46% of patients could be spared from unnecessary chemotherapy
The first results of the MINDACT trial give hope to many women with early-stage breast cancer.
in future, it is possible that up to 46% of patients who would have received chemotherapy in the past could be spared from this treatment and its side effects.
MINDACT, validating a new prognostic tool

Patient categories

- **Clinical & genomic tests indicate low risk of recurrence**
- **Clinical & genomic tests indicate high risk of recurrence**
- **Clinical & genomic tests are discordant**

70-gene prognosis signature can help with decision-making about giving chemotherapy or not.

46% of patients could be spared unnecessary chemotherapy.

- The trial enrolled 6,693 early-stage breast cancer patients.
- 112 cancer centres and hospitals.
- 9 countries.
- 47 million € to fund the trial.

De-escalation of therapies
- Pioneering precision medicine
- Better and personalised treatment
- Potential savings for society
- Goldmine for future research

Highest scientific evidence level 1A

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Assessing the risk of cancer relapse

After surgically removing a patient’s tumour, it is crucial to evaluate the risk of cancer returning or spreading to other parts of the body. If the risk is high, the patient may be advised to receive chemotherapy. As each person’s risk depends on many factors, it is not easy to define “high” risk accurately.

The tumour is first analysed by pathologists. Traditionally, the factors considered to evaluate this risk include the patient’s age, the tumour’s size, the number of lymph nodes containing cancer, the presence of hormone-receptors, HER2*-receptors and other features that affect how quickly a tumour will grow and how well a treatment is likely to work.

Based on this assessment, if the risk of recurrence is high, doctors will generally propose chemotherapy. Unfortunately, this traditional clinical way of assessing risk is not homogenous and not always consistent.

The effects of chemotherapy

Chemotherapy is an anti-cancer treatment that has real benefits and that can save lives. However, it also has a number of unwanted side effects. This happens because chemotherapy is not a specific treatment and not only kills tumour cells but also some good or ‘normal’ cells in the body.

Tumours can grow very quickly because they contain rapidly dividing cells.

Simone was diagnosed in 2002. She received chemotherapy for six months. During treatment, she experienced many unwanted side effects.

“When I was told I would receive chemotherapy, my first thought was ‘oh no, I’m going to lose my hair… I need a wig’. Before starting therapy, I wanted my daughter to come with me to the shop and buy a wig. Having one, I felt ready to start the treatment. But when you start therapy, you feel other things can go wrong. That’s when you understand that losing your hair is not important at all. The first session is really heavy because the effects are rapidly in the follicles. That is why hair can fall out when chemotherapy attacks these cells.”

“Nowadays, because we don’t know how to pick up the patients who really need this type of treatment, and we know that once breast cancer has spread it becomes an incurable disease, we tend to give chemotherapy anytime we are in doubt, because as an oncologist, you don’t want to take a risk as this is the only opportunity you have to cure the patient”

says Dr Fatima Cardoso, Chair of the EORTC (European Organisation for Research and Treatment of Cancer) Breast Cancer Group (member of BIG), Study Chair of the MINDACT trial.

“The success story of an academic trial that has the potential to change the future of breast cancer treatment

Patients’ needs and quality of life are at the heart of our clinical research. We now understand that breast cancer is not one single disease, but many different subtypes. Therefore, all patients are different and require a unique treatment approach. Our aim is to find the right treatment for every patient.

This is exactly what the MINDACT trial is about: enabling women who would not benefit from chemotherapy to avoid this heavy treatment.

Discover how research impacts lives.

*HER2 = Human EGF Receptor 2 (EGF = Epidermal Growth Factor)
unexpected. You don’t know if the pain you feel is from the chemotherapy or not. And you are not confident, because even if the physician explained the effects in detail, you didn’t experience such pain and discomfort before. And then it comes at you. You feel very uncomfortable. I had a lot of pain in my joints and everywhere in my body.”

Chemotherapy can be hard to handle. “They say it’s like having a bad hangover” says Ilaria. “But I would say it’s like having the worst hangover ever on top of having the worst flu you’ve ever had. And on top of that, you feel pretty depressed.”

Ilaria was 33 when she was diagnosed with breast cancer. Because of her age and the type of cancer she had, she received a particularly aggressive form of chemotherapy. “It’s an attack on every single cell of your body. You really do feel attacked. And it’s a mental struggle as well because you know that next Friday at 3 o’clock you’re going to feel absolutely terrible for a week or ten days. On top of that you put on weight, you lose hair and you have hot flushes and … (silence). You know, it’s grim.”

There are also some side effects from chemotherapy that can occur after treatment. One of them is intense fatigue, which can last for several months. Another side effect that was underestimated in the past is memory loss, which is a problem that women occasionally report to their doctors. Fortunately, this usually improves with time.

There are two long-term side effects of chemotherapy that are much more serious, but fortunately are extremely rare. One of them is toxicity to the heart, which weakens the heart muscle. It mainly occurs with certain specific chemotherapies, and can be treated by a cardiologist. Nevertheless, the effect on quality of life can be substantial. The second very rare but potentially serious side effect is chemotherapy-induced leukaemia. Leukaemia is a deficient condition of the blood, in which white blood cells are produced uncontrollably. This disease can be lethal, and it must be treated with chemotherapy as well. Luckily it is seen in less than 1% of patients with breast cancer treated with chemotherapy, but when it does occur, it can be devastating.

Prof Martine Piccart, Co-founder and Chair of the Breast International Group (BIG) and Study Chair of the MINDACT trial states:

“Clearly, when we look at all the side effects of chemotherapy in the short and long term it becomes obvious that we don’t want to give this treatment to a woman who doesn’t need it.”

Journey to finding a new prognostic tool
Dr Laura Van ’t Veer, world renowned molecular biologist, Professor at the University of California, San Francisco, and Chief Research Officer at Agendia, is one of the inventors of the MammaPrint® test (the 70-gene prognosis signature), developed while she worked at the Netherlands Cancer Institute. “Early 2000 at the Netherlands Cancer Institute, we had the opportunity to work with a small start-up company that had developed a technology where one could analyse the activity of all genes of a cell in just one experiment. This microarray technology has revolutionised molecular biology research and we took it upon ourselves to see if we could use it for premenopausal breast cancer to find the genes whose activity would be related to either ‘no breast cancer recurrence’ or ‘recurrence within five years’.

When you start therapy, you feel other things can go wrong. That’s when you understand that losing your hair is not important at all. The first session is really heavy because the effects are unexpected. You don’t know if the pain you feel is from the chemotherapy or not.

Simone, diagnosed in 2002
We wanted to use this knowledge to understand who needed chemotherapy, and for whom the risk of recurrence was so low that they could safely forego chemotherapy and not suffer from the side effects."

The results of a first study that identified a 70-gene signature to help with decision-making about chemotherapy were very promising. The prognostic information seemed good and reliable.

“It almost looked too good to be true. We could possibly hold a key that would help clinicians make better decisions, sparing many women from a chemotherapy they would not benefit from.”

Prof Emiel Rutgers

How did it work?

After the protocol (design of the study) had been approved, the logistical complexity of the trial had been tested and validated, and the initial funding had been secured, the MINDACT trial could start recruiting patients.

From 2007 to 2011, doctors at 112 centres in nine countries enrolled in the trial 6,693 patients (out of 11,288 women screened) who had undergone surgery for early-stage breast cancer. All participants were categorised as low or high risk for tumour recurrence in two ways: first, through the genomic analysis of tumour tissue using MammaPrint (= innovative method, genomic test) by Agenda in Amsterdam; and second, using Adjuvant! Online, a tool that calculates the risk of breast cancer recurrence based on common clinical and biological criteria (= traditional method, clinical test).

The participants were then divided into different groups:
When both the genomic and the clinical tests showed high risk, the patients received chemotherapy. When both tests showed low risk, no chemotherapy was proposed. However, when the two tests disagreed, patients were randomly assigned to follow the advice provided by one of the two tests.

The trial was not easy to explain, but patients embraced MINDACT

This trial would not have been possible without the support and collaboration of hundreds of healthcare professionals across multiple disciplines and, above all, without the trust and participation of all 6,693 patients.

Europa Donna - The European Breast Cancer Coalition, a patient advocacy organisation, has representation on the MINDACT Steering Committee and was instrumental in preparing informational material to help make the study accessible and understandable. Leaflets and presentations at conferences helped to communicate about MINDACT, in particular its innovative character. The Patient Informed Consent form was carefully written to ensure that the trial could be easily understood despite its complexity, and a DVD was prepared to help physicians and study nurses explain the trial to patients.

