Together we will find a cure for breast cancer.
About BIG

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

The BIG network unites 55 groups and reaches across more than 50 countries and 6 continents. 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 the international level. We are proud to be both global AND local, helping breast cancer patients from all over the world.

www.BIGagainstbreastcancer.org
15 years of collaboration

Since founding BIG in 1999 after our first exchange of ideas, 15 years have passed. 15 years of collaboration to move breast cancer research forward while reducing duplication of effort. Moving more globally, more rapidly and more innovatively towards better treatments and finding cures.

We are delighted to celebrate this 15th anniversary year with you: members, partners, supporters and donors. Everything that we achieved during the last decade and a half was possible because we did it TOGETHER.

Together, we have run landmark trials with a real impact on patients’ lives.

Together, we have changed practice in the treatment of women and men affected by breast cancer.

Together, with the breakthrough technologies at our disposal and considering recent findings about the molecular complexity and heterogeneity of breast cancer, we are able to conduct the most innovative research.

Together, we are able to build close collaborations with our pharmaceutical partners, all the while following the same Principles of Research Conduct that are the pillars of our mission, safeguarding our patients’ interests and leading to highly credible results.

It is your collaboration and your support that has made all of this possible!

We now have an obligation to continue to join forces and succeed together in the future. We know we can continue to count on the strong collaborative spirit among researchers around the world and on your support to achieve our common vision: find a cure for breast cancer.

We will not stop our efforts. Patients need us. And we need all of you to achieve even more in the next fifteen years.

Prof Martine Piccart-Gebhart
BIG Chair

Prof Aron Goldhirsch
BIG Vice-Chair

BIG Executive Board 2014-2018
Front, from left to right: Sibylle Loibl, Michael Gnant (Treasurer), Martine Piccart (Chair), Angelo Di Leo, Karen Gelmon
Back, from left to right: David Cameron, José Baselga, Fabrice André
Absent: Aron Goldhirsch (Co-chair)
In 2014, BiG launched new studies that represent the next generation of breast cancer research, and delivered results that changed clinical practice to better serve patients.

Together, BiG researchers, patients and supporters made real progress in identifying the needs of women and men with breast cancer and improving their treatments. This year was a culmination of 15 years of collaboration and, together, we can accomplish even more.
SOFT  
(Suppression of Ovarian Function Trial)

In 2014, researchers presented the results of the SOFT clinical trial, conducted by the International Breast Cancer Study Group (IBSCG) under the BIG umbrella, at two major global oncology conferences: the American Society of Clinical Oncology (ASCO) Annual Meeting and the San Antonio Breast Cancer Symposium (SABCS). Results were also published online in the New England Journal of Medicine (nejm.org). The SOFT trial, along with its sister trial, TEXT, was cited in several articles* as the “year’s best” trial in a year of significant developments in breast cancer research.

The trial’s practice changing results indicated that for young women with early, hormone-sensitive breast cancer who remained pre-menopausal after chemotherapy, selective ovarian suppression reduces the risk of breast cancer recurrence. The drug tamoxifen has been the standard treatment after surgery for pre-menopausal women with hormone-sensitive breast cancer. However, the benefit of adding ovarian suppression to the tamoxifen treatment had been uncertain. SOFT showed that this group of women do benefit from adding ovarian suppression to tamoxifen, reducing the risk of recurrence by 22%, compared to tamoxifen alone.

Even better results were achieved by treating this group of women with a combination of ovarian suppression and exemestane, an aromatase inhibitor. In this arm of the randomized trial, the risk of disease recurrence was reduced by 35%, compared to tamoxifen alone, resulting in 7 or 8 fewer women out of 100 having a breast cancer recurrence within 5 years.

The benefit of adding ovarian suppression to tamoxifen was most pronounced in women younger than 35, an age group at particularly high risk of recurrence. This benefit was even greater with exemestane plus ovarian suppression: after 5 years, 1-in-6 women under age 35 receiving exemestane plus ovarian suppression experienced further breast cancer, compared to 1-in-3 under age 35 receiving tamoxifen alone.

“These results will change clinical practice,” said study co-chair Prudence Francis, M.D., Head of Breast Medical Oncology, Peter MacCallum Cancer Centre, Australia. “For the youngest women with hormone-sensitive breast cancer, ovarian suppression will increasingly be recommended. For women who have not reached menopause and have hormone-sensitive breast cancer that carries sufficient risk of recurrence to warrant chemotherapy, doctors are likely to discuss the option of treatment with ovarian suppression plus an aromatase inhibitor as an alternative to tamoxifen.”

* Sources:
Metastatic Breast Cancer GPS (scientific name: AURORA)

Just as a GPS guidance system helps you locate and avoid traffic problems, finding the best route to your destination, the GPS programme aims to identify breakdowns (genetic aberrations) and to map the routes that cancer cells take to invade other organs. Knowing this, we can stop them, or change their course by choosing the best possible route to treatment.

