately 70 countries on 6 continents. An overview can be found on page 58 and 59

HANDMADE BIG-BRANDED FACE MASKS: BY AND FOR BIG HQ COLLEAGUES

At the beginning of the pandemic, face masks had been the advised preventive measure but were hardly available. Two of our amazing colleagues, **Heidi De Swert** and **Valeria Karusinova** from the Research Operations team, sewed a pair of BIG-branded face masks for everyone working at BIG HQ.



Heidi De Swert and Valeria Karusinova, BIG HQ colleagues from BIG's Research Operations team



Gia Questiaux and Joëlle Leemans, BIG HQ colleagues from the BIG against breast cancer team (BIG's philanthropy unit)



HOW THE BIG NETWORK ADDRESSED THE COVID-19 CHALLENGES

HOW THE BIG NETWORK ADDRESSES THE COVID-19 PANDEMIC, DEMONSTRATING RESILIENCE AND PERSISTENCE

Long-term resilience and persistence are needed in academic research

Research is the only way to understand breast cancer, how and why it progresses, and how it can ultimately be stopped. For over 20 years, BIG has been conducting global breast cancer clinical trials and research programmes. By engaging its network to rapidly enrol large numbers of patients into complex international clinical trials, and by sharing best practices, expertise, and data in pursuit of answers to important scientific questions, BIG has the ability to achieve faster results and greater patient benefits. BIG trials also follow patients long after the experimental treatment ends, with the aim to detect long-term side effects, improve treatment therapies and patients' quality of life. **This requires resilience and persistence at every stage, from planning to completion, as well as sufficient funding.**

Over the years, breast cancer has been classified into multiple sub-types, each requiring different approaches to treatment. To test new treatments on enough patients within a sub-group, and to be confident about the results, most research cannot be limited to one institution or even to one country. **Large-scale international cooperation** is crucial to make significant advances in treating breast cancer, reduce the wasteful duplication of efforts, and best serve those affected by the disease.

Over 30 international clinical trials or research programmes are being run or are under development under the BIG umbrella at any one time. Since 1999, more than 97,000 patients have participated in BIG's studies.

Much of BIG's research is considered landmark, introducing particularly innovative designs, contributing to significant breakthroughs, or paving the way towards more personalised treatment of the disease.

"NONE OF BIG'S ACHIEVEMENTS WOULD BE POSSIBLE WITHOUT THE WILLINGNESS TO WORK TOGETHER. DESPITE THE COVID-19 PANDEMIC AND ALL THE CHALLENGES IT POSES, BIG'S NETWORK HAS CONTINUED ITS EFFORTS TO ADVANCE BREAST CANCER RESEARCH, DEMONSTRATING GREAT RESILIENCE AND PERSISTENCE"

Below are a few examples of how BIG member groups addressed the challenges of COVID-19.

HOW SOUTHERN EUROPE LED THE WAY: SOLTI & GOIRC

With high levels of COVID-19 in many parts of Southern Europe during the early stages of the pandemic, clinicians such as **Professor Aleix Prat, President of the SOLTI Breast Cancer Research Group (Spain)** and **Professor Gabriele Zoppoli, member of the Board of Directors of the Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC)**, were concerned about its impact on breast cancer research.

“In Spain, trial recruitment fell and research facilities closed but, by the Summer, things were back to normal. I am optimistic that, unless there is a change in the next few months, clinical, translational and basic research will not be hugely impacted overall,” says Prat.

His main concern is that the huge investment being made in COVID-19 prevention and patient care will affect resources for treatment of patients with cancer.

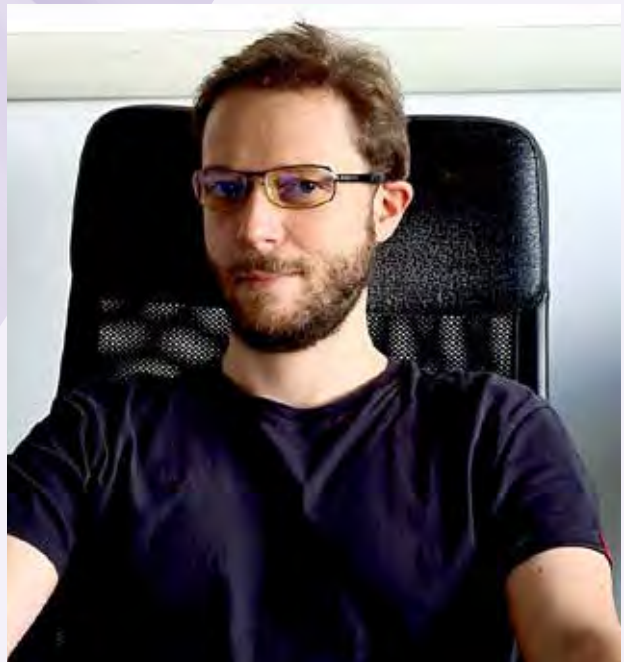
“It is understandable that COVID-19 was the priority, but we now need to catch up with breast cancer screening because of the risk of delayed diagnosis and the potential for worsening mortality a few years down the line,” he says.



Professor Aleix Prat

In Italy, which was the first European country to be hit by COVID-19, telemedicine played an important part in supporting patient care and, in Lombardy and Emilia Romagna – two of the worst hit regions of Italy – huge efforts were made to deliver cancer treatment in patients’ homes and ensure continuation of clinical trials.

“Lombardy and Veneto were the hotspots of the pandemic in Italy but, in several centres, they actually managed to increase accrual of new patients in clinical trials through a structured parallel care pathway for those with cancer,” recalls Zoppoli. “I think we can be very proud of how Italian centres dealt with the crisis and cared for patients,” he adds.



Professor Gabriele Zoppoli



ABCSG

Carrying on in challenging times

What to learn from the unexpected in clinical research? The COVID-19 pandemic had far-reaching consequences for daily clinical research routines. Best practice examples can be identified in countries and individual centres, but how the situation will develop over time and what implications this will have for clinical routine, research, translational work and study groups remains to be seen.

For the **Austrian Breast and Colorectal Cancer Study Group (ABCSG)**, the implications of the pandemic are impacting daily operations as well as strategic scenarios. **Professor Michael Gnant, President of the ABCSG**, describes challenges, opportunities and lessons learned.



Professor Michael Gnant

INTERVIEW FROM DECEMBER 2020

How does the COVID-19 pandemic affect clinicians, and the study landscape? What are the learnings for ABCSG so far?

Professor Gnant: “The pandemic has hit us unexpectedly, like everybody else. Probably the biggest challenge for clinicians in late Winter 2019 and Spring 2020 was the uncertainty about how dramatic the impact on our health care systems would be. Like everybody else in Europe, I was greatly moved and concerned after the alarming reports from our brave colleagues in Northern Italy came in. Some countries suffered more than others (in terms of health care capacity), and obviously the reaction (times) by political leaders was difficult. Personally, I would have hoped for a bit more unity and solidarity between EU countries and globally, but obviously politics is not yet as mature as we have developed in international research collaboration. While hospital capacities were blocked by and/or for COVID-19 patients, “nonessential” patient visits were postponed in many environments, which clearly affected clinical trials. However, with a lot of spirit and dedication, the study teams were able to maintain “damage control”, also supported by regulators and ethics committees, who helped in conquering the extraordinary situation.

In addition to the things you have mastered in your study activities with the ABCSG, what is your personal motivation to continue clinical breast cancer studies in these difficult times?

Professor Gnant: “Clinical research multiplies the creativity and dedication of caregivers. Developing ideas, discussing improvements in diagnosis and therapy, transforming exciting new achievements into clinical practice, mentoring young people – all of this keeps me going. In the last 30 years of clinical research, we have saved thousands of lives, achieved improvements in patient quality of life through modernisation and de-escalation, de-ciphered part of the enemies’ code – and made important friendships around the globe. I am very grateful for all of that.”



BCT-ANZ

Accelerating the digital

Staff at BCT-ANZ worked from home for a period of three months, returning to the office at the start of July 2020. But rather than allowing this disruptive environment to halt their activities in the research, fundraising, communications, and business departments, BCT-ANZ identified opportunities to streamline processes and create new ways to engage its stakeholders. These include system improvements such as implementing a Sharepoint portal to allow for real time collaboration of documents for multiple users from any location; implementation of initiatives to overcome source data verification difficulties associated with increased remote monitoring activities; enhancement of online training tools and conduct of site initiation meetings; virtual public workshops; and online fundraising events.

COVID-19 brought forward and expedited the development and implementation of an electronic patient-reported outcome-measures platform, known as **e-PROMs**, which was launched with the **BCT 2001 (Breast-MRI)** trial in July 2020. The e-PROMS platform now allows for important patient questionnaires to be completed by participants (at the appropriate time) electronically on a computer or smart device, including remotely away from the clinic, if necessary. Participants are provided a link via email as their next round of study questionnaires falls due, enabling them to complete the questionnaires in their own time. The system is completely customisable to all forms of questionnaires and usable on all platforms. Now that this has been successfully launched, BCT-ANZ will be utilising this e-platform for all future trials requiring PROMs completion.

Similarly, BCT-ANZ is developing a platform for providing a digital patient information and consent form, known as **e-CONSENT**, with the aim of patient consent forms being available for all future clinical trials in an electronic format. Patients will still be able to receive the traditional paper version of the consent materials. However, the digital version will provide the opportunity to present and explain the clinical trial in a more interactive

way through the inclusion of video and animation. The e-CONSENT platform will also allow patients to remotely provide their consent from anywhere at any time. It is anticipated that this system will provide more condensed, intuitive, and easy-to-understand information about each clinical trial.