The participants grasped the importance of this study to help other patients potential-
Initially avoid chemotherapy when not needed in the future. “It was the first time that a patient advocacy organisation was involved so deeply in a clinical trial”, said Karen Benn, deputy CEO and Head of Public Affairs at Europa Donna.

**Extra challenges**

**Funding the trial: € 47 million**

“There’s no science without finance” says Dr Denis Lacombe, Director General of the EORTC, which sponsored and ran MINDACT under the auspices of BIG. The first step was to knock on the door of the European institutions to demonstrate that this trial was a unique opportunity to transform the lives of breast cancer patients, and that it had the potential to save millions of Euros in government health budgets. After BIG received an “EU Framework 6” grant of €47 million to support MINDACT, scientists became extremely motivated. Prof Martine Piccart was impressed by the level of their engagement: “it was touching to have a group of persons that were ultra-motivated by this fantastic opportunity to de-escalate therapy”.

**Logistics and data management**

The MINDACT trial was very demanding in terms of logistics as well. It was described as a true “logistical nightmare”, involving surgeons, oncologists, pathologists, research nurses and many other professionals.

For example, a sample of the tumour of each participant had to be collected by the surgeons and then fresh frozen for further analysis. During the trial, 10s of 1000s of high quality samples frozen tumour tissue, whole blood and plasma had to be transported in strictly regulated conditions to a specialised biological storage facility. With the analysis of 44,000 genes of each tumour, a huge amount of data had to be collected and stocked in a genomic database, in addition to all the medical data collected from each patient and stored in the clinical database. Web-based registration forms were developed to allow tracking of samples and to inform doctors about their patients’ screening results, the genomic and clinical test results, whether patients would need to receive chemotherapy, and how patients were randomised.

MINDACT demanded tremendous collaborative efforts. Today, it is a successful example of how, by working together across borders and disciplines, we can develop better treatments – and eliminate those that are not needed – while increasing the likelihood of finding cures.

**Impressive results: 46%**

The MINDACT trial, published in the New England Journal of Medicine in 2016, demonstrates that research offers the opportunity to transform both patient’s lives and that of healthcare professionals. The results of the trial indicate that the use of MammaPrint can potentially reduce overtreatment of breast cancer patients by 46%, even in the presence of high risk clinical features. This means that nearly half of the early-stage breast cancer patients identified as high risk for recurrence based on clinical factors were identified as low risk when using the MammaPrint test. The patients who avoided chemotherapy during the trial thanks to this signature were closely monitored over five years. The data demonstrated that chemotherapy provided no clinically meaningful benefit for these patients.

“MINDACT trial results provide evidence that using MammaPrint could change clinical practice by substantially de-escalating the use of adjuvant chemotherapy and sparing many patients an aggressive treatment they will not benefit from.” says Prof Martine Piccart.

“MINDACT demonstrates how our joining efforts have a direct impact on patients’ lives. It takes optimism and the unwavering belief in a grander purpose that enables us to succeed, despite the many daily challenges that broad-scale, international collaboration entails,” said Dr Carolyn Straehle, Managing Director of BIG.
Changing the future of breast cancer treatment

One of the main challenges in oncology today has become to accurately distinguish between patients who need adjuvant treatment and those who do not. This, together with the identification of the best type of therapy for each individual patient and the development of drugs targeting specific characteristics of tumour cells, are the goals of treatment tailoring or personalised medicine. It is our mission to find ways of ensuring patients receive the treatments most appropriate for them.

The results prove that the MammaPrint gene test could identify women who will not benefit from chemotherapy, thus sparing them the often gruelling side effects. This is very promising news and demonstrates that working together across disciplines on an international scale contributes to the faster development of better treatments, and increases the likelihood of cures for patients.

We look forward to further results from this and other trials in the future.

The future is bright. Together, we will find a cure for breast cancer.

A goldmine for future research

The physicians and scientists who designed MINDACT made sure that the study would serve as a long-term investment in future breast cancer research. Not only did they analyse the 70 genes using MammaPrint, but they also processed over 44,000 genes from the tumours of each of the 6,693 participating patients. This genomic information, together with the tumour samples and blood donated by the patients, and the clinical data collected during the study, represents a tremendous resource for the future. Researchers from around the world will be able to access these materials for research projects that will be carefully reviewed for their potential scientific value.

According to Dr Denis Lacombe, “MINDACT is not only pioneering in precision medicine, it contributes to something important to the patients and society as a whole: de-escalating therapies. It also created a huge resource for future research, because research using the participants’ tumour samples, blood samples, and clinical outcomes data could allow us to gain a substantially better understanding of the biology of breast cancer.”

The MINDACT Trial is managed and sponsored by the European Organisation of Research and Treatment of Cancer (EORTC) as part of an extensive and complex partnership in collaboration with BIG, Agendia, and many other academic and commercial partners, as well as patient advocates. The study was supported by grants from the European Commission Framework Programme VI (FP6-LSHC-CT-2004-503426, “TRANSBIG Network of Excellence”), the Breast Cancer Research Foundation, Novartis, F. Hoffman La Roche, Sanofi-Aventis, Eli Lilly, Veridex, the U.S. National Cancer Institute, the European Breast Cancer Council-Breast Cancer Working Group (BCWG grant for the MINDACT biobank), the Jacqueline Sieroussi Memorial Foundation (2006 JSMF award), Prix Mois du Cancer du Sein (2004 award), Susan G. Komen for the Cure (SG05-0922-02), Fondation Belge Contre le Cancer (ISCIE 2005-271, Dutch Cancer Society IKWFI, Association Le Cancer du Sein, Parlons-en!), the Brussels Breast Cancer Walk-Run and the American Women’s Club of Brussels, NIF Trust, Deutsche Krebshilfe, the Grant Simpson Trust and Cancer Research UK. This trial was also supported by the EORTC Charitable Trust. Whole genome analysis was provided in kind by Agendia. Total funding: approx. EUR 47 million.

More detailed scientific information about this trial can be found here: www.BIGagainstbreastcancer.org
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 by 2016 it represented 56 like-minded research groups from around the world and reached 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 an international level. We are proud to be both global AND local, helping breast cancer patients from all over the world.

www.BIGagainstbreastcancer.org
Message from the Co-chairs

2016 has been a tremendous year for BIG with the release of the MINDACT study’s positive results, which we expect will lead to a reduction in chemotherapy prescription for many patients in the future.

MINDACT, which involved more than 6,000 women from nine countries, is an achievement we can be particularly proud of. Sponsored and led by the European Organisation of Research and Treatment of Cancer (EORTC) under the BIG umbrella, and launched in the context of the BIG-coordinated TRANSBIG project, it combined close collaboration with patient advocates, scientific innovation, and unwavering perseverance, especially to raise the € 47 million needed to support the trial! It is the perfect example of how, through collaboration and global research, we as academics can have a real impact on the lives of patients affected by breast cancer.

We can be very proud of the continuous dedication and hard work of BIG’s 56 collaborative member groups, which represent an impressive network of more than 10,000 breast cancer experts worldwide. In this 2016 annual report, we highlight both some of our joint and their individual activities.

Recognising that the “global cancer problem” has particularities in each region and country, BIG has been actively pursuing closer relationships with its members outside of Western Europe. One fruit of these exchanges was an enthusiastically received pilot programme to train young research-physicians from Latin America in clinical trial development and academic collaborative group management.

The following pages also give you a flavour of BIG’s fundraising activities and corporate partnerships established throughout the past year, directly benefiting studies such as BIG Time for Baby (scientific name: the POSITIVE study).

Finally, we wish to extend our heartfelt thanks to all our member groups, partners, faithful supporters and staff for their tireless determination and strong collaborative spirit to help advance breast cancer research and treatment. In addition, but just as importantly, we wish to thank and honour the thousands of patients who participate in our trials and work with us to develop tomorrow’s cures.

Together, we have the opportunity to make a real difference in patients’ lives, both today and in the future.
A BIG network to facilitate research and collaboration

Each of the 56 BIG member groups 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.

Each group is associated with one to several hundred hospitals and scientists, which represents a collaboration between thousands of institutions worldwide.

“The

International collaboration is crucial to moving breast cancer research forward, moving more rapidly and efficiently towards one goal: to find better treatments and cures for all patients affected by breast cancer.

