ANNUAL REPORT

2018

Spreading Hope
advancing breast cancer research

BIG
Breast International Group
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>MESSAGE FROM THE CHAIR</td>
<td>1</td>
</tr>
<tr>
<td>BIG</td>
<td>2</td>
</tr>
<tr>
<td>BIG RESEARCH</td>
<td>4</td>
</tr>
<tr>
<td>BIG PHILANTHROPY</td>
<td>10</td>
</tr>
<tr>
<td>BIG NETWORK</td>
<td>20</td>
</tr>
<tr>
<td>BIG TRIALS</td>
<td>36</td>
</tr>
<tr>
<td>BIG PUBLICATIONS</td>
<td>38</td>
</tr>
<tr>
<td>BIG FINANCIALS</td>
<td>39</td>
</tr>
<tr>
<td>BIG ACKNOWLEDGEMENTS</td>
<td>40</td>
</tr>
</tbody>
</table>
MESSAGE FROM THE CHAIR

2018 was another year of hard work to prepare the ground and sow the many seeds needed to launch new breast cancer clinical trials and research programmes – and secure necessary funding for them. This annual report highlights the key activities of BIG’s network and its 59 member groups (made up of breast cancer experts across the globe), while also providing information about our structure, governance, and financial performance.

In the feature article, “Two decades of breast cancer research: more patients living longer than ever before”, some of BIG’s leading researchers discuss the impact of advances in the understanding and treatment of breast cancer since BIG was established in 1999. They also give their view on future developments and therapies.

BIG’s dedicated philanthropy unit conducts vital fundraising to support clinical trials and research programmes that have no commercial interest but are crucial for patients. The funds raised provide the means for BIG member groups and their affiliated hospitals to finance their efforts and patient participation in a study. This is made possible by foundations, companies, ambassadors and individuals. 94.8% of the raised funds are invested directly into BIG’s own research.

In 2018, and in continuation of the organisation’s governance review that began in 2016, BIG completed the expansion of its Executive Board. It is now composed of 16 members reflecting the multiculturalism and scientific know-how of the BIG network and its member groups. To mirror this growth and evolution, BIG’s Headquarters, located in Brussels (Belgium), also underwent restructuring to enable a dynamic, younger generation with deep scientific knowledge and clinical trials expertise to support the organisation.

In the upcoming year 2019, BIG is celebrating its 20th anniversary. Women and men diagnosed with breast cancer 20 years ago had limited treatment options and a suboptimal survival rate. Fortunately, we are making progress and mortality rates are falling thanks to the research conducted to date. BIG’s ambition is to see the current and next generations of women and men reaping the fruits of its research to beat breast cancer, which continues to touch the lives of so many in our communities. Let’s keep spreading hope!

We wish to say thank you to our member groups, partners, faithful ambassadors, donors and staff for their support and strong collaborative spirit to help advance breast cancer research. We also wish to thank and honour the thousands of patients who participate in our trials and work with us to develop tomorrow’s cures.

Prof Martine Piccart-Gebhart
BIG Chair

INTRODUCTION

PROGRESS IS IMPOSSIBLE WITHOUT COLLABORATION

ONCE YOU CHOOSE HOPE, ANYTHING’S POSSIBLE
2,1 MILLION PEOPLE
diagnosed with breast cancer in 2018

72 PEOPLE / HOUR
die from breast cancer

± 95 000 PATIENTS
have participated in BIG trials

 Patients are at the heart of BIG’s research

> 30 clinical trials and research programmes are run at any one time

59 academic research groups. The largest international network dedicated to breast cancer research!

Connecting ± 10 000 breast cancer specialists
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.

BIG was founded as a network of collaborative groups in 1999 to address fragmentation in European breast cancer research. However, groups from other parts of the world rapidly expressed interest in joining BIG, and in 2018 it represented 59 like-minded research groups from around the world and reached across more than 65 countries and 6 continents.

Through these groups, BIG connects thousands of hospitals and world-class breast cancer experts who collaborate on pioneering 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.

BIG is supported in part by its philanthropy unit, known as BIG against breast cancer. This denomination is used to disseminate information to the general public as well as partners and donors.

www.BIGagainstbreastcancer.org
TWO DECADES OF BREAST CANCER RESEARCH: MORE PATIENTS LIVING LONGER THAN EVER BEFORE

By medical journalist Jenny Bryan

In 2000, a year after BIG was founded, approximately one million women and men were diagnosed with breast cancer and nearly 470,000 died from the disease. By 2018, when the latest data were published, just over two million people were diagnosed and nearly 627,000 died (source: GLOBOCAN 2018).

Women and men with breast cancer are living longer than ever before thanks to earlier diagnosis, more effective treatment, and better tailoring of treatment to each patient’s tumour.

Here, some of BIG’s leading researchers discuss the impact of advances in understanding and treatment of breast cancer since BIG was established in 1999 and look forward to future developments.
BREAST CANCER: NO LONGER A SINGLE DISEASE, BUT MANY

IN THE EARLY 2000s, BREAST CANCER WAS DIVIDED INTO FOUR TYPES (LUMINAL A, LUMINAL B, HER2 POSITIVE [HER2+] AND BASAL/TRIPLE NEGATIVE BREAST CANCER [TNBC]), BUT RESEARCHERS NOW KNOW OTHER DIFFERENCES THAT CAN HELP DRIVE NEW APPROACHES TO TREATMENT.

“Thanks to our improved understanding of the biology of breast cancer, we can now diagnose it earlier and develop better therapies to cure more patients, improve survival and quality of life, and reduce the number of patients who need chemotherapy,” says Dr Ander Urruticoechea, medical oncologist and scientific director, Onkologikoa, San Sebastian, Spain.

Three drugs (palbociclib, ribociclib and abemaciclib) are available for patients with luminal B, HER2 negative breast cancer that inhibit CDK4/6 cyclin-dependent kinases, which are essential for cell division and are often overactive in cancer cells.

Promising results have been reported with the alpha-specific PI3K inhibitor alpelisib for tumours with mutations in the PI3K cell-signalling pathway.

Patients with metastatic breast cancer and the inherited BRCA1/2 mutation can benefit from the PARP inhibitor olaparib, which exploits DNA repair deficiencies in cancer cells.

“There are many drugs in early-phase clinical trials, and the challenge is now to match them with the tumour alterations and show that they are useful to patients,” says Professor Aleix Prat, head of medical oncology at the University of Barcelona, Spain.

> Relevant BIG studies/trials:
  AURORA (BIG 14-01)
  PYTHIA (BIG 14-04)
  PALLAS (BIG 14-03)
  LORELEI (BIG 3-13)

HOW TRASTUZUMAB HAS TRANSFORMED THE OUTLOOK FOR WOMEN WITH HER2+ DISEASE

WHEN THE MONOCLONAL ANTIBODY TRASTUZUMAB WAS LICENSED FOR THE TREATMENT OF HER2+ METASTATIC BREAST CANCER IN 1998, HER2+ TUMOURS WERE AMONG THE HARDEST TO TREAT. FAST FORWARD TWO DECADES AND ANTI-HER2 THERAPY IS ONE OF THE BIGGEST SUCCESS STORIES IN MODERN CANCER TREATMENT – FOR METASTATIC AND EARLY STAGE HER2+ BREAST CANCER.

“Progress has been astonishing and anti-HER2 therapies are now lifesaving for women with early stage disease because they increase the chance of cure. For women with advanced disease, they prolong survival without altering quality of life because most are extremely well tolerated,” says Professor Martine Piccart, professor of oncology at the Université Libre de Bruxelles and Director of Research at Jules Bordet Institute, Brussels, Belgium. Professor Piccart is also co-founder and chair of BIG.

Even so, one in four women with node-positive HER2+ breast cancer still relapses and dies within 10 years, despite trastuzumab therapy, so the battle is far from won.

Considerable hope rests on the newer anti-HER2 therapies, such as the monoclonal antibody pertuzumab, the anti-HER1/2 tyrosine kinase inhibitor lapatinib, and trastuzumab emtansine (T-DM1), which uses trastuzumab to target chemotherapy directly at HER2+ cells. But biomarkers are needed to identify women most likely to benefit from these new approaches.

> Relevant BIG studies/trials:
  HERA (BIG 1-01)
  APHINITY (BIG 4-11)
  ALTTO (BIG 2-06)
  NeoALTTO (BIG 1-06)
  SOLD (BIG 1-10)
SURGERY: SMALLER OPERATIONS WITH BETTER RESULTS

GONE ARE THE DAYS WHEN 80-90% OF WOMEN WITH BREAST CANCER HAD A MASTECTOMY. INSTEAD, BREAST CONSERVATION HAS BECOME STANDARD CARE, WITH NEOADJUVANT THERAPIES OFTEN USED TO SHRINK LARGER TUMOURS BEFORE SURGERY.

“Our surgical techniques are better, and the use of systemic therapies to shrink tumours means that 90-95% of women can now have breast conserving surgery,” says Professor Michael Gnant, MD, FACS, Austria.

For women who do need a mastectomy, breast reconstruction can often be done at the same time – reducing the need for repeat surgery and offering women more rapid resolution of their cancer surgery.

In many countries, local recurrence rates have fallen significantly due to better surgery, pathology, radiotherapy and radiology, and greater standardisation of procedures.

Even so, there are still questions to be answered, and BIG has established a task force to consider how surgical questions can be integrated into clinical trials.

Research is also exploring whether, in the future, some patients with breast cancer may be able to avoid surgery, but that is unlikely to happen for at least a decade.
RADIOTHERAPY:
TAILORING TREATMENT TO INDIVIDUAL PATIENT NEEDS

FOR MANY YEARS, RADIOTHERAPY HAS BEEN AN INTEGRAL PART OF TREATMENT FOR EARLY STAGE AND ADVANCED BREAST CANCER, AND REMARKABLE TECHNOLOGICAL ADVANCES OVER THE LAST THREE DECADES HAVE IMPROVED TREATMENT PRECISION AND DECREASED TOXICITY.