Using the latest technologies, the GPS programme aims to help us understand both why breast cancer spreads (metastasises) and why some metastases respond poorly to standard treatment, while others respond very well. Whenever possible, patients enrolled in the GPS programme will be offered the opportunity to participate in clinical trials testing new and promising drugs that target the specific genetic characteristics of their tumours. The hope is that the GPS programme will one day lead us both to better treatments and to cures for the women and men affected by metastatic disease.

This study was launched in the second quarter of 2014 and up to 80 hospitals in 14 countries will participate in the programme. AURORA is being conducted by BIG with the Breast European Adjuvant Study Team and Frontier Science Scotland. It is made possible in part by generous grants from the Breast Cancer Research Foundation®, the Fondation Cancer (Luxembourg), the National Lottery (Belgium), NIF Trust, and individual donors.

* Source:
  1) World Cancer Report 2014, Edited by Bernard W. Stewart and Christopher P. Wild, Published by the International Agency for Research on Cancer
BIG Time for Baby (scientific name: POSITIVE)

The BIG Time for Baby trial will evaluate the pregnancy outcomes and safety of interrupting endocrine therapy for young women with ER+ breast cancer who wish to become pregnant.

It represents a unique opportunity to allow young women with breast cancer to safely plan and become pregnant without waiting many years after completing their endocrine treatment.

It will also improve our scientific understanding of issues related to conception and pregnancy in young women who have had breast cancer by helping us obtain solid data. 59 breast cancer centres around the world are interested in participating in the study.

*Source: Pagani et al., BCRT 2011;129(2):309-17

BIG Annual Report 2014

“...It’s a good feeling being part of something global that will help science and help patients in the future.”

Sarah Jane, participant in the DCIS study

Finely Tuned Radiotherapy (scientific name: DCIS)

Ductal Carcinoma in Situ (DCIS) is the earliest form of breast cancer (stage 0) and the most common type of non-invasive breast cancer. DCIS is considered a growing health problem since the introduction of mammographic screening has substantially increased our ability to diagnose it. Today, up to 25% of screen-detected breast cancers are DCIS.

There is currently no best practice and no standard of care worldwide when it comes to DCIS.

This international study, involving over 1,600 patients in 11 countries, will tailor radiotherapy to minimise the risk of invasive cancer recurrence in high-risk patients while sparing unnecessary treatment toxicity in low-risk patients. An additional objective of the study is to enable physicians to discover predictive biomarkers that identify which patients are at low risk for recurrence and can be safely prescribed a lighter course of radiation treatment, with the same success in curing their DCIS, and which patients are at high risk for recurrence and require more intense therapy.

* Sources:

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

Up to 25% of screen-detected breast cancers are a non-invasive form called DCIS*
BIG scientists, staff and supporters came together in May 2014 to celebrate BIG’s 15th anniversary and raise funds for BIG against breast cancer. The event raised over 52,000 EUR to fund BIG research studies.

The 2nd edition of the “Sapins de Noël des Créateurs belges” raised 118,000 EUR for BIG against breast cancer. More than 30 designers participated in the second edition of the event, including Raf Simons, Diane von Fürstenberg, and special guest designer Stella McCartney.

Together we raised over 170,000 EUR during our BIG events.
Together we can do more

How to help, if you are a …

**Attend an event in 2015**

SAVE THE DATE!

- **20 September 2015**
  BIG Garden Party

- **10 October 2015**
  BIG-athlon
  A never-before-seen sporting and charity team challenge
  www.BIG-athlon.org

- **30 November 2015**
  Sapins de Noël des Créateurs belges

And more events to come: check www.BIGagainstbreastcancer.org/events

**Company / Organisation**

Set up a “Look and Feel” health workshop at your workplace
BIG staff can present our “Look and Feel” guide to your employees, to raise awareness of breast cancer and promote early detection, for the well-being of your colleagues and their families.

**Collector / Art Aficionado**

Attend the “Sapins de Noël des Créateurs belges” event in Belgium
You can support BIG by taking part in the auction of unique pieces created by internationally renowned designers.

Or host an event to donate an artwork from your own collection for auction to benefit BIG.

**Community Leader**

Introduce BIG to your personal or professional network
Or organise an event - you can support BIG against breast cancer by volunteering to host a meeting, dinner, or other type of party to raise awareness and funds for BIG.

**Breast Cancer Research Champion**

Make a donation
By making a tax-deductible donation to BIG, you directly support breast cancer research, enabling the discoveries needed to end breast cancer once and for all!
Together we celebrated BIG’s 15th anniversary

Top 15 moments in 2014

1. Awarded BCRF Grant (2.2 million USD)
2. Launched GPS Programme (AURORA)
3. Co-hosted IMPAKT conference
4. Celebrated 15th anniversary
5. Welcomed new BIG Executive Board members
6. Awarded Fondation Cancer (Luxembourg) Grant (1.3 million EUR)
7. Participated in 4 major breast cancer conferences
8. Connected with our members at General Assembly

9. Presented BIG trial results at major conferences

10. Partnered with Liberty Global

11. Exchanged ideas with Latin American BIG member groups

12. Crowdfunded research at the Schuman Festival

13. Raised funds at the Sapins de Noël des Créateurs belges

14. Launched BIG Time for Baby trial (POSITIVE)

15. Conducted world class research
Together we are stronger

BIG encompasses 55 member groups worldwide, which are breast cancer focused collaborative research groups or data centres.