BIG and the North American Breast Cancer Group (NABCG)

For over a decade BIG has been collaborating closely with its American counterpart, the North American Breast Cancer Group (NABCG) – a network of major US and Canadian-based research groups supported by the US National Cancer Institute (NCI). BIG and NABCG have been meeting annually with the aim of identifying difficult aspects of breast cancer research, focusing on research areas not supported by the pharmaceutical industry, and collaborating to improve treatments and cures for patients around the world.

A current focus of the BIG-NABCG collaboration is precision medicine. Experts have also been tackling the following issues: novel immunotherapies, data sharing in the context of molecular screening programmes and the analysis of circulating biomarkers (circulating tumour cells, and circulating tumour DNA). This collaboration is supported by the generous help of the Breast Cancer Research Foundation®.
BIG Member Groups

ABCSG    Austrian Breast & Colorectal Cancer Study Group
AGO-B    Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group
ANZBCCTG Australia & New Zealand Breast Cancer Trials Group
ARCAGY-DINECO Association de Recherche dans les Cancers dont Gy-nécologiques – Groupe d’Investigateurs Nationaux pour l’Etude des Cancers Ovariens et du Sein
BGICS    Breast-Gynecological International Cancer Society
BIEI      Breast Intergroup of Eastern India
BOOG      Borstkanker Onderzoek Group
Cancer Trials Ireland

CCTG      Canadian Cancer Trials Group
CEEOG     Central and East European Oncology Group
CTRIG     Cancer Therapeutics Research Group
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
GAICO     Grupo Argentino de Investigación Clínica en Oncología
GBECAM    Grupo Brasileiro de Estudos do Câncer de Mama
GBG       German Breast Group
GECOPERU Grupo de Estudios Clínicos Oncológicos Peruano
GBCAM     Grupo Español de Investigación en Cáncer de Mama
GOCCHI    Grupo Oncológico Cooperativo Chileno de Investigación
GOCUR     Grupo Oncológico Cooperativo Uruguayo
GOIRC     Gruppo Oncologico Italiano di Ricerca Clinica
GONO      Gruppo Oncologico del Nord Ovest
HBSS      Hellenic Breast Surgeons Society
HeCOG     Hellenic Cooperative Oncology Group
HKBOG     Hong Kong Breast Oncology Group
HORG      Hellenic Oncology Research Group
IBCO      Icelandic Breast Cancer Group
IBCSCG    International Breast Cancer Study Group
IBG       Israel Breast Group
IBIS      International Breast Cancer Intervention Studies
ICCG      International Collaborative Cancer Group
ICON ARO Indian Co-operative Oncology Network
ICRC      Iranian Cancer Research Center
ICR-CTSU  Institute of Cancer Research - Clinical Trials & Statistics Unit
IB-CTSU   Institut Jules Bordet - Clinical Trials Support Unit (formerly BREAST - Breast European Adjuvant Study Team)
IOSG      Indian Oncology Study Group
ITMO      Italian Trials in Medical Oncology
JBCRG     Japan Breast Cancer Research Group
LACOG     Latin American Cooperative Oncology Group
MICHELANGELO Fondazione Michelangelo
NBCG      Norwegian Breast Cancer Group
NCR-BCSG  National Cancer Research Institute - Breast Cancer Clinical Studies Group
SABO      Swedish Association of Breast Oncologists
SAKK      Swiss Group for Clinical Cancer Research
SBCCG     Sheba Breast Collaborative Group
SweBCG    Swedish Breast Cancer Group
SKMCH & RC Shaukat Khanum Memorial Cancer Hospital & Research Centre
SLO       Société Luxembourgoise d’Oncologie
SOLT      SUCCESS

SUCCESS Study Group
TCOG      Taiwan Cooperative Oncology Group
TROG      Trans Tasman Radiation Oncology Group
UCBG      Unicancer Breast Group
WSG       Westdeutsche Studiengruppe

Country covered by a BIG member

56 member groups across all continents
BIG Members’ activities

BIG member groups represent the top breast cancer experts worldwide. Here is a peek at some of their activities in 2016.

CANCER TRIALS IRELAND WON IRISH HEALTHCARE AWARD FOR “JUST ASK” CAMPAIGN

In November 2016 Cancer Trials Ireland won the Irish Healthcare Award for its “Just Ask” campaign. The campaign was designed to encourage patients and their families to ask their doctor about cancer trials. It won the award for the Best Patient Education Project – Non pharmaceutical.

The “Just Ask” campaign was also part of the organisation’s name change programme from ICORG to Cancer Trials Ireland, which was kindly supported by the Irish Cancer Society, the Health Research Board, Bayer, Amgen and Merck Serono. Attendance at the awards event was supported by Bayer and MSD.

ITMO’s 22nd National Congress took place on 01 July 2016. As modern oncology is moving towards a global sharing of guidelines and clinical practice, the aim was to organise an educational congress to underline the new frontiers in oncological medicine and the current evidence for every-day clinical practice. Experts from different regions of Italy participated in and contributed to the success of this congress, during which the most important cancer diseases were addressed. The group esteems that global sharing is of great importance for health education and must be continuously updated and renewed.

ITMO team (credit: ITMO)
INTERNATIONAL BREAST CANCER STUDY GROUP (IBCSG)

IBCSG partnered with Race for Life

For the first time, IBCSG partnered with ‘Race for Life’, a charity bicycle marathon that has been held in Switzerland since 2010. The event took place on Sunday 11 September 2016, in front of the parliament in Bern.

The donated (or rather “cycled”) money benefited the various cancer research projects of the involved partner organisations. Besides the sportive aspect, ‘Race for Life’ is also a social event with an appealing frame-work programme. As expressed by the IBCSG team: “we are very grateful to all our supporters who volunteered to cycle for IBCSG and for all other ‘Race for Life’ partners.”

IBCSG’s research

In November 2016, the Journal of Clinical Oncology released its annual compilation of the most-accessed articles in breast cancer. Out of the seven most popular breast cancer articles of 2016, three were authored by investigators of the International Breast Cancer Study Group (IBCSG):

• ‘Absolute Benefit of Endocrine Therapies for Breast Cancer’, by IBCSG Group Statistician Meredith M. Regan, ScD (USA) et al.
• ‘Estrogen Levels in Premenopausal Women Receiving Triptorelin’, by Meritxell Bellet, MD (Spain) et al.
• ‘Late Recurrences in Operable Breast Cancer’, by IBCSG Scientific Committee Chair Marco Colleoni, MD (Italy) et al.

2016 ‘Best of JCO’ breast cancer edition highlighted IBCSG’s research

GRUPO ONCOLÓGICO COOPERATIVO CHILENO DE INVESTIGACIÓN (GOCCHI)

GOCCHI’s Director Dr Bettina Müller honoured with award

Dr Bettina Müller, Director of GOCCHI and Head of the Medical Oncology Department of the National Cancer Institute of Chile, received an award for her role in oncologic cooperative research in Latin-America at the last meeting of the Latin-American Cancer Societies (FLASCA).

GOCCHI 2009-01 PRECISO trial received distinction

GOCCHI’s PRECISO trial*, a phase II one arm prospective trial of Perioperative Chemotherapy in Locally Advanced Gastric Carcinoma, was awarded the “Best Work” distinction during the last meeting of the Chilean Cancerology Society meeting that took place in October 2016.

GOCCHI’s Director Dr Bettina Müller (credit: GOCCHI)
There has been a string of achievements for the IBIS-II trials in 2016. In January, the first results of the IBIS-II DCIS trial were published in the Lancet (Forbes et al) reporting on the first seven years of follow-up of nearly 3,000 women. In December 2016, the findings of the IBIS-II Prevention trial were implemented through updated guidance from the National Institute of Clinical Excellence endorsing use of anastrozole for postmenopausal women with a family history of breast cancer. Professor Jack Cuzick also received two prestigious awards in 2016 acknowledging his work on the IBIS trials and for his long standing services to cancer prevention and screening. He became a fellow of the Royal Society, as well as a Commander of the Order of the British Empire (CBE) in the Queen’s New Year Honours list.

On 21 October 2016, the Breast & Gynecological International Cancer Society (BGICS) held an exceptional event in the Bibliotheca Alexandrina of Alexandria, Egypt, to raise awareness about breast cancer and to provide support to patients and survivors through multiple sessions and workshops held throughout the day. The event also marked the launch of BGICS’ groundbreaking project ‘the National Breast & Gynecological Cancers Awareness & Prevention Campaign’ conducted in collaboration with the National Council of Motherhood and Childhood and the National Population Council. Its aim is to work through different channels to reach different segments of the population, starting with the nine different governates/districts of the country that are most affected by the disease.