Research has shown that, after breast conserving surgery, conventional daily radiotherapy for five to six weeks has no safety or effectiveness benefits over modestly larger daily doses of radiation typically given over three weeks. The newer approach, called hypofractionated radiotherapy, has obvious advantages for patients and healthcare providers.

“Hypofractionated whole breast radiotherapy is being adopted as a standard of care for women with early breast cancer in an increasing number of countries,” explains Professor Boon Chua, radiation oncologist and director of Cancer and Haematology Services, University of New South Wales and Prince of Wales Hospital in Sydney, Australia.

Patients at low risk of recurrence may only need partial breast irradiation, targeting the primary tumour site where recurrence is most likely to occur and further accelerating treatment to one week or less.

“I think the future of personalised radiotherapy will be driven by integrating our current knowledge with new understanding of tumour biology and efficacy of systemic therapy in a multidisciplinary setting,” says Chua.

> Relevant BIG studies/trials:
  EXPERT (BIG 16-02)
  SUPREMO (BIG 2-04)
  DCIS (BIG 3-07)

HORMONE THERAPY:
LEADING THE WAY IN TARGETED TREATMENT

MANY OF TODAY’S TREATMENTS FOR HORMONE SENSITIVE TUMOURS WERE AVAILABLE LONG BEFORE BIG WAS ESTABLISHED. HOWEVER, RESEARCH IN THE LAST 20 YEARS HAS HELPED TO DIFFERENTIATE THE ROLES OF TAMOXIFEN, AROMATASE INHIBITORS (AIs) AND OTHER HORMONE THERAPIES, BASED ON DISEASE SEVERITY AND RISK OF RECURRENCE.

Premenopausal women at intermediate risk of recurrence benefit from tamoxifen combined with ovarian suppression, while those at highest risk may do better with exemestane and ovarian suppression. In postmenopausal women, results of the BIG 1-98 showed that adjuvant treatment with the AI letrozole is better at preventing recurrence than tamoxifen alone.

Newer agents, such as CDK4/6 and mTOR inhibitors, have been used to boost the effectiveness of hormonal treatment. Following reassuring long-term safety data in advanced disease, the combination of hormone treatment and CDK4/6 inhibitors is being investigated as adjuvant hormone therapy in early stage breast cancer.

“Endocrine therapy will always be needed for blocking progression of hormone responsive breast cancer, and improved selection of patients for additional tailored therapies will enable us to optimise results. Identifying the best way of combining these agents is the true challenge for the future,” says Professor Aron Goldhirsch, medical oncologist, Italy/Switzerland. Professor Goldhirsch is also co-founder and, until recently, was vice-chair of BIG.

> Relevant BIG studies/trials:
  SOFT / TEXT (BIG 2-02 / BIG 3-02)
  AROMATASE INHIBITORS (BIG 1-97 / BIG 2-97 / BIG 1-98)
CHEMOTHERAPY: FEWER WOMEN NEED TOXIC DRUGS FOR BREAST CANCER THAN EVER BEFORE

IN THE LAST THREE YEARS TWO MAJOR TRIALS, MINDACT AND TAILORX, HAVE CONFIRMED THAT FEWER WOMEN WITH EARLY BREAST CANCER NEED CHEMOTHERAPY THAN EVER BEFORE.

“In the 1990s and early 2000s, the vast majority of patients with early stage breast cancer received chemotherapy, but we now know that patients with tumours which are highly sensitive to hormone treatment do not need chemotherapy,” says Dr Angelo Di Leo, medical oncologist, Head of Sandro Pitigliani Medical Oncology Unit, Istituto Toscani Tumori, Prato, Italy.

Patients with early stage, luminal A breast cancer that has spread to axillary lymph nodes are no longer automatic candidates for chemotherapy, though chemotherapy is still needed for luminal B breast cancer or triple-negative breast cancer (TNBC). It is also combined with anti-HER2 therapy in patients with HER2+ breast cancer.

In advanced breast cancer, many patients can be offered chemotherapy at a later stage than in the past, and a ‘kinder’ treatment such as frequent, low dose, oral treatment at home is often possible.

For the future, cancer specialists want to target chemotherapy at patients most likely to benefit from it, and there is great interest in how it can be combined with immunotherapy.

> Relevant BIG studies/trials:
  MINDACT (BIG 3-04)

IMMUNOTHERAPY REVEALS POTENTIAL IN BREAST CANCER

IN 1999, ACTIVATING THE IMMUNE SYSTEM TO DESTROY BREAST CANCER CELLS WAS LITTLE MORE THAN AN IDEA. BUT CHECKPOINT INHIBITORS THAT RELEASE THE BRAKES ON THE IMMUNE SYSTEM’S NATURAL RESPONSE AGAINST CANCER CELLS NOW HOLD GREAT PROMISE FOR BREAST CANCER TREATMENT, INCLUDING TRIPLE-NEGATIVE BREAST CANCER.

“During the last 20 years, advances in scientific understanding of how immune cells recognise cancer cells as abnormal and, most importantly, how cancer cells inhibit that immune response, have provided the foundation for today’s immunotherapy,” explains Professor Fabrice André, medical oncologist, professor of medical oncology at the Institut Gustave Roussy, Villejuif, France.

The most interesting checkpoint inhibitors are antibodies that interfere with how breast cancer cells deactivate immune cells called T lymphocytes when they arrive in tumours to kill them. Combining checkpoint inhibitors with chemotherapy helps boost responses.

There is also progress in developing cancer vaccines to ‘educate’ the immune system to recognise abnormal protein markers on breast cancer cells, and attack them.

“Over the next five to 10 years, we can expect increasingly sophisticated immunotherapy for breast cancer, including personalised cancer vaccines and adoptive T-cell therapy, and we will hopefully start to develop vaccination strategies for breast cancer prevention,” says Dr Michail Ignatiadis, senior attending physician, Medical Oncology Department at the Jules Bordet Institute, Brussels, Belgium.

> Relevant BIG studies/trials:
  ALEXANDRA / IMPASSION 030 (BIG 16-05)
  PANACEA (BIG 4-13)
  ULTIMATE (BIG 16-01)
GETTING MALE BREAST CANCER ON THE RESEARCH AGENDA

FOR THE 1% OF PATIENTS WITH BREAST CANCER WHO ARE MALE, THE MOST SIGNIFICANT CHANGES OF THE LAST 20 YEARS HAVE BEEN INCREASING AWARENESS AND DIAGNOSIS, AND EFFORTS TO GET MORE MEN INTO LARGE CLINICAL TRIALS OF NOVEL TREATMENTS.

“If men participate in clinical trials of new treatments – even in small numbers – they are more likely to be included among the patient groups who can access those treatments when they are approved by the regulatory authorities,” says Dr Fatima Cardoso, medical oncologist, director of the Breast Unit of the Champalimaud Clinical Center, Lisbon, Portugal.

Nearly all men with breast cancer have hormone sensitive tumours, but diagnosis is often delayed and fewer men receive hormone therapy than would be expected, or radiotherapy for node-positive disease.

Men are not yet benefitting as much as women from recent advances in breast cancer treatment, partly due to reimbursement issues for newer agents, and trial sponsors may exclude men in breast cancer trials in case they ‘dilute’ treatment benefits achieved in female patients.

“I remain optimistic that, if we work together, we can change attitudes and get more male patients into breast cancer trials. We must also educate all clinicians and the public about the need to recognise symptoms so that it can be diagnosed and treated earlier,” says Cardoso.

> Relevant BIG studies/trials:
  Male Breast Cancer (BIG 2-07 / EORTC 100-85P / BCG)
BIG PICTURE OF PHILANTHROPY

> 95,000 patients in BIG clinical trials since its conception
> 3,500 donor base
5 foundations
46 corporate & event partners
1,100 attendees at our 2018 fundraising events
9 influential ambassadors

94.7% INVESTED DIRECTLY INTO BIG’S OWN RESEARCH
PHILANTHROPIC COMMUNITY

BIG comprises a two-sided coin, namely, a scientific community and a philanthropic community, sharing the same vision to eradicate breast cancer.

Our dedicated philanthropy unit conducts vital fundraising to support academic clinical trials and research programmes that have no commercial interest but are crucial for patients. These collaborative efforts have led to practice-changing achievements in the field of breast cancer.

The funds raised provide the means for BIG member groups (made up of breast cancer experts across the globe) and their affiliated hospitals to finance their efforts and patients’ participation in a study.

This is made possible by foundations, companies, ambassadors and individuals; in other words, by our philanthropic community.
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.

From the generous support over the years, real progress has been made in better understanding breast cancer and improving the treatments of women and men with the disease. Among the key academic initiatives run within the BIG network are the Metastatic Breast Cancer GPS (scientific name: AURORA), BIG Time for Baby (scientific name: POSITIVE) and BIG Radio Tuning (scientific name: EXPERT). All three are ongoing and still require financial support to enrol the number of patients needed to answer important questions.

BIG RADIO TUNING (EXPERT)

Which women could be spared from radiotherapy following breast conserving surgery? Generally, in the treatment of breast cancer, 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.

The aim of the BIG Radio Tuning study is to better analyse the risk profile of tumours to identify which women could safely avoid radiation therapy after surgery in the future.

To do this, the tumours of patients potentially interested in the study will be analysed for risk of recurrence using a genetic test of 50 genes. Those qualifying as low-risk according to the test will then receive either endocrine therapy alone or endocrine therapy plus radiotherapy. The study hopes to show that both groups do well and that therefore patients classified as low-risk according to the 50-gene test may be spared radiotherapy in the future. In 2018, 28 of about 90 hospitals that will participate in the study got on board.
BIG TIME FOR BABY (POSITIVE)

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

In 2018, 57 women participating in the study had their dream come true, and gave birth. Of the needed 500 patients, 339 are currently enrolled.

METASTATIC BREAST CANCER GPS (AURORA)

The Metastatic Breast Cancer GPS is an innovative, international research programme set up to improve our understanding of metastatic breast cancer, to identify breakdowns (genetic aberrations) and to map the routes that cancer cells take to invade other organs. Approximately one in three cancers metastasises.

