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Northern Europe
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Note from the editors

It is with great sadness that we learned of the passing away of Professor José Baselga, a friend and colleague of so many of us. The breast cancer community has lost one of its leading researchers and most brilliant scientists. He will continue to inspire future generations of cancer scientists and oncologists. Our prayers and thoughts are with his family, friends, and colleagues. Professor Baselga died at the age of 61 on 21 March 2021. An In Memoriam can be found on page 15.

With COVID-19 still impacting our everyday lives, the arrival of the vaccines brings optimism. As we are entering a new phase of the pandemic, the light at the end of the tunnel is slowly getting brighter. Let’s hope that we may soon return to some kind of normalcy.

BIG’s editorial team wishes to thank all the BIG member groups who contributed to this issue of BIG Research in Focus. Thank you especially to the breast cancer experts who accepted to be interviewed for the themed article “Fighting breast cancer around the globe: Northern Europe”. You provided us with very valuable insights into breast cancer research in your countries. The countries of Northern Europe have frequently been at the forefront of breast cancer research that has shaped worldwide clinical practice, and they continue to carry out important studies nationally, and as valued participants in collaborative trials. Medical journalist Jenny Bryan discusses recent studies and future plans with leading Nordic breast cancer researchers. For the full article, see as of page 5.

None of BIG’s achievements would be possible without the BIG network and its willingness to work together. Despite all the challenges COVID-19 poses, BIG continues its efforts to advance breast cancer research, demonstrating persistence and resilience, which is needed when conducting large international academic trials. The section “Other trials and activities by BIG Member Groups” gives a peak at BIG member’s research and related activities around the world. You will also find a few examples of how some BIG member groups address(ed) the pandemic. See as of page 30.

BIG against breast cancer, BIG’s dedicated philanthropy unit, conducts vital fundraising to support BIG’s clinical trials and research programmes that have no commercial interest but are crucial for breast cancer patients. The funds raised – through the generosity of foundations, companies, ambassadors, and other individuals – contribute to the work of BIG member groups and their affiliated hospitals, and help support patient participation in a study. Due to the COVID-19 pandemic and related public health measures, planned events had to be cancelled and we had to re-invent how to reach BIG’s community of supporters, as described in the section “BIG Network”. See as of page 14.

The section “Clinical Trials and Activities” gives an update on BIG trials, their status and abstracts presented at Virtual SABCS 2020 and Virtual St Gallen Breast Cancer Conference 2021. See as of page 20.

Finally, you will find the “Overview of the current clinical studies run within the BIG network” as of page 40.

We hope you enjoy the reading and look forward to our on-going collaboration with you.

Together, we make a difference

BIG’s Editorial Team

The countries of Northern Europe have frequently been at the forefront of breast cancer research that has shaped worldwide clinical practice and they continue to carry out important studies nationally, and as valued participants in collaborative trials. Medical journalist, Jenny Bryan, discusses recent studies and future plans with leading Nordic breast cancer researchers.

In 1985, when Swedish breast cancer researchers reported that mammographic screening had reduced breast cancer mortality by 31% after seven years, they started a revolution in breast cancer care.1 It was the key evidence that many countries had been awaiting before giving the green light to their own national programmes.

Thirty-five years later, Nordic countries have among the lowest breast cancer mortality rates in the world and, as Professor Jonas Bergh, Professor of Oncology at the Karolinska Institutet University Hospital, Stockholm, explains, nationwide screening is likely to have played an important role.

“It took some 10 years for mammography to be introduced in all regions of Sweden and adherence has been higher than some would have expected. There is a history of positive attitudes to innovation in Sweden and, thanks to regularly updated national guidelines focused on the highest international standards, patients with breast cancer have had access to all the latest treatment strategies,” says Bergh, a former chair of the Swedish Breast Cancer Group (SweBCCG).

National healthcare registration and a comprehensive breast cancer registry in Sweden for over 20 years have been used to monitor implementation of breast care recommendations and treatment outcomes and have also contributed to the current low mortality rate. In other Nordic countries, there have been similar reductions in mortality. Minna Tanner, Adjunct Professor in Oncology and Senior Consultant in Clinical Oncology and Radiotherapy at Tampere University Hospital, Finland, explains that, despite the relatively high incidence of breast cancer in Finland, five-year breast cancer survival is over 90%.

“We saw a remarkable improvement in survival following the introduction of national screening and adjuvant therapies, such as taxanes, and breast cancer guidelines. The implementation of multidisciplinary teams, including oncologists, surgeons, radiologists and pathologists, for deciding treatment has also contributed to improved outcomes for patients,” says Tanner, who chairs the Finnish Breast Cancer Group (FBGC).

With five university hospitals and 15 regional hospitals, patients in Finland can expect the same standards of care wherever they are treated. Indeed, it has been shown that availability of breast cancer treatment in Finland is more equitable than for many other diseases.

1 It was the key evidence that many countries had been awaiting before giving the green light to their own national programmes.
In recent years, Bergh and colleagues at the Karolinska Institute have focused on neoadjuvant studies in patients with human epidermal growth factor receptor 2 (HER2)-positive breast cancer.

In 2019, promising results were reported from the randomised Phase 2 PREDIKX HER2 study carried out in Sweden and coordinated by researchers at the Karolinska Institutet University Hospital, Stockholm. This showed similar pathological complete response (pCR) and less toxicity with trastuzumab emtansine compared to standard care with docetaxel, trastuzumab and pertuzumab in patients with hormone receptor (HR)-positive, HER2-positive tumours and positive nodes. A further de-escalation randomised study is under discussion. It will compare the combination of trastuzumab emtansine, CDK 4/6 inhibition and fulvestrant with best available chemotherapy.

“This will really challenge whether this type of de-escalation therapy is effective in this group of patients,” says Bergh.

In the large NordicTrip study, initiated by SweBCG and SABO, researchers from Sweden, Finland, Denmark and Iceland will join forces to investigate the effect of adding oral capcitabine to platinum-based preoperative chemotherapy in a planned 820 patients with ER-negative and HER2-negative Stage 2-3 breast cancer. The primary endpoint of the study is pathological complete response (pCR) rate at the time of radical surgery, and secondary endpoints include invasive disease-free survival (IDFS), DFS, and overall survival.

Swedish researchers are also investigating checkpoint inhibitors in breast cancer, including in PREDIKX HER2, a randomised Phase 2 trial of pre-operative treatment with or without atezolizumab in programmed death-ligand 1 (PD-L1) positive HER2-positive breast cancer.

Linderholm is the principal investigator for the I-CONIC study – a window-of-opportunity trial run at Sahlgrenska University Hospital in collaboration with Professor Kristian Pietras, at Lund University. This follows pre-clinical research by Pietras’ group that showed the potential of inhibition of platelet-derived growth factor (PDGF)-CC to convert basal-like breast cancers into HR-positive tumours with enhanced sensitivity to endocrine therapy. I-CONIC will now investigate the use of the tyrosine kinase inhibitor, alpelisib, in patients with breast cancer with one to five metastases in one or two organs.

In the pan-Nordic Affibody-3 study led by Dr Henrik Lindman from Uppsala Akademiska University Hospital, PET scanning with the radioactive tracer, ABY-025, has been shown to accurately evaluate HER2 expression in patients with metastatic breast cancer.

“The Affibody research has shown that there is heterogeneity in HER2 positivity in different metastases in the same patient, and there is a common conversion in HER2 status between primary and metastatic tumours,” explains Linderholm.

“The next stage of the research, which is being carried out by researchers in Sweden and Denmark, is to find out whether measurement of HER2 status using ABY-025 PET scanning or conventional biopsy is the best predictor of response to HER2 therapies,” she adds.
Precision medicine is high on the agenda in Norway

As well as contributing a significant number of patients to multiple ongoing international studies, researchers in Norway are actively involved in ground-breaking research sponsored or heavily supported through the Norwegian Breast Cancer Group (NBCG) – an organisation for breast surgeons and oncologists, pathologists, radiologists and others involved in breast cancer research.