The day ended with a concert for patients. In addition, the Bibliotheca Alexandrina was lit in pink the whole evening, in solidarity with patients and to show support for all the efforts done to combat the disease everywhere. This extraordinary feat was witnessed for the first time ever in Egypt, announcing the country’s support in the fight against cancer everywhere, and taking a historic step to join the global stand against breast cancer.
BIG Network

BIG Annual Report 2016

In Summer 2016, ABCSG organised two important investigator meetings for the ABCSG’s global trial PALLAS (ABCSG 42/BIG14-03) in Vienna, Austria and Sydney, Australia. More than 350 participants from all over the world attended these meetings. Approximately 600 patients had been recruited worldwide by the end of 2016 (target: 4,600) in this adjuvant academic study, which means enrollment is within schedule.

Another important international trial managed by ABCSG is LORELEI (ABCSG 38/SOLTI 1205/BIG3-13). This neoadjuvant study completed recruitment three months ahead of schedule in August 2016 – record time! 334 patients worldwide are involved in this trial. The top recruiting countries were Spain, the US and Austria.

Lastly the vaccine trial ABCSG 34, although it turned out to be a “negative study”, gives the important opportunity to conduct a lot of translational research, and ABCSG is getting more and more active in this field. The results of this Austrian study, which finished randomisation in 2014, were presented by Dr Christian Singer at the San Antonio Breast Cancer Symposium 2016 and shall be published in 2017.

SOLTI’s Educational Programme for Medical Oncologists

SOLTI collaborated with the Catalan Institute of Oncology and the Vall d’Hebron Institute of Oncology to drive a training programme to improve the knowledge and skills of medical oncologists in the emerging field of cell cycle modulator drugs, supported by a grant from Pfizer Inc.

The goal of this blended educational programme is to inform and train specialists regarding the clinical implications of new therapeutic targets in the treatment and management of breast cancer, particularly in the metastatic hormone receptor-positive setting, focusing on the pharmacological aspects of these therapies as well as the development of preclinical and clinical trial studies.

Upon completion of the programme, participants will be able to determine the role of CDK 4/6 inhibitors in the management of patients with metastatic breast cancer, understand the available data of biomarker targets, sensitivity and resistance mechanisms, and know how to manage the toxicities of CDK 4/6 inhibitors.

The programme consists of a Satellite Symposium that took place during the Annual Conference of the Spanish Society of Medical Oncology in October 2016, and a national workshop to be held in Barcelona in 2017, the content of which will be turned into a course that will be launched online for professionals abroad through the e-oncología platform.

AUSTRIAN BREAST & COLORECTAL CANCER STUDY GROUP (ABCSG)

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Another important international trial managed by ABCSG is LORELEI (ABCSG 38/SOLTI 1205/BIG3-13). This neoadjuvant study completed recruitment three months ahead of schedule in August 2016 – record time! 334 patients worldwide are involved in this trial. The top recruiting countries were Spain, the US and Austria.

Lastly the vaccine trial ABCSG 34, although it turned out to be a “negative study”, gives the important opportunity to conduct a lot of translational research, and ABCSG is getting more and more active in this field. The results of this Austrian study, which finished randomisation in 2014, were presented by Dr Christian Singer at the San Antonio Breast Cancer Symposium 2016 and shall be published in 2017.
The SOFT clinical trial, which produced practice changing results in the treatment of breast cancer in young women, was recognised as a finalist in the inaugural Australian Clinical Trials Alliance’s (ACTA) Clinical Trial of the Year Awards. SOFT is an international trial coordinated by the International Breast Cancer Study Group (IBCSG) under the BIG umbrella (IBCSG 24-02/BIG2-02). The study was one of five finalists in the awards and was conducted in Australia and New Zealand by the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG). More than 3,000 women were enrolled in the clinical trial worldwide, which found that treatment with tamoxifen plus ovarian function suppression did not significantly benefit all premenopausal women. However, the addition of ovarian suppression to tamoxifen reduced the relative risk of developing invasive breast cancer recurrence by 22% in women who did not transition into menopause after receiving chemotherapy, when compared to treatment with tamoxifen alone. A secondary analysis showed that further benefit could be gained by treating these women with an aromatase inhibitor exemestane plus ovarian suppression, which reduced their relative risk by 35%, compared to tamoxifen alone, resulting in 7 to 8 fewer women out of 100 having a breast cancer recurrence within five years. This is a globally significant result that will increasingly see this therapy recommended for the very youngest women with hormone-receptor-positive breast cancer.

Associate Professor Prue Francis is the International Co-Chair of the SOFT clinical trial and presented the study results at the 2014 San Antonio Breast Cancer Symposium in Texas, USA, and was the lead author of the publication in the New England Journal of Medicine.

MA. 17R clinical trial recognised as one of the highest impact studies in the world

Extended AI Therapy Improves DFS in Postmenopausal HR-Positive Breast Cancer

The Canadian Cancer Trials Group (CCTG) MA. 17R study (BIG 1-97) was recognised as among the highest impact studies in the world. This breast cancer study was chosen to be featured in the plenary session of the American Society of Clinical Oncology (ASCO) annual meeting in Chicago in June, 2016.

“The MA. 17R paper was chosen to represent the best and most significant advances in cancer treatment and care, with the greatest potential influence” said Dr Wendy Parulekar, the CCTG Senior Investigator who supervised the trial. “Only four papers were selected by ASCO for their plenary session out of more than 5,000 submissions.”

The MA.17R trial discovered that extending therapy with a commonly used hormone drug called an aromatase inhibitor from five to ten years in postmenopausal women with early breast cancer reduces the risk of recurrence by 34%.

The findings were published in the New England Journal of Medicine. The lead author and study chair is Dr Paul Goss (Harvard Medical School).

“This is the first study to report the impact of extended aromatase inhibitor therapy on breast cancer recurrence, side effects and quality of life in women with receptor positive breast cancer,” says Dr Parulekar. “Based on the results of this trial, women and their healthcare providers can make an informed decision about taking this type of treatment beyond five years, which is the current standard of care. The results of this study will immediately impact treatment practices on a global basis.”
SAKK activities in the field of breast cancer

The SAKK project groups are made up of medical oncologists and representatives of other disciplines, and they concern themselves with the disease areas defined as research priorities. The SAKK project group for breast cancer is an active group – in 2016, it recruited a total of 278 patients into clinical trials, a figure that is in the same range as last year. Looking more closely, accrual is now originating more from interventional trials and SAKK’s own activities than in the previous two or three years, when patients were mainly recruited from non-interventional and international trials from other cooperative groups.

The first surgical trial, SAKK 23/13, recruited fast and completed its accrual on time. The surgical colleagues made a tremendous effort, and their contribution to SAKK’s project group for breast cancer is essential. The group has applied for various grants for the ambitious “Swiss Sentinel Study” surgical project and hopes to succeed in activating this international flagship trial soon.

Another important international trial is SAKK 96/12, which compares fewer denosumab injections to the standard monthly recommendation in patients with bone metastases. If the trial’s hypothesis is borne out, this trial can contribute critically to the further tailoring of treatment to patients and to the reduction of over-treatment.

SAKK 24/14 was activated in October 2016. This innovative project investigates anti-EGFR immunoliposome therapy in metastatic, triple-negative breast cancer and represents genuine bench-to-bedside research originating in Switzerland.

SAKK expects increased accrual of breast cancer patients in 2017 as several projects are in the pipeline, in particular the adjuvant PALLAS trial.

In December 2016, four years after the first site initiation visit, the 10,000th patient was enrolled in the CANTO project!

CANTO is a prospective trial fully dedicated to survivorship and treatment toxicities. It includes patients who present early breast cancer from 25 centres. It collects prospective data on social sciences, quality of life, exercise, nutrition, and all possible side effects.