The programme, launched in 2014, will enrol 1,000 patients from 11 European countries and aims to understand why breast cancer spreads (metastasises) and why some patients respond poorly to standard treatment while others respond very well. Through the findings, we aim to develop better treatments and potentially offer cures one day to patients with this still incurable disease. Since November 2018, already 602 of the 1,000 needed patients are participating. Preliminary findings are anticipated in 2019.

For more information on BIG’s achievements in the field and current trials, visit www.BIGagainstbreastcancer.org
DONOR EVENTS

A BIG EVENING IN ST PETERSBURG
4 October - 6th annual gala

The vibrant colours of the matryoshka dolls, the joyful music of gypsies and the atmosphere of an autumn evening in St Petersburg set the tone at the Cercle de Lorraine in Brussels. Beautiful prizes were raffled, surprising gifts and unique experiences were auctioned.

PINK IS THE NEW BLACK
11 October - dinner party

The exceptional setting of the desacralised GESU church in the heart of Brussels mesmerised the participants, who did not hesitate to express their enthusiasm for the auction and to bring the dance floor alive until the wee hours of the morning.
The BIG philanthropic community comes together regularly; in 2018 we invited our supporters to the following events, with proceeds benefiting BIG’s research.

PATRICK BRUEL CONCERT
20 March - Brussels
A private concert was offered to our supporters, at la Madeleine in Brussels. The crowd went wild for this second edition of such an exclusive occasion.

GIUSEPPE VERDI’S ‘REQUIEM’
17 November - Brussels
We offered some of the best seats in the house at Bozar. This piece was performed by the Brussels Choral Society and the Philharmonischer Chor Bonn - with no fewer than 150 singers on stage - accompanied by the Ensemble Orchestral de Bruxelles.

THANK YOU COCKTAIL
We celebrated our philanthropic community at the Thank You Cocktail on April 26 at the Castle of Groot-Bijgaarden (Brussels).

A BIG THANK YOU TO OUR 2018 EVENT SPONSORS:
Altavia Act • Axel Kuborn Management • Banque Bruxelles Lambert • Be Close Protection International • Belfius • Benoit Colette-Photographe • Blue Beach House • Brussels Expo • Champagne de Castellane • Château Brande-Bergère • Château de Bioul • Comité Octobre Rose Comines • Comptoir des vins • Denis Meyers • Enjoy by Alex • Festi-Rent • GTS Gold Team Service • JML • L’Une ou l’Autre • L’Usine • La ville de Bruxelles • Leonidas • Les Gloutons • Media Expo • NA Production • Nuxe • Panda GIN • Pernod Ricard • Quilak • Rothschild • Sabam • Salon de coiffure Mitchell’s • Securitas • Sharing Box • Shows on the Road • UBU • Veluvins
How Individuals Can Make a Difference

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

- Join our community and stay in touch with news from the philanthropy unit.
- Introduce BIG to your professional network.
- Donate for any occasion. Think BIG for a birthday, Mother’s Day, anniversary or make a gift in memory of a loved one, or to commemorate a family member or friend who has battled breast cancer.
  
  www.BIGagainstbreastcancer.org/donate

- Attend an event.
- Give in-kind (e.g. artwork from your own collection or an exquisite experience) for auction to benefit BIG.
- Create a Facebook birthday fundraiser.

Thank you to our supporters who “thought BIG” in 2018 and asked their loved ones to donate for their special occasion. This past year BIG was the grateful beneficiary of a wedding gift wish list.

For more information on how you can support BIG, contact philanthropy@BIGagainstBC.org

Follow us on

@BIGagainstbreastcancer
@BIGagainstBC
BIG against breast cancer
BIG is tremendously grateful to the foundations, corporate partners and individuals - who, through supporting its research - bring us one step closer to finding cures for breast cancer.

HONORARY PRESIDENT

“Breast cancer affects women and men of all ages. It is crucial to identify the most appropriate and personalised therapies to increase the chances of recovery and cure. BIG fosters collaboration among the world’s leading breast cancer experts and advances in research.”

Her Majesty the Queen of the Belgians, Honorary President

COMMITTEE OF AMBASSADORS

“By supporting BIG against breast cancer, we all help the world’s best researchers unite their expertise in the fight against one of the most devastating cancers worldwide. We also have the privilege of participating in a real challenge: making treatments less invasive and giving comfort and hope to many patients.”

Nathalie de Merode, President of the Committee of Ambassadors
A FEW HIGHLIGHTS OF OUR CORPORATE COLLABORATIONS IN 2018

BAOBAB COLLECTION

With the support of the Baobab Collection in 2018, nearly 60 patients have found hope by being able to participate in a clinical study crucial to them: BIG Time for Baby. It not only brings its financial support through the sale of its ‘Women’ and ‘Gentlemen’ candles, of which a percentage is donated to BIG, but Baobab Collection is also our partner in many events, through in-kind giving and specific sponsorships.

"The 'Women' candle represents the female symbol. I chose to support BIG because my mother also lost her life to breast cancer. The launch of ‘Women’ proved to be the most successful in our line in the shortest amount of time."

Corinne Bensahel, Creative Director, Baobab Collection

NUXE

NUXE's commitment to breast cancer is 360°. Nuxe partners with BIG in many events, both with financial support and by generously offering many products such as ‘Prodigieuse Oil’ to all participants. Moreover, Nuxe is the first partner that has committed to launch a sports challenge through Atlas GO, thus enabling a diverse audience to convert their daily fitness activity into credits for a good cause.
HOW CORPORATE PARTNERS CAN GENERATE IMPACT

CSR PATRONAGE PACKAGES
As a corporate partner you share BIG’s values (sharing and combining resources, expertise, accountability, innovation) and embrace the cause. Your company is a changemaker and wishes to save lives by supporting breast cancer research.

MY-EMPLOYEES-COUNT PACKAGES
With such a high incidence rate, breast cancer greatly impacts business life. Employees, or their family members, are likely to be confronted with the disease one day. Showing solidarity and mobilising your entire team can stimulate their motivation and enhance retention. You can choose among truly attractive packages, including the “adopt-a-future mother” programme, in-house information sessions, sports activities and challenges, team building occasions, the surprising “Boobs Art” exhibition, private concerts, and more. This package entails a long-term, stable engagement between your company and BIG.

PINK MARKETING PACKAGES
What about taking the opportunity to engage your customers with your brand? Simply allocate a percentage of your total turnover or a percentage of the sales of a specific product or service to support breast cancer research. This package offers you the opportunity to communicate your support for a cause that touches many women and men in the world.
BIG NETWORK: INTERNATIONAL COLLABORATION TO MOVE RESEARCH FORWARD

BIG designs and conducts its own research through its 59 members groups worldwide and their extended network of hospitals and breast cancer experts. In 2018, it reached across more than 65 countries and 6 continents. Together, BIG members represent the largest global network dedicated to breast cancer research. Each BIG group plays a crucial role in today’s research. Their expertise, collaborative spirit, dedication and hard work are essential to improving the lives of patients confronted with breast cancer.

SPREADING HOPE THROUGH OUR NETWORK OF BREAST CANCER EXPERTS

AFRICA
BGICS Breast Gynaecological International Cancer Society

ASIA
BIEI Breast Intergroup of Eastern India
BDPCC Breast Disease Professional Committee of CMEA
CTRG Cancer Therapeutics Research Group
HKBOG Hong Kong Breast Oncology Group
ICON ARO Indian Co-operative Oncology Network
IOSG Indian Oncology Study Group
JBCRG Japan Breast Cancer Research Group
KCSG Korean Cancer Study Group
SKMCH & RC Shaukat Khanum Memorial Cancer Hospital & Research Centre
TCOG Taiwan Cooperative Oncology Group
TSCO Thai Society of Clinical Oncology

AUSTRALASIA
BCT-ANZ Breast Cancer Trials Australia and New Zealand
TROG Trans-Tasman Radiation Oncology Group

EUROPE
ABCSG Austrian Breast & Colorectal Cancer Study Group
AGO-B Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group
BOOG Borstkanker Onderzoek Groep
CEEOG Central and East European Oncology Group
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
FBI Francilien Breast Intergroup
GBG German Breast Group
GCSG Georgian Cancer Study Group
GEICAM Spanish Breast Cancer Group
GOIRC Gruppo Oncologico Italiano di Ricerca Clinica
GONO Gruppo Oncologico del Nord Ovest
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
COMPLETION OF BIG EXECUTIVE BOARD’S EXPANSION

In continuation of the organisation’s governance review that began in 2016, BIG was proud to welcome five new members to BIG’s Executive Board (EB) in June 2018: Dr Carlos Barrios, Dr Philippe Bedard, Dr Etienne Brain, Dr Eva Carrasco and Dr Nick Turner.

They joined Prof Judith Bliss, Dr Boon Chua, Dr Marco Colleoni, Dr Barbro Linderholm, Dr Shinji Ohno, Dr Aleix Prat, and Dr Ander Urruticoechea, members of the EB since 2017, as well as Dr David Cameron, Dr Angelo Di Leo and Dr Sybille Loibl, who were re-elected in 2018 to serve additional terms.

This expanded board reflects the multiculturalism and diverse scientific know-how of the BIG network. It develops BIG’s scientific strategy and, with BIG Headquarters, implements decisions of the General Assembly and provides oversight of the organisation.

BIG AND THE NORTH AMERICAN BREAST CANCER GROUP

For over a decade, BIG has collaborated closely with the North American Breast Cancer Group (NABC) – a network of major US and Canadian-based research groups. BIG and NABC have been meeting annually to identify and address some of the most challenging aspects of breast cancer research, answer critical questions, focus on research areas not supported by the pharmaceutical industry such as male breast cancer, and collaborate to improve treatments and cures for patients around the world.

In 2018, the group focused on preparing for the future of international clinical trials in breast cancer. The aim of the annual meeting was to resolve challenges in international trial collaboration, to provide recommendations to improve trial design and to explore opportunities to apply machine learning.

This long standing, academically-driven collaboration is supported by the generous help of the Breast Cancer Research Foundation®.
BIG HEADQUARTERS’ RESTRUCTURING

In 2016, BIG launched an intensive governance review and succession-planning process, which led to the decision to expand the Executive Board (EB) in two phases. The second phase was completed in 2018, with the board growing from 9 members to 16. This new expanded board reflects the multiculturalism and scientific know-how of the BIG network.