Some BIG groups are regional, some are national and some are international. Each is associated with one to several hundred member hospitals and investigators. This represents thousands of institutions worldwide.
Together we welcomed 6 new research groups

Association de Recherche dans les Cancers dont Gynécologiques – Groupe d’Investigateurs Nationaux pour l’Étude des Cancers Ovariens et du sein (ARCAGY-GINECO)
Comprising more than 700 investigators, ARCAGY-GINECO was created in 1993. In particular, GINECO is a cooperative clinical trials group of clinicians dedicated to gynaecological cancer research and metastatic breast cancer research in France.
www.arcagy.org

Breast-Gynecological International Cancer Society (BGICS)
BGICS is a non-profit society aiming at promoting optimal standards of care for patients with breast gynaecological cancers. It represents a committee of international and national members from different disciplines. Its mission can be divided into three main categories: education, research, and patient support.
www.bgicc.eg.net

”ARCAGY-GINECO has many international connections in gynaecological oncology, but not in breast cancer. We hope to benefit from BIG’s international network to share experience and knowledge, participate in international phase III trials, and promote international phase III trials.”
Anne-Claire Hardy Bessard, Head of the GINECO breast working group and BIG voting representative

”Bringing worldwide breast cancer experts together adds to our dedication to foster the science of breast and gynecological oncology and improve the care of cancer patients and their families throughout the world. Our aim is to lessen the human suffering from cancer all over the world.”
Hesham Elghazaly, President of the BGICS and BIG voting representative

Société Luxembourgeoise d’Oncologie (SLO)
Founded in 1999 the SLO is a group made of medical oncologists and radiologists working in Luxembourg. The group aims to improve the treatment of cancer patients. SLO, in collaboration with the Fondation Luxembourgeoise Contre le Cancer, also acts in the field of cancer prevention.
www.slo.lu

”International collaboration makes it possible to conduct studies that would not be possible for our research group to carry out on its own, especially as treatments become increasingly targeted.”
Catherine Herremans, MD at Centre Hospitalier de Luxembourg and member of SLO
Fondazione Michelangelo (MICHELANGELO)

Originally launched by Gianni Bonadonna in 1993, when he convened a small group of Italian oncologists to cooperate in a non-randomized neoadjuvant study in early breast cancer, MICHELANGELO is now a non-profit organisation that proposes and coordinates multicentric prospective studies in various malignant tumours, including breast cancer.

www.fondazionemichelangelo.org

Hong Kong Breast Oncology Group (HKBOG)

Constituted in February 2014, the HKBOG is the first and foremost comprehensive collaborative group in Hong Kong, with representatives of all the key opinion leaders for breast oncology, including both clinical oncologists and medical oncologists.

HKBOG Founding Council Members believe that interactions with other regional and international collaborative research groups are crucial to help HKBOG to further enhance innovation and have a positive impact on breast cancer care and research in the best interests of our patients.”

Janice Tsang, Director of the Cancer Centre at Queen Mary Hospital and Founding Convenor of HKBOG and BIG voting representative

Fondazione Michelangelo (MICHELANGELO)

Originally launched by Gianni Bonadonna in 1993, when he convened a small group of Italian oncologists to cooperate in a non-randomized neoadjuvant study in early breast cancer, MICHELANGELO is now a non-profit organisation that proposes and coordinates multicentric prospective studies in various malignant tumours, including breast cancer.

www.fondazionemichelangelo.org

Israeli Breast Group (IBG)

The Israeli Breast Cancer Group (IBG) consists of medical oncologists and radiation therapists whose main clinical and basic research interest is breast cancer. We meet as a group up to 4 times a year, and hold additional educational activities as well. IBG also participates in the decision-making process around the introduction of new breast cancer medication for reimbursement in Israel. Recently we established a website for the group, including a central database of all breast cancer clinical trials that are active in Israel.

The global nature and burden of cancer necessitate multidisciplinary and multinational collaborations. Only through such collaborations, will we achieve the goal of understanding and controlling breast cancer. We look forward to taking part in BIG’s clinical trials and research programmes and helping to achieve these goals.”

Noa Efrat (Ben-Baruch), Head of the Department of Oncology at Kaplan Medical Center and BIG voting representative

MICHELANGELO joined BIG to avoid isolation in a time of major new advances in cancer medicine, a growing need for a collaborative academic effort in translational medicine, and growing challenges in the relationship between the academy and the industry.”