In addition to clinical data, biological samples are also collected, including blood samples at baseline and after three years, plasma and serum samples every two years. So far, about 5,000 DNA have been extracted from the blood samples. The scientific exploitation of CANTO is just starting as sufficient data and follow-up is needed to ensure the significance of the analysis. This project is open to partnerships with both academic and industrial partners.
In 2016 LACOG presented the results of the most comprehensive retrospective study of real world patterns of care for metastatic breast cancer in Brazil. More than 700 patients from 20 centres were included in this study, which showed that half of HR+/HER2- patients received chemotherapy as first-line treatment. A prospective breast cancer registry, AMAZONA III, was also initiated last year to include approximately 3,000 new cases of breast cancer from 23 centres in Brazil. This study is conducted in collaboration with the Grupo Brasileiro de Estudos do Câncer de Mama (GBECAM) and supported by grants from the Ministry of Health, ITAU Bank and the AVON Institute. Both studies aim to identify inequalities in breast cancer care and propose actions to health authorities and policy makers. In parallel LACOG proudly presented the “Projeto CURA”, a fundraising initiative to support cancer research projects in Latin America. Lastly, in collaboration with BIG and EORTC, LACOG organised the first clinical research management training programme for young oncologists from Latin America, which took place in October 2016. “Certainly 2016 was a very productive year for LACOG with several initiatives in different areas. The group is growing rapidly and we hope to increase our contribution with BIG and its members” said Gustavo Werutsky, Chair of LACOG.

One of the constituents of the Indian Oncology Study Group, the Tata Memorial Centre, organised the 14th Annual Breast Cancer Conference in the scenic locale of Amby Valley, about 100 km far from Mumbai, from 14-16 October 2016. This conference is conducted annually in partnership with an NGO, Women’s Cancer Initiative, and deliberates on a specific aspect of breast cancer management. The Conference Oration was delivered by academic luminaries including Dr Bernard Fisher who delivered the Oration at the inaugural Conference in 2003. The Oration was delivered in 2016 by Dr Steven Narod on ‘Breast Cancer Genetics and Healthcare Policy’. The Conference was attended by about 200 delegates from India and many other countries. The Tata Memorial Centre is India’s largest and most prestigious cancer centre.

INdIAN OnCOLOGY STUDY GROUP (IOSG)

IOSG’s 14th Annual Breast Cancer Conference (credit: IOSG)

LATIN AMERICAN COOPERATIVE ONCOLOGY GROUP (LACOG)

LATIN AMERICAN COOPERATIVE ONCOLOGY GROUP (LACOG) (credit: LACOG)

Fernanda Schwyter, Laura Voelcker, Aytén Heidrich and Dr Márcio DeBiasi (Projeto Cura event) (credit: LACOG)

INdIAN ONCOLOGY STUDY GROUP (IOSG)

Sudeep Gupta Deputy Director, ACTREC, Tata Memorial Centre), Rajiv Sarin (Radiation Oncologist, Tata Memorial Centre), Steven Narod (Medical Oncologist, University of Toronto) and Devieka Bhojwani (Vice-President, Women’s Cancer Initiative, Mumbai).
Supporting clinical research in Latin America

In 2016 BIG organised its first clinical research management training for young oncologists from Latin America. From 13 October to 10 November 2016, three early-career medical oncologists and one radiation oncologist from Latin American academic research groups that are members of BIG were in Brussels to follow a training programme dedicated to clinical research development and management: Dr Márcio Debiasi (Latin American Cooperative Oncology Group, LACOG, Brazil), Dr María Clara Rodríguez Palleiro (Grupo Oncológico Cooperativo Uruguayo, GOCUR, Uruguay), Dr Javier Retamales (Grupo Oncológico Cooperativo Chileno de Investigación, GOCCHI, Chile), Dr Zaida Denisse Morante Cruz (Grupo de Estudios Clínicos Oncológicos, GECO, Peru).

During this 4-week programme initiated by BIG and the Latin American Cooperative Oncology Group (LACOG), and developed in close collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), the group attended a variety of activities (presentations, interactive exercises, classroom courses, site visits, etc.) and had the opportunity to exchange experience, know-how and ideas about the management of clinical research groups, as well as the negotiation, set-up and running of clinical trials.

The objective of this training was to nurture and support early-career cancer researchers in the Latin American region in their mission to build the solid infrastructure required to conduct high quality national and regional clinical research, as well as to take part in large international research programmes, while dealing with the many local challenges specifically faced by their region.

The ultimate goal is to boost clinical research in Latin America and thereby to improve the lives of cancer patients from the region.

Cancer research groups in Latin America have rung the alarm and are joining efforts Latin America is struggling to build a qualified and sustainable infrastructure able to develop clinical research. Several factors can explain this precarious situation, among them: limited and unequal access to drugs and medical devices, bad health infrastructures, lack of public health programmes and lack of funding to support research. Cancer research groups in Latin America have rung the alarm and are joining efforts to tackle this issue.

The idea for the training programme on clinical research management materialised from discussions that took place during a meeting in Porto Alegre, Brazil in 2014. This regional ‘Retreat’, the first of its kind initiated by BIG, brought to the table leading Latin American cancer experts from the BIG network, together with representatives of the BIG Executive Board and BIG Headquarters.

The goal of the meeting was to better understand the better understand the situation of clinical research in Latin America – with a focus on breast cancer – and to determine how cancer experts could work hand-in-hand to optimise their collaborations, whether within their individual countries, within their region, or internationally through the BIG network.

During the meeting it was agreed that although some challenges needed to be dealt with locally – such as educating local populations about the importance of research or addressing lengthy regulatory approval processes –, providing training and support for young
oncologists in the management of clinical research groups and the development of clinical studies was a priority for the region that could be achieved together.

To be continued …

Since the training, the focus has been on establishing a mentorship programme to provide support and advice to each of the participants after their return to their home countries, so that they can contribute to the strengthening of the clinical trials infrastructure and expertise within their groups locally.

**BIG affiliated cancer research groups from Latin America**

- **GAICO** - Grupo Argentino de Investigación Clínica en Oncología
  www.gaico.org.ar
- **GBECAM** – Grupo Brasileiro de Estudos do Cáncer de Mama
  www.gbecam.org.br
- **GECOPERU** - Grupo de Estudios Clínicos Oncológicos Peruano
  www.gecoperu.pe
- **GOCCHI** – Grupo Oncológico Cooperativo Chileno de Investigación
  www.gocchi.org
- **GOCUR** - Grupo Oncológico Cooperativo Uruguayo
  www.sompu.org.uy
- **LACOG** - Latin American Cooperative Oncology Group
  www.lacog.org.br

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**Some of the key scientific articles published by member groups about BIG breast cancer trials in 2016**

- Trastuzumab re-treatment following adjuvant trastuzumab and the importance of distant disease-free interval: the HERA trial experience. Metzger-Filho O et al., Breast Cancer Research and Treatment. 2016; 155:127-132, 2016. (BIG 1-01)
- The genomic grade assay compared with Ki67 to determine risk of distant breast cancer recurrence. Ignatiadis M et al., JAMA Oncology 2016, 2:217-224, 2016. (BIG 1-98)
- Twelve-month estrogen levels in premenopausal women with hormone-receptor positive breast cancer receiving adjuvant triptorelin plus exemestane or tamoxifen in the SOFT trial: the SOFT-EST substudy. Bellet M et al., Journal of Clinical Oncology. 2016; 34:1584-1593, 2016. (BIG 2-02, BIG 3-02)


• Liquid biopsy-based clinical research in early breast cancer: The EORTC 90091-10093 Treat CTC trial. M. Ignatiadis et al., European Journal of Cancer 63 (2016) 97e104. (BIG 1-12)


• Poor prognosis after second locoregional recurrences in the CALOR trial. Wapnir IL et al., Annals of Surgical Oncology. 2016 Sep 23. (BIG 1-02)


• RNA Sequencing to Predict Response to Neoadjuvant Anti-HER2 Therapy. A Secondary Analysis of the NeoALTO Randomized Clinical Trial. Furnagalli D et al., JAMA Oncology, September 29, 2016. doi:10.1001/ jamaoncol.2016.3824 (BIG 1-06)

BIG trials
Overview of the current clinical studies run within the BIG network.