To mirror this growth and evolution, BIG HQ also underwent restructuring. These changes were implemented to meet the needs and demands of a growing organisation and changing environment. As of February, Dr Theodora Goulioti took over the role of CEO from Dr Carolyn Straehle, who assumed the role of deputy-CEO and Research Support Director.

Theodora Goulioti: “My vision is to further nurture this team and work even more closely with the headquarters of our member groups to ensure that we provide optimal support to breast cancer research and ultimately to those affected by the disease.”

Carolyn Straehle: “Just as it is important to periodically “refresh” BIG’s governance to meet the demands of a growing organisation and changing environment, it is essential to adapt BIG’s HQ structure to be able to do the same. Our restructuring aims on the one hand to be more streamlined, while at the same time to enable a dynamic, younger generation with deep scientific and clinical trials expertise to lead BIG HQ and support the organisation.”

DR MARTINE PICCART HONoured WITH TWO PRESTIGIOUS CANCER RESEARCH AWARDS

In 2018, co-founder and president of the Breast International Group Dr Martine Piccart was honoured with two important cancer research awards.

Dr Martine Piccart and Michel Pébereau, President of Fondation ARC (credit: Fondation ARC)

The first, which she received in April, was the 46th Fondation Arc Léopold Griffuel award for translational and clinical research, one of the most prestigious European prizes for cancer research.

Then, in November, she was awarded the KNAW Bob Pinedo Cancer Care award for her many contributions to breast cancer research, her role as an educator to many breast cancer specialists, and her dedication to advocating the importance of clinical cancer research.

AS OUR WORK IS MOSTLY COLLABORATIVE, THIS IS A RECOGNITION FOR THE WHOLE GROUP OF OUR COLLABORATORS

TOGETHER, WE ACHIEVE MORE
On Friday 23 November 2018, the first BIG-East Asia workshop for young investigators took place in Singapore and involved the seven east-Asian member groups from the BIG network.

The workshop - co-chaired by Dr Shinji Ohno (JBCRG), Dr Janice Tsang (HKBOG) and Dr Sung-Bae Kim (KCSG) - stemmed from the wish of the BIG Asian groups to develop young investigators’ experience in international collaboration and participation in international clinical trials, from within the region or under the BIG umbrella. The event, held during the ESMO-Asia Congress in Singapore, was attended by early career breast cancer specialists and senior investigators who serve as their mentors.

The main objectives of the workshop were:

- To develop breast cancer clinical trial ideas under the BIG umbrella, with young investigators serving as the trials’ principal investigators, and run by the Asian groups from the network.
- To have a series of manuscripts touching on topics relevant to Asian countries written for publication.

Over the course of the workshop, the early-career investigators presented 9 clinical trial ideas relevant to the East-Asian region. Although all trial ideas were excellent and will likely be further developed in close collaboration with the mentors and early career investigators in the future, three clinical trials ideas were selected as potentially interesting for the BIG network. The projects of Dr Iris Ka Ming Wong, Dr Jae Ho Jeong, and Drs Yukinori Osaki and Makiko Ono will be further developed and presented to BIG member groups at the BIG Scientific Meeting in September 2019.

Groups participating in the BIG-East Asia clinical trials workshop for young investigators:

- Breast Disease Professional Committee of CMEA (BDPCC)
- Cancer Therapeutics Research Group (CTRG)
- Hong Kong Breast Oncology Group (HKBOG)
- Japan Breast Cancer Research Group (JBCRG)
- Korean Cancer Study Group (KCSG)
- Taiwan Cooperative Oncology Group (TCOG)
- Thai Society of Clinical Oncology (TSCO)
ABCSG supports young scientists with a new research grant and the Young Investigator Award

In November 2018, for the first time, the Austrian Breast & Colorectal Cancer Study Group (ABCSG) conferred a grant for clinical and translational research to promising young investigators. The total amount of EUR 25,000, to be shared between two young scientists for their study projects, was awarded during ABCSG’s annual meeting in Saalfelden (Salzburg, Austria).

Dr Maximilian Marhold, oncologist in Vienna, presented his project “Establishing a patient-derived metastatic breast cancer organoid platform for drug resistance screens and translational research applications”. The Viennese gynaecologist Dr Elisabeth Reiser will use the grant to implement her research about the “Prognostic and predictive value of the FRAX score – reanalysing the ABCSG 18 trial”.

“We are very happy that ABCSG supports young researchers with great ideas for new study projects. Our new research grant will surely help to realise innovative strategies, and we are proud to be part of such a network to help young colleagues make their way to innovative research”, say Drs Florian Fitzal and Christoph Tausch, chairs of the scientific session and presenters of the award.

Also, the Young Investigator Award, well-established since 2012 and representing EUR 2,500, was awarded in Saalfelden to the young Viennese surgeon Dr Kerstin Wimmer, who will use the money to attend a scientific meeting overseas.
The Canadian Cancer Trials Group (CCTG) had some changes in leadership in 2018. The group is grateful for the many years of superb leadership from Drs Karen Gelmon and Tim Whelan, the two previous co-Chairs of our Breast Disease Site Group. Dr Stephen Chia, a medical oncologist from BCCancer, Vancouver, took over from Karen in the spring of 2018, and Dr Eileen Rakovitch, a radiation oncologist from Sunnybrook in Toronto, is replacing Tim. We are excited to have Stephen and Eileen at the helm.

Throughout the year, our trial activities continued to be a mix of CCTG-led studies, NCI’s National Clinical Trials Network (NCTN) trials with our US partners, or trials run in collaboration with BIG. The CCTG is currently participating in OLYMPIA (BIG 6-13), PALLAS (BIG 14-03) (to which we contributed 173 patients by the end of 2018 in spite of starting the trial very much later than many other participating groups), and POSITIVE (BIG 8-13). The latter was widely publicised and enthusiastically received by physicians and young women alike. We are grateful for the support offered by RETHINK Canada, who have been helping us to publicise the trial and have provided financial support. And we continued to provide central pathology review for TROG 07.01 DCIS / BIG 3-07, the outcome of which we are anxiously awaiting.

CCTG MA.32 (BIG 5-11) was ongoing in 2018, and all patients continue to be followed for the invasive disease-free primary outcome measure. Secondary analyses examining the impact of metformin on metabolic outcomes are ongoing, including those presented at meetings in 2018:


CCTG MA.38, a randomised phase II study comparing two different schedules of palbociclib plus second-line endocrine therapy in women with oestrogen receptor-positive, HER2-negative advanced/metastatic breast cancer, was presented at the 2018 San Antonio Breast Cancer Symposium in one of the Spotlight Sessions (PD1-10).

A newly activated study in 2018 was CCTG MA39 Tailor RT, a randomised trial of regional radiotherapy in biomarker low-risk node-positive breast cancer, which is active in North America within the NCTN. This noninferiority trial will evaluate the impact of de-escalation of regional radiotherapy in patients with breast cancer with an Oncotype Dx® Score lower than 18.

We continue to look forward to our collaborations with BIG and are pleased that one of our CCTG members, Dr Phil Bedard from the Princess Margaret Cancer Centre, is now a member of the expanded BIG Executive Board.
The Central and East European Oncology Group (CEEOG) was established in 1983, initially as the South and East European Oncology Group (SEEEOG). At the time, SEEEOG consisted of 15 institutions from Bulgaria, Czechoslovakia, Hungary, Poland, Romania and Yugoslavia. Over the next 16 years, the group was chaired by Prof. Sandor Eckhardt from the National Cancer Institute in Budapest. SEEEOG was then the only drug-oriented cancer research organisation in the region. In the 1980s and 1990s the group conducted a series of phase II and III clinical trials in breast, ovarian, lung and head and neck cancer patients.

In 1988 SEEEOG changed its name to Central and East European Oncology Group (CEEOG), as the latter better reflected the geographical location of its member countries.

In 1999 CEEOG chairmanship was transferred to Prof. Jacek Jassem from the Medical University of Gdańsk, Poland, and Gdańsk became the home of the new data centre.

Since then, CEEOG has greatly expanded and now includes around 35 academic and community hospitals from Bosnia and Herzegovina, Bulgaria, Croatia, Czechia, Estonia, Hungary, Israel, Latvia, Lithuania, Poland, Romania, the Russian Federation, Serbia, Slovakia and Slovenia.

CEEOG performs translational and investigator-initiated phase II clinical studies, and participates in large phase III trials carried out within international consortia. The group’s main focus is breast cancer.

CEEOG is a member of BIG and has participated in pivotal BIG studies for many years. Other global partners for cooperative activities in breast cancer include the EORTC (European Organisation for Research and Treatment of Cancer), IBCSG (International Breast Study Group) and the National Cancer Institute, Bethesda, USA (see http://ceeog.eu/publications.html for the list of publications).

CEEOG recently initiated a translational project to investigate the predictive role of quantitative HER2/HER3 heterodimer measurement in advanced breast cancer patients receiving pertuzumab. Interested institutions can contact Prof. Jassem at info@ceeog.eu or jjassem@gumed.edu.pl.

In 2005 CEEOG established its working party, the Polish Brain Metastasis Consortium (PBMC), chaired by Dr Renata Duchnowska from the Military Institute of Medicine in Warsaw. PBMC has conducted several translational studies and now includes around 30 Polish and international research institutions (see http://www.pbm.org.pl/en/publications/publications1.html for the list of publications).
A few years ago, the GEICAM Spanish Breast Cancer Group identified two challenges related to young investigators:

First, there is no regular training in clinical trial design and methodology in medical schools, so medical specialists, when they want to become involved in clinical trials, do not have the foundation needed to develop high-quality clinical research. Even more importantly, they are unable to design both innovative and feasible clinical trials.

Second, GEICAM, as a cooperative group focused on breast cancer research, needs to nurture and develop well-trained junior investigators to become its future leaders. This is essential to carry on with the GEICAM mission developed during its more than 20 years of existence.