CCTG

The 2020 trial activity of the **Canadian Cancer Trials Group (CCTG)** (www.ctg.queensu.ca) focused on ensuring the continued development and safe conduct of cancer clinical trials during the COVID-19 pandemic in addition to the activation of new trials aimed at improving outcomes in patients with cancer.

Below are three COVID-19 trials that allow enrolment of patients with breast cancer:

CCTG IC.8 COV-IMMUNO – a randomised, phase III trial of Immunisation with IMM-101 versus Observation for the Prevention of Severe Respiratory and COVID-19 Related Infections in Cancer Patients at Increased Risk of Exposure (NCT04442048)

The purpose of the trial is to find out if immunisation with a new immune-stimulator will prevent or reduce severe respiratory and COVID-19 infections in cancer patients. A new type of immune stimulating therapy is being developed for the treatment of cancer. It works by activating the parts of your immune system involved with protecting against viral and bacterial infections. It has been studied in over 300 cancer patients who have also been receiving other cancer treatments and seems promising. But it is not yet clear if it can offer better results than not having the immunisation at all.

Cancer patients, while undergoing treatment, are at higher risk for COVID-19 because of a compromised immune system and the need for frequent visits to a cancer centre. The new immune stimulator also shows promise in tolerability for individuals with compromised immune systems.



CCTG ICC.1: NCI COVID-19 in Cancer Patients Study (N-CCaPS) – a Longitudinal Natural History Study of COVID-19 in people with cancer (NCT04387656)

In this study, researchers are following people and collecting medical and other information about them over time to learn more about how a disease and its symptoms develop and change. The knowledge gained through this study will help doctors better manage treatment for people with cancer and COVID-19 in the future.

As part of the N-CCaPS study, researchers will collect blood samples, medical information, and medical images from 2,000 people with cancer who also have COVID-19. Each person will be followed for up to 2 years to help doctors understand how cancer affects COVID-19 and COVID-19 affects cancer.

CCTG SC.27: Living with Cancer in the Time of COVID-19 - a Cohort Study of the Impact of the COVID-19 Pandemic on Cancer Patients During Treatment and Survivors

The goal of CCTG SC.27 is to examine the impact of the COVID-19 pandemic on the experience of Canadian cancer patients at all stages of treatment, focusing on self-reported emotional, social and physical symptoms, quality of life, changes in cancer care, satisfaction with care, and use of a variety of positive and negative coping strategies.

Drs Linda Carlson, University of Calgary, and Lynda Balneaves, University of Manitoba, with CCTG Senior Investigator, Dr Harriet Richardson, are leading the study team. They will be looking at the unique challenges and potential benefits of these changes in care during the current pandemic by conducting a series of online surveys over a 12-month period asking cancer patients and survivors about their experiences, including people currently receiving cancer treatment and up to 10 years post-treatment. Participants will complete online surveys and investigators will interview cancer patients, survivors and their caregivers to better understand their experiences during the pandemic and how they have coped and adjusted to changes to their care.

Investigators hope that the results of the trial will help to provide a better understanding of the nature of challenges encountered by cancer patients and that identifying potential solutions and developing

appropriate supports that can be implemented and evaluated in future emergency planning and research will help to better support patients with cancer.

GAICO

COVID-19 recommendations for cancer patients

Since the start of the COVID-19 pandemic, we have all been forced to take many precautions to maintain the safety and the integrity of our patients participating in clinical trials. To this end, GAICO created a document with recommendations regarding COVID-19 and oncology patients and shared it with all its sites. GAICO members had frequent teleconferences to discuss the problems that arose during this pandemic. **The good news is that the clinical trials remained open and that all the sites continued working.**

GEICAM

COVID-19 information for cancer patients

TABLA DE EJERCICIOS NIVEL AVANZADO
¡MUÉVETE CON GEICAM!

5 **Movilización de hombros:** Tumbado, elevar los brazos, intentando tocar el suelo con los pulgares por encima de la cabeza. 6 repeticiones.

Observaciones: El arte amparar la zona anterior, llegar hasta donde se pueda sin forzar los codos.

6 **Tumbado, con las palmas de las manos hacia arriba, de los brazos hacia los laterales sin despegar las manos y los codos del suelo.** 6 repeticiones.

Observaciones: Diferenciación zona anterior, llegar hasta donde se pueda sin forzar los codos. Codos y manos laterales que hace siempre el suelo.

7 **Movilización gato - vaca:** 4 repeticiones, subir y bajar cuatro veces 1 repetición.

Observaciones: Manos apoyadas a la altura y anchura de los hombros y rodillas apoyadas a la altura y anchura de la cadera. Solo mover la columna. Después de hacer este ejercicio, levantar los brazos arriba y bajar los puños 10 veces.

Si se tiene indigestión o vómitos, evitar preferiblemente no hacer este ejercicio (consultar con el oncólogo).

8 **Restricción torácica:** Tumbado en el estómago, el fémur no afectado. 4 repeticiones.

Observaciones: No mover las piernas, el movimiento parte de la rotación del brazo, no el movimiento con el brazo. Tocar el suelo si no se llega. La rodilla que está en flexión puede apoyar sobre el suelo.

9 **Abducción de cintura:** Mantener la posición 3 segundos, levantar y volver a bajar 4 repeticiones.

Observaciones: Después de cada ejercicio, intentar tirar del pecho hacia abajo. Pueden apoyar los brazos en una mesa cercana a él.

Geicam
 Investigación en
 cáncer de mama
 Para esta información, contacta a través de www.geicam.org

As other parts of the world, Spain was hit by the COVID-19 crisis in the first months of 2020 and a national lockdown was announced on 14 March. At that time, there was not a lot of information about the virus, but it was suspected that infected cancer patients could suffer from a larger number of complications than the healthy population. This is due to their cancer itself as well as to the immunosuppressive effect of its treatments. Cancer patients worried about their specific situation and demanded quality information about the relationship between cancer and COVID-19.

Via its website and social media, the **Spanish Breast Cancer Group (GEICAM)** decided it was critical to underline the importance of cancer patients, their families and their caregivers to be particularly careful when following the international guidelines for COVID-19 prevention. GEICAM added some nuances to the information provided by Spain's National Health System. In addition to these recommendations, GEICAM created a specific section on its website where it collected the latest information on the coronavirus and the risks for cancer patients. GEICAM also prepared a series of support documents and media of interest, including infographics on how breast cancer patients can exercise at home, a collection of frequent Q&A, and webinars hosted by experts in cancer treatment and psycho-oncology.

Visit the “Breast cancer and COVID-19” section on GEICAM's website:

<https://www.geicam.org/cancer-de-mama/coronavirus/informacion-para-pacientes-oncologicos>

In this spirit, GEICAM started its podcast platform **GEICAM T-Habla** (which translates into **GEICAM speaks to you**), a space where experts and patients debate different topics related to breast cancer in a simple and rigorous way. The first podcast was about the benefits of physical exercise for cancer patients. After that, experts and collaborators covered topics such as lymphedema, metastatic cancer, psychology, the role of research in the development of new treatments, and male breast cancer.

GOIRC

The DOMONCOVID project (Italy): a homecare model for cancer patients during and after the COVID-19 pandemic

Cremona, a city in the Lombardy region in the north of Italy, was the Italian city with the 5th highest incidence of COVID-19. The pandemic added a significant strain on healthcare resources due to the sheer volume of patients presenting to emergency departments, often within a short space of time.

It became very difficult for cancer patients to be assisted and hospitalised. COVID-19-positive (COVID-19+) cancer patients, even with mild symptoms, were hospitalised in COVID wards and completely isolated from their family members and from the treating oncologists themselves. Patients were faced with enormous stress and terror due to the risk of death in a situation of isolation and total abandonment.

In the middle of March 2020, during the crucial phase of the pandemic, the **Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC)**, decided to create a homecare project called **DOMONCOVID** with the aim of avoiding hospital admissions of cancer patients and their families, by following patients with mild to moderate symptoms at home and admitting only those with severe symptoms who needed invasive respiratory support.

Within a few days, and in agreement with the hospital management, a team composed of oncologists and nurses from the Oncology Division of Cremona Hospital was formed. It was supported by a secretary with a dedicated telephone number. The team worked for 6 days a week from 8 AM to 5 PM in collaboration with local operators and general practitioners. It assisted cancer patients at home with confirmed diagnosis or symptoms suggestive of COVID-19, without clear clinical or radiological criteria for hospitalisation.

The assistance was provided for residents living within a radius of 50 km from the hospital, from Monday to Saturday, 8 AM to 5 PM. Cancer patients and their cohabitants were tested with at least two nasopharyngeal swabs (NPS). Blood tests, medical examinations and vital parameters were performed.

All screened individuals were advised to follow the quarantine procedures and received an information leaflet. Oral/infusion treatments, including antiviral drugs, were administered.