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>
<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, P. Altmanos</td>
<td>Lead trial • Coordinating groups: BIG HQ (Sponsor) / JB-CTSU (BrEAST) / FSS • Pharma partner: N/A</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 - NCT01905392</td>
<td>N. Turner, J. Balmaña, D. Cameron, W. Audeh</td>
<td>Co-lead trial • Coordinating groups: EORTC / BIG HQ • Pharma partner: Tesaro (sponsor)</td>
</tr>
<tr>
<td>Breast Cancer in Pregnancy</td>
<td>BIG 2-03</td>
<td>Registry of women treated for breast cancer while pregnant - NCT00196833</td>
<td>S. Loibl, G. von Minckwitz</td>
<td>Supporter trial • Coordinating group: GBG (sponsor) • Pharma partner: N/A</td>
</tr>
<tr>
<td>LORELEI</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 • Coordinating Groups: ABCSG, SOTI and BIG HQ • Pharma partner: Genentech (sponser)</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 neoadjuvant chemotherapy - NCT02032823</td>
<td>A. Tutt, B. Kaufman, J. Garber, C. Geyer</td>
<td>Lead trial • Coordinating groups: BIG HQ / FSTRF • Sponsors: Astrazeneca (Rest of the World), NRG Oncology (US)</td>
</tr>
<tr>
<td>PALLAS</td>
<td>BIG 14-03</td>
<td>Palbociclib with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for hormone receptor positive IHR+ / human epidermal growth factor receptor 2 HER2-negative early breast cancer - NCT02513394</td>
<td>M. Grant, E. Mayer, A. DeNicolle</td>
<td>Co-Lead trial • Sponsors: ABCSG (RoW) / AFT (US) • Pharma partner: Pfizer (grant)</td>
</tr>
<tr>
<td>PANACEA</td>
<td>BIG 4-13</td>
<td>Anti-PD-1 monoclonal antibody in advanced, trastuzumab-resistant, HER3-positive metastatic breast cancer - NCT02192556</td>
<td>S. Loi, F. André</td>
<td>Supporter trial • Coordinating group: IBCSG (sponser) • Pharma partner: Merck</td>
</tr>
<tr>
<td>PENELOPE-B</td>
<td>BIG 1-13</td>
<td>Post-neoadjuvant palbociclib 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 (sponser) • Pharma partner: Pfizer</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, A.H. Partridge, H. Azim, F. Peccatori</td>
<td>Supporter trial • Coordinating group: IBCSG (sponser) • Pharma partner: N/A</td>
</tr>
<tr>
<td>PYTHIA</td>
<td>BIG 14-04</td>
<td>A Phase II Study of Palbociclib plus Fulvestrant for pretreated patients with ER+/HER2- Metastatic Breast Cancer - NCT02336742</td>
<td>L. Malorni</td>
<td>Co-lead trial • Coordinating Groups: BIG HQ/IBCSG (sponser) • Pharma partner: Pfizer (grant)</td>
</tr>
</tbody>
</table>

To test new treatments, BIG collaborates closely with, but independently from the pharmaceutical industry. BIG studies apply specific Principles of Research Conduct to maintain scientific independence and keep the patients' best interests at heart. Together we develop and run clinical trials that will best meet patients’ needs, while following BIG’s principles of research conduct.

In 2016 BIG conducted clinical trials in collaboration with: Novartis, Roche, Tesaro, Servier, AstraZeneca, Genentech, Apotex, Sanofi, Agenda, Pfizer, Merck, Celgene.
## Active, but not recruiting

<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>ALTO</td>
<td>BIG 2-06</td>
<td>Adjuvant lapatinib and trastuzumab - sequence and combination for patients with HER2/Erbb2 positive breast cancer - NCT00490139</td>
<td>M. Piccart, A. Moreno-Aspilua</td>
<td>Lead trial • Coordinating groups: BIG HQ / BrEAST / FSS / Alliance (former NCCTG; sponsor for the US) • Pharma partner: Novartis (global sponsor for all countries with the exception of US)</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, J. Baselga, J. Bines</td>
<td>Lead trial • Coordinating groups: BIG HQ / BrEAST / FSS • Pharma partner: Roche (sponsor)</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 - NCT00004205</td>
<td>B. Thurlimann</td>
<td>Supporter trial • Coordinating group: IBCSG (sponsor) • Pharma partner: Novartis</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. Chu, I. Ollivato, T. Whelan, I. Kunkler, H. Westenberg, J. Jassern, K. Rabinowitch, G. Graub</td>
<td>Supporter trial • Coordinating group: TROG (sponsor) • Pharma partner: N/A</td>
</tr>
<tr>
<td>FINESSE</td>
<td>BIG 2-13</td>
<td>Oral letrozib for patients with FGRF1 ER+ metastatic breast cancer - NCT02053636</td>
<td>F. André, J. Cortés</td>
<td>Lead trial • Coordinating groups: BIG HQ / BrEAST / FSS • Pharma partner: Servier (sponsor)</td>
</tr>
<tr>
<td>IBIS-II Prevention</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 NCT000072462 - NCT00078832</td>
<td>J. Cuzick</td>
<td>Supporter trial • Coordinating group: IBIS (sponsor) • Pharma partner: AstraZeneca</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 - NCT01010438</td>
<td>P. J. Goodwin</td>
<td>Supporter trial • Coordinating group: NCIC (sponsor) • Pharma partner: Apotex</td>
</tr>
<tr>
<td>Male BC</td>
<td>BIG 2-07</td>
<td>Registration and biologic characterisation programme of breast cancer in men - NCT01101425</td>
<td>F. Cardoso, S. Giordano</td>
<td>Supporter trial • Coordinating groups: EORTC (sponsor) / NABCG (US) • Pharma partner: N/A</td>
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<tr>
<td>MINDACT</td>
<td>BIG 3-04</td>
<td>Can the addition of 70-gene signature to common clinical-pathological criteria safely spare patients with 0 to 3 node positive breast cancer from adjuvant chemotherapy? - NCT00433339</td>
<td>E. Rutgers, F. Cardoso, M. Piccart</td>
<td>Co-lead trial • Coordinating groups: EORTC (sponsor) / BIG HQ • Commercial partners: Roche, Sanofi, Novartis and Agenda</td>
</tr>
<tr>
<td>NEO-ALTO</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, J. Huober</td>
<td>Co-lead trial • Coordinating groups: Breast / FSS / SOLTI / BIG HQ • Pharma partner: Novartis (global sponsor for all countries with the exception of US, where Alliance is the sponsor)</td>
</tr>
<tr>
<td>REACT</td>
<td>BIG 1-03</td>
<td>A Phase III Multicentre Double Blind Randomised Trial of Celemoxib versus Placebo in Primary Breast Cancer Patients REACT - Randomised EuropeAn Celemoxic Trial - NCT02429427</td>
<td>C. Coombes, J. Bliss, G. von Minckwitz</td>
<td>Supporter trial • Coordinating group: ICGC (sponsor) • Pharma partner: Pfizer</td>
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<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>SOFT</td>
<td>BIG 2-02</td>
<td>Evaluation of ovarian suppression and of exemestone as adjuvant therapy for premenopausal women with endocrine responsive breast cancer – NCT000066490</td>
<td>P. Francis, G. Fleming</td>
<td>Supporter trial • Coordinating group: IBCSG (sponsor) • Pharma partner: Pfizer</td>
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<tr>
<td>SOLD</td>
<td>BIG 1-10</td>
<td>Short (9 week) vs 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: Roche</td>
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<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 - NCT000533410</td>
<td>M. Colleoni, P. Karlsson, S. Aebi, J. Chirgwin</td>
<td>Supporter trial • Coordinating group: IBCSG (sponsor) • Pharma partner: Novartis</td>
</tr>
<tr>
<td>SUPREMO</td>
<td>BIG 2-04</td>
<td>Adjunct chest wall irradiation for ‘intermediate risk’ breast cancer following mastectomy - NCT00966888</td>
<td>I. Kunkler, P. Canney</td>
<td>Supporter trial • Coordinating group: SCIBG (sponsor) • Medical Research Council • Pharma partner: N/A</td>
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<tr>
<td>TEXT</td>
<td>BIG 3-02</td>
<td>Evaluation of exemestone plus GNRH analogue for premenopausal women with endocrine responsive breast cancer - NCT009664147</td>
<td>O. Pagani, B. Walley</td>
<td>Supporter trial • Coordinating group: IBCSG (sponsor) • Pharma partner: Pfizer</td>
</tr>
</tbody>
</table>

Legend: • AFT: Alliance Foundation Trials, LLC • FSS: Frontier Science Scotland, LTD • FSTRF: Frontier Science and Technology Research Foundation, Inc • TBRC: Translational Breast Cancer Research Consortium • NCCTG: North Central Cancer Treatment Group • SCIBG: Scottish Cancer Trials Breast Group • N/A: not applicable

NB: This table does not include the trials in development and the closed trials. For more information, please visit [www.BIGagainstbreastcancer.org](http://www.BIGagainstbreastcancer.org)
Support BIG: Donors and fundraisers with a BIG heart

Individuals support BIG

**Can you make a difference as an individual?**
Research budgets seem huge. And people often wonder if their support makes a real difference. Of course it does!