To tackle these challenges, Professor Miguel Martín, Dr Ander Urruticoechea, Dr Alberto Ocaña and Dr Eva Carrasco designed and launched the first edition of the GEICAM Clinical Trials Design Course in 2016. Two years later, the Group initiated the second edition.

The main objective of the course is to train early-career investigators in the methodology needed to be able to develop innovative clinical trials that meet high quality standards. The small group of junior specialists (including oncologists, surgeons and radiologists) receive a combination of on-line theoretical training modules, together with personalised mentoring, as the size of the group facilitates close interaction. The intention is to generate direct, positive interactions between the expert mentors and trainees to maximise learning and skills development. By the end of the course, every participant will have designed his or her own clinical research project that can be carried out under the umbrella of GEICAM, benefitting from its infrastructure and experience.

The course lasts five months and includes various theoretical modules relevant for developing a study proposal, e.g., clinical trial design from phase I to phase IV, new approaches in design (basket, umbrella and adaptive trials, etc.), pharmacodynamics, pharmacokinetics, biomarker development, and statistics. The course also covers more practical issues, such as how to prepare a study budget or what to take into consideration from a legislative perspective to comply with international standards and local requirements. These modules, which will be evaluated and adapted as required, are available on an e-learning platform that trainees can access at their convenience. In addition, two face-to-face meetings are scheduled within the programme, at the beginning and at the end of the course. These meetings provide an important opportunity for the trainees and mentors to interact in a less formal networking environment. In the last session, the trainees present the research proposals to their peers and mentors to generate interactive, constructive discussion and feedback, which is useful for their final proposals.

Until now, 22 early-career investigators from different hospitals in Spain have enjoyed this course (with 11 trainees participating in the second edition). The 11 participants from the first edition evaluated this course with a score of 9.5 on a 10-point satisfaction scale.

GEICAM wants to strategically support such initiatives to help young investigators be well prepared to contribute to the development of high-quality research, with the ultimate aim to develop new diagnostic and therapeutic approaches for breast cancer patients in an effort to improve clinical outcomes and quality of life.
The #AyúdameInvestigar (#Helpmeinvestigate) campaign

In October 2018, during Breast Cancer Awareness Month, GEICAM launched the social and traditional media campaign #AyúdameInvestigar (which translates as “#HelpmeInvestigate”), with the dual goal of encouraging the participation of breast cancer patients in clinical trials and requesting support from public and private institutions for breast cancer academic research.

As Professor Miguel Martín, GEICAM President and Head of the Medical Oncology Service at Gregorio Marañón Hospital (Madrid, Spain), explains: “Society as a whole must be aware of the important role that clinical trials play in advancing knowledge and treatment of this disease, and patients need more information to learn about the possibilities of participating in clinical trials.”

The campaign tells the story of a woman from Gipuzkoa, Maite, who had breast cancer and decided to participate in a clinical trial. “For my own benefit and for those who will come after me: only science can contribute to our survival,” as she says in the campaign video.

#AyúdameInvestigar was supported by several well-known faces among Spanish celebrities, including television personalities, actresses and musicians.

In parallel, GEICAM carried out a national survey to evaluate the population’s knowledge and perceptions of clinical trials. The survey concluded that 56% of the respondents know that clinical trials assess the efficacy and safety of a treatment. By contrast, 16% think that they are carried out to investigate rare or terminal diseases only. Confusion was also perceived about who can participate in these studies: 12% believe that any patient who is willing to can participate, whereas 58% think that women at very high risk of developing breast cancer are eligible. Finally, 71% believe that both patients and former patients can participate.

“Clinical trials in oncology are generally performed in breast cancer patients who participate altruistically and must meet certain eligibility criteria detailed in the protocol,” explains Professor Martín.
The scientific activity of the **Italian Clinical Research Oncology Group (GOIRC)** in the BIG network has increased over the last two years thanks to active participation in BIG’s lead and co-lead trials as well as GOIRC’s constant frontline clinical research. GOIRC’s mission is to advance clinical research in several cancer types, as well as to promote independent, academia-driven studies amongst its affiliated centres.

In 2018 GOIRC’s structure underwent radical changes to be aligned with a more modern approach to research. These changes were strongly encouraged by current GOIRC President Dr Rodolfo Passalacqua. New members – not just oncologists but experts from all areas of medicine – have been joining GOIRC to increase its potential to design and launch new studies.

Novel trials have been conceived in different cancer settings and aim to answer everyday issues in the oncology practice. For example, a trial coordinated by the Policlinico Hospital of Modena will establish a national registry for the follow-up of breast cancer patients treated with palbociclib. For patients with hormone receptor-positive breast cancer exposed to the first CDK4/6 inhibitors in clinical practice, it is unclear which subsequent treatment they will receive and how they will respond. GOIRC will collect valuable information with the goal of optimising the sequence of therapies in this large subpopulation of patients.

For the neoadjuvant setting, GOIRC is designing a trial to evaluate the role of steroids in relation with immunotherapy and the potential of CDK4/6 inhibitors to treat breast cancers showing poor endocrine sensitivity.

With over ten international clinical trials ongoing, GOIRC is the main Italian interface between BIG and Italian clinical centres involved in breast cancer clinical research.
HKBOG

The Hong Kong Breast Oncology Group (HKBOG) is a formal platform with representatives from all the key opinion leaders in breast oncology from all the seven public cancer centres under the Hospital Authority as well as private oncology centres in Hong Kong, including both medical schools.

HKBOG was appointed by the “Best of SABCS” Head Office as the official exclusive presenter and organiser for the Best of SABCS Review, not only for 2018 but for many more years to come and exclusively for Hong Kong, Macau and the Grand Bay Area. We are so blessed and grateful with this new opportunity and further international recognition of the HKBOG, on top of our group being part of BIG. To facilitate better knowledge exchange among breast cancer experts in the field around the world, across regions and within local communities, and with the aim to enhance breast cancer care and research in Hong Kong, we hosted the ‘Best of SABCS 2018’ at the Sheraton Hong Kong. The event received considerable positive feedback.

The HKBOG was formally established during the Inauguration Ceremony and Scientific Meeting held on 15 February 2014, with guest of honour Professor Sophia Chan, the Under-Secretary of the Food & Health Bureau (FHB) at that time, now serving as FHB Secretary.

We hope that through this comprehensive platform, we can continue to contribute to breast cancer research and clinical and translational trial priorities, facilitate updates of local standard guidelines, and enhance knowledge exchange activities within the community! The HKBOG joined BIG in 2014, at that time being the third Asian member group just after Taiwan and Japan.

Over the last four years, we have conducted various formal scientific programmes and symposiums dedicated to healthcare professionals, from oncologists to general practitioners and paramedics; as well as workshops and knowledge exchange programmes intended for breast cancer patients, survivors and their family members and caregivers. We have also been leading various translational research programmes and general surveys among the general public and practicing oncologists.

WE ARE BLESSED AND DELIGHTED TO CELEBRATE OUR 5TH ANNIVERSARY IN 2019 AND LOOK FORWARD TO FURTHER ENHANCING BREAST CANCER CARE AND RESEARCH IN HONG KONG
The 23rd National Congress of the Italian Trials in Medical Oncology group (ITMO) took place on 25 May 2018. The aim was to organise an educational congress to underline the new frontiers in oncological medicine and the current evidence for everyday clinical practice. ITMO will organise another National Congress on 10 July 2019, where all the latest updates in the field of oncology will be discussed and shared.

ITMO is always on the frontline to cooperate with Italian and international research groups in order to follow the best path to find effective treatments for cancer. That is why it is dedicated to conducting clinical trials with the ultimate aim to beat cancer once and for all.

ITMO’s most recent publication is “Everolimus in combination with octreotide long-acting-repeateable in a first-line setting for patients with neuroendocrine tumours: a 5-years update”, published in Neuroendocrinology in 2018.
On 18-19 May 2018, the Korean Cancer Study Group (KCSG) held a meeting to celebrate its 20th anniversary and take a look back on its successes and achievements. Over the last two decades, KCSG not only has conducted many national multicentre clinical trials, but it has also reinforced its collaborative networking with government agencies, companies and medical associations involved in international clinical research.

The ceremony was particularly memorable because KCSG’s breast cancer committee officially joined the BIG network just on the cusp of its 20th anniversary.

Various articles on oncology, including breast cancer, have been published by KCSG. KCSG-BR07-02, for example, was a representative practice-changing trial in Korea, demonstrating the role of maintenance chemotherapy versus observation in patients with metastatic breast cancer who achieved disease control with an initial six cycles of paclitaxel plus gemcitabine chemotherapy (J Clin Oncol. 31:1732-9, 2013). The group was also involved in many meaningful and potentially practice-changing international trials such as ALITTO, Neo-ALITTO, NeoSphere, APHINITY, KRISTINE, CLEOPATRA, OlympiAD, OlympiA and PALOMA-2.

During the ceremony, invited speakers Drs. Dennis J. Slamon and Bruce J. Giantonio extended their congratulations to KCSG and gave the following talks respectively: 'Future global clinical trials perspective through TRIO experience' and 'ECOG-ACRIN perspective on clinical trials’. The 20th anniversary was also an opportunity for KCSG to present its new slogan “KCSG: Paving the way to a cancer-free world!”