From 23 March to 30 April 2020, 71 cancer patients were assisted at home, with a total of 191 visits. Of the 71 patients tested with NPS, 26 were COV-19+. Twelve COV-19+ cancer patients had mild symptoms, such as low-grade fever, cough, olfactory alterations and mild dyspnea. Seven patients showed clinical and radiological signs of initial pneumonia with stable parameters; they were successfully treated at home with hydroxychloroquine, antivirals and NSAIDs and did not require hospitalisation. Seven patients with severe symptoms were promptly hospitalised. Four of them died, two due to the infection and two due to disease progression. 52 cohabitants were screened with NPS, of which 28 lived with a COV-19+ cancer patient; in this subgroup, more than half ($n = 16$) were COV-19+ by NPS. Interestingly, most of them ($n = 15$) were totally asymptomatic. In Italy, NPS screening is not routinely performed, not even in cohabitants of COV-19+ patients.

This project demonstrated the feasibility of an innovative model based on homecare assistance for COV-19+ cancer patients with mild symptoms. This strategy, limiting hospital access for COV-19+ patients, might be useful to contain the spread of the infection. Further studies are needed to test this strategy in COV-19-negative cancer patients, and the plan is to implement this model of assistance in this population, who will receive oral therapy at home. Finally, this experience indicates a high probability of identifying asymptomatic COV-19+ individuals among cohabitants, and there is an urgent need to extend the screening to this population.



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Acknowledgement

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The **DOMONCOVID** Project was designed by Rodolfo Passalacqua, Director of the Oncology Department of Cremona and member of the Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC), and by the oncologists Federica Negri, Margherita Ratti, Maria Bonomi, Giulia Grizzi, Bruno Perrucci, Maria Olga Giganti, Matteo Brighenti, Stefano Panni, Maddalena Donini, Benvenuto Ferrari, Alessandra Curti, and the nurses Roberta Marchi and Gianvito Donati.

The results of the DOMONCOVID Project were presented by Margherita Ratti as an oral presentation at the **ESMO Virtual Congress in September 2020**.

OTHER BIG MEMBER GROUPS' ACTIVITIES

ABCSG

Digitalisation and promotion of young talent – the ABCSG year 2020

2020 was a year full of challenges that will have lasting impact on our lives as individuals and particularly on the working life and professional environment of clinical research. The pandemic hit us unexpectedly, and it had far-reaching consequences for our clinical operations and the daily clinical research routines, thus having a major (and ongoing) impact on clinical studies all around the globe.

However, every crisis also harbours its learnings and provides opportunities: existing operations, plans, and systems must suddenly be re-evaluated, or even completely re-designed. In addition to maintaining the high quality of our clinical and translational studies, **the Austrian Breast and Colorectal Cancer Study Group (ABCSG)** is particularly concerned with the **continuing country-wide education** of clinicians and investigators in the state-of-the-art diagnosis and treatment of breast cancer.

ABCSG goes digital had started, even before the pandemic hit, as a digitalisation initiative to render our many breast cancer continuing education courses and discussion formats increasingly available virtually and for remote participation. However, 2020 deprived us of the “classic” alternatives and forced us to develop, optimise and use digital tools in an expedited manner. This offered us many new opportunities: we were able to attract new target audiences, and we were highly motivated to test new and innovative forms of scientific dialogue and collegial exchange. Eventually, this even led to a process of re-thinking our ways of acquiring knowledge: suddenly, it appeared easy to abandon manifested concerns about organising purely virtual events, or the use of social media for science communication. These means offered us a vital way to stay in close touch with our network, including doctors, nurses, and patients. We are keen to move ahead for **more virtual continuing education content and digital communication**

in 2021, and we have already observed raised awareness of its impact. Even once we all may attend long-awaited on-site congresses again, the digitalisation of learning and knowledge will already have further integrated into our daily lives and routines.

“When I announced the **ABCSG goes digital** initiative in 2019, I clearly did not expect that 2020 would bring a major boost and acceleration to this modernisation programme. The deadly pandemic, that will hopefully come to an end in the coming months, also brought huge creativity, innovative formats and wonderful new collaborations to our great team”, ABCSG president Professor Michael Gnant said, “once more confirming the principle *“The bigger the challenge, the bigger the opportunity.”*”

Another great achievement for ABCSG in 2020 was the successful establishment of a junior talent platform – the newly formed **ABCSG Task Force FutureNow**. **Dr Christoph Suppan** from the Department of Internal Medicine, Medical University Graz (Austria), and member of the Task Force **FutureNow**, describes the group and its activities as follows: “The Task Force was founded in late 2019 in order to bring together and support younger members of the ABCSG. Currently we are working on establishing a new platform for continuing education, giving younger doctors a stage to ask questions in an encouraging environment. Moreover, we are planning interactive roundtables with principal investigators who are willing to take us on a journey through time and tell us about hurdles and successes of previous studies.” As ABCSG president Professor Michael Gnant worded it: “I am very happy that a dream is coming true for me, now that we have finally identified the optimal structure and, most importantly, a number of great persons with almost unlimited potential to continue and to build on current ABCSG successes. This initiative will strongly benefit from our new digital communications and provides us with new options for knowledge transfer and networking throughout the country, beyond our existing member community.” The next steps of the Task Force might include identifying potential partners on the international level to create and strengthen a joint young investigator network for breast cancer research.



BCT-ANZ

Founded in 1978, **Breast Cancer Trials (BCT-ANZ)** is the largest, independent, oncology clinical trials research group in Australia and New Zealand. Our research involves multicentre national and international clinical trials and brings together almost 800 researchers in 107 institutions. Over 16,000 women have participated in our clinical trials over the last 40 years.

Board of Directors

BCT-ANZ welcomed **Professor Sherene Loi** to the Board of Directors. Professor Loi is the BCT-ANZ Study Chair of the **Neo-N** and **DIAmOND** clinical trials and a member of the BCT-ANZ Scientific Advisory Committee. She is the Head of the Translational Breast Cancer Genomics and Therapeutics laboratory at the Peter MacCallum Cancer Centre, Melbourne, as well as Consultant Medical Oncologist in the Breast Service and Head of the Breast Cancer Clinical Trials Unit. **Professor Sunil Lakhani** and **Dr Richard Isaacs** were re-elected to the Board. Professor Lakhani is the Executive Director of Research and Senior Staff Specialist at Pathology Queensland and Head of the Breast Group, Centre for Clinical Research, University of Queensland, Brisbane, Australia. Dr Isaacs is a Medical Oncologist and Head of Medical Oncology at Palmerston North Hospital, New Zealand.



Professor Sherene Loi

New Trials Commenced

Three new trials opened in 2020:

> **BCT 1901 (CAPTURE)** is an Australian clinical trial open to both women and men diagnosed with oestrogen-receptor (ER) positive and human epidermal growth factor receptor 2 (HER-2) negative breast cancer that has returned after treatment with a CDK4/6 inhibitor (such as ribociclib, palbociclib, abemaciclib). It will investigate if treatment with a PI3K inhibitor (alpelisib), in combination with fulvestrant, will improve outcomes for patients with metastatic breast cancer when compared with standard treatment. **Professor Sarah-Jane Dawson is the Study Chair.**

> **BCT 1902 (Neo-N)** is an international clinical trial for women or men diagnosed with unilateral triple negative early breast cancer. It will investigate if using an immunotherapy drug alone prior to the combination of immunotherapy and standard chemotherapy is safe and effective in treating breast cancer before surgery. **Professor Sherene Loi is the Australian Study Chair.**

> **BCT 2001 (Breast-MRI)** is an Australian study that is open to women diagnosed with breast cancer and where the medical treatment team suggest that magnetic resonance imaging (MRI) of the breast will help plan treatment. This study aims to find out if having a breast MRI after being diagnosed with breast cancer might change plans for treating the breast cancer and how this might affect patient outcomes. **Professor Christobel Saunders is the Study Chair.**

GBG

As a leading cooperative study group in the field of breast cancer in Germany, the **German Breast Group (GBG)** manages clinical trials across all major therapeutic areas: neoadjuvant, (post-neo)adjuvant, prevention, surgical and palliative.

GBG consistently delivers high-quality results contributing to improvement breast cancer treatment and patients' quality of life. Being accompanied by broad translational research programmes, GBG-led clinical trials also allow for analysis of biomaterial in academic co-operations worldwide.

Clinical trial status and results

In 2020, results of three major early-stage GBG studies, as well as various high-impact translational research projects have been presented, and results of several clinical trials were released as full publications.

Invasive-disease-free survival and safety results of the **GAIN-2** study were presented at the **ASCO 2020 Virtual Meeting**. In this phase III study, patients with high-risk early breast cancer were randomised to intense, dose-dense epirubicin, nab-paclitaxel, and cyclophosphamide (iddEnPC) vs dose-dense, dose-tailored epirubicin/ cyclophosphamide followed by dose-dense, dose-tailored docetaxel (dtEC-dtD) as adjuvant or neoadjuvant chemotherapy. Overall, there was no difference in invasive-disease-free survival between arms and no new safety concerns were raised, so that the use of both regimen appears feasible in this setting ^[1].

Long-term follow-up results of the phase III **GeparOcto** study were presented at the **ESMO 2020 Virtual Congress**. Overall, no difference was found for invasive disease-free and overall survival following neoadjuvant chemotherapy with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide, or weekly paclitaxel/liposomal doxorubicin plus carboplatin in case of triple-negative breast cancer (TNBC) in the high-risk breast cancer population. The subgroup of hormone receptor-positive/HER2-negative breast cancer, however, significantly benefitted from treatment with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide, supporting the concept of effective therapy beyond pathological complete response (pCR) in patients with luminal breast cancer ^[2].