In 2016, we highlighted one specific project: BIG Time for Baby (pregnancy after breast cancer, see our campaign on the following pages). The total budget of this study amounts to over € 7 million and will involve 500 patients for a period of ten years.

If you look at the needed funds differently, you can also conclude that the participation of one patient costs about € 14,000. This equals to a bit less than € 30 per week. If one person supports one week of participation, another one another week and so on... the budget can be largely supported by individual donors.

And think about the impact. If this study delivers the expected results, every year, over 100,000 young women could benefit from the conclusions and have the opportunity to safely try to have a baby.

Every donation counts.

**BIG Music Night**

In October, the iconic Grand Place of Brussels turned pink. To celebrate the 20th anniversary of the idea that led to the creation of the BIG network, a special event was organised in the City Hall.

BIG’s Honorary President, Her Royal Majesty the Queen of the Belgians, stressed the ambitious vision of the founders of BIG: “Twenty years ago a plan was developed to build an international network of thousands of scientists and hospitals, all dedicated to making the fight against breast cancer more targeted and more efficient. Meanwhile, this vision has become reality.”

Donors and partners were invited to a lyrical concert by the students of the International Opera Academy of Ghent. An exquisite performance.

**Femmes Fatales**

A tattoo and a photo exhibition to support BIG against breast cancer.

With his pictures, Jurgen Rogiers wanted us to change our view on the disease to a more human and empathetic look. Isabelle Lenfant developed a temporary tattoo that was sold at the exhibition and in several shops to support breast cancer research, giving buyers a unique way of proudly showing their support.
4th Belgian edition of The Designers’ Christmas Trees

On 24 November 2016, The Hotel. Brussels played host to an evening of fine dining, fun and philanthropy. The gala-dinner highlight was the auctioning of 15 original Christmas trees designed by eminent Belgian artists. The event raised €180,000 in support of BIG clinical trials. Making a BIG difference.

Artwork by Fred Eerdekens

Artwork by Jean-François D’Or

Zoë’s testimonial

Since she was a young girl, Zoë dreamed of being a mom. Affected by hormone-sensitive breast cancer at the age of 30, her dreams almost shattered. But she did not give up. Her speech at the gala event inspired many and gives strength to women confronted with breast cancer.

Discover her emotional video testimonial and learn what you can do on www.BIGtimeforbaby.org

In four editions, 50+ artists & designers contributed to raise over €600,000 to support BIG.
BIG Time for Baby campaign

#AllStorks

A campaign to support young women who survived breast cancer and dream of having a baby

We all know the story of the stork delivering babies to people’s houses. Everyone can now join the campaign and, just like the stork, bring good luck and hopefully babies to women fighting the return of breast cancer.

To collect the vital funds needed for the BIG Time for Baby study, we launched a crowdfunding campaign. The idea was to convey a simple and original message that triggers the public to take action and donate.

The campaign was recognisable on social media with the #AllStorks hashtag. Every participant was asked to address his/her online network to help make this campaign go viral. Because with #AllStorks, together, we can make a BIG difference in the lives of these patients.

About the study
BIG Time for Baby is an international clinical study evaluating whether it is safe for women to interrupt their endocrine therapy to attempt pregnancy after breast cancer. Specifically, the study hopes to determine whether treatment can be paused for up to two years to allow for conception without increasing the risk of breast cancer recurrence.

Prof Martine Piccart stresses the societal importance of this study: “The research associated with pregnancy after breast cancer is limited, making it challenging for a woman to navigate her fertility options. This study is vital – the results will allow to determine the risk of interrupting hormonal treatment for oestrogen-receptor positive (ER+) breast cancer on solid scientific ground, in order to give time to the patient to try for a baby. This information is of great importance to thousands of women worldwide!”

www.facebook.com/ BIGagainstbreastcancer
Key results of the campaign

**Facebook**
- The video of Zoë's testimonial touched the masses and went viral.
- The Facebook campaign reached 790,775 unique users and generated 17,750 website clicks.
- Social media proved its ability to target a large-scale audience and to provide adequate reach & frequency to sensitise and mobilise potential donors.

**Blogger moms**
- Asked to talk about the campaign and study (video posts, social media, articles).
- Ten influential bloggers supported the campaign on their channels, allowing a potential reach of 201,780 individuals.

**Celebs**
- Four Belgian celebrities supported the campaign by calling on their followers on social media to take action.

**Press**
- Press release launched in September.
- Interviews organised with Prof. Martine Piccart.
- 17 media outlets with a potential audience reach of 12,289,126 individuals.

**Potential audience reach of 12,289,126 individuals**
Support BIG: Corporate partnerships

We are grateful to the many companies, brands, businesses and employees that are involved in the fight against breast cancer. Their engagement, energy and creativity makes a BIG difference in the lives of the patients we serve.

Why do they support BIG?

Research saves lives
Research is the only way to understand breast cancer, how and why it progresses, and how it can ultimately be stopped. For more than 15 years we have been conducting innovative clinical trials and research that have helped to develop better and more personalised treatments, improving patient survival and quality of life. By supporting clinical research, our partners contribute to giving people more time with their loved ones.

GLO-CAL impact
Global research increases our chances of finding a cure. To test new treatments with enough patients and be confident about the results, clinical research cannot be limited to one institution or one country. But the impact of our work is local, involving many hospitals around the world. Findings and ideas are shared with the global scientific community, for the sake of all patients.

Merge expertise and innovation
Creativity, innovation and generosity. These elements are essential for scientific research aimed at developing the innovative treatments of tomorrow. Those that will save lives.

A Corporate Social Responsibility policy with a serious partner
BIG is a credible partner who values scientific excellence – several of our clinical trials are considered to be landmark – and transparency. Our team works meticulously to ensure that every cent is accounted for, and then provides reports for our donors. Partnering with BIG is also a great opportunity to mobilise and engage employees to help fight a disease that has impacted many lives.

As well as helping to do good, supporting a charity can help our business in many ways. For example, it helps defining our corporate identity and enhances employee relations and motivation.

Every action makes a difference.
They joined our fight against breast cancer in 2016.

Babeth
www.facebook.com/Babeth.be
Pink October gave Babeth (an online women’s fashion shop) the opportunity to sensitise clients and to raise funds for breast cancer research. 10% of all sales in October were donated to BIG.

Babiage
www.babiage.com
The Doodoo, baby’s best friend, is a cuddly toy helping the little ones and their parents to catch a good night of sleep. Since 2016, a percentage of the Rabbit cuddly toy is donated to support mothers-to-be in the BIG Time for Baby study.

Artists with a BIG heart at B19
Three Belgian artists - Tiline Courcelles, Evelyne Cuylits and Gérald de Patoul – participated in Pink October by donating a percentage of their sales at the opening of their collective exhibition at B19, a business centre in Brussels.
During Pink October, customers of CAMELEON were invited to round up the amount of their purchase to support breast cancer research. An action that was welcomed by many clients and staff members. CAMELEON also hosted the first edition of BIG’s Light & Shadow, an event where young Belgian designers sold their work during an auction, in support of BIG’s research.

Octobre Rose Tournai asbl
www.octobrerose.be

The association supported BIG’s research with the profit made from the sale of a catalogue containing photographs by Aurore Delsoir.

COMMUNICATION PARTNERSHIPS

Vivio
www.vivio.com

As Belgium’s leading custom publisher in the field of health and well-being, Vivio supported the #AllStorks campaign by donating advertising space.

Antennes Nostalgie

BIG was one of the laureates of the contest “100 Minutes pour changer le monde” (100 minutes to change the world), benefiting 100 minutes of airtime to promote our work for a better world.

EMPLOYEE ENGAGEMENT

Groupe Vlan
www.vlan.be

Groupe Vlan is one of Belgium’s major players in the field of free press and local information. The group supported the #AllStorks campaign by engaging their readers, journalists, employees and customers to take action against breast cancer.

“
We are all concerned by the disease that affects our loved ones.
Joëlle de Surgères - Babeth
"

CORPORATE DONATIONS

Buy Way
www.buyway.be

Buy Way decided to make a corporate donation and to sensitize their employees and clients by communicating internally on the importance of breast cancer research.

Fimaser
www.carrefourfinance.be

Fimaser supported the BIG Time for Baby study by adopting a patient. They support the enrollment and close monitoring of one patient in this study for a period of 10 years.