“The NBCG plays an important role in advances in breast cancer care, including the development of national guidelines and patient care pathways. It also brings together a network of clinicians and scientists who are interested in research in a large number of areas, ranging from translational to clinical development. NBCG researchers are also contributing to the OPTIMA study which is investigating the use of Prosigna molecular profiling for personalising treatment in patients with node-positive breast cancer.”

On a national scale, IMPRESS Norway is a clinical study starting in 2021 to investigate the use of gene mutation testing in patients with cancer to help inform off-label use of medicines that have been approved for other indications. Modelled on the Dutch DRUP precision medicine initiative, IMPRESS Norway will get government funding and active support from pharmaceutical sponsors to develop national infrastructure for precision diagnostics and treatment. IMPRESS Norway plans to recruit 250-500 patients per year with advanced cancer who have been referred by their GPs or hospital clinicians, based on molecular profile, cancer diagnosis and previous treatment. Cohorts of eight patients will be treated according to their molecular profiles, and if one or more respond to treatment, a further 16 patients will be recruited. Cohorts will be considered positive if five or more of the total 24 patients respond to treatment.

There is also continuing focus on the potential of immunotherapy approaches in breast cancer. The ALICE study, which is being carried out in collaboration with researchers in Denmark, is recruiting patients to investigate the effects of anacizumab in combination with immunogenic chemotherapy in patients with metastatic TNBC. In collaboration with Belgian researchers, the ICON study, which completed recruitment at the end of 2020, is evaluating the checkpoint inhibitor, ipilimumab and nivolumab, in combination with immunogenic chemotherapy in patients with metastatic lobar B breast cancer.

“In a different area of breast cancer research, the primary aims of the fully recruited EBBA-II study are to determine whether a 12-month exercise programme of strength and endurance training among newly diagnosed patients with breast cancer patients undergoing adjuvant therapy will influence factors associated with metabolic profile, tumour growth, and cardiopulmonary function. Secondary aims are to determine training effects on disease-free survival, overall mortality, and breast cancer specific mortality.”

Treatment de-escalation studies take priority in Finland

In Finland, a programme of nationwide, population-based studies, many done under the umbrella of the Finnish Breast Cancer Group (FBCG), means that all patients with breast cancer may have the opportunity to participate in clinical trials, explains Tanner.

The FinHer study showed improved recurrence-free survival (RFS) with docetaxel on recurrence-free survival compared with vinorelbine in early breast cancer and the efficacy of trastuzumab in those with HER2-positive disease. The FinXX study, carried out in collaboration with Swedish researchers, failed to show an RFS advantage when capecitabine was added to docetaxel, epirubicin, and cyclophosphamide, though a significant improvement in overall survival was shown with capecitabine in an exploratory subgroup analysis of patients with TNBC.

“In Finland, capecitabine is used more commonly in adjuvant breast cancer specific mortality. We have good data pools from our registries to collect this sort of data and it doesn’t require a lot of financial support,” says Tanner.

Although basic research is not carried out by the FBCG, it is underway in many university and other departments in Finland. A national programme of research is using next generation sequencing (NGS) to guide targeted breast cancer treatment for many patients and to monitor efficacy based on molecular profiles.

“Centres have been established in Helsinki, Tampere, and Turku to perform Phase 1/2 studies, as these need fewer patients and will give Finnish researchers more opportunities to participate.”

“This is a very interesting area of research to be involved in earlier phase studies. It will take investment to set up, but we believe it is a good option in Finland where we have high-quality researchers,” says Tanner. “It has taken a few years to establish a track record but, as we progress, we hope it will become easier to get more studies.”

As in many countries, precision medicines are high on the agenda in Norway. EMIT1 is a de-escalation study investigating the use of Prosigna® molecular profiling to determine individualised therapy for patients with early breast cancer.

“We are establishing the diagnostic possibility to use gene expression profiling in node-negative patients across Norway and monitoring the effects of this on treatment decision-making, health economic outcomes, and changes in quality of life and adverse effects due to treatment alterations,” Naume explains. “This study also provides the basis for planned translational refinement studies based on the analysis of additional biomaterial.”

NBCG researchers are also contributing to the OPTIMA study which is investigating the use of Prosigna molecular profiling for personalising treatment in patients with node-positive breast cancer.

He adds that several studies (PETREMAC, NeoAVA, I-BCT) carried out under the NBCG umbrella, and separately, are endeavouring to identify mechanisms of tumour sensitivity or resistance to neoadjuvant therapy, including olaparib, CDK4/6 inhibitors, bevacizumab, and carboplatin.

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“In Finland, capecitabine is used more commonly in adjuvant breast cancer than in some countries because of the survival benefits seen in patients with TNBC. While it would be nice to carry out a randomised controlled trial in patients with TNBC, we believe that the clear benefits in this population-based study are sufficient to guide practice,” says Tanner.

Treatment de-escalation studies are also a priority in Finland. In the SOLD study in patients with HER2-Positive early breast cancer, short-course trastuzumab was shown to be non-inferior to one year of trastuzumab when given with similar chemotherapy. The BOLD-1 study in patients with HER2-positive early breast cancer is now comparing short-course trastuzumab and pertuzumab and docetaxel therapy with standard trastuzumab and docetaxel therapy for one year.

“Recruitment to BOLD-1 has been slow partly because the treatment of HER2-positive disease has moved towards the neoadjuvant setting but, at the FBCG, we feel it is a very worthwhile study to complete,” says Tanner.

In addition, several real-world FBCG studies are underway to investigate the use of new agents such as atezolizumab.
Bergh points out that, although Nordic countries have small populations, they have other advantages for research, including long term follow-up studies, due to the quality of their cancer registries12 and their guidelines-based consistency of breast cancer care.

“Our relatively small population means that we are sometimes left out of pharmaceutical studies but, although we may not be able to contribute large numbers, ‘lost to follow up’ is almost non-existent in our cohorts, and this is well understood to be an important advantage in performing clinical trials,” he says.

“I hope that discussions about planned trials can be more inclusive of Nordic researchers so that their additional and complementary insights may add value to future research,” he adds.

Linderholm stresses the importance of being involved with BIG. “Being a member of BIG not only enables us to hear about the new trial proposals that have been accepted and participate in discussions, it also provides opportunities to expand our network into other parts of Europe. I would never have got to know researchers from organisations, such as GEICAM and SOLTI in Spain, so quickly if I had not been involved with BIG,” she says.

She explains that obtaining national funding for clinical trials is challenging as Swedish grant-giving bodies have typically favoured pre-clinical research. However, more recently, breast cancer researchers have been more successful in financing clinical trials through the Swedish Research Council, including for the TAORMINA, PREDIX2HER2 and NordicTrips studies.

In Finland, lack of funding for investigator-led studies and exclusion from studies sponsored by pharmaceutical companies are also an issue. “All small countries are facing the same problem of being unable to recruit sufficient patients to be considered for the larger international trials sponsored by pharmaceutical companies. The best way forward is to collaborate with breast cancer groups in other countries and participate in BIG trials,” says Tanner.

Naume agrees that Nordic collaborative studies, such as NordicTrips and NATURAL, are one option. However, he also points out that different national and local regulatory systems can lead to delays in starting trials. In Norway, getting approvals from each hospital where researchers want to take part can take a lot of time. A recent government initiative has tried to address timelines and taxinates in the adjacent setting. DBCG studies also contributed to the development of aromatase inhibitors and targeted adjuvant treatment for HER2-positive breast cancer.

As a result of scientific interest in the anti-cancer potential of cholesterol-lowering, statin treatment, the MASTER study is comparing standard neoadjuvant therapy and placebo with standard neoadjuvant therapy and atorvastatin in patients with early breast cancer. Over 3,000 patients from across Denmark with ER-positive breast cancer, who are candidates for systemic cancer therapy before or after breast surgery, are being recruited. The primary endpoint is invasive disease-free survival. Treatment with atorvastatin or placebo will continue for two years unless side-effects are experienced and further treatment with atorvastatin or the placebo is deemed inadequate.

Future directions

For the future, Bergh hopes that research will lead to a better understanding of the heterogeneity of breast cancer and a better appreciation of the genetic and other drivers of the disease.

“I hope this will mean that targeted treatment can take the place of the more toxic forms of chemotherapy and radiotherapy in use today. In particular, I hope this will include novel treatments for triple negative breast cancer for which we are already starting to see progress with the first approval of sacituzumab govitecan,” he says.

Naume also hopes for more possibilities for precision medicine, with targeted treatment including in patients with early breast cancer.

For Tanner, the goal is to be able to report better survival rates for the more aggressive tumour types, such as TNBC, and cure more patients.

“Having made so much progress with screening and the treatments we already have, the only way to really make progress is with new and better drugs. However, as survival is already so good, we probably need to accept that new steps forward will be important but may be quite small,” she concludes.

A broad spectrum of breast cancer research in Denmark

For more than 40 years, Danish breast cancer specialists contributing to studies coordinated by the Danish Breast Cancer Cooperative Group (DBCG) have helped to improve outcomes for patients with breast cancer.11 DBCG trials have led to the survival advantages of post-mastectomy radiation in high-risk patients and the effectiveness of breast-conserving surgery and radiotherapy have had a significant impact on clinical practice.

Continuing studies aimed at de-escalating radiotherapy to reduce toxicity while maintaining efficacy have also affected practice worldwide. In 2015, the SKAGEN1 study was initiated to investigate the difference in late radiation morbidity between hypo-fractionated and normo-fractionated loco-regional breast irradiation in high risk patients, with participation from Norway and other European countries as well as Australia.

In the NATURAL de-escalation trial, initiated by the DBCG, with collaborators in Norway and Sweden, female patients over 60 years with early breast cancer and negative nodes and negative margins after surgery are being randomised to partial or no radiotherapy. The aim is to find out if low-risk patients can safely omit adjuvant radiotherapy from their care.

Early DBCG studies on tamoxifen and cyclophosphamide-based chemotherapy were instrumental for the development of adjuvant systemic therapy and establishing the relative importance of anthracyclines and taxanes in the adjuvant setting. DBCG studies also contributed to the development of aromatase inhibitors and targeted adjuvant treatment for HER2-positive breast cancer.

For the future, Bergh hopes that research will lead to a better understanding of the biology of breast cancer cells that are lying dormant, he says.

As well as looking forward to results from TAORMINA and from new treatment de-escalation studies, such as NATURAL and BIG’s planned DECRESCENDO trial in patients with HER2-positive breast cancer, Linderholm hopes for better treatment for brain metastases.

“Patients with disseminated treatment are living longer thanks to more effective treatment, so we are seeing more patients with brain metastases who now need more research into better treatments,” she says.

For Tanner, the goal is to be able to report better survival rates for the more aggressive tumour types, such as TNBC, and cure more patients.

“We also need to understand more about tumour biology in delayed relapses to help improve the management of delayed relapse. We are collaborating with researchers in the UK to try to characterise single tumour cells in bone marrow to better understand the biology of breast cancer cells that are lying dormant,” he says.

Research challenges of working with smaller populations

Breast cancer researchers in Northern Europe would like to play a more significant role in the development and leadership of international trials – given the significant patient numbers they recruit relative to their population size.
References


Meet the experts

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BIG strategy statement

At the end of 2020, BIG’s Executive Board proposed the following strategy statement to the General Assembly, which was approved:

We believe that it is possible to develop cures for breast cancer through global research and collaboration; our mission is therefore to facilitate and accelerate academic breast cancer research at an international level, and to do so by enabling groups to do more than their individual parts.

BIG commits to prioritising research that otherwise would not be possible and cannot be done by one research group alone by

- having a network of collaborative research groups and data centres, represented by their individual members, who are world-class experts in breast cancer research
- bringing together these individuals to discuss, prioritise and conduct clinical trials and research programmes that will help address the unmet related needs of individuals with breast cancer, without unnecessarily duplicating efforts
- appointing working groups and task forces to develop new research ideas that can only be done within a network such as BIG’s
- facilitating access to bio-samples and data collected in the context of BIG studies for the conduct of translational research, aiming to optimise individualised diagnosis and treatment
- providing a headquarters with trained and qualified staff who
  - work closely with BIG members to plan, develop and run BIG studies and translational research
- provide support in various forms, ranging from scientific input to legal advice, communications, fundraising, and the organisation of meetings and other events for BIG members and partners
- working according to specific research principles that will preserve academic freedom, even when partnering with commercial entities.

With this framework, the BIG network will thrive and continue to inspire future generations of cancer scientists and oncologists. He will leave a lasting legacy through his contributions to oncology, and to patients suffering from cancer.

Today the breast cancer community has lost one of its leading researchers and most brilliant scientists. He will continue to inspire future generations of cancer scientists and oncologists.

Our prayers and thoughts are with his family, friends, and colleagues.

In memory of his father, Clara Baselga-Garriga has launched a crowdfunding campaign to fund research for Creutzfeldt-Jakob disease.

World renowned oncologist and researcher, Professor José Baselga died at the age of 61 on Sunday 21 March 2021.

Throughout his career, Professor Baselga made significant contributions to breast cancer treatment and paved the way towards personalised medicine. His main research interests were the development of molecular targeted agents and novel anti-HR2 drugs, the identification of strategies to overcome mechanisms of resistance, and new therapeutic approaches to target the PI3K pathway.

Professor Baselga started his career in Spain, where he was Founding Director of the Vall d’Hebron Institute of Oncology (VHIO) at the Vall d’Hebron University Hospital in Barcelona. In 2010, he became Chief of the Division of Haematology / Oncology, Associate Director of the Massachusetts General Hospital Cancer Centre, and Professor of Medicine at Harvard Medical School, before moving to the Memorial Sloan Kettering Cancer Center (MSKCC) in New York in 2013. There he served as Physician-in-Chief and was also Chief Medical Officer and Professor of Medicine at Weil Cornell College in New York City until 2018. Since 2019, Professor Baselga was Executive Vice-President, Research & Development Oncology at AstraZeneca.

He was recognised as a visionary in the field of oncology, playing a key role in drug development at the international level, leading a number of neo-adjuvant trials in breast cancer, and being at the forefront of developing biomarker-based early and translational clinical research. As member of the SOLTI Breast Cancer Research Group, Professor Baselga has been involved in many international trials run in collaboration with BIG. As BIG Executive Board Member from 2010 to 2018, he was also particularly influential in large studies such as NeoALTTO, ALTTO and APHINITY.

"Dr Baselga was an extraordinary human being who led the field of precision oncology, treating many patients and mentoring many oncologists around the world, including me. His vision, passion, determination, and hard work allowed many patients suffering from breast cancer to benefit. His death is a big loss for patients and the whole cancer community. Our thoughts are with his family". Dr Aleix Prat, BIG Executive Member and member of SOLTI Breast Cancer Research Group.

Professor Baselga was past President of ESMO and AACR, and a past member of the Board of Directors of AACR and ASCO. He received numerous awards throughout his career, including the prestigious 2017 ESMO Lifetime Achievement Award as recognition for his outstanding contributions to oncology, and to patients suffering from cancer.

Today the breast cancer community has lost one of its leading researchers and most brilliant scientists. He will continue to inspire future generations of cancer scientists and oncologists.

Our prayers and thoughts are with his family, friends, and colleagues.

In memory of her father, Clara Baselga-Garriga has launched a crowdfunding campaign to fund research for Creutzfeldt-Jakob disease.
BIG thank you

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

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

Today, the BIG network consists of 54 like-minded research groups. An overview of them can be found on page 45.

World Cancer Day 2021

Every year, 4 February marks World Cancer Day. As this year’s theme was “Together, all our actions matter”, BIG launched a communications campaign highlighting BIG’s de-escalation trials and the importance of international collaboration to optimise personalised treatment of breast cancer.

BIG and World Cancer Day: communication and key messages

The following content was developed into a press release and issued to a global list of media contacts. It was also distributed via various social media posts and channels, published on BIG’s website, and shared with BIG HQ, BIG’s member groups, BIG against breast cancer’s philanthropy community and other stakeholders:

BIG’s large global network of over 50 academic breast cancer research groups is at the fore of today’s breast cancer research. Founded on the idea that working together internationally is essential to making strides towards curing breast cancer, BIG’s clinical trials have led to practice-changing achievements, paving the way towards more personalised treatment of breast cancer.

A number of BIG’s trials aim to test the possibility to safely reduce the amount and/or the length of some treatments – or avoid them entirely –, without increasing the risk of the cancer coming back or affecting a patient’s quality of life. The use of cutting-edge genomic tests is closely linked to some of these de-escalation studies.

BIG’s de-escalation studies contribute to tailoring treatment more precisely to individual patient needs. Today, three large international, long-term breast cancer de-escalation trials are being run or about to be launched under the BIG umbrella: MINDACT (BIG 3-04 / EORTC 10041), EXPERT (BIG 16-02 / ANZ 1601) and DECRESCENDO (BIG 19-02 / JBB-EBG-Decrescendo-2020). A fourth one, DCIS (BIG 3-07 / TROG 07.01), focuses specifically on ductal carcinoma in situ (DCIS), which is not an invasive breast cancer but if left untreated, may turn into one.

None of BIG’s achievements would be possible without the willingness to work together. For over 20 years, BIG has been conducting global breast cancer clinical trials and research programmes. Despite the COVID-19 pandemic and all the challenges it poses, BIG’s network has continued its efforts to advance breast cancer research, demonstrating persistence and resilience.

Together, we will make a difference.

Read BIG’s press release for World Cancer Day 2021
With all the restrictions that were put in place in 2020 by the Belgian Government to quell the spread of the COVID-19 virus, BIG’s philanthropic team had to re-invent how to reach its community of supporters. This led to the development of new digital events, direct mailings, and corporate partnerships.

Although gala and other in-person events could not take place as planned, these new concepts helped to raise close to EUR 900,000. These precious funds will help support POSITIVE, EXPERT and AURORA, three purely academic studies run under the BIG umbrella.

The new digital events included the following:

* **Move for BIG Research virtual challenge (June & July)** Organised at the height of the lockdown in Belgium, during this first ever BIG virtual challenge, BIG’s community was invited to run, walk, garden, do yoga and cycle at home, all with the goal of reaching 28,800 steps each.

* **“1 note, 1 donation” crowdfund campaign in collaboration with Fanny Leeb (September & October)** This crowdfund campaign was launched in collaboration with French singer Fanny Leeb. For each donation of EUR 11, a note of her song “Show them how it goes”, which she specifically produced for BIG, was revealed.

**BIG's Extraordinary Raffle**

Furthermore, towards the end of the year, BIG’s philanthropic team organised an online raffle for the BIG against breast cancer community. The sale of tickets took place between 18 November and 27 December, with the winner taking home a hybrid Fiat 500.

The tickets were sold exclusively online, with the enthusiasm and support of the philanthropic community being highlighted by the success of the campaign. In total, the raffle raised over EUR 28,000.

**BIG Together e-news**

Over the course of 2020, a tri-lingual (English, French and Dutch) electronic newsletter entitled “BIG Together” was developed.

The aim of this e-newsletter is not only to keep an open line of communication between BIG and the wider community, but also to share updates on the BIG network at large and its research highlights.

The BIG against breast cancer philanthropic team hopes to be able to organise COVID-friendly events in 2021 to re-connect in person with its community of supporters, as well as raise funds.

If you would also like to be kept up to date on upcoming activities, do not hesitate to sign-up to the newsletter here: www.BIGagainstbreastcancer.org/BIG-Together
The trial is a partnership between Breast International Group (BIG), NRG Oncology, the US National Cancer Institute (NCI), Frontier Science & Technology Research Foundation (FSTRF), AstraZeneca and MSD. It is sponsored by NRG Oncology in the US and by AstraZeneca outside the US.

21 research groups from the BIG network are participating in this trial.

Manuscripts recently published


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Could patients avoid radiotherapy after surgery?

In the EXPERT trial (public name: BIG radio tuning), BIG, together with Breast Cancer Trials Australia & New Zealand (BCT-ANZ), is studying whether some patients with low risk early breast cancer could be spared radiotherapy after breast conserving surgery. A genomic test on breast cancer tumours is being used to determine the risk of the cancer coming back. In patients at low risk of recurrence, the combination of standard radiotherapy and hormone treatment is being compared with hormone treatment alone.

As we write these lines, 400 patients have already been enrolled in the study.

The results of the EXPERT trial, which will be run in 9 countries around the globe and enrol a total of 1,170 patients, could influence how 2 in 5 women with breast cancer are treated.


If the study proves that certain patients do not need radiation therapy, many women affected by this disease may be spared its potential side effects, and healthcare systems could also make significant savings.

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The OlympiA Phase III trial will move to early primary analysis and reporting following a recommendation from the Independent Data Monitoring Committee (IDMC).

Based on the planned interim analysis, the IDMC concluded that the trial crossed the superiority boundary for its primary endpoint of invasive disease-free survival (iDFS) and demonstrated a sustainable, clinically relevant treatment effect for olaparib (Lynparza) versus placebo for patients with germline BRCA-mutated (gBRCAm) high-risk human epidermal growth factor receptor 2 (HER2)-negative early breast cancer, and recommends primary analysis now take place.

In its communication, the IDMC did not raise any new safety concerns. The trial will continue to assess the key secondary endpoints of overall survival and distant disease-free survival.

The OlympiA trial was set up to assess if using olaparib can reduce the risk of breast cancer recurrence in patients with high-risk HER2-negative primary breast cancer who have an inherited BRCA1 or BRCA2 gene mutation and who have completed all standard anticancer treatments.

The Olympus (BIG 6-13) trial will move to early primary analysis and reporting following a recommendation from the Independent Data Monitoring Committee (IDMC). Based on the planned interim analysis, the IDMC concluded that the trial crossed the superiority boundary for its primary endpoint of invasive disease-free survival (iDFS) and demonstrated a sustainable, clinically relevant treatment effect for olaparib (Lynparza) versus placebo for patients with germline BRCA-mutated (gBRCAm) high-risk human epidermal growth factor receptor 2 (HER2)-negative early breast cancer, and recommends primary analysis now take place.

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The Olympus trial was set up to assess if using olaparib can reduce the risk of breast cancer recurrence in patients with high-risk HER2-negative primary breast cancer who have an inherited BRCA1 or BRCA2 gene mutation and who have completed all standard anticancer treatments.
Due to the global pandemic, the annual San Antonio Breast Cancer Symposium took place virtually from 8 to 11 December 2020. The symposium aims to provide the most up-to-date information on the experimental biology, etiology, prevention, diagnosis, and therapy of breast cancer and premalignant breast disease.

Several oral presentations and posters related to BIG trials and research collaborations were presented over the course of these four days; here is a peek at some of them.

**DCIS (TROG 07.01 / BIG 3-07)**

**Individualising radiotherapy can reduce DCIS recurrence**

Important results from the DCIS study were presented by Professor Boon Chua, study Principal Investigator, showing that individualising radiotherapy for women with DCIS of the breast reduces recurrence after surgery.

The study reported that after breast conserving surgery, higher radiation doses to the part of the breast where DCIS was found, in addition to radiotherapy of the whole breast, significantly reduced its risk of returning in patients with higher-risk DCIS. Compared to 5 weeks of whole breast radiotherapy, the study also shows that the shorter, more convenient 3 weeks of radiotherapy did not increase recurrence.

These results will likely have a significant impact on how patients with DCIS are best managed worldwide. It could also lead to better use of healthcare resources by minimising over or under-treatment of patients with DCIS.

The study is one of the few large-scale clinical trials in DCIS that used highly standardised protocols for radiation treatment, detailed patient data collection, robust quality assurance, and development of one of the world’s largest DCIS tissue resources. Collectively, this comprehensive study has the potential to generate the high-quality evidence necessary for improving radiotherapy in patients with DCIS to ameliorate patient outcomes.

Research using the unique DCIS resource of the study may identify markers for recurrence, in particular invasive recurrence. If this future research is successful, a test could be developed to predict the recurrence risks of DCIS and guide treatment decisions by patients and clinicians.

**Trans-Tasman Radiation Oncology Group (TROG) Cancer Research** is the coordinating group and study sponsor. The study was activated in Australia and New Zealand in 2007, and internationally in 2009 in collaboration with the BIG network including the Canadian Cancer Trials Group (CCTG), European Organisation for Research and Treatment of Cancer (EORTC), Scottish Cancer Trials Breast Group (SCTBG), International Breast Cancer Study Group (IBCSG) and Cancer Trials Ireland (CT-IRE).

With the powerful momentum generated by the global investigator team, the accrual of 1,608 patients from 136 centres in 11 countries was completed on 30 June 2014, two years ahead of schedule.

This achievement demonstrates that research on DCIS is a high priority for many patients and researchers. The final analysis of the DCIS study is planned for 2024. The successful conduct to date of this academic, investigator-led study is made possible only by the strong and enduring international alliance of the BIG network.

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


**PENELOPE-B (GBG 78 / BIG 1-13)**

First results show no benefit of palbociclib

Professor Sibylle Loibl presented the results of the phase III PENELOPE-B trial. They show that the CDK4/6 inhibitor palbociclib did not improve invasive disease-free survival (iDFS) when given in addition to standard endocrine therapy for a period of one year to patients with hormone receptor-positive (HR+), HER2-negative primary breast who are at high risk of recurrence following neoadjuvant chemotherapy.

After a median follow-up of 43 months the addition of 1 year palbociclib to endocrine therapy did not improve iDFS (stratified hazard ratio 0.93, 95% CI [0.74, 1.16], 2-sided CHWP p=0.525; estimated 3-year iDFS rate: 81.2% with palbociclib vs 77.7% with placebo). No new safety signals were observed, and there was no difference observed for overall survival at interim analysis.

CDK 4/6 inhibitors have proven to prolong survival in the metastatic breast cancer setting, hence the interest in their potential role in the treatment of early breast cancer. Nevertheless, the results of PENELOPE-B are concordant with the recent second interim analysis of the PALLAS study (BIG 14-03), presented in September 2020, which showed that the addition of two years of palbociclib to endocrine therapy had no effect on iDFS compared to standard of care (endocrine therapy alone) in patients with HR+, HER2-negative, early-stage breast cancer. These results contrast with those of the monarchE trial, which met its primary endpoint iDFS after 15/19 months follow-up.

The study, which enrolled 1,250 patients, is sponsored and conducted by the German Breast Group (GBG) under the BIG umbrella, and in cooperation with the Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) Study Group and The National Surgical Adjuvant Breast and Bowel Project (NSABP) Foundation Inc.

**References:**


PYTHIA (IBCSG 53-14 / BIG 14-04)
Presentation of first results
By IBCSG

Professor Luca Malorni presented the first results of the IBCSG and BIG co-led phase II PYTHIA (Palbociclib in molecularly characterised ER-positive/HER2-negative metastatic breast cancer) trial. Its primary objective is to interrogate a series of potential biomarkers, which will be assessed for their association with progression-free survival in post-menopausal women with HR+/HER2-negative advanced breast cancer who are treated with CDAK (an inhibitor of palbociclib) in combination with fulvestrant when their breast cancer has progressed after prior endocrine therapy (1st or 2nd line). PYTHIA is a “downstream” trial of the European AURORA research programme (BIG 14-01 + NCT0210165), run under the BIG umbrella. This international initiative collects and characterises biological samples, including metastatic tissue, from patients with advanced breast cancer. Detailed molecular information (including somatic mutations, copy number variation, gene expression profiling and circulating biomarkers) are being analysed from the AURORA programme for patients enrolled in PYTHIA.

The first presented results investigated circulating thymidine kinase activity (TKa) as a potential prognostic and monitoring marker for patients treated with palbociclib+fulvestrant. High baseline TKa and incomplete suppression of TKa during treatment may identify patients with poor prognosis and primary resistance to palbociclib+fulvestrant. TKa may represent a novel biomarker to select patients for alternative treatment modalities and warrant further investigation in prospective comparative trials.

Other research related to BIG trials presented at SABCS 2020

- Lamberti M, Aghor-Tari D, Metzger-Filho O et al. Prognostic role of distant disease-free interval from completion of adjuvant trastuzumab in HER2-positive early breast cancer: analysis from the ALTTO (BIG 2-06) trial. Spotlight Poster Discussion 3-04
- Frenzau MA, Procter M, Emond O et al. Timelines to initiate an adjuvant phase III trial across the globe: a sub-analysis of the APHINITY trial. PS7-21
- Gelber RD, Wang X, Cole BF et al. 6-year absolute invasive disease-free survival (DFS) benefit of adding adjuvant pertuzumab to trastuzumab plus chemotherapy for patients with early HER2-positive breast cancer: a STEPP analysis of the APHINITY (BIG 4-13) trial. PS10-01
- Van’t Veer LJ, Cardoso F, Poutre C et al. How low is low risk? MINDACT updated outcome data for clinical low risk patients by genomic stratification and treatment benefits by age and nodal status. General Session 4
- Lopes Cardoso JM, Byng D, Drucker CA et al. Outcome without adjuvant systemic treatment in breast cancer patients included in the MINDACT trial. PS11-01
- Chic N, Lauren S, Nuciforo P et al. Celtil score and long-term survival outcome in early stage HER2-positive (HER2+) breast cancer treated with anti-HER2-based chemotherapy: a correlative analysis of NeoALTTO trial. PS5-03
- Mayer EL, Fear C, Docek A et al. Treatment persistence and dose modifications in the PALLAS trial: PALbosid Collaborative Adjuvant Study of palbociclib with adjuvant endocrine therapy for HR+/HER2- early breast cancer. Spotlight Poster Discussion 2-03
- Burridge AH, Nimain SM, Raggett M et al. Baseline Characteristics of Women Enrolled in the POSITIVE Trial (Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIVe breast cancer). PS12-17
- Munzone E, Arbi S, Martinez Juarez N et al. Phase III open-label, multicenter, randomized trial of adjuvant palbociclib in combination with endocrine therapy versus endocrine therapy alone for patients with hormone receptor-positive / HER2-negative resected isolated locoregional recurrence of breast cancer – the POLAR Trial. OT-26-02
- Goeta MP, Fleming GF, Kuffel M et al. The role of CYP2D6-mediated Tamoxifen Metabolism in the Suppression of Ovarian Function Trial (SOFT). Spotlight Poster Discussion 2-09

Reference:

St Gallen International Breast Conference 2021
(virtual congress, 17 - 21 March 2021)

The 17th St. Gallen International Breast Cancer Conference took place virtually from 17 to 21 March 2021. Held every two years, the congress brings together breast cancer experts from all around the world, and the consensus recommendations on the optimal treatment of early breast cancer are highly respected.

Could you describe Aron’s role in the evolution of adjuvant therapies across time and in the evolution of academic research?

His role has been KLEY, setting standards for trial design and the questions, and providing leadership in building multi-centre, multi-national trials and building consensus about how patients should be treated.

BIG has been active for over 20 years; what challenges do you perceive for academic research groups and the BIG network in the future?

A need for greater collaboration and increasing challenges in securing non-commercial funding for clinical trials.

Lecture to honour Professor Aron Goldhirsch

For the first time, a lecture1 was given to honour the memory of Professor Aron Goldhirsch, co-founder of BIG, who passed away in February 2020. Professor David Cameron, Chair of BIG, was entrusted to give this presentation, and we had the pleasure to ask him a few questions before his talk.

How effective are adjuvant therapies today compared to 20 years ago?

Apart from trastuzumab (not available 20 years ago), the individual therapies are not that much better. However, an area where some success is evident, is combining many different therapies into a treatment programme.

Could you list the key stages in the evolution of adjuvant therapies to its current role in patients with breast cancer?

- Early investigators being brave enough to try chemotherapy and endocrine therapy
- Recognising the existence of predictive markers for some treatments (i.e., endocrine therapy is only for hormone receptor-positive tumours, not all)
- Longer duration of endocrine therapy
- Large, multi-centre, multi-national trials!
- Meta-analyses of trials to get precise estimates of benefits from all the women who enrolled in trials – none of the information is wasted!

Reference:
on patients’ quality of life. Veronesi’s contributions are crucial at the level of breast and the axilla. This had a great impact. Umberto Veronesi and Bernard Fisher in the US are the use of chemotherapy through the help of a genomic example of treatment de-escalation. In this study we decreased The of de-escalation trials that have been practice-changing. The problem is that we keep on trying to give the maximum escalation should not be limited to the treatment of early breast cancer. We are seeing a shift in mentalities also in the metastatic setting. While the old way of thinking is that, since metastatic disease is incurable, you have to give everything and as much as you can in the hope that you can somehow control the disease and prolong the life of the patient. Doctors and researchers now understand the need to optimise treatments according to the characteristics of the disease and of each individual patient. How have academic cooperative groups contributed to this process in the past and how can a network like BIG continue to contribute? MINDACT was a great example of academic collaboration that led to practice-changing results and impacted the lives of many patients with early breast cancer. The academic community took a long time to pay attention to metastatic breast cancer. There are now different research programmes dedicated to the metastatic disease, such as AURORA (BIG 14-01), but the majority of studies run in this metastatic setting are still pharma driven and that leaves a lot of important questions unanswered for the patients. Because metastatic breast cancer clearly has fewer patients (about 1/3 compared to 2/3 of patients with early breast cancer), international cooperation between academic groups is crucial to run trials in the metastatic setting that may not have commercial interests but tackle academic questions that really matter to patients.

From my perspective, to run effective de-escalation studies, we also need innovative trial designs, and this must be done in close collaboration with regulators and pharmaceutical companies. These studies have to be statistically sound and accurate, but they can’t be run as non-inferiority trials, which demand a huge patient population. The same happened in the field of biosimilars, and a new methodology was developed and is approved by regulators. I strongly support the development of an equally effective methodology, approved by regulators, for de-escalation trials as well as for trials that aim at approving a new drug formulation or the use of lower (but similarly effective) doses. I think that an academic network like BIG has the potential to play a key role here, to help change mentalities from the beginning of drug development, and to raise a voice in the discussions with pharmaceutical companies and regulators.

What is Umberto Veronesi’s main contribution to the de-escalation of breast cancer therapies?

Umberto Veronesi’s motto was “from the maximum tolerated to the minimum necessary”. Back in the 1970s-80s, this new notion that we could treat as well as we were doing at the time, while being less aggressive, completely changed the mentalities and had an impact on all breast cancer specialties, including surgery, medical oncology and radiotherapy.

What progress have we seen in the field of de-escalation of early breast cancer therapy? Are these practice-changing?

I think that the best word is not really “de-escalation” but “optimisation”; it’s not always about providing less treatment, but optimising treatment based on several characteristics of the disease and the patient.

In the early breast cancer setting, there are various examples of de-escalation trials that have been practice-changing. The MINDACT study (EORTC 10041 / BIG 3-04) is a typical example of treatment de-escalation. In this study we decreased the use of chemotherapy through the help of a genomic signature, the MammaPrint test. This study has been practice-changing, since it showed that patients considered as high-risk of cancer recurrence based on traditional factors, but identified as low risk by the MammaPrint test and treated with endocrine therapy alone (without chemotherapy), still had very good outcomes at 8 years of follow-up. Particularly for post-menopausal women, we see no clinically meaningful benefit from chemotherapy and, therefore, it can be safely omitted.

Another example is the phase II APT3 trial, which evaluated de-escalation strategies in women with small, node-negative HER2-positive breast cancer. Sara M. Tolaney and her team evaluated a chemotherapy backbone of adjuvant paclitaxel in combination with trastuzumab and found a 7-year disease-free survival rate (DFS) of 93%. Although this regimen is not adequate for all breast cancer patients, it allows for de-escalation of both a type of chemotherapy and a type of anti-HER2 therapy for “low risk” HER2-positive cases.

I think it’s important to emphasise that the notion of de-escalation should not be limited to the treatment of early breast cancer. We need to start changing this from the preclinical stage up to the clinical stage, while being less aggressive, completely changed the mentalities and had an impact on all breast cancer specialties, including surgery, medical oncology and radiotherapy.

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How have academic cooperative groups contributed to this process in the past and how can a network like BIG continue to contribute? MINDACT was a great example of academic collaboration that led to practice-changing results and impacted the lives of many patients with early breast cancer.

For the future, I think that we investigators need to discuss with statisticians about how to run these de-escalation trials in an appropriate way that provides the level of evidence that we need, but without taking so many years as MINDACT did, for example (about 15 years).

We need to start changing mentalities in drug development itself, in terms of doses and in terms of trial design.

What we typically do is find the maximum tolerated dose. This traditionally comes from chemotherapy development. The problem is that we keep on trying to give the maximum tolerated dose even with targeted agents. But these agents were developed to hit a certain target and the efficacy is linked to “hitting the target”. We should therefore be looking for the minimum dose required, sometimes called “minimum effective dose”, to hit the target. This would allow us to retain efficacy and greatly decrease toxicity.

We need to start changing this from the preclinical stage up until the way phase I and then phase III trials are run. As academic groups, I believe that we need to pay attention to that, particularly in the field of targeted and biological therapies.
What are the most burning questions that still need to be answered and standardised in early disease? Obviously, we have to pursue the ultimate goal of personalised medicine, which is still a long and winding road to go. The path we follow not only consists of escalating breast cancer therapies for a small but important group of patients, but also, to a greater extent, of de-escalating treatment for the majority of patients with good prognosis. The vast majority of these patients may be cured without maximal adjuvant therapy. Furthermore, as the current surgical approach is unsatisfactory, the management of patients with high risk of developing breast cancer needs to be improved. Additional information may help to individualise the approach: polygenic risk-scores are one of the promising tools. The approach to the axilla (axillary dissection versus no axillary dissection) was put on the agenda by Aron (and others) more than a decade ago and it will stay on it for many conferences to come.

Finally, the lack of access to innovation, in particular to new tests and drugs, remains an issue to address: innovative drugs and technology are ineffective if patients don’t have access to them.

What are the most burning questions that still need to be answered and standardised in early disease?

For many years, Professor Beat Thürlimann was Chief Physician and Head of the Breast Centre at the Kantonsspital St. Gallen (Switzerland). He also serves as Past-President of the Swiss Group for Clinical Cancer Research (SAKK).

Since its early days, Prof Thürlimann has been involved in the establishment and organisation of the St Gallen International Breast Conference.

BIG asked Prof Thürlimann the following questions:

Professor Aron Goldhirsch was Scientific Co-Chair of the St. Gallen conference for about 30 years. A special lecture will be given in his honour. What is his main contribution to the conference and what has changed compared to 30 years ago, when the conference was launched?

Together with Dr Alan Coates and Dr Richard Gelber, Dr Aron Goldhirsch was the main driver behind the conference and the consensus, Aron, who always remained humble, had one ideal: to combine science and research with patient-care. When he was urged (for example by policy-makers) to provide firmer statements on treatment recommendations in the consensus paper, he said to me: "A certain uncertainty must remain!" For him room for optimal individual patient care remained a priority.

On the other hand, as a policy-maker Aron initiated the paradigm change from risk-adapted adjuvant therapy to tailored treatment in 2003, but it was only in 2005 that the panel would follow him. Indeed, 2005 was an extraordinary year of progress that significantly changed the landscape in adjuvant breast cancer therapy. The panel recommended a fundamental change in the criteria for selection of adjuvant systemic therapy, giving prime attention to endocrine responsiveness.

Today, the debate on endocrine responsiveness, proliferation and benefit of chemotherapy continues. Considerable improvements have been made, with new tools and new data emerging from clinical research.

How do you expect the St. Gallen Conference to evolve in the next decade?

Any prediction is difficult, especially when it comes to predicting the future. The conference will adapt to the new technologies, regulations and travel behaviours. Virtual access will allow for a larger attendance and, importantly, from low and middle incomes in particular. I continue to acknowledge the value of personal interactions by face-to-face meetings during and after the conference, both for clinicians and researchers. However, it remains a challenge to find the best ways to accommodate all these different needs.

What is your main contribution to the conference and what was the impact of the St. Gallen International Expert Consensus Conference?

Professor Aron Goldhirsch, the “father” of BIG and a founder of the International Breast Cancer Study Group (IBCSG), passed away at the age of 73 on 26 February 2020.

Throughout his career, Prof Goldhirsch made significant contributions to breast cancer medicine and education and, besides his many national duties, he worked tirelessly to foster international collaboration and preserve academic independence in cancer research. Much of this work was conducted in the context of his leadership within the International Breast Cancer Study Group (www.ibcsg.org), of which he was a founder.

In 1996, together with Dr Piccart, Prof Goldhirsch created the Breast International Group (BIG) with the aim of bringing together academic research groups.

He was also one of the main contributors to the St. Gallen International Expert Consensus Conference, which gives practicing oncologists recommendations on how to optimise treatment for patients with early breast cancer.
Other trials & activities by BIG member groups

BCT-ANZ

Breast Cancer Trials (BCT-ANZ): achievements and update of key clinical trials

The EXPERT clinical trial

The first international patient has been randomised on the EXPERT clinical trial at the National Taiwan University Hospital. EXPERT is an international clinical trial, co-led by Breast Cancer Trials-ANZ and BIG, which will enrol 1,170 patients worldwide. It is open to women aged 50 years or older, with Hormone Receptor (HR) positive, Human Epidermal Growth Factor Receptor 2 (HER2) negative, early-stage breast cancer. EXPERT will use a genomic test of breast cancer tissue to select women who can safely avoid radiation therapy. The trial aims to improve personalised use of radiation therapy in early breast cancer patients, according to individual risk of local recurrence. Regulatory submissions have commenced in Ireland, Chile, Argentine and Argentina. The IBIS-II DCIS clinical trial will soon commence in Spain, Switzerland, and Italy, with the first BIG sites to begin recruitment in Q2 2021.

Professor Boon Chua is the Study Chair and Dr Gunther Gruber is the international Co-Chair.

IBIS-II DCIS results

Long-term follow-up of the IBIS-II DCIS clinical trial has found that anastrozole and tamoxifen are both effective in preventing breast cancer and DCIS (ductal carcinoma in situ), providing more treatment options for postmenopausal women with this condition. The results were announced at the San Antonio Breast Cancer Symposium in the United States (virtual symposium, December 8-11, 2020). 2,980 women were recruited to the IBIS-II DCIS clinical trial worldwide, including 178 women at 24 institutions in Australia and New Zealand where the study was coordinated by Breast Cancer Trials – ANZ.

The IBIS-II DCIS trial demonstrated that anastrozole and tamoxifen are similarly effective in preventing future DCIS or breast cancer over the 12 years of follow-up of the trial. Interestingly, anastrozole was more effective whilst taking the medication for 5 years, but after stopping at 5 years, there was no longer a difference compared with tamoxifen. After 12 years, 9.7% of patients on tamoxifen and 8.5% of patients on anastrozole were diagnosed with DCIS or breast cancer. There was no difference in survival between the two drugs.

Professor Sherene Loi

In addition, and for the third year in a row, Professor Loi has been included in the worldwide Web of Science Highly Cited Researchers list in the category of Clinical Medicine. This highly prestigious list identifies the top scientists and researchers from around the world who produced multiple papers ranking in the top 1% by citations for their field and year of publication. This demonstrates significant research influence among their peers.

Professor Loi is the Study Chair of BCT-ANZ’s CHARIOT, DIAnO ND and Neo-N clinical trials, and is a member of the BCT-ANZ Board of Directors.

The Breast Cancer Trials (ANZ) Podcast

BCT-ANZ Podcast has over 10,000 listeners and features breast cancer research news, clinical trial updates, and an explanation of breast cancer related topics such as recurrence, myths, and treatment during COVID-19. You can subscribe to the podcast by searching for Breast Cancer Trials in Apple podcasts, Spotify or Google Podcasts.

Over this period, GAICO grew from eight founding members to more than 21 throughout the country, all of them dedicated to clinical research in oncology.

During all these years, GAICO has been working hard to standardise all site’s SOPs (Standard Operating Procedures) and to train its staff in clinical research. Until 2018, and as part of this training, GAICO annually held the Oncology Research and Development Conference (JIDO). Seven editions took place, during which GAICO discussed the ethical and scientific problems of clinical research with all its stakeholders.

BIG clinical trials

Thanks to these years of strengthening, GAICO has achieved cooperation agreements with private-public entities and organisations like GAICO to collaborate in different ways. GAICO’s collaboration with BIG is very important and has allowed the group to participate in multiple clinical trials that are run under BIG’s umbrella such as ALTTO, NEOALTTO, APHINITY, and OLYMPIA. Some of these have changed the standard therapy in breast cancer.

Today, this collaboration continues with GAICO being involved in BIG clinical trials such as IMPASSION 132, DECRESCENDO and EXPERT.

COVID-19

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

Registry of clinical trials

An important contribution of GAICO to the community is its registry of clinical trials (REC), which is the only registry created for the physicians that can also be used by patients. The registry contains information about all open clinical trials in Argentina and recruiting sites to help potential patients and to refer patients.

The principal objective of GAICO is to keep working on strengthening itself, thereby following the example of BIG and striving for an independent vision of clinical research with the sole objective to contribute to improving the quality of life and survival of patients.

Recognition for BCT-ANZ researcher

Professor Sherene Loi was awarded the 2020 ESMO Breast Cancer Award, which is presented annually to experts with major research contributions to their name, and the Outstanding Investigator Award for Breast Cancer from the American Association for Cancer Research.
Male Breast Cancer Research Initiative: ARDERNE® Project

ARDERNE. In memorial of the first male breast cancer clinical report described by John of Arderne in the 14th century

Male breast cancer is a rare entity and its clinical management is mainly based on the experience generated from women with breast cancer (BC). However, the biological, diagnostic and clinical knowledge of male BC is still limited.

GEICAM is running a male BC registry that includes a comprehensive sample collection, with the ultimate objective to define a molecular predictor for the personalised clinical management of this condition. A better molecular characterisation of male BC would help us understand if it is biologically and molecularly different from BC in women. This registry will also allow us to establish more effective therapeutic strategies and clinical guidelines for disease management. Nevertheless, this complex project would not be possible without the collaboration of a multidisciplinary consortium made up of different national and international research groups bringing their expertise in this area. This is a very ambitious project for which GEICAM is looking for funding through competitive calls and fundraising activities.

GEICAM hopes it can soon share some interesting results with the entire BC research community.

The manuscript is freely available in the Journal of Clinical Oncology.

GEICAM

The PEARL trial

Publication in Annals of Oncology. “Palbociclib in combination with endocrine therapy versus capecitabine in hormonal receptor-positive, human epidermal growth factor 2-negative, aromatase inhibitor-resistant metastatic breast cancer: a phase III randomised controlled trial—PEARL.”

This study is led by GEICAM, the Spanish Breast Cancer Group, in collaboration with the Central European Cooperative Oncology Group (CECOG). The study enrolled more than 600 patients from Spain (81%), Hungary (9.8%), Israel (6.5%) and Austria (2.5%). This is the first clinical trial comparing palbociclib plus endocrine therapy (ET) ( exemestane or fulvestrant) versus oral chemotherapy (capecitabine) in postmenopausal women with hormone receptor-positive and HER2-negative, aromatase inhibitor’s (AI) resistant, metastatic breast cancer (MBC).

The results showed that:
- Palbociclib plus fulvestrant did not provide evidence of progression-free survival (PFS) superiority over capecitabine in MBC patients resistant to AIs
- Palbociclib plus ET did not show PFS superiority over capecitabine in wild-type ESR1 MBC patients resistant to AIs
- Palbociclib plus ET was better tolerated and offered better quality of life than capecitabine

The manuscript is available online (click here).

Practice changing results of RxPONDER study at SABCS 2020

GEICAM participated in the international network of different research groups led by SWOG Cancer Research Network in the RxPONDER study. The results were presented at the 43rd San Antonio Breast Cancer Symposium (virtual SABCS, December 8-12, 2020) by Dr Kevin Kalinsky. The principal conclusions reported were:
- Postmenopausal women with hormone receptor-positive (HR+) and HER2-negative breast cancer, with 1-3 positive nodes and a recurrence score (RS) 0-25, can likely safely forego adjuvant chemotherapy without compromising invasive disease-free survival (IDFS)
- Premenopausal women with positive nodes and RS 0-25 significantly benefit from chemotherapy

These are practice-changing results that could avoid unnecessary chemotherapy for an important group of postmenopausal hormone receptor-positive and HER2-negative breast cancer patients.

GEICAM investigators contributed almost 20% of the patients enrolled, with the participation of 21 sites throughout Spain.

IBCSG

News from the SOFT and TEXT Front

Absolute improvements in freedom from distant recurrence to tailor adjuvant endocrine therapies for pre-menopausal women published in the Journal of Clinical Oncology

The SOFT and TEXT trials involve 5,738 women who were pre-menopausal at the initiation of adjuvant endocrine therapy for hormone receptor-positive early breast cancer. To help with tailoring the SOFT/TEXT results “on average” for individual women, the trials recently reported on the absolute improvement in freedom from distance recurrence at 8 years since randomisation, according to a composite measure of recurrence risk. Women with low recurrence risk have minimal potential benefit in escalating endocrine therapy, while women with high-recurrence risk may experience a 10-15% absolute improvement in 8-year freedom from distant recurrence with exemestane+OFS versus tamoxifen+OFS or tamoxifen alone.

The manuscript is freely available in the Journal of Clinical Oncology.

Composite Risk web application

To accompany the analyses published in the Journal of Clinical Oncology, IBCSG made a web application that allows the user to enter an individual set of clinical-pathologic characteristics, then calculates the composite risk value and shows how similar patients in SOFT and TEXT have performed:

https://rconnect.dfci.harvard.edu/CompositeRiskSTEPP/.

The web application was supported by grants from the Breast Cancer Research Foundation and Friends of Dana-Farber Cancer Institute.

Analysis plans and continuation of follow-up for 5 more years

In the course of 2021, the SOFT and TEXT trials will report a second update of results, after median follow-up of approximately 12 to 13 years, with all participants being followed for at least 10 years since their enrollment in the study. As of December 2020, approximately 4,500 women continue in follow-up. The protocols and informed consent specified “life-long follow-up” and IBCSG plans to continue with the follow-up of these women for 5 more years (from 2021 until end 2025). The median will then be approximately 18 years since the start of their adjuvant endocrine therapy. At the time of the final analyses, these patients will have been followed, on average, into their mid-60s.
Clinical trials
The Japanese Breast Cancer Research Group (JBCRG) is running the following clinical trials:

- JBCRG-M06 (EMERALD): a phase III clinical study to compare the combination therapy of eribulin mesylate + pertuzumab + trastuzumab with paclitaxel or docetaxel + pertuzumab + trastuzumab
- JBCRG-C07 (REIWA): an observational study to evaluate the impact of the gene panel test on treatment decision-making in breast cancer throughout Japan as a whole
- JBCRG-ABCD project: Advanced Breast Cancer Database (ABCD) project

Presentations at congresses

ESMO Virtual Congress 2020 (19-21 September 2020): Japan Breast Cancer Research Group-M05 (PRECIOUS) study and the socio-economic impact of breast cancer in Latin America. “The partnership between BIG and LACOG strengthens our research collaboration and provides the opportunity for patients to participate in high-quality research in Latin America.” said Dr Gustavo Werutsky, LACOG Chair.

JBCRG is involved in the following trials run under the Participation in global trials

- TAXIS (SAKK 23/16): a unique large phase III trial randomising 1,500 patients with axillary lymph node involvement. By comparing standard axillary lymph node dissection to limited axillary surgery, the trial aims to contribute significantly to de-escalation of axilla surgery. Thanks to an international effort bringing together Switzerland, Hungary, Germany, Austria and Lithuania, the recruitment is proceeding as planned, with currently 400 randomised patients.

Another successfully recruited trial is WISE (SAKK 95/17), aiming to improve quality of life. This phase III study assessed the impact of a 24-week activity programme (monitored by a tracking device) on arthralgia induced by aromatase inhibitors. The target recruitment of 350 patients was reached more than one year ahead of schedule.

SAKK 21/18, an international collaboration and a phase III trial investigating a therapeutic strategy, is comparing the upfront combination of ribocilib-endocrine therapy versus a short-term induction chemotherapy followed by maintenance with the endocrine combination. Women with visceral metastases are the target population, and an original composite endpoint was chosen, taking into account cancer response and quality of life.

SAKK Project Group Breast Cancer is a long-term member of IBCSG and BIG and is proud to have contributed actively to some major practice-changing trials conducted by these two collaborative groups.

References:
1. TAXIS (SAKK 23/16)
2. WISE (SAKK 95/17)
3. IBCTSG and IBAC: IBCSG is a long-term member of IBCTSG and IBAC and is proud to have contributed actively to some major practice-changing trials conducted by these two collaborative groups.

The LACOG Breast Cancer Group

The LACOG Breast Cancer Group is part of the Latin American Cooperative Oncology Group (LACOG), the largest multinational cooperative group in Latin America exclusively dedicated to clinical and translational cancer research.

LACOG Breast aims to develop real world data studies and clinical trials in Latin America as well as to collaborate with international intergroup studies to improve breast cancer care in the region. Currently, there are over 80 investigators from several countries in Latin America participating in LACOG Breast studies. LACOG Breast works in partnership with BIG.

“"The partnership between BIG and LACOG strengthens research collaboration and provides the opportunity for patients to participate in high-quality research in Latin America.” said Dr Gustavo Werutsky, LACOG Chair.

Ongoing studies
LACOG is currently participating in two trials under the BIG umbrella: ALEXANDRA/IMpassio030, OlympiA, POSITIVE, PenelopeB and PALLAS.

For details about the trial leadership, please refer to the