Results of the international phase III **PenelopeB** study, conducted under the BIG umbrella, were presented at the **SABCS 2020 Virtual Symposium**. The study evaluated the addition of the CDK4/6

inhibitor palbociclib to endocrine therapy as post-neoadjuvant treatment for hormone receptor-positive/HER2-negative patients with high relapse-risk. After a median follow-up of 43 months the addition of 1 year of palbociclib to endocrine therapy did not significantly improve invasive disease-free survival. No new safety signals were observed. PenelopeB is the first study showing mature invasive disease-free survival results on a CDK4/6 inhibitor as part of a (post-neo)adjuvant therapy in early breast cancer. Further translational research and subgroup analyses are ongoing ^[3].

Two analyses related to the neoadjuvant **GeparX** study were also presented. Interestingly, a high RANK expression was associated with significantly higher pCR rates, especially in patients with luminal breast cancer, as shown at the **ESMO Virtual Congress 2020**. However, a clinical benefit of denosumab in relation to RANK expression could not be shown ^[4]. A substudy investigating the potential eradication of disseminated tumour cells (DTCs) with denosumab was presented at the **ASCO 2020 Virtual Meeting**. While DTC-eradication was observed at a slightly higher rate after denosumab plus chemotherapy than after chemotherapy alone, the presence of DTCs at baseline or DTC-eradication after denosumab treatment did not influence pCR rates. With regards to breast cancer subtypes, a potential effect of DTC-eradication on pCR in TNBC was proposed to be further investigated ^[5].

Results of the randomised, non-comparative phase II trial **GeparOLA**, investigating neoadjuvant treatment with paclitaxel plus olaparib vs paclitaxel plus carboplatin in HER2-negative early breast cancer patients with a homologous recombination deficiency (HRD), were recently published in *Annals of Oncology* ^[6]. This paper is the first one to compare a poly(adenosine diphosphate [ADP]-ribose) polymerases (PARP) inhibitor containing neoadjuvant regimen with a platinum containing regimen in a HRD early breast cancer population. Additional analyses concerning germline *BRCA1/2* (*gBRCA1/2*) and other panel genes were presented at the **ESMO 2020 Virtual Congress**. Germline *BRCA1/2* mutation status predicted therapy outcome even in patients with HRD tumours. For patients without *gBRCA1/2* mutations, higher pCR rates were observed in the paclitaxel plus olaparib than in the paclitaxel plus carboplatin arm ^[7].

A notable success at the **ESMO Breast Cancer Virtual Meeting 2020** was the presentation of the research project on tumour mutational burden and immune gene expression profile of TNBC patients



from the **GeparNuevo** trial. The results were recently published in *Annals of Oncology*^[8]. This study showed for the first time that tumour mutational burden and immune gene expression profile are independent predictors of response to neoadjuvant immune checkpoint inhibition.

Two retrospective analyses including patients from the **GBG Brain Metastases in Breast Cancer (BMBC)** registry were recently conducted. The results presented at **ESMO Breast Cancer Virtual Meeting 2020** revealed that several clinical parameters as well as Graded Prognostic Assessment (GPA)-scores were significantly associated with overall survival^[9]. An analysis that is of clinical relevance in the context of potential trials examining the benefit of early detection and treatment of brain metastases was recently published in *Cancers (Basel)*. Asymptomatic patients seem to have less severe metastatic brain disease and, despite less intensive local brain metastasis therapy, outcome is still better, especially for patients with HER2-positive breast cancer compared to patients with symptomatic brain metastases^[10].

The use of sentinel lymph node biopsy (SLNB) versus no axillary surgery in patients with early invasive breast cancer (clinically/imaging ≤ 5 cm, c/iN0) who were candidates for breast-conserving surgery (BCS), including postoperative whole-breast irradiation, is investigated in the randomised **INSEMA** trial. Recently, an integrated radiation therapy quality assurance review was published in the *International Journal of Radiation Oncology, Biology, Physics*^[11]. Assuming $\geq 80\%$ of prescribed breast dose as the optimal dose for curative radiation of low-volume disease in axillary lymph nodes, at least 50% of reviewed patients received an adequate dose in level I, even with contemporary 3-dimensional techniques. Dose coverage was much less in axillary levels II and III, and far below therapeutically relevant doses.

The final results of the **MALE** study, the first prospective, randomised, multicentre trial evaluating the efficacy and safety of different endocrine treatment options in male patients with breast cancer, were recently published in *JAMA Oncology*. Aromatase inhibitor or tamoxifen plus gonadotropin-releasing hormone analogue vs tamoxifen led to a sustained decrease of estradiol. The decreased hormonal parameters were associated with impaired sexual function and quality of life, however^[12].

Ongoing trials and future research

> The phase III, placebo-controlled **GeparDouze** (GBG 96 / NSABP B-59) study is investigating the addition of the immune-checkpoint inhibitor atezolizumab to neoadjuvant chemotherapy in patients with TNBC.

> The phase III **SASCIA** (GBG 102) study started recruitment in 2020 to evaluate the efficacy and safety of post-neoadjuvant treatment with sacituzumab govitecan compared to treatment with physician's choice (capecitabine or platinum-based chemotherapy or observation) in primary HER2-negative breast cancer patients with high relapse-risk after standard neoadjuvant treatment.

> The phase III **TAXIS** (GBG 101; SAKK 23/16/ IBCSG 57-18/ABCSG-53) study was launched in 2020 to investigate the value of tailored axillary surgery.

> In metastatic breast cancer, the **AMICA** (GBG 97) and **PADMA** (GBG 93) trials on CDK4/6 inhibitors ribociclib and palbociclib were amended to include a molecular screening programme that may benefit patients by identifying actionable alterations within the context of precision medicine.

> The prospective and retrospective registry study on **breast cancer in pregnancy and young women (BCP)**, in cooperation with BIG (GBG 29/BIG 03-02), successfully continued and included 2,659 patients as of 31 December 2020.

Two new studies were planned and set-up in 2020 and will start recruitment in 2021:

> The phase III **TruDy** (GBG 103 / DESTINY-Breast01: AGO-B-050; NSABP B-60; SOLTI-2001) study, a collaboration between NSABP, Arbeitsgemeinschaft Gynäkologische Onkologie (AGO-B) and the SOLTI Breast Cancer Research Group, is a multicentre, randomised, open-label, active-controlled trial that was initiated for a head-to-head comparison of trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1) as adjuvant treatment in a subset of patients with high-risk HER2-positive primary breast cancer.

> The **EUBREAST-01** (GBG 105) study is a surgical trial about the omission of sentinel lymph node biopsy (SLNB) in TNBC and HER2-positive breast cancer patients with radiologic and pathologic complete response in the breast after neoadjuvant systemic therapy. The study will evaluate the 3-year rate of axillary recurrence-free survival after breast cancer surgery in patients without SLNB.

GBG will continue to develop clinical trials and translational research to investigate new therapeutic agents for breast cancer.

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GEICAM

GEICAM's 25th anniversary: #GeneracionesGEICAM Campaign

On the occasion of its 25th anniversary, the **Spanish Breast Cancer Group (GEICAM)** launched the **#GeneracionesGEICAM campaign** aiming to raise awareness about the reality of breast cancer and requesting society's support for cancer research. This initiative was carried out and made public via several videos with testimonies of both patients and professionals.

In the main testimonial, Guiomar, a 25-years-old metastatic breast cancer patient, and Julia, a 25-year old resident oncologist, thank each other for their participation in scientific research, thereby showing the audience that the generosity of patients participating in clinical trials and the work of researchers contribute to advances that increase survival rates and improve quality of life for people with breast cancer. The audio-visual fragments also show brief dialogues between Guiomar and Maria Luisa, a patient diagnosed with breast cancer 20 years ago. They exchange their experiences as cancer patients and highlight the advances that have been made over a period of 20 years, the contribution of research, the role of patient associations, and the need for patients to have access to reliable information about the disease.



From left to right, Guiomar and Julia thanking each other for their participation in scientific research (video-campaign image)

Collaborating with patient associations: metastatic and male breast cancer

Teaming up with patient associations allows collaborative research groups like GEICAM to go further with their research and outreach about the disease.

In 2020, GEICAM established collaboration agreements with two associations representing realities in breast cancer that may not be so frequently discussed: the **Association for Metastatic Breast Cancer** and the **INVI Association for Male Breast Cancer**. Together we have begun to conduct visibility activities.

Research and communications awards

In 2020, GEICAM received two awards of which they are especially proud:

The first award is the annual prize from the **Spanish Group of Cancer Patients (Grupo Español de Pacientes con Cáncer, GEPAC)**, which honours the best initiative in social and scientific research in oncology and which was awarded to GEICAM's study **RegistEM**. RegistEM is the first national registry of patients with advanced breast cancer in Spain. Its results will show in detail the way Spanish professionals manage the breast cancer and the outcomes of these patients.