Luca Gianni, Director of the Department of Medical Oncology at San Raffaele Hospital - Scientific Institute

The global nature and burden of cancer necessitate multidisciplinary and multinational collaborations. Only through such collaborations, will we achieve the goal of understanding and controlling breast cancer. We look forward to taking part in BIG’s clinical trials and research programmes and helping to achieve these goals.”

Noa Efrat (Ben-Baruch), Head of the Department of Oncology at Kaplan Medical Center and BIG voting representative
Together we achieve more

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.

Collaborating through the largest international network of research groups

With a network of 55 academic research groups, covering over 50 countries from Canada to China, BIG is a leading force in the breast cancer research arena. BIG research groups are tied to thousands of hospitals and breast cancer specialists.

With today’s knowledge about breast cancer showing us that it is not one but multiple diseases, clinical trials cannot be limited to one single institution, or even to one country. Through the network structure of BIG, research groups make it possible to test new anticancer treatments in a truly effective way. Through the wide reach of the BIG network, and our strong partnerships with industry and other collaborators, we can quickly recruit patients and generate highly credible results. Such large-scale cooperation is crucial to making significant advances in breast cancer research.

BIG has GLOBAL reach

Ensuring high quality 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.

INTEGRATE project

The INTEGRATE project aimed to develop innovative infrastructures to enable data and knowledge sharing and to foster large-scale collaboration in biomedical research. Partially funded by the European Commission under the 7th Framework Programme, INTEGRATE was conducted by a Consortium of seven partners from different European countries, including: BIG, Custodix, German Breast Group (GBG), FORTH, Institut Jules Bordet, Philips, and Universidad Politécnica de Madrid (UPM). It ended last October 2014. A final review meeting was held mid-January 2015 to present the outcomes of the project to the European Commission.

IMPAKT Breast Cancer Conference

Co-chaired by Giuseppe Curigliano and Alastair Thompson, the 6th edition of the IMPAKT Breast Cancer Conference took place on 8 to 10 May 2014 in Brussels. On the occasion of BIG’s 15th anniversary, a special panel session was organised on how international collaboration can benefit young researchers. Early-career breast cancer specialists shared their own experience with international collaboration, explaining what have been the benefits, but also the challenges of working on international, collaborative research efforts and how they got involved with such projects.