Atos Worldline
www.worldline.com

Being particularly sensitive to the cause, Atos decided to sponsor the participation of 10 patients in the BIG Time for Baby study.

Nestlé
www.nestle.be

As one of the leading nutrition, health and wellness companies, Nestlé supported BIG’s research by setting up a fundraiser and sensitizing doctors, health professionals and nurses in their network.

Tamahris
www.tamahris.com

Tamahris, a consultancy network group, helping businesses to define their HR strategy, made a corporate donation to support breast cancer research.

The Baillet-Latour Fund
www.fondsbailetlatour.com

The Baillet-Latour fund supports the BIG Time for Baby study (cf. p.26). Their substantial grant -over three years- gives a strong boost to the study and helps convincing other philanthropists to fund this research.

The societal relevance of this trial was a key factor. More than 100,000 women could benefit from the results of this study yearly.
## Financials

### Balance Sheet

<table>
<thead>
<tr>
<th>ASSETS</th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fixed assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible fixed assets</td>
<td>0</td>
<td>4,396</td>
</tr>
<tr>
<td>Tangible fixed assets</td>
<td>207,420</td>
<td>64,147</td>
</tr>
<tr>
<td>Financial fixed assets</td>
<td>72,627</td>
<td>69,574</td>
</tr>
<tr>
<td><strong>Total Fixed Assets</strong></td>
<td>280,047</td>
<td>138,117</td>
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<tr>
<td><strong>Current assets</strong></td>
<td></td>
<td></td>
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<tr>
<td>Receivables up to one year</td>
<td>4,277,524</td>
<td>6,587,041</td>
</tr>
<tr>
<td>Current investments</td>
<td>5,910,218</td>
<td>4,086,298</td>
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<tr>
<td>Cash at bank</td>
<td>5,361,575</td>
<td>4,948,447</td>
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<tr>
<td>Deferred charges and accrued income</td>
<td>343,189</td>
<td>371,370</td>
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<tr>
<td><strong>Total current Assets</strong></td>
<td>15,892,506</td>
<td>15,993,156</td>
</tr>
<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>16,172,553</td>
<td>16,131,273</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LIABILITIES</th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Equity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrestricted net assets</td>
<td>5,493,549</td>
<td>5,170,847</td>
</tr>
<tr>
<td><strong>Total Equity</strong></td>
<td>5,493,549</td>
<td>5,170,847</td>
</tr>
<tr>
<td><strong>Debts</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amounts payable within one year</td>
<td>10,647,074</td>
<td>10,870,181</td>
</tr>
<tr>
<td>Trade debts</td>
<td>9,847,170</td>
<td>10,294,017</td>
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<tr>
<td>Tax, remuneration and social security</td>
<td>799,904</td>
<td>576,164</td>
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<tr>
<td>Deferred charges and accrued income</td>
<td>31,930</td>
<td>90,245</td>
</tr>
<tr>
<td><strong>Total Debts</strong></td>
<td>10,679,004</td>
<td>10,960,426</td>
</tr>
<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>16,172,553</td>
<td>16,131,273</td>
</tr>
</tbody>
</table>

Over the last five years, we invested over €60,000,000 in breast cancer research, making a huge difference in the lives of the patients. A heartfelt thank you to all our partners and donors for making this possible.
### Income & Expenses Statement

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operating Income &amp; Expenses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turnover (research)</td>
<td>9,563,551</td>
<td>12,717,941</td>
</tr>
<tr>
<td>Other goods &amp; services</td>
<td>-6,743,845</td>
<td>-10,374,686</td>
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<tr>
<td><strong>Operating margin</strong></td>
<td>2,819,706</td>
<td>2,343,255</td>
</tr>
<tr>
<td>Remuneration, social security &amp; pension costs</td>
<td>-2,730,817</td>
<td>-2,403,277</td>
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<tr>
<td><strong>Operating result</strong></td>
<td>88,889</td>
<td>-60,022</td>
</tr>
<tr>
<td>Financial result</td>
<td>243,874</td>
<td>13,843</td>
</tr>
<tr>
<td>Extraordinary income (+)</td>
<td>0</td>
<td>3,257</td>
</tr>
<tr>
<td>Extraordinary expenses (-)</td>
<td>-10,061</td>
<td>-10,060</td>
</tr>
<tr>
<td><strong>Result for the financial year</strong></td>
<td>322,702</td>
<td>-52,982</td>
</tr>
</tbody>
</table>

From 2012 to 2016, 94.5% of BIG’s income was invested in breast cancer research.
Acknowledgements

Our donors
Mrs Estelle Benatar
Mr Marc Bogaerts
Mr Philippe Bossard
Mrs Lisa Boulet
Mr and Mrs Alain and Cristina Camu
Mr Yves de le Court
Mrs Anne-Marie Delhougne
Prince and Princess de Merode
Knight Gerald de Patou
Mr Alain De Pauw, president CDP
Mr and Mrs Bruno and Isabelle Dethomas
Count and Countess de Traux de Wardin
Baron and Baroness de Vaucleroy
Countess Louis du Chastel de la Howarderie
Mr Yvon Englert, Rector ULB
Mr François Gerard and Mrs. Jessica Parser
Mrs Alain Grisay
Mr and Mrs Nissim Israël
Mrs Barbara Kandiyoti
Mr and Mrs Xavier Pelgrims de Bigard
Mrs Axelle Pintiaux, Erasme
Mr and Mrs Xavier Roland
Mrs Virginie Sailléz
Mr Olivier Schaar - Brand it
Prof Maurice Sosnowski
Baron and Baroness Vaxelaire
Mrs Anne Vierstraete
Mr and Mrs Luc and Inge Vierstraete
Mr Michel Wajs

Our sponsors
Artmaniac – Xavier Dujardin
Atelier Isabelle de Borchgrave
Aurum Drinks
Cattleya
Catwalk Pictures
CdS Location
City of Brussels
Château de Bioul
Escrtoire
Hoel&Hoel Brandsetters
International Opera Academy, Ghent
Les Vins de Julien
Maison Wittamer
MODEIGN Academy
My Be Pop
Petroissan
Rouge Pivoine
Silversquare
Sotheby’s
Stockmans kalenders
The Hotel, Brussels
Traiteur Lefevere

Artists with a BIG heart
Atelier Relief, Wim Bruynooghe, Isabelle de Borchgrave, Jean-François D’Or, Fred Eerdekens Philippe Geluck, Clio Goldbrenner, Marie-Jo Lafontaine, Guy Leclef, Isabelle Lenfant, Ali Mahdavi, Kris Martin, Pol Quadens, Annemie Verbeke
Akinto, Ariane Lesprie, BShirt, Delphine Quirin, Juggle Angels, JustEve, Louise Assoma, Mère et Fille, Olivia Hainaut, Orane et Enara, Sarah Josis, Tenue de Ville, World of Wonder

Tilene Courcelles, Evelyne Cuylits and Gérald de Patou

The Chefs
Pascal Devalkeneer - Restaurant le Chalet de la Forêt
Isabelle Arpin - Restaurant WY
Pierre Balthazar - The Restaurant
Joost Arijs - pastry chef and master confectioner
César Román - “Best Sommelier” by Gault & Millau in 2015

The Committee of Ambassadors
Jessica Parser, President
Nathalie de Merode
Patsy Israël
Nathalie Misson
Edith Roland
Frédéric Van der Schueren
Catherine Vaxelaire

“Finding a cure for breast cancer is one of the biggest challenges faced by researchers from around the world. Significant progress has been made to improve both the chances of survival and the quality of life of women affected by the disease. However, breast cancer remains the second most common cancer in the world and is still responsible for too many deaths annually.

By bringing together the top breast cancer experts from around the world to conduct innovative research, BIG has the global reach and expertise required to find a cure. We need to support such critical research to give hope to women affected by this devastating disease, and their families.

HRM the Queen of the Belgians
Honorary President of BIG against breast cancer
Hello. I´m Charly.

You may not know it yet, but you saved my mom.
Thank you.

Your support makes a BIG difference in the lives of the patients we serve.

Support breast cancer research today and help save lives.

Evidence shows that younger women are increasingly being affected by breast cancer. Of the 1.67 million new cases in 2012, one third were patients under the age of 50. We are on a mission to change that. Join us today.

Make a donation on our bank account
BE57 5230 8072 9135

Or visit our website to make your contribution in just a few clicks.

www.BIGagainstbreastcancer.org/donate