The second award GEICAM received is the silver **"ASPID" health communication and creativity award for "best digital communication"**, which honoured **GEICAM's 2019 Breast Cancer World Day campaign, #ElAcentoQueloCambiaTodo** ("The emphasis that changes everything"). The most important emphasise of this campaign was: **through scientific research, promoting a future with no fear of breast cancer.**

IBCSG

Changes in the IBCSG Scientific Committee

In 2020 the **International Breast Cancer Study Group (IBCSG)** was pleased to announce **Professor Sherene Loi** as co-chair of the IBCSG Scientific Committee. Professor Loi is a medical oncologist specialised in breast cancer treatment as well as a clinician-scientist with expertise in genomics, immunology, and drug development. She is an internationally recognised leader whose work has led to new insights into the breast cancer immunology field. Professor Loi leads the Breast Cancer Clinical Trials Unit as well as the Translational Breast Cancer Genomics and Therapeutics Laboratory at the Peter MacCallum Cancer Centre in Melbourne, Australia. She is a Professor at the University of Melbourne, the current holder of the Inaugural

National Breast Cancer Foundation (NBCF) of Australia Endowed Chair and a research fellow of the Breast Cancer Research Foundation (BCRF), New York. Professor Loi received the AACR Outstanding Investigator Award for Breast Cancer Research during the 2020 San Antonio Breast Cancer Symposium (SABCS) and the 2020 European Society of Medical Oncology (ESMO) Breast Cancer Award.

The IBCSG thanks **Dr Angelo Di Leo**, Head of Sandro Pitigliani Medical Oncology Unit, Hospital of Prato Istituto Toscani Tumori, Prato, Italy who served for 4 years as co-chair of the IBCSG Scientific Committee with **Dr Marco Colleoni**, Director of the Division of Medical Senology at the European Institute of Oncology, Milan, Italy. Drs Di Leo and Colleoni are members of BIG's Executive Board.

JBCRG

BIG studies

The **Japan Breast Cancer Research Group (JBCRG)** is currently participating in the following studies run under the BIG umbrella: **POSITIVE**, **ALEXANDRA/IMpassion030**, **OlympiA**, **PENELOPE-B** and **PALLAS**.

Organisation

JBCRG reorganised its Standing Committee, which is responsible for the organisation's group activities. It also welcomed many new members who will be dedicating their time to research development. In addition, JBCRG revised its Standard Operating Procedure manuals related to research conduct principles.

Activities

With the aim to improve cancer care and raise further awareness about breast cancer and clinical trials, JBCRG doctors in charge of public relations gave presentations on this topic at leading Japanese companies.



Dr Chikako Shimizu from the **National Centre for Global Health and Medicine** was invited to present at **ELC Japan K.K.**



Dr Atsuko Kitano from **St. Luke's International Hospital** presented at **Japan Airlines Co., Ltd.**

Japan Air Lines (JAL) supports breast cancer awareness. The famous Japanese crane logo of JAL was presented showcasing that airplanes have similarities with **medical care and clinical research**: they carry our **dreams** and **hopes** for new destinations.



JBCRG's annual meeting

JBCRG's 10th Educational Meeting took place on 15 February 2020. The theme was "Revolution of diagnosis and treatment for breast cancer through artificial intelligence and precision medicine". Around 100 investigators attended.





LACOG

2020 was unique and challenging for all of us. Despite the pandemic, we were able to continue our studies with the great effort and commitment of LACOG's staff, investigators, and sites. 2020 was also remarkable to LACOG as we presented our first study in prostate cancer in an oral abstract session at the **ASCO 2020 Annual Meeting**.

LACOG's new visual identity



In 2020, as part of the group's communication strategy, an update of LACOG's visual identity was developed. The LACOG logo was updated and a specific logo for each LACOG cancer group and specialty, such as the LACOG Breast Group, was created. Additionally, LACOG launched a new website where current information regarding studies, groups, and events can be found. More information is available at www.lacogcancerresearch.org



Ongoing Studies

LACOG is currently participating in two trials under the BIG umbrella: **ALEXANDRA/IMpassion 030** (BIG 16-05), which is open for recruitment in Brazil and Mexico, and **PALLAS** (BIG 14-03), with the participation of Mexican sites. PALLAS' first study results were presented at the **ESMO Virtual Congress 2020** and published in *The Lancet Oncology*.

With the **LATINA** study (LACOG 0615), LACOG is conducting the most comprehensive breast cancer prospective registry in Latin America. In December 2020, the study included more than 1,600 patients of a planned 4,500 from 35 sites in 11 countries.

In 2020, the LACOG Breast group and GBECAM published the first results of the **AMAZONA III** prospective registry regarding the impact of sociodemographic factors and health

insurance coverage in the diagnosis of breast cancer in Brazil. The results showed that patients from the public health system were diagnosed more frequently with symptomatic disease, at later stages, and with more aggressive breast cancer subtypes than patients with private health coverage. This study brings to light important information to identify gaps to optimal care in healthcare systems in Brazil. Two posters were presented at the **Virtual San Antonio Breast Cancer Symposium 2020 (Virtual SABCS 2020)**. A sub-analysis of AMAZONA III showed that around 10% of patients in Brazil do not return to work, get divorced, or end their partner relationship within 1 year of their breast cancer diagnosis. Personal income and surgery type were associated with higher risk of not returning to work, whereas no specific variable was related to marital status change. The main message of this analysis is that government social support, specifically to help people to get back to work, remains critical for breast cancer patients, especially shortly after they have been diagnosed with the disease.

Another study presented at the **Virtual SABCS 2020** is **LACOG 1218**, which evaluated the influence of physicians' lifestyles on prescribing healthy habits to their breast cancer patients. The study, led by Dr Renata Cangussu, showed that the majority of physicians treating breast cancer patients have a healthy lifestyle. Physicians who regularly practise physical activity or who are older than 50 were more likely to advise lifestyle modification. Only half of the physicians treated obesity or referred these patients to specialists. This may have an impact on patient outcome.

Several study proposals from breast investigators in Latin America are being evaluated to be developed by LACOG in the years to come.



Dr Renata Cangussu, PI of LACOG 1218 Study

Dr Gustavo Werutsky, PI of LACOG 0615/LATINA Study

Biobank and Translational research

In years, LACOG has been implementing biological material collection into its clinical and epidemiological studies. Recently, a biobank partnership was established with the Pontificia **Universidade Católica do Rio Grande do Sul (PUCRS)** to manage all the samples from LACOG studies. “LACOG’s wish for the near future is to provide support and collaborate in translational research projects in order to better describe molecular and genetic characteristics of our patients”, said **Dr Gustavo Werutsky**, Chair of LACOG.

The Instituto Projeto Cura in 2020

Despite the tough scenario we all faced in 2020 due to the pandemic, the **Instituto Projeto Cura (CURA)** continued its work. Its efforts consisted in making 2020 memorable and positive even during hard times. For example, a crowdfunding campaign was developed to raise funds to pay for 1,000 laboratory tests needed for four research projects led by LACOG’s Head & Neck Cancer Group. It also promoted the **1st Brazilian Workshop on the “Benefits of Research in the Fight against Cancer”**, for which awareness of non-governmental organisations (NGOs) leaders and patients was raised. Additionally, the **2nd edition of the Renata Thorman Procianoy Award** was held, with Dr Fernando Maluf as the recipient.

CURA, with its headquarters in Brazil, and working closely with LACOG, is the only organisation in Latin America dedicated to planning and executing actions to raise awareness and to collect funds to support multiple research activities that aim to combat cancer. According to Fernanda Schwyter, president of the Institute: “Such initiatives are essential to foster a philanthropic culture in Brazil. As far as we know, this has been the largest fundraising campaign carried out in Brazil to support scientific research. And that is just the beginning”.

CURA collects over R\$ 180,000 to support head and neck cancer research

From July throughout September 2020, the “1,000 lab tests for research against cancer” crowdfunding campaign raised R\$ 184,000 to be invested in various scientific projects to combat head and neck cancer in Brazil. The initial objective of collecting funds to pay for the basic costs to collect and store 1000 laboratory tests on blood and biopsy samples donated by patients exceeded the projected target by 143%, gathering an amount equivalent to the basic costs of 1,430 tests.

This result was only made possible thanks to the dedication of doctors and researchers from Brazilian Group on Head & Neck Cancer (GBCP) and LACOG, which, using an innovative digital strategy, mobilised 335 donors for the cause. The campaign also involved the strong digital participation and support of doctors, celebrities, digital influencers, and patients. Despite the difficulties posed by the Covid-19, the donation webpage recorded over 7,000 digital accesses. In addition to collecting funds, the initiative raised awareness about the importance of supporting scientific research in Brazil.





1st Brazilian workshop on “Benefits of Research in the Fight against Cancer”

The event, which took place on 7 and 8 October, was attended by over 200 participants. CURA gathered physicians, cancer patients, leaders of NGOs and other interested individuals in a virtual and historical event designed to exchange knowledge. Based on a pedagogical concept, the workshop was a pioneering in Latin America. It enabled discussions with the different audiences about the importance of scientific research, including 8 lectures and the presence of renowned experts to clarify doubts. The event was kindly sponsored by Roche. Registration was free.

The workshop could count on the presentations of the following scientific lecturers and investigators: Dr Andreia Melo (INCA), Dr Lilian Arruda (IBCC), Dr Juliana Mauri (IBCC), Dr Carlos Barrios (LACOG), Dr José Márcio Barros de Figueiredo and Dr Paulo Fernandes (IQVIA), Dr. Heloisa Resende (Hospital HINJA), and Dr Fabio Franke (Aliança Pesquisa Clínica).

Discussions were also held in small groups, thus ensuring direct access of participants to medical coordinators and investigators: Dr William William (Hospital Beneficência Portuguesa), Dr Gustavo Werutsky (LACOG), Dr Renata Cangussú and Dr Samira Mascarenhas (Oncologia D’Or), Dr Fernando Moura (ICESP), Dr Ricardo Caponero (Hospital Alemão Oswaldo Cruz) and Dr Graziela Del Molim (Hospital Beneficência Portuguesa). These group discussions also involved facilitators from CURA, namely Lisiane Mota, Marie Caponero, Alcina Mara Rodrigues and Fernanda Schwyter.