* Consult BIG’s Mission and Principles of Research Conduct on www.BIGagainstbreastcancer.org
<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>AURORA (Metastatic Breast Cancer GPS)</td>
<td>BIG 14-01</td>
<td>The AURORA programme: Aiming to Understand the Molecular Aberrations in Metastatic Breast Cancer - NCT02102165</td>
<td>M. Piccart</td>
<td>Lead trial Coordinating groups: BIG (Sponsor) / BrEAST / FSS Pharma partner: N/A</td>
</tr>
<tr>
<td>POSITIVE (BIG time for Baby)</td>
<td>BIG 8-13</td>
<td>Endocrine therapy interruption to enable conception for young women with ER+ breast cancer - NCT02308085</td>
<td>O. Pagani</td>
<td>Supporter trial Coordinating group: IBCSG (sponsor) Pharma partner: N/A</td>
</tr>
<tr>
<td>OLYMPIA</td>
<td>BIG 6-13</td>
<td>Olaparib vs. placebo for patients with BRCA-mutated, high-risk HER2-negative breast cancer, having completed local treatment and (neo) adjuvant chemotherapy - NCT02032823</td>
<td>A. Tutt, B. Kauflman, J. Garber, C. Geyer</td>
<td>Lead trial Coordinating groups: BIG / FSTRF Pharma partner: AstraZeneca (sponsor)</td>
</tr>
<tr>
<td>BRAVO</td>
<td>BIG 5-13</td>
<td>Niraparib for patients with HER2-negative, germline BRCA mutation-positive, locally advanced or metastatic breast cancer - NCT01903392</td>
<td>N. Turner, J. Bolmanna, D. Cameron, W. Audeh</td>
<td>Co-lead trial Coordinating groups: EORTC / BIG Pharma partner: Merck</td>
</tr>
<tr>
<td>PANACEA</td>
<td>BIG 4-13</td>
<td>Anti-PD-1 monoclonal antibody in advanced, trastuzumab-resistant, HER2-positive metastatic breast cancer - NCT01639556</td>
<td>S. Loi, F. André</td>
<td>Supporter trial Coordinating group: IBCSG (sponsor) Pharma partner: N/A</td>
</tr>
<tr>
<td>LORELEI</td>
<td>BIG 3-13</td>
<td>Oral lactulamb for patients with FGFR1 ER+ metastatic breast cancer - NCT025553636</td>
<td>C. Sauro, E. de Azambuja</td>
<td>Co-lead trial Coordinating groups: ABCSG / SOLTI / BIG HQ Pharma partner: Genentech (sponsor)</td>
</tr>
<tr>
<td>FINESSE</td>
<td>BIG 2-13</td>
<td>Treatment for HER2-negative, early stage breast cancer with high relapse risk after neoadjuvant chemotherapy - NCT01684746</td>
<td>F. André, J. Corbés</td>
<td>Lead trial Coordinating groups: BIG HQ / BrEAST / FSS Pharma partner: Seriver (sponsor)</td>
</tr>
<tr>
<td>PENELOPE-B</td>
<td>BIG 1-13</td>
<td>Post-neoadjuvant palboclib for patients with hormone-receptor-positive, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy - NCT01864746</td>
<td>G. von Minckwitz</td>
<td>Supporter trial Coordinating group: GBG (sponsor) Pharma partner: Pfizer</td>
</tr>
<tr>
<td>SNAP</td>
<td>BIG 2-12</td>
<td>Evaluation of different schedules of nab-paclitaxel for metastatic breast cancer - NCT01746225</td>
<td>A. Gennari, G. Jerusalem</td>
<td>Supporter trial Coordinating group: IBCSG (sponsor) Pharma partner: Celgene</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 tumor cells (CTC) - NCT01548677’</td>
<td>M. Ignatadis, M. Piccart, M. Y. Pierga, B. Rock, C. Sotiriou</td>
<td>Supporter trial Coordinating group: EORTC (sponsor) Pharma partner: Roche</td>
</tr>
<tr>
<td>Neo-PHOEBE</td>
<td>BIG 6-11</td>
<td>Buparlisib for HER2-positive, PIK3CA wild-type and PIK3CA mutant primary breast cancer - NCT01816594</td>
<td>S. Loi, S. Loi</td>
<td>Co-lead trial Coordinating groups: GBG / SOLTI / BIG Pharma partner: Novartis (sponsor)</td>
</tr>
<tr>
<td>MA.32 Metformin</td>
<td>BIG 5-11</td>
<td>Effect of metformin on recurrence and survival in early stage breast cancer - NCT01001438</td>
<td>P. J. Goodwin</td>
<td>Supporter trial Coordinating group: NCIC (sponsor) Pharma partner: Apotex</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 - NCT01358877</td>
<td>G. von Minckwitz, M. Piccart, J. Baselga, J. Baines</td>
<td>Lead trial Coordinating groups: BIG / BrEAST / FSS Pharma partner: Roche (sponsor)</td>
</tr>
<tr>
<td>SOLD</td>
<td>BIG 1-10</td>
<td>Short (9 weeks) versus long (1 year) treatments of early HER2-positive breast cancer with trastuzumab - NCT00593697</td>
<td>H. Joensuu</td>
<td>Supporter trial Coordinating group: FBCG (sponsor) Pharma partner: N/A</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, I. A. Olivetta, T. J. Whelan, I. Kunkler, H. Westenberg, J. Jassem, R. Robinovitch</td>
<td>Supporter trial Coordinating group: TROG (sponsor) Pharma partner: N/A</td>
</tr>
<tr>
<td>Study Name</td>
<td>BIG number</td>
<td>Short description</td>
<td>Principal Investigator(s)</td>
<td>Trial model &amp; partners</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Male BC</td>
<td>BIG 2-07</td>
<td>Registration and biologic characterisation programme of breast cancer in men - NCT01010425</td>
<td>F. Cardoso S. Giordano</td>
<td>Supporter trial Coordinating groups: EORTC (sponsor) / NABC (US) Pharma partner: N/A</td>
</tr>
<tr>
<td>SOLE</td>
<td>BIG 1-07</td>
<td>Continuous versus intermittent letrozole following endocrine treatment for postmenopausal women disease-free of hormone-receptor-positive, node-positive early stage breast cancer - NCT00553410</td>
<td>M. Colleoni P. Karlsson  S. Aebi  J. Chughin</td>
<td>Supporter trial Coordinating trial: IBCSG (sponsor) Pharma partner: Novartis</td>
</tr>
<tr>
<td>ALTTO</td>
<td>BIG 2-06</td>
<td>Adjuvant lapatinib and trastuzumab: sequence and combination for patients with HER2/Erbb2 positive primary breast cancer - NCT00490139</td>
<td>M. Piccart E. Perez</td>
<td>Lead trial Coordinating groups: BIG / BrEAST / FSS / NCCTG (US) Pharma partner: GSK</td>
</tr>
<tr>
<td>NEO-ALTTO</td>
<td>BIG 1-06</td>
<td>Comparison of dual HER2 inhibition (lapatinib, trastuzumab) plus chemotherapy before surgery versus single HER2-targeted therapy - NCT00553358</td>
<td>J. Baselga H. Edtmann</td>
<td>Co-lead trial Coordinating groups: BrEAST / FSS / SOLTI / BIG Pharma partner: GSK (I)</td>
</tr>
<tr>
<td>MINDACT</td>
<td>BIG 3-04</td>
<td>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</td>
<td>E. Rutgers F. Cardoso M. Piccart</td>
<td>Co-lead trial Coordinating groups: EORTC (sponsor) / BIG Pharma partner: Roche, Sanofi, Novartis</td>
</tr>
<tr>
<td>SUPREMO</td>
<td>BIG 2-04</td>
<td>Adjuvant chest wall irradiation for 'intermediate risk' breast cancer following mastectomy - NCT00956888</td>
<td>J. Kunleer P. Canney</td>
<td>Supporter trial Coordinating group: SCTBG Sponsor: Medical Research Council Pharma partner: N/A</td>
</tr>
<tr>
<td>AZURE</td>
<td>BIG 1-04</td>
<td>Adjuvant zoledronic acid for patients with high-risk, localised breast cancer - NCT00072020</td>
<td>R. Coleman</td>
<td>Supporter trial Coordinating group: NCRi Pharma partner: Novartis Sponsor: University of Sheffield</td>
</tr>
<tr>
<td>Breast Cancer in Pregnancy</td>
<td>BIG 2-03</td>
<td>Registry of women treated for breast cancer while pregnant - NCT00194833</td>
<td>S. Loibl G. von Minckwitz</td>
<td>Supporter trial Coordinating group: GBG (sponsor) Pharma partner: N/A</td>
</tr>
<tr>
<td>REACT</td>
<td>BIG 1-03</td>
<td>Trial of celecoxib for patients with primary breast cancer - NCT02429427</td>
<td>C. Coombes J. Bliss G. von Minckwitz</td>
<td>Supporter trial Coordinating groups: ICG (I) / GBG Pharma partner: Pfizer</td>
</tr>
<tr>
<td>IBIS-II</td>
<td>BIG 5-02</td>
<td>Prevention study of anastrozole for postmenopausal women of increased risk of breast cancer, and of effects of tamoxifen vs. anastrozole in postmenopausal women with DCS - NCT00072462 - NCT00078832</td>
<td>J. Cusick</td>
<td>Supporter trial Coordinating group: IBIS (I) Pharma partner: AstraZeneca</td>
</tr>
<tr>
<td>TEXT</td>
<td>BIG 3-02</td>
<td>Evaluation of exemestane plus GnRH analogue as adjuvant therapy for premenopausal women with endocrine responsive breast cancer - NCT00963417</td>
<td>O. Pagan B. Walley</td>
<td>Supporter trial Coordinating group: IBCSG (I) Pharma partner: Pfizer</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 - NCT00066690</td>
<td>P. Francis G. Fleming</td>
<td>Supporter trial Coordinating group: IBCSG (I) Pharma partner: Pfizer</td>
</tr>
<tr>
<td>HERA</td>
<td>BIG 1-01</td>
<td>Comparison of different regimes of trastuzumab for women with HER2-positive primary breast cancer - NCT00045032</td>
<td>M. Piccart</td>
<td>Lead trial Coordinating groups: BIG / BrEAST / FSS Pharma partner: Roche (sponsor)</td>
</tr>
<tr>
<td>IBCSG 18-98</td>
<td>BIG 1-98</td>
<td>Letrozole as adjuvant endocrine therapy for postmenopausal women with receptor positive tumours - NCT0004205</td>
<td>B. Thürmann</td>
<td>Supporter trial Coordinating group: IBCSG (I) Pharma partner: Novartis</td>
</tr>
</tbody>
</table>