### KCSG No | Title
--- | ---
KCSG-BR 11-06 | Randomised phase II study of lapatinib plus vinorelbine versus vinorelbine in patients with HER2 positive metastatic breast cancer progressed after lapatinib and trastuzumab treatment
KCSG BR 14-07 | Prospective cohort and analysis of clinical outcomes of patients with metastatic or recurrent breast cancer
KCSG BR 15-01 | A randomised, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboPlatin as (neo)adjuvant therapy in patients with EARLY triple-negative breast cancer (PEARLY)
KCSG BR 15-10 | A phase II randomised study of palbociclib in combination with exemestane plus GnRH agonist versus capecitabine in premenopausal women with hormone receptor-positive metastatic breast cancer
KCSG BR 15-17 | Randomised phase II trial of pemetrexed plus vinorelbine versus vinorelbine in patients with recurrent or metastatic breast cancer previously treated with or resistant to anthracycline and taxane
KCSG BR 16-09 | Clinical manifestation and prognosis in Korean male type breast cancer according to intrinsic subtypes, retrospective multicenter trial
KCSG BR 17-04 | Phase II trial of durvalumab and tremelimumab in the hormone receptor-positive, hyperMUTATed metastatic breast cancer identified by whole exOme sequencingN (MUTATIONIT)
NBCG

The Norwegian Breast Cancer Group (NBCG) is involved in supporting, facilitating and/or running multicentre trials in Norway. Some of these studies are run under the BIG umbrella, including the ALTTO and NeoALTTO trials (follow-up still ongoing), the Exceptional Responders Programme, and the POSITIVE study (Pregnancy Outcome and Safety of Interrupting Therapy for Women With Endocrine Responsive Breast Cancer). Fourteen patients from Norwegian sites had been included in POSITIVE by the end of 2018, and recruitment is still ongoing.

The NBCG was founded in 1988. Breast surgeons and breast oncologists from university clinics and the four Norwegian health regions form the core of the organisation. Surgeons and oncologists from selected other hospitals across the health regions are also represented, as well as two pathologists, two radiologists, one geneticist and a plastic surgeon. The steering committee consists of 30 members who elect an executive committee (EC) of 5 persons. The latter is responsible for bringing topics for discussion to the steering committee and executing the decisions taken. The EC also coordinates research and manages NBCG on a day-to-day basis.

NBCG’s steering committee meets at least biannually, whereas the EC holds additional regular meetings throughout the year. Several working groups (surgical, medical oncology, radiotherapy, and pathology) have been established to draft recommendations and facilitate the work and discussion in NBCG concerning treatment, diagnostics and research. The NBCG organises a national breast cancer meeting twice yearly, which focuses on both clinical updates and research issues. The group is also responsible for writing and updating the national guidelines for breast cancer, which are published by the Norwegian Directorate of Health and revised once or twice per year. Furthermore, the NBCG has played a key role in establishing the National Breast Cancer Quality Registry – both as initiator, planner and author – in close collaboration with the Cancer Registry of Norway. This registry can now be used to monitor the quality of breast cancer diagnosis and treatment in Norway, to run decision-impact studies, and to provide clinicopathological data to clinical and translational studies.

Beyond participating in BIG trials, NBCG has focused on breast cancer research in several other ways. Studies have been conducted for which NBCG was the initiator and served as executive board. Over the years, more and more key clinical scientists (many of them members of the NBCG) have presented trial ideas or protocol drafts to NBCG. This is followed by a collaborative discussion and frequently leads to trial-initiation and execution. NBCG’s involvement in most of these studies has been instrumental to achieving participation from hospitals all over the country, securing both successful recruitment and access to clinical trials for patients. All new clinical trial proposals (either investigator-initiated or industry-sponsored, irrespective of being suitable as an NBCG study) are presented during steering committee meetings.

The NBCG therefore plays a major role in breast cancer research conducted in Norway. It provides the forum through which investigators can be informed about and discuss new studies; it also facilitates the initiation of these studies and provides various forms of support, both for Norwegian breast cancer studies in general, and for the active conduct of its own studies.
Despite the size of the country (nearly 600,000 inhabitants) and the availability of high quality technological platforms, centralisation and harmonisation efforts have only been recently introduced in cancer care in Luxembourg. Indeed, national health policies were initiated in 2014 through an ambitious “Plan Cancer” and the continuation of this process is now further supported by the recently created Institut National du Cancer (INC). This entity has just launched an accreditation programme for all breast cancer units in the country.

In the research arena, professionalisation of research activities has been achieved by establishing the Luxembourg Institute of Health, a public biomedical research organisation that includes an oncology department. It has allowed oncologists from the Société Luxembourgeoise d’Oncologie (SLO) to develop local projects (both fundamental and clinical) in the field of breast cancer research, including the following:

- Actin cytoskeleton remodeling drives breast cancer cell escape from natural killer-mediated cytotoxicity (published by Al Absi, Cancer Research. Aug. 2018);
- Biobanking of blood, breast tissue and tumour in Luxembourg: a pilot study (3B) in collaboration with IBBL integrative Biobanking Luxembourg (ongoing);
- “E-dherence”: importance of oral therapy adherence in breast cancer survivorship - E-health as a new intervention tool (ongoing);
- MIPAClux: feasibility and effectiveness of motivational interviews to alter behaviour of breast cancer patients with regard to physical activity: a randomised study (paper submitted as of late 2018).

In the clinical arena, centralising breast cancer care in a few breast units has enabled SLO members to develop specific structures like the “integrative oncology centre” dedicated to women with breast cancer. This centre will start its activities in 2019, offering patients non-drug therapies integrated into the classic hospital-based cancer journey: acupuncture, mindfulness, yoga, sports coaching, and weight control programmes, among others.

However, international research collaboration is even more crucial for SLO than for any larger country: the group is happy and proud to be one of BIG’s 59 members and to be able to actively recruit patients into the ongoing AURORA programme, BIG’s large international initiative dedicated to improving our understanding of metastatic breast cancer.
## BIG TRIALS

Overview of the clinical studies run within the BIG network in 2018

Open, recruiting patients

<table>
<thead>
<tr>
<th>Study name</th>
<th>BIG number</th>
<th>Short description</th>
<th>Principal investigator(s)</th>
<th>Trial model &amp; partners</th>
</tr>
</thead>
</table>
| 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 | Lead trial  
(Co)-Leading partners: BIG HQ / UB-CTSU, FSTRF and AFT  
Pharma partner: Roche/Genentech (sponsor)  
Funding: Roche / Genentech |
| 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) / UB-CTSU (BrEAST) / FSS  
Pharma partner: N/A  
Funding: BCRF, Fondation Cancer, NIF Trust, the National Lottery (Belgium), 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: BCRF, 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. Irthum (coordinator)  | BIG-sponsored programme  
(Co)-Leading partner: BIG HQ  
Pharma partner: N/A  
Funding: BCRF |
| EXPERT                                         | 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 breast cancer - NCT02889874 | B. Chua  | Co-lead trial  
(Co)-Leading partners: BCT-ANZ (sponsor) and BIG HQ  
Pharma partner: N/A  
Funding: BCRF, 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 - NCT01001425 | F. Cardoso, S. Giordano  | Supporter programme  
(Co)-Leading partners: EORTC (sponsor) / NABCG (US)  
Pharma partner: N/A  
Funding: BCRF |
| 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 CoLlaborative 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. Giunti, A. DeMichele  | Co-Lead trial  
Coordinating groups: ABCSG (RoW) / AFT (US) (sponsors)  
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 Ballet-Latour, national and local funding bodies, individual donors |
| PYTHIA                                         | BIG 14-04  | Palbociclib plus fulvestrant for pretreated patients with ER+/HER2-negative metastatic breast cancer - NCT02536742 | L. Malorni  | Co-lead trial  
(Co-Leading partners: IBCSG (sponsor) and BIG HQ  
Pharma partner: Pfizer  
Funding: Pfizer grant |
| ULTIMATE                                       | BIG 16-01  | Immunotherapy combined with standard endocrine therapy as neoadjuvant treatment for women with ER+/HER-negative breast cancer - NCT02997995 | F. André, A. Prat  | Co-lead trial  
(Co-Leading partners: UCBG (sponsor) and BIG HQ  
Pharma partner: Astrazeneca  
Funding: Astrazeneca grant |
## Follow-up or post-study activities