2nd edition of the Renata Thorman Procianoy Award

Oncologist **Dr Fernando Maluf** was the recipient of the Renata Thormann Procianoy Award, granted by CURA to honour Brazilian scientific researchers who have been contributing to improve the treatment and survival of patients.

The winner was announced on 9 June during the Brazilian edition of the Online 2020 Best of ASCO. This event is officially authorised by ASCO (American Society of Clinical Oncology), which promotes, on a yearly basis, the largest and most important worldwide oncology congress.

Dr Fernando is the principal investigator of a 100% Brazilian study addressing a new drug to combat prostate cancer in advanced stages. Traditionally, the treatment procedure for this type of cancer is hormonal castration – chemical or surgical – as testosterone is the main nutrient for the malignant cell of prostate cancer. However, according to Dr Maluf: “The reduction of testosterone among men results in several side effects: loss of libido, sexual potency, bone and muscle mass and neurological effects, in addition to hot flashes, usually reducing the quality of life to a very low level.”

The study presented at ASCO involved 128 patients who received drugs that prevent the delivery of testosterone to the cancer cells. According to the oncologist: “This is a global pioneering study that assesses new strategies to face prostate cancer in advanced stages, with the objective of, after a confirmatory study, replacing hormonal castration with these new drugs, preserving the same efficacy, but increasing quality of life”. Coordinated by LACOG, with headquarters in Porto Alegre (RS), the clinical trial involved 14 research centres and several Brazilian oncologists.

Dr Fernando Maluf works at the Beneficência Portuguesa Hospital of São Paulo and The Israeli Albert Einstein. He is a faculty member at the Medical School of the Santa Casa de São Paulo.



Dr Fernando Maluf, recipient of the 2nd edition of the “Renata Thormann Procianoy Award” and Fernanda Schwyter, president of Projeto Cura Institute

SAKK

The **Swiss Group for Clinical Cancer Research (SAKK)** is a non-profit organisation that has been conducting clinical trials in oncology since 1965. Its primary objective is to research new cancer therapies, to further develop existing treatments, and to improve quality of life for patients with cancer. This takes place through cooperative projects within Switzerland and in collaboration with centres and study groups abroad.

With regular training opportunities, events, and symposia, SAKK promotes the cooperation and further education of researchers in clinical cancer research.

SAKK organises annual events such as:

- **Chicago in the Mountains**, to discuss the most important news from the **ASCO Annual Meeting**
- **ESMO in the Alps**, organised in parallel with the **ESMO Congress**
- **Swiss PostESMO**, to present the most important data from **ESMO**



SAKK's annual mentoring programme for young oncologists, the **Young Oncology Academy**, focuses on providing young talents with insights into the successful development, management, execution, and publication of a clinical trial. As part of the academy, participants also attend the **ESMO congress**, the **EHA** (for haematologists) or **ESTRO** (for radio-oncologists) congresses.

SAKK, a long-term member of IBCSG and BIG, is or has been working closely with prominent breast cancer experts such as **Professor Aron Goldhirsch**, **Professor Monica Castiglione-Gertsch**, **Professor Beat Thürlimann** and **Professor Stefan Aebi**.

In 2020, the **SAKK Project Group Breast Cancer (PG BC)**, which centralises about fifty members including university hospitals, public hospitals, and private cancer centres, recruited 560 patients in breast clinical trials. The group is proud to have contributed actively to some major practice-changing trials conducted under the umbrella of

two collaborative networks, **IBCSG** and **BIG**. The collaboration continues with SAKK being involved in the following trials: **OlympiA** (BIG 6-13 / NSABP B-55), **PALLAS** (BIG 14-03 / ABCSG 42), **POLAR** (IBCSG 59-19 / BIG 18-02), **POSITIVE** (IBCSG 48-14 / BIG 8-13), and **TOUCH** (IBCSG 55-17).

The SAKK PG BC is also the initiator of several ongoing trials exploring loco-regional, systemic, or quality of life interventions.

TAXIS trial (SAKK 23/16)

This trial is a unique large phase III trial randomising 1,500 patients with axillary lymph node involvement. Standard axillary lymph node dissection is compared to tailored axillary surgery, a new technique that aims at selectively removing the positive lymph nodes. The trial aims to contribute significantly to the de-escalation of axilla surgery. Thanks to an international effort bringing together Switzerland (25 sites), Germany (7 sites), Austria (7 sites), Hungary (3 sites), Italy (1 site) and Lithuania (1 site), the recruitment is proceeding as planned, with 400 randomised patients as of this writing.

WISE trial (SAKK 95/17)

This phase III trial assesses the impact of a 24-week activity programme (monitored by a tracking device) on aromatase inhibitors induced arthralgia (joint pain). The target recruitment of 350 patients was reached more than one year ahead of schedule, underlining the interest of the patients and the centres in participating in trials aiming to improve quality of life.

REDUSE trial (SAKK 96/12)

This phase III trial compares denosumab administered every 4 weeks versus every 12 weeks in term of prevention of symptomatic skeletal events in patients with metastatic breast or prostate cancer. The trial is being conducted in Austria, Germany, and Switzerland.

VISION (SAKK 23/18)

In this trial, vacuum assisted biopsy immediately before surgery is used as a surrogate for patient's response to neoadjuvant chemotherapy for breast cancer. The investigators will attempt to resolve any limitations of previous trials conducted in the past and that failed.



SOLTI

Interview with Dr Tomás Pascual



Dr Tomás Pascual is the newly appointed Chief Scientific Officer of the SOLTI Breast Cancer Research Group (SOLTI). In his words: “At SOLTI we focus our research on tumour biology because we know that it is the key to the paradigm shift”.

What do you think is SOLTI’s main contribution as a cooperative group dedicated to clinical and translational research?

Dr Tomás Pascual: “Cooperative academic research groups are very necessary because they promote independent research of excellence and, in the case of SOLTI, we also encourage the creativity of researchers in the generation of ideas, turning scientific-medical concepts into clinical trials. In recent years, SOLTI has promoted disruptive and innovative trials such as **CORALLEEN**, **PAMELA** and **PATRICIA**.”

Where do ideas for designing original clinical studies come from?

Dr Pascual: “Day-to-day clinical experience with patients gives us an endless pool of ideas because cancer is a complex disease that, even when we’re dealing with the same type of tumour, behaves in very different ways. This is one of the reasons why SOLTI’s research programme is focused on studying the biology of tumours from a clinical point of view. This new vision allows us to better understand why a drug is not effective in a group of patients, to search for new treatment regimens or to select a specific population with a high possibility of responding to a drug, for example.”

Many cancer patients do not respond to standard treatment and, after several treatments, they remain without a therapeutic alternative. What is SOLTI’s strategy for those patients?

Dr Pascual: “SOLTI provides the expertise of 25 years of developing very specific clinical studies based mainly on tumour biology. Our fundamental purpose is to carry out studies that have a direct impact on the patient and that respond to fundamental questions about the disease and to unmet medical needs. That’s why we prioritise conducting studies that focus on new therapeutic targets and the application of new treatment protocols that can change the paradigm of clinical practice in the approach and treatment of the disease.”

Of the studies currently being carried out by SOLTI, which ones do you think could make a difference in current clinical practice?

Dr Pascual: “At SOLTI we group the studies into three programmes, according to their design: the **Clinical Trial Programme**, the **Window Programme** and the **Biomarker Programme**. However, we can look at the same studies from another point of view and group them based on a **functional perspective**: a **first group** that includes studies aimed at improving the prognosis of **metastatic tumours** with hormone receptor and HER2-negative expression, selecting subgroups of patients who present a poor prognosis factor or resistance to an established treatment. The **second category** includes studies aimed at better characterising the **biomarkers** that could determine response-probability to a specific drug. And, finally, the **third category** includes studies in **early breast cancer**, mainly in residual disease, which includes new treatment strategies that improve prognosis.”

What do you think are the main contributions that SOLTI has made during its 25 years’ history?

Dr Pascual: “In the last 25 years, there have been many **advances in the knowledge and treatment of breast cancer** and SOLTI has definitely contributed to these achievements. One of our main singularities has been to differentiate ourselves by having opened pioneering lines of research, such as in the field of the neoadjuvant treatment, and generating hypotheses based on biomarkers.”

How do you think cancer research should evolve?

Dr Pascual: “From my point of view, the fundamental thing is that we learn to look at the whole picture of the disease, and not only at parts of it. This reminds me of the Indian folk tale of ‘The six blind wise men and the elephant’. In short, it tells the story of six blind men who spend hours competing to see who is the wisest. One day, an elephant passes through the village and they discuss its shape. Undoubtedly, all the wise men were partially right, since all the forms they described were true. However, undeniably all of them were also wrong because they were unable to depict the real, whole image of the elephant.”

“Just like the elephant, cancer is an entity that all experts must observe, each from his or her perspective and specialty. But only by putting together all this collective knowledge, will we be able to draw a silhouette that is as close to reality as possible.”