**Study status in 2014:**
- Open, recruiting patients
- In follow up

NB: This table does not include the trials in development and the closed trials. For more information, please visit www.BIGagainstbreastcancer.org
Together we had a true impact on practice in the last 15 years

**HERA trial: a new standard of treatment**

The HERA trial, which was conducted from 2001 to 2005, is an example of a successful practice-changing clinical study. Involving 27 BIG research groups and recruiting 5,100 women from 480 sites across 39 countries in just over four years – in itself a remarkable achievement – HERA contributed to a new standard of treatment for women with HER2-positive, early breast cancer, a highly aggressive form of the disease. HERA helped accelerate the approval of the drug trastuzumab which has cut relapse rates by 50% and is now the standard treatment for this type of breast cancer.

**Putting aromatase inhibitors on the map!**

Three studies, BIG 1-97/MA.17, BIG 2-97/IES and BIG 1-98, together recruiting a total of 17,958 patients, contributed to the body of evidence that aromatase inhibitors could be used as a safe alternative to tamoxifen, a drug used to treat oestrogen receptor (ER) positive breast cancer that is associated with dangerous side effects for some women. Not only did these trials prove the effectiveness of the new drugs, but they also answered important additional questions about whether the drugs should be given in combination or in sequence with others, the likelihood of side effects with long-term use, and patients’ overall quality of life. The findings of those trials had a real impact on the treatment given to women affected by ER-positive breast cancer. The consequent change in practice greatly improved the quality of life of these women.

**ALTTO and Neo-ALTTO: the strength of international collaboration**

ALTTO and its “sister” trial NeoALTTO – together involving more than 8000 patients and a huge prospecitive collection of biological materials for future translational research – are a testimony to the strength and richness in terms of scientific expertise, creativity and flexibility of BIG’s network research groups to conduct international and complex clinical studies.