**Table:**

<table>
<thead>
<tr>
<th>Study name</th>
<th>BIG number</th>
<th>Short description</th>
<th>Principal Investigator(s)</th>
<th>Trial model &amp; partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTTO</td>
<td>BIG 2-06</td>
<td>Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation: sequence and/or combination for patients with HER2/erbB2 positive primary breast cancer - NCT00970199</td>
<td>M. Piccart A. Maroño-Aspila</td>
<td>Lead trial - (Co)-Leading partners: BIG HQ / BCS (Euro-BrASt) / FSTRF / Alliance (former NCCTG) / Pharma partner: Novartis global sponsor for all countries with the exception of USA where NCI is the sponsor - Funding: GSK (past) / Novartis</td>
</tr>
<tr>
<td>APHINITY</td>
<td>BIG 4-11</td>
<td>Comparison of single-versus dual-anti HER2 therapy (trastuzumab, pertuzumab) for patients with HER2-positive primary breast cancer - NCT01558677</td>
<td>M. Piccart S. Loli J. Bines</td>
<td>Lead trial - (Co)-Leading partners: BIG HQ / BCS (Euro-BrASt) / FSTRF - Pharma partner: Roche (sponsor) - Funding: Roche</td>
</tr>
<tr>
<td>AZURE</td>
<td>BIG 1-04</td>
<td>Does Adjuvant Zoledronic acid reduce Recurrence in patients with high-risk, localised breast cancer? - NCT00702200</td>
<td>R. Coleman</td>
<td>Supporter trial - (Co)-Leading partner: IBCSG (sponsor) - Pharma partner: Novartis - Funding: Novartis</td>
</tr>
<tr>
<td>BIG 1-98</td>
<td>BIG 1-98</td>
<td>Letrozole as adjuvant endocrine therapy for postmenopausal women with receptor positive tumours - NCT00042005</td>
<td>B. Thürlimann</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Novartis - Funding: Novartis</td>
</tr>
<tr>
<td>BRAVO</td>
<td>BIG 5-13</td>
<td>Niraparib for patients with HER2-negative, germinal BRCA mutation-positive, locally advanced or metastatic breast cancer - NCT01905592</td>
<td>N. Turner J. Balmaña D. Cameron J. Eiben</td>
<td>Co-lead trial - (Co)-Leading partners: EORTC / BIG HQ Pharma partner: Tesaro (sponsor) - Funding: Tesaro</td>
</tr>
<tr>
<td>CALOR</td>
<td>BIG 1-02</td>
<td>A randomised clinical trial of adjuvant chemotherapy for radically resected loco-regional relapse of breast cancer - NCT01047912</td>
<td>S. Aebi I. Wapnir</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: N/A - Funding: BCSG</td>
</tr>
<tr>
<td>DCIS</td>
<td>BIG 3-07</td>
<td>Radiation doses and fractionation schedules for women with DCIS - NCT00470236</td>
<td>B. Chua</td>
<td>Supporter trial - (Co)-Leading partner: TROG (sponsor) - Pharma partner: N/A - Funding: National Health &amp; Medical Research Council Project Grant, Susan G. Koman</td>
</tr>
<tr>
<td>FINESE</td>
<td>BIG 2-13</td>
<td>Oral lutein for patients with FGFR1/erb1 metastatic breast cancer - NCT00536356</td>
<td>F. André J. Cortés</td>
<td>Lead trial - (Co)-Leading partners: BIG HQ / BCS / FSTRF - Pharma partner: Server (sponsor) - Funding: Server</td>
</tr>
<tr>
<td>IBIS-II</td>
<td>BIG 5-02</td>
<td>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 - NCT00724626</td>
<td>J. Cuzick</td>
<td>Supporter trial - (Co)-Leading partner: BIS - Pharma partner: AstraZeneca - Sponsor: Queen Mary University of London - Funding: Cancer Research UK, Queen Mary University of London</td>
</tr>
<tr>
<td>LORELI</td>
<td>BIG 3-13</td>
<td>Different regimens of letrozole (or letrozole + taselisib) in postmenopausal women with ER positive/HER2-negative, early stage breast cancer - NCT02273973</td>
<td>C. Saura E. de Azambuja</td>
<td>Co-lead trial - (Co)-Leading partners: ABCSG, SOLT and BIG HQ Pharma partner: Genentech (sponsor) - Funding: Genentech</td>
</tr>
<tr>
<td>MA.32</td>
<td>BIG 5-11</td>
<td>Effect of metformin on recurrence and survival in early stage breast cancer - NCT01043483</td>
<td>P. J. Goodwin</td>
<td>Supporter trial - (Co)-Leading partner: CCTG (sponsor) - Pharma partner: Apexon - Funding: NCI/NIH grants, Cancer Research UK, Canadian Cancer Society, BCFR and Canadian Breast Cancer Foundation</td>
</tr>
<tr>
<td>INDACT</td>
<td>BIG 3-04</td>
<td>Can addition of 7-gene signature to common clinical-pathological criteria safely spare patients with 0 to 3 node positive breast cancer from adjuvant chemotherapy? - NCT00435589</td>
<td>E. Rutgers F. Carod-Arbois M. Piccart</td>
<td>Co-lead trial - (Co)-Leading partners: EORTC (sponsor) / BIG HQ Commercial partners: Roche, Sanofi, Novartis and Agenda Funding: European Commission, Roche, Sanofi and Novartis grants, BCRF, Susan G. Koman for the Cure, Cancer Research UK, EORTC Charitable Trust, numerous national cancer societies and many other charitable grants*</td>
</tr>
<tr>
<td>NEO-AL-</td>
<td>BIG 1-06</td>
<td>Comparison of dual HER2 inhibition (lapatinib, trastuzumab plus chemotherapy before surgery versus single HER2-targeted therapy - NCT00533558</td>
<td>P. Nucifora J. Huber</td>
<td>Co-lead trial - (Co)-Leading partners: IBB-CTSU (BEAST) / SSDI / SOLT / BIG HQ - Pharma partner: Novartis (sponsor) - Funding: GSK (past) / Novartis</td>
</tr>
<tr>
<td>TTO</td>
<td>BIG 4-13</td>
<td>Anti-PD-1 monoclonal antibody in AdviCed, trastuzumab-resistant, HER2-positive breast cancer - NCT0229556</td>
<td>S. Loi F. André</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Merck - Funding: Merck grant</td>
</tr>
<tr>
<td>PENELO-</td>
<td>BIG 1-13</td>
<td>Post-neoadjuvant palbociclib for patients with HR+, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy - NCT01647476</td>
<td>G. van Minckwitz</td>
<td>Supporter trial - (Co)-Leading partner: GBG (sponsor) - Pharma partner: Pfizer - Funding: Pfizer grant</td>
</tr>
<tr>
<td>REACT</td>
<td>BIG 1-03</td>
<td>Randomised European Cli boasted trial: placebo versus placebos in primary breast cancer patients - NCT02492427</td>
<td>C. R. Coombs G. van Minckwitz</td>
<td>Supporter trial - (Co)-Leading partner: ICGC (sponsor) / GBG Pharma partner: Pfizer - Funding: Pfizer grant, Cancer Research UK, ECMC, GBG, Imperial College London and NCIIRN</td>
</tr>
<tr>
<td>SNAPP</td>
<td>BIG 2-12</td>
<td>Schedules of nab-Paclitaxel: evaluation of different schedules of nab-paclitaxel for metastatic breast cancer - NCT00746225</td>
<td>A. Gennari G. Jerusalem</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Celgene - Funding: Celgene grant</td>
</tr>
<tr>
<td>SOFT</td>
<td>BIG 2-02</td>
<td>Evaluation of ovarian suppression and of exemestane as adjuvant therapy for premenopausal women with endocrine responsive breast cancer - NCT00966888</td>
<td>P. Francis G. Fleming</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Pfizer - Funding: Grant support from Pfizer, Ipsen, US, NCI, BCISG and many participating collaborative academic groups, BCRF, as well as various charities</td>
</tr>
<tr>
<td>SOLD</td>
<td>BIG 1-10</td>
<td>The Synergism Of Long Duration (SOLD) Study: short 19 weeks versus long 11 year treatment of early HER2-positive breast cancer with trastuzumab - NCT00536967</td>
<td>H. Joensuu</td>
<td>Supporter trial - (Co)-Leading partner: FBCG (sponsor) - Pharma partner: Roche - Funding: Pharmmac/NZ, Saoani-Aventis and Novartis grants</td>
</tr>
<tr>
<td>SOLE</td>
<td>BIG 1-07</td>
<td>Study Of Letrozole Extension: continuous versus intermittent letrozole following endocrine treatment for postmenopausal women disease-free of HR+, node-positive early stage breast cancer - NCT00535410</td>
<td>M. Colleoni P. Karlson S. Aebi J. Chergwin</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Novartis - Funding: Novartis grant</td>
</tr>
<tr>
<td>SUPREMO</td>
<td>BIG 2-04</td>
<td>Selective Use of Postoperative Radiotherapy ARF to Prevent Ovarian Metastases in women with HER2-positive breast cancer - NCT00966888</td>
<td>I. Kunzler P. Conway</td>
<td>Supporter trial - (Co)-Leading partner: SCTRBC - Sponsor: UK Medical Research Council Project Grant, Pharma partner: N/A - Funding: UK Medical Research Council, EORTC, Cancer Australia, William and Elizabeth Davies Charitable Trust, Peter Chan Jay Yai Foundation, Young Ying Yin and Way Young Foundation</td>
</tr>
<tr>
<td>TEXT</td>
<td>BIG 3-02</td>
<td>Tamoxifen and Exemestane Trial: evaluation of exemestane plus GnRH analogue for premenopausal women with endocrine responsive breast cancer - NCT00066703</td>
<td>O. Pagani B. Walley</td>
<td>Supporter trial - (Co)-Leading partner: BCSG (sponsor) - Pharma partner: Pfizer - Funding: Grant support from Pfizer, Ipsen, US, NCI, BCISG and many participating collaborative academic groups, BCRF, as well as various charities</td>
</tr>
<tr>
<td>TREAT CTC</td>
<td>BIG 1-12</td>
<td>Trastuzumab treatment for HER2-negative early breast cancer in the presence of circulating tumour cells (CTC) - NCT01548677</td>
<td>M. Ignatias M. Piccart J. Y Piaggio</td>
<td>Supporter trial - (Co)-Leading partner: EORTC (sponsor) - Pharma partner: Roche - Funding: Roche grant</td>
</tr>
</tbody>
</table>

* full information available on the BIG website  
NB: This table does not include the trials in development and the closed trials. For more information, please visit: www.BIGegancerbia.org
• Association of p27 and Cyclin D1 Expression and Benefit from Adjuvant Trastuzumab Treatment in HER2-Positive Early Breast Cancer: A TransHERA Study Filipin M. et al., Clin Cancer Res. 2018 July 1, doi: 10.1158/1078-0432.CCR-17-3473. (BIG 1-01 HERA)


• A RB-1 loss of function gene-signature (RBSig) as a tool to predict response to neoadjuvant chemotherapy (CT) plus anti-HER2 agents (H): A substudy of the NeoALTTO trial (BIG 1-06), Rui E. et al., Journal of Clinical Oncology 20 May 2018, doi: 10.1200/JCO.2018.36.15_suppl.577 Journal of Clinical Oncology 36, no. 15_suppl (May 2018) 577-577. (BIG 1-06 NeoALTTO)

• Cardiac biomarkers for early detection and prediction of trastuzumab and/or lapatinib-induced cardiotoxicity in patients with HER2-positive early-stage breast cancer: a NeoALTTO substudy (BIG 1-06), Ponde N. et al., Breast Cancer Res Treat. 2018 Apr, doi: 10.1007/s10549-017-4628-3. (BIG 1-06 NeoALTTO)

• Circulating tumor DNA in HER2 amplified breast cancer: A translational research substudy of the NeoALTTO phase 3 trial, Ignatiadis M. et al., Cancer Research February 2018, doi: 10.1158/1538-7445.SABCS17-PD3-03. (BIG 1-06 NeoALTTO)

• Deregulation of A-to-I RNA editing is associated with poor prognosis in HER2+ breast cancers in the NeoALTTO trial. Venet D. et al., Cancer Research February 2018, doi: 10.1158/1538-7445.SABCS17-PD3-05-04. (BIG 1-06 NeoALTTO)

• Identifying clinically relevant subgroups of women with HER2-positive breast cancer: An analysis of Neo-ALTTO using the 41-gene TRAR score. En Cosimo S. et al., Cancer Research February 2018, doi: 10.1158/1538-7445.SABCS17-PD3-04-03. (BIG 1-06 NeoALTTO)