TROG

The DCIS study (BIG 3-07 / TROG 07.01)

BIG and the Trans Tasman Radiation Oncology Group (TROG) Cancer Research's decade of collaboration on the DCIS study has reached the key milestone of main analysis

The principal goals of treatment of ductal carcinoma in situ (DCIS), which accounts for up to 25% of new breast cancer diagnoses, are to minimise the risk of progression to invasive breast cancer and impact on quality of life of patients. Radiotherapy after breast conserving surgery for non-low risk DCIS reduces the risk of local recurrence but is associated with radiation-related toxicity. In contrast to invasive breast cancer, there is no high-level evidence on the optimal radiation dose fractionation for DCIS to guide patients and clinicians in achieving the principal goals of treatment.

The DCIS study is an academic, investigator-led, randomised phase III study of radiation doses and fractionation schedules for DCIS of the breast. It aims to individualise radiotherapy for patients with non-low risk DCIS following breast conservative surgery to achieve long-term disease control with minimal toxicity.

The study was activated in Australia and New Zealand in 2007, and internationally in 2009 in collaboration with the BIG network including the Canadian Cancer Trials Group (CCTG), the European Organisation for Research and Treatment of Cancer (EORTC), the Scottish Cancer Trials Breast Group (SCTBG), the International Breast Cancer Study Group (IBCSG) and Cancer Trials Ireland (CT-IRE). With the powerful momentum generated by the global investigator team, the accrual of 1,608 patients from 136 centres in 11 countries was completed on 30 June 2014, two years ahead of schedule.

The international collaboration has successfully reached the key milestone of the 5-year main analysis on the primary endpoint of time to local recurrence, and the results were presented at the **San Antonio Breast Cancer Symposium (virtual SABCS 2020, 8-12 December, 2020)** by **Professor Boon Chua**. In addition, the investigator team has also completed the first international study of cosmetic outcomes in patients with DCIS treated by breast conserving surgery and adjuvant radiotherapy. It represents the largest prospective evaluation of cosmetic outcomes



for women with DCIS published to date (*Radiotherapy and Oncology* 2020;142:180–85). The team has also published an analysis of patient reported outcomes including fatigue, physical functioning, body image and perceived risk of developing invasive breast cancer following breast conserving surgery and radiotherapy for DCIS (*The Lancet* 2019;394:2165-2172). Collectively, these results provide the data to support informed treatment decision and will likely have a significant impact on clinical practice internationally.

Importantly, the prospectively collected DCIS tumour specimens of BIG 3-07 / TROG 07.01 are being centrally reviewed by an international panel of expert breast pathologists, and provide a unique biological resource to develop and validate a clinical diagnostic test that will predict the likelihood of recurrence, in particular invasive recurrence. The ability to distinguish patients with DCIS at high or low risk of recurrence will facilitate personalised management to optimise patient outcomes. Analyses are actively in progress.

Final analysis of the DCIS study is planned for 2024. The successful conduct to date of this academic, investigator-led study is made possible only by the strong and enduring international alliance of the BIG network.

The study is funded by the Australian National Health and Medical Research Council, Susan G. Komen for the Cure®, Breast Cancer Now, OncoSuisse Swiss Federation Against Cancer, Dutch Cancer Society and Canadian Cancer Society.



For further information, please contact Study Chair, Professor Boon H Chua (Boon.Chua@health.nsw.gov.au).



WSG

For 27 years, the **West German Study Group (WSG)**, an academic study group, has been designing, organising and conducting breast cancer clinical trials. With our trials, we aim to develop new therapeutic strategies that significantly improve efficacy and tolerability in comparison with existing standard therapies. Our scientific work focusses on the individualisation of breast cancer treatment (which patient needs which treatment?) and the development of de-escalated therapeutic strategies. More than 12,000 patients have already participated in our studies.

Germany-wide, WSG collaborates closely with over 200 breast centres, thereby contributing to bringing the latest findings in the therapy of breast cancer directly into everyday clinical treatment. Through this large network of study centres, WSG also collaborates with several international partners such as **Barts Cancer Institute** (BCI, Queen Mary University of London) and the **European Organisation for Research and Treatment of Cancer (EORTC)**. WSG is responsible for the conduct of collaborative trials in Germany. Currently, there are 2 international collaborative studies **conducted in Germany under the responsibility of WSG: BARBICAN and ECLIPSE.**

Activities in 2020

At the **ASCO 2020 Annual Meeting**, the first efficacy results from the **TP-II trial** were presented. It was shown that in early HR+/HER2+ breast cancer, a de-escalated chemotherapy regimen (paclitaxel + double HER2 blockade) was superior to a de-escalated chemotherapy-free regimen (endocrine therapy + double HER2 blockade) with regard to achieving pCR (pathologic complete response). However, the trial's survival results are still awaited, and these will determine what recommendations for a de-escalated chemotherapy regimen in HR+/HER2+ early breast cancer can be made.

At the **ESMO Virtual Congress 2020**, survival data from the **ADAPT HR+/HER2+** study were presented, showing excellent 93% 5y DFS (disease-free survival) in patients with pCR after only 12 weeks of T-DM1 +/- ET (even without further chemotherapy). These promising data may serve as a basis for further prospective trials aimed at determining how to avoid overtreatment in carefully selected patients with HER2+ early breast cancer. Moreover, translational analyses showed that mutations associated with endocrine resistance and metastatic breast cancer are enriched in short-term endocrine treated primary luminal breast cancers with impaired Ki67 response.

ESMO Lifetime Achievement Award 2020 for Professor Nadia Harbeck

Professor Nadia Harbeck, one of the Medical Directors at WSG, Head of the Breast Centre and Chair of Conservative Oncology at the LMU University Hospital's department of Obstetrics and Gynaecology, Germany, has won ESMO's Lifetime Achievement Award in **recognition of her career-long commitment to global cancer research and education.**



Professor Nadia Harbeck

The WSG-ADAPT-HR+/HER2- study

The study was conducted by the West German Study Group and 5-year survival data were presented orally at the Virtual **San Antonio Breast Cancer Symposium**. Within ADAPT HR+/HER2- adjuvant treatment decision-making was guided by a predefined algorithm combining information from the 21-gene expression assay (Recurrence Score, RS) and Ki-67 response to 3-week preoperative endocrine therapy.

In summary, about half of the 5,000 patients in the study population (all candidates for chemotherapy by conventional criteria) could be spared chemotherapy. Building on the findings from **TAILORx** and **RxPONDER**, ADAPT HR+/HER2- generates important information, especially for pre-menopausal women. In endocrine-responsive tumours we could not detect age dependent effects in the low and intermediate risk score (RS) populations in patients with pN0-1 disease. Survival data for these patients are excellent, so it is unlikely that they will obtain a clinically meaningful benefit from chemotherapy.

Data presented from the neoadjuvant part of the study by **Dr Sherko Kümmel** showed pCR data from 427 patients in the nab-paclitaxel arm and 437 in the paclitaxel arm. PCR was significantly higher in the nab-paclitaxel arm. RS > 25 and tumour size were independent predictors of pCR. Patients with high RS > 25 but endocrine response had a low rate of pCR (5,6%).

Ongoing and future trials

ADAPTcycle

WSG-ADAPTcycle is a prospective, (neo)adjuvant, randomised phase III trial. It is investigating whether patients with HR+/HER2- early breast cancer identified during screening as intermediate risk (based on Oncotype DX and response to 3 weeks of endocrine therapy [ET]) derive additional benefit from 2 years of the CDK4/6 inhibitor ribociclib combined with ET compared to chemotherapy (CT) (followed by adjuvant ET). Co-primary endpoints are disease-free survival (DFS) and distant DFS. 5,600 patients will be screened, of which 1,670 will be randomised. The study started in July 2019 and by the end of December 2020, 1,291 patients had been screened and 314 randomised.

ADAPTlate

WSG-ADAPTlate is a prospective, randomised phase III trial. ADAPTlate seeks to evaluate whether enhancing endocrine therapy (ET) with a CDK 4/6 inhibitor is superior to ET alone in patients with clinical or genomic high risk early breast cancer, even 2-6 years after their initial diagnosis. Primary objective is to demonstrate superiority of invasive disease-free survival (iDFS) of abemaciclib + ET vs. standard ET. It is planned to screen 1,250 patients of which 903 will be randomised. The study started in September 2020 and by end December 2020, 21 patients had been screened and 12 randomised.

Keyriched 1

WSG-Keyriched 1 is a prospective, single-arm neoadjuvant phase II single arm study. This hypothesis-generating trial is investigating the rate of pCR in patients with HER2-enriched breast cancer receiving four cycles of the dual anti-HER2 blockade (trastuzumab and pertuzumab) in combination with the checkpoint inhibitor pembrolizumab. The intention is to screen 82 patients of which 46 will be included. The study started in August 2020 and by the end of December 2020, 41 patients had been screened and 18 enrolled.

Concepts for future trials are being elaborated, especially to address the clinical needs in triple-negative and HER2+ breast cancer.



THE BIG NETWORK: GLOBAL RESEARCH COLLABORATION TO CURE BREAST CANCER

For over 20 years, BIG's academic research groups have been working together to find better treatments and cures for breast cancer

The Breast International Group (BIG) is an international not-for-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, more than two decades later, BIG represents over 50 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 enrolls 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 Shaikat 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

FBCG Finnish Breast Cancer Group

GBG German Breast Group

GCSG Georgian Cancer Study Group

GEICAM Spanish Breast Cancer Group

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 Clínicos Oncológicos 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, BIG MEMBER GROUPS ARE STRONGER, MORE RESILIENT AND PERSISTENT IN FINDING CURES FOR BREAST CANCER

4 / BIG TRIALS

Overview of the current clinical studies run within the BIG network

Open trials / research programmes

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 (BrEAST) / FSTRF and AFT Pharma partner: Roche/Genentech (sponsor) Funding: Roche / Genentech
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
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. Oliveira	BIG-sponsored programme (Co)-Leading partners: BIG HQ (sponsor) / IJB--CTSU (BrEAST) / FSS Pharma partner: N/A Funding: BCRF, Fondation Cancer (Luxembourg), NIF Foundation, the National Lottery (Belgium), Barrie and Deena Webb, Think Pink Belgium (SMART Fund) and many individual donors
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
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
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, and BIG HQ fundraising initiatives
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 (US) Pharma partner: N/A Funding: Breast Cancer Research Foundation
POLAR	BIG 18-02	Palbociclib for HR+ isolated local or regional recurrence of breast cancer - NCT03820830	E. Munzone S.Aebi	Supporter trial Coordinating group: IBCSG (sponsor) Pharma partner: Pfizer

Follow-up or post-study activities

Study name	BIG number	Short description	Principal Investigator(s)	Trial model & partners
ALTO	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 (BrEAST) / 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 (BrEAST) / FSTRF Pharma partner: Roche (sponsor) Funding: Roche
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: Australian National Health and Medical Research Council, Susan G. Komen for the Cure®, Breast Cancer Now, OncoSuisse Swiss Federation Against Cancer, Dutch Cancer Society and Canadian Cancer Society
FINESSE	BIG 2-13	Oral lucitanib for patients with FGFR1 ER+ metastatic breast cancer - NCT02053636	F. André J. Cortés	Lead trial (Co)-Leading partners: BIG HQ / BrEAST / FSS Pharma partner: Servier (sponsor) Funding: Servier
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
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, Canadian Cancer Society, BCRF and 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*



Follow-up or post-study activities

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 B. Kaufman J. Garber C. Geyer	Lead trial (Co)-Leading partners: NRG Oncology (sponsor in US), BIG HQ and FSTRF Pharma partner: AstraZeneca (sponsor in Rest of the World) Funding: AstraZeneca
PALLAS	BIG 14-03	PALbociclib CoLaborative Adjuvant Study: palbociclib with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for HR+ / HER2-negative early breast cancer - NCT02513394	E. Mayer M. Grant A. DeMichele	Co-Lead trial (Co)-Leading partners: ABCSG (RoW), AFT (US) (sponsors) and BIG HQ Pharma partner: Pfizer Funding: Pfizer grant
PENE-LOPE-B	BIG 1-13	Post-neoadjuvant palbociclib for patients with HR+, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy - NCT01864746	G. von Minckwitz	Supporter trial (Co)-Leading partner: GBG (sponsor) Pharma partner: Pfizer Funding: Pfizer grant
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: IBCSG (sponsor) Pharma partner: N/A Funding: IBCSG, Fonds Baillet-Latour, 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: IBCSG (sponsor) and BIG HQ Pharma partner: Pfizer Funding: Pfizer grant
SNAP	BIG 2-12	Schedules of nab-Paclitaxel: evaluation of different schedules of nab-paclitaxel for metastatic breast cancer - NCT01746225	A. Gennari G. Jerusalem	Supporter trial (Co)-Leading partner: IBCSG (sponsor) Pharma partner: Celgene Funding: Celgene grant
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: IBCSG (sponsor) Pharma partner: Pfizer Funding: Grant support from Pfizer, Ipsen, US NCI, IBCSG and many participating collaborative academic groups, Breast Cancer Research Foundation, as well as various charities
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 (Co)-Leading partner: IBCSG (sponsor) Pharma partner: Pfizer Funding: Grant support from Pfizer, Ipsen, US NCI, IBCSG and many participating collaborative academic groups, BCRF, as well as various charities
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.



Follow-up or post-study activities

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: IBCSG (sponsor) Pharma partner: Pfizer Funding: Grant support from Pfizer, Ipsen, US NCI, IBCSG and many participating collaborative academic groups, BCRF, as well as various charities
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. Sofiriu	Supporter trial (Co)-Leading partners: EORTC BCG, SUCCESS, UNICANCER Sponsor: EORTC Pharma partner: Roche, Janssen Diagnostics Funding: Roche educational grant/ medication; Janssen test kits
ULTIMATE	BIG 16-01	Immunotherapy combined with standard endocrine therapy as neoadjuvant treatment for women with ER+/HER2-negative breast cancer - NCT02997995	F. André A. Prat	Co-lead trial (Co)-Leading partners: French Breast Cancer Intergroup Unicancer (UCBG) (sponsor) and BIG HQ Pharma partner: AstraZeneca Funding: AstraZeneca grant

* full information available on the BIG website.

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; **NCCTG:** North Central Cancer Treatment Group; **NCI:** US National Cancer Institute; **SCTBG:** Scottish Cancer Trials Breast Group; **TBCRC:** Translational Breast Cancer Research Consortium

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

“TO CONDUCT LARGE INTERNATIONAL CLINICAL TRIALS AND TO FOLLOW PATIENTS FOR SEVERAL YEARS AFTER TREATMENT ENDS, REQUIRES THE RESILIENCE AND PERSISTENCE OF BOTH PATIENTS AND RESEARCHERS. TOGETHER, WE FACILITATE AND ACCELERATE BREAST CANCER RESEARCH.”

5 / BIG PUBLICATIONS

PEER-REVIEWED PAPERS PUBLISHED BY MEMBER GROUPS ABOUT THE BIG NETWORK AND ITS ACTIVITIES IN 2020

Gelber RD, Coates AS, Gelber S et al. The legacy of Professor Aron Goldhirsch. *Ann Oncol* 2020;31(6):671-673. doi: 10.1016/j.annonc.2020.03.288. Epub 2020 Mar 23

Leone JP, Cole BF, Regan MM et al. Clinical behavior of recurrent hormone receptor-positive breast cancer by adjuvant endocrine therapy within the Breast International Group 1-98 Clinical Trial. *Cancer* 2021;127(5):700-708. doi: 10.1002/cncr.33318. Epub 2020 Dec 8 (BIG 1-98)

Rabaglio M, Sun Z, Maibach R et al. Cumulative incidence of cardiovascular events under tamoxifen and letrozole alone and in sequence: A report from the BIG 1-98 trial. *Breast Cancer Res Treat* 2021;185(3):697-707. doi: 10.1007/s10549-020-05981-z. Epub 2020 Nov 7 (BIG 1-98)

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“BIG patients, researchers and supporters share the same goal: to eradicate breast cancer. **Together, we achieve more.**”



6 / BIG FINANCE

BIG BALANCE SHEET

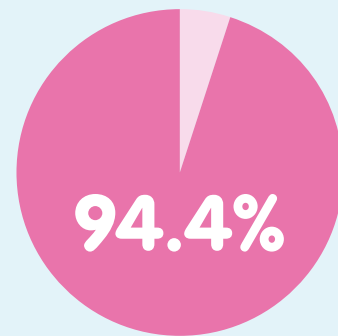
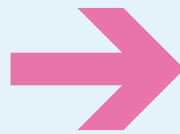
ASSETS	2020	2019
Fixed Assets		
Intangible fixed assets	15,401	0
Tangible fixed assets	56,132	119,398
Financial fixed assets	146,668	140,637
Total Fixed Assets	218,201	260,035
Current Assets		
Receivables up to one year	7,737,508	5,125,002
Current investments	1,544,366	3,144,370
Cash at bank	9,539,875	10,768,868
Deferred charges and accrued income	140,237	148,341
Total Current Assets	18,961,986	19,186,581
TOTAL ASSETS	19,180,186	19,446,616
LIABILITIES		
Equity		
Unrestricted net assets	460,408	1,113,195
Restricted net assets	4,552,180	3,891,624
Total Equity	5,012,588	5,004,819
Debts		
Amounts payable after more than one year	0	0
Amounts payable within one year	14,077,598	14,441,636
Trade debts	13,563,231	14,113,383
Tax, remuneration and social security	514,367	328,253
Deferred charges and accrued income	90,000	161
Total Debts	14,167,598	14,441,797
TOTAL LIABILITIES	19,180,186	19,446,616

INCOME & EXPENSES STATEMENT

Operating Income & Expenses		
Turnover (research)	17,551,462	18,046,390
Other goods & services	-13,648,390	-14,820,796
Operating margin	3,903,072	3,225,594
Remuneration, social security & pension costs	-3,870,787	-3,442,878
Operating result	32,285	-217,284
Financial result	-11,070	238,607
Extraordinary income (+)	459	24,076
Extraordinary expenses (-)	-13,904	-5,359
Result for the financial year	7,770	40,040

Between 2012
and 2020,
BIG received over
€ 132 696 663 *

* funding for study collaborations involving pharmaceutical and other partners, as well as from the philanthropic work of *BIG against breast cancer*



was spent directly on research conducted under the BIG umbrella, making a huge difference in the lives of women and men with breast cancer



BIG Executive Board

BIG's EB represents the leadership and the main scientific and decision-making authority of the organisation. It aims to reflect the geographical extent of the network, as well as its multiculturalism and the broad range of expertise among its members; such as medical oncology, gynaecological oncology, surgical oncology, radiation oncology, medical statistics, clinical trials methodology, translational research and business.

The EB members develop BIG's scientific strategy. With BIG headquarters, they implement decisions of the General Assembly and provide oversight of the organisation.

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TOGETHER, we are stronger,
more resilient and persistent
in finding cures for breast cancer

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