Launched in 2007, ALTTO involved 947 hospitals from 18 BIG collaborative groups covering 44 countries and enrolled 8381 patients in just 49 months. It is considered to be the largest-ever adjuvant clinical trial in HER2-positive breast cancer. Its objective was to compare single trastuzumab therapy to a dual HER2-targeted therapy combining trastuzumab plus lapatinib, given after breast cancer surgery (i.e. adjuvant treatment).

Developed in parallel, ALTTO’s ‘sister’ trial NeoALTTO was also launched in 2007 and recruited 455 women with HER2-positive primary breast cancer from 86 different centres in 23 countries. Its objective was to evaluate the benefit of dual HER2-targeted therapy (trastuzumab plus lapatinib), compared to a single HER2-targeted therapy (either trastuzumab or lapatinib alone) before cancer surgery (i.e. neoadjuvant treatment). The results of NeoALTTO showed a near doubling of the pathologic complete response rate (pCR) with the dual HER2-targeted therapy rather than the single agent alone (trastuzumab or lapatinib) before surgery. These results were considered promising for ALTTO and the adjuvant setting.

However, the 2014 ALTTO findings did not confirm the predicted benefit of using both anti-HER2 therapies (trastuzumab plus lapatinib). Despite its unexpected results, the ALTTO trial can be considered to be a landmark study. Not only did this large collaboration trial answer important questions about the adjuvant treatment of women with HER2-positive breast cancer – namely, the findings confirmed that the standard adjuvant treatment for early stage HER2-positive breast cancer should remain trastuzumab in combination with chemotherapy – but the data and samples collected will be very valuable for the conduct of promising translational research.
## Financials

### Balance Sheet

<table>
<thead>
<tr>
<th>Assets</th>
<th>2014</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed assets</td>
<td>123,540</td>
<td>60,731</td>
</tr>
<tr>
<td>Intangible fixed assets</td>
<td>21,328</td>
<td>25,875</td>
</tr>
<tr>
<td>Tangible fixed assets</td>
<td>54,045</td>
<td>34,357</td>
</tr>
<tr>
<td>Financial fixed assets</td>
<td>48,167</td>
<td>500</td>
</tr>
<tr>
<td>Current assets</td>
<td>16,753,377</td>
<td>17,455,083</td>
</tr>
<tr>
<td>Receivables up to one year</td>
<td>7,068,276</td>
<td>5,325,090</td>
</tr>
<tr>
<td>Current investments</td>
<td>4,612,065</td>
<td>7,999,609</td>
</tr>
<tr>
<td>Cash at bank</td>
<td>4,923,961</td>
<td>4,037,015</td>
</tr>
<tr>
<td>Deferred charges and accrued income</td>
<td>149,075</td>
<td>93,474</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td><strong>16,876,917</strong></td>
<td><strong>17,515,920</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liabilities</th>
<th>2014</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity</td>
<td>5,223,829</td>
<td>5,245,686</td>
</tr>
<tr>
<td>Unrestricted net assets</td>
<td>5,223,829</td>
<td>5,245,686</td>
</tr>
<tr>
<td>Debts</td>
<td>11,653,088</td>
<td>12,270,234</td>
</tr>
<tr>
<td>Amounts payable after more than one year</td>
<td>1,326</td>
<td>1,326</td>
</tr>
<tr>
<td>Amounts payable within one year</td>
<td>11,502,324</td>
<td>11,702,091</td>
</tr>
<tr>
<td>Current portion of amounts payable after more than one year falling due within one year</td>
<td>0</td>
<td>4,959</td>
</tr>
<tr>
<td>Trade debts</td>
<td>11,197,072</td>
<td>11,528,236</td>
</tr>
<tr>
<td>Tax, remuneration and social security</td>
<td>305,251</td>
<td>168,896</td>
</tr>
<tr>
<td>Deferred charges and accrued income</td>
<td>149,438</td>
<td>566,817</td>
</tr>
<tr>
<td><strong>Total liabilities</strong></td>
<td><strong>16,876,917</strong></td>
<td><strong>17,515,920</strong></td>
</tr>
</tbody>
</table>

### Income & Expenses Statement

<table>
<thead>
<tr>
<th>Operating income &amp; expenses</th>
<th>2014</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnover (research)</td>
<td>12,635,447</td>
<td>13,476,223</td>
</tr>
<tr>
<td>Other goods &amp; services</td>
<td>-10,411,800</td>
<td>-11,961,505</td>
</tr>
<tr>
<td>Operating margin</td>
<td>2,223,647</td>
<td>1,514,718</td>
</tr>
<tr>
<td>Remuneration, social security &amp; pension costs</td>
<td>-2,380,762</td>
<td>-1,653,334</td>
</tr>
<tr>
<td>Operating result</td>
<td>-157,115</td>
<td>-138,616</td>
</tr>
<tr>
<td>Financial result</td>
<td>141,573</td>
<td>118,571</td>
</tr>
<tr>
<td>Extraordinary income (+)</td>
<td>369</td>
<td>1,822</td>
</tr>
<tr>
<td>Extraordinary expenses (-)</td>
<td>-6,684</td>
<td>-55,386</td>
</tr>
<tr>
<td><strong>Result for the financial year</strong></td>
<td><strong>-21,858</strong></td>
<td><strong>-73,610</strong></td>
</tr>
</tbody>
</table>
Messages of hope for the next 15 years of research

“I am always struck by the high number of breast cancer cases, the most common cancer among women today. Although progress has been made in recent years, research in this field remains a big challenge, and it is so very important.

I support researchers from all over the globe who are looking for cures for this disease. BIG researchers and their colleagues worldwide have proven that they have the expertise needed to find advanced and innovative treatments that will help women survive breast cancer and get their lives back on track. This research brings hope to millions of women and their families that they can fight the disease successfully. BIG researchers contribute towards this goal.

They all need our support in various ways.”

Her Majesty the Queen of the Belgians, Honorary President of BIG

“My great hope is to see a cure for metastatic breast cancer. It’s still the most lethal form of breast cancer and we need to help those patients. I would also hope that breast cancer screening becomes truly universal, so that more women are diagnosed before their breast cancer has a chance to spread.”

Jessica Parser, President of the Committee of Ambassadors of BIG against breast cancer

“As a network of collaborative groups, BIG has the expertise and global reach required to conduct innovative research to best serve the needs of women and men with breast cancer. We hope that breast cancer collaboration will become even stronger over the next 15 years, so that we can continue to make a real difference in patients’ lives.”

Carolyn Straehle, BIG Managing Director and Theodora Goulioti, BIG Scientific Director

“In 2014, employees of cable company Liberty Global took part in “Look and Feel” workshops presented by BIG, in an effort to understand the importance of early detection of breast cancer, and the simple steps we can take for our own health. I hope that in the coming years, this message can be spread to empower even more women and men worldwide. Early detection has the power to save so many lives.”

Crystal Crawford, Corporate Responsibility Manager, Liberty Global

“My great hope is that in 15 years from now, researchers will have found a cure for cancer. As a young woman who won the fight against breast cancer, I also hope that increased knowledge of the disease will give the opportunity to all patients to resume a normal life after treatment: going back to work, being able to start families if they wish, or pursuing any other dreams that they have.”

Laura, participant in the POSITIVE clinical trial

Moving research forward is essential to breast cancer advocacy and to patients. The hope for patients in the future rests in the hands of researchers and research groups to develop new and better treatments for the many types of breast cancers that exist. Research represents the hope, the future, and the real possibility of eradicating this disease once and for all.”

Susan Knox, Europa Donna Executive Director
In recent years, we have discovered that breast cancer, like all cancers, is an immensely complex disease, whose management requires a concerted effort of various stakeholders. Only by building effective partnerships amongst all stakeholders involved in the scientific discovery and clinical research process can we hope to make further advances in the management of breast cancer. BIG has been a leader in building bridges between academia and industry and in pioneering innovative models of collaboration to accelerate clinical research. I am confident that BIG will continue to advance the science and management of breast cancer by connecting patients and other stakeholders in the drug development process and thus ensuring that patients’ needs are fully addressed."

Tamas Suto, Chief Medical Officer, Sanofi Asia

We hope that breast cancer opinion leaders and their cooperative groups will continue to recognise the need to “groom” the younger generation, by giving them the opportunity to take the lead in moving research forward. This, together with a spirit of “all for one and one for all” in international collaboration will ensure that we keep patients at the heart of our endeavours. Certainly, this is what we have done within BIG in the past and will continue to do in the future."

Carlos Barrios, BIG Member, Latin America

My great hope is that every woman and man with breast cancer will have access to relevant treatments and have the same chances to be cured worldwide, no matter where they are born and live. BIG, with its member groups and highly motivated researchers in many corners of the globe, has the potential to turn this hope into a reality."

Boon Chua, BIG Member, Australia

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."

Raf Simons, Belgian fashion designer at the Sapins de Noël des Créateurs belges

Personally, supporting BIG against breast cancer means a lot to me because a close friend of mine who lost her mother and aunt to breast cancer then had to fight the disease herself. I hope that in the coming years, more and more people will support the charity so that we can save more women like her."

We would also like to thank our donors who elected to remain anonymous.

Thank you to the King Baudouin Foundation for their collaboration and advice in BIG's development activities.
Thank you

Danke  شكرا  благодаря  谢谢  감사합니다
hvala  tak  Gracias  kiitos  Merci  ευχαριστώ  تّاّك  köszönöm  ee-may-nah  go raibh maith agat
enkosi  siyabonga  þakka þér  Grazie  有り難うありがとうございます

Dank U  takk  shukriya  dziękuję  Obrigado  mulțumesc
спасибо  ćakujem  hvala  tack  děkuji