• Low levels of HER2 extracellular domain (ECD) compared to intracellular domain (ICD) in NeoALTTO may segregate benefit from lapatinib and trastuzumab in breast cancer. Rimm D.L. et al., Cancer Research February 2018, doi: 10.1158/1538-7445.SABCS17-PD3-09-09. (BIG 1-06 NeoALTTO)

• T-cell receptor beta chain variable region (TRBV) expression patterns predict response to combined trastuzumab/lapatinib treatment in the NeoALTTO/BIG-1-06 trial. Powles R. et al., Cancer Research doi: 10.1158/1538-7445.SABCS17-PD3-09-01. (BIG 1-06 NeoALTTO)

• The use of breast imaging for predicting response to neoadjuvant lapatinib-trastuzumab (T) and/or trastuzumab in HER2-positive breast cancer: Results from Neo-ALTTO. Di Cosimo S. et al., Eur J Cancer 2018 Jan, doi: 10.1016/j.ejca.2017.10.056. (BIG 1-06 NeoALTTO)


• Characterisation of the HLA-DRB1*07:01 biomarker for lapatinib-induced liver toxicity during treatment of early-stage breast cancer patients with lapatinib in combination with trastuzumab and/or taxanes. Spragg C.F. et al., Pharmacogenomics J 2018 May 22, doi: 10.1007/s12967-018-0471-0. (BIG 2-06 Male BC)


• Impact of body mass index (BMI) and weight change after treatment in patients (pts) with HER2-positive (HER2+) early breast cancer (EBC): Secondary analysis of the ALTTO BIG 2-06 trial. Marrel S. et al., Journal of Clinical Oncology May 20 2018, doi: 10.1200/JCO.2018.36.15_suppl.1006 Journal of Clinical Oncology 36, no. 15_suppl (May 2018) 10065-10065. (BIG 1-06 NeoALTTO & BIG 2-06 ALTTO)


## BIG BALANCE SHEET

### ASSETS

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fixed Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible fixed assets</td>
<td>2,952</td>
<td>5,904</td>
</tr>
<tr>
<td>Tangible fixed assets</td>
<td>175,331</td>
<td>194,757</td>
</tr>
<tr>
<td>Financial fixed assets</td>
<td>137,769</td>
<td>147,477</td>
</tr>
<tr>
<td><strong>Total Fixed Assets</strong></td>
<td>316,052</td>
<td>348,138</td>
</tr>
<tr>
<td><strong>Current Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receivables up to one year</td>
<td>14,831,225</td>
<td>8,858,530</td>
</tr>
<tr>
<td>Current investments</td>
<td>64,336</td>
<td>534,901</td>
</tr>
<tr>
<td>Cash at bank</td>
<td>8,422,909</td>
<td>8,034,099</td>
</tr>
<tr>
<td>Deferred charges and accrued income</td>
<td>655,376</td>
<td>390,657</td>
</tr>
<tr>
<td><strong>Total Current Assets</strong></td>
<td>23,973,847</td>
<td>17,818,187</td>
</tr>
<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>24,289,899</td>
<td>18,166,325</td>
</tr>
</tbody>
</table>

### LIABILITIES

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Equity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrestricted net assets</td>
<td>1,073,155</td>
<td>5,002,714</td>
</tr>
<tr>
<td>Restricted net assets</td>
<td>3,891,624</td>
<td></td>
</tr>
<tr>
<td><strong>Total Equity</strong></td>
<td>4,964,779</td>
<td>5,002,714</td>
</tr>
<tr>
<td><strong>Debts</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amounts payable after more than one year</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Amounts payable within one year</td>
<td>19,324,818</td>
<td>13,131,681</td>
</tr>
<tr>
<td>Current portion of amounts payable after more than one year falling due within one year</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt; Trade debts</td>
<td>19,027,763</td>
<td>12,778,395</td>
</tr>
<tr>
<td>&gt; Tax, remuneration and social security</td>
<td>297,054</td>
<td>353,286</td>
</tr>
<tr>
<td>Deferred charges and accrued income</td>
<td>302</td>
<td>31,930</td>
</tr>
<tr>
<td><strong>Total Debts</strong></td>
<td>19,325,120</td>
<td>13,163,612</td>
</tr>
<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>24,289,899</td>
<td>18,166,325</td>
</tr>
</tbody>
</table>

### INCOME & EXPENSES STATEMENT

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operating Income &amp; Expenses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turnover (research)</td>
<td>14,218,053</td>
<td>20,903,057</td>
</tr>
<tr>
<td>Other goods &amp; services</td>
<td>-11,434,687</td>
<td>-18,632,682</td>
</tr>
<tr>
<td><strong>Operating margin</strong></td>
<td>2,783,367</td>
<td>2,270,375</td>
</tr>
<tr>
<td>Remuneration, social security &amp; pension costs</td>
<td>-2,952,007</td>
<td>-2,784,181</td>
</tr>
<tr>
<td><strong>Operating result</strong></td>
<td>-168,641</td>
<td>-513,807</td>
</tr>
<tr>
<td>Financial result</td>
<td>170,314</td>
<td>31,841</td>
</tr>
<tr>
<td>Extraordinary income (+)</td>
<td>-39,016</td>
<td>0</td>
</tr>
<tr>
<td>Extraordinary expenses (-)</td>
<td>-592</td>
<td>-8,870</td>
</tr>
<tr>
<td><strong>Result for the financial year</strong></td>
<td>-37,935</td>
<td>-490,835</td>
</tr>
</tbody>
</table>

Between 2012 and 2018, we invested over $97,000,000 € in breast cancer research, making a huge difference in the lives of patients.
A SPECIAL THANK YOU

Mr Stéphane Henrard
Count and Countess Tanguy de Villegas de Saint Pierre Jette
Mr and Mrs Bernard and Marie-Noëlle Amory
Mrs Françoise Montfort
Mrs Véronique Paulus de Châtelet
Mr Patrick Simon
Mrs Marianne Fraeys
Mr and Mrs Alain De Pauw
Mr Philippe de Spirlet
Mr and Mrs Cédric Grandjean
Count and Countess Eric d’Humilly de Chevilly
Mr and Mrs Xavier Deleval
Baroness Hubinont
Mr and Mrs Alain et Cristina Camu
Mr and Mrs Jean-Philippe et Alix Hubin
Mrs Reem Boustany
Mrs Louise Descamps
Mr Jean-Pierre Maurice
Mr and Mrs Daniel and Nicole Lebard
Mrs Chantal Beineix-Gillion
Mrs Maae Juengers
Mr and Mrs Amaury de Sèze
Mrs Tatiana Cornet de Ways-Ruart
Mr and Mrs Hubert and Tinou d’Ansembourg
Mr Daniel Abelew (Bouvy)
Mrs Maïté Relcom
Mrs Levke King
Baron and Baroness Brotchi
Mrs Marie-Thérèse de Liedekerke
Mr and Mrs Marc and Judith Decorte
Mr and Mrs Loïc Waucquez

B Blue Beachouses - Itacimirim Bahia Brésil –
Mr Bernard Welbes
Mr and Mrs David and Lina Lebard
Marquis and Marquess de Chaumont-Quitry
Baron and Baroness Rodolphe van der Straten Waillet
Baron Charles-Albert Snoy
Mr Walter De Toffol
Mr and Mrs François de Hennin
Mr Xavier Smekens and Miss Laure Smekens
Mr and Mrs Thomas Spiller
Mr and Mrs Cédric Pelgrims de Bigard
Mr and Mrs Pierre Kuborn
Mrs Céline Frémault, Ministre bruxelloise
Mr and Mrs Jacques Berrebi
Mr and Mrs Andy Wyckmans
Baron and Baroness Thomas de Mevius
Prince and Princess de Merode
Mr and Mrs Nissim Israël
Mr and Mrs Erol Kandiyoti
Mr and Mrs Thierry Misson
Mrs Jessica Parser and Mr François Gérard
Mr and Mrs Vladimir Cardon de Lichtbuer
Mrs Patrick Sylvia Chiche
Mrs Evelyn Gessler
Baron and Baroness Gillion Crowet
HE Ambassador and Mrs Juan Prat Y Coll
Mr and Mrs Xavier Roland
Baron and Baroness Raymond Vaxelaire
Mr Frédéric Van der Schueren
Baron Marc de Villenfagne de Vogelsanck

FOUNDATIONS

BCRF
Fondation Cancer
Fonds Ballet Latour
Foundation KIABI
Loterie Nationale Loterie
Colophon

MANAGING EDITORS:
CAROLYN STRAHELE
ORIANA SPAGNOLO
VALERIE VAN DER VEEKEN
GIA QUESTIAUX
SERGE SCHMITZ
CAIT CAMERON

DESIGNED BY:
VANDEN BROELE
PHOTOS @ SHUTTERSTOCK

THE OPINIONS OR CONCLUSIONS STATED OR IMPLIED IN THE ARTICLES HEREIN ARE THOSE OF THE AUTHORS AND DO NOT NECESSARILY REFLECT THOSE OF THE PUBLISHER.

BIG HEADQUARTERS’ CONTACT ADDRESS:
BREAST INTERNATIONAL GROUP (BIG)-AISBL
BLVD DE WATERLOO 76
1000 BRUSSELS, BELGIUM
TEL.: +32 2 486 16 00

VAT: BE 0468 176 240

E-MAIL: INFO@BIGAGAINSTBC.ORG
WWW.BIGAGAINSTBREASTCANCER.ORG

COPYRIGHT 2019
BREAST INTERNATIONAL GROUP
ALL RIGHTS RESERVED
TOGETHER, we have the opportunity to make a real difference in patients’ lives, both today and in the future.

SUPPORT BIG:
IBAN BE08 0689 0916 0213
(communication: BIG Spreading Hope)

OR DONATE ONLINE:
www.BIGagainstbreastcancer.org/donate

#BIGAGAINSTBC
WWW.BIGAGAINSTBREASTCANCER.ORG

FOLLOW US ON
@BIGagainstbreastcancer  @BIGagainstBC  BIG against breast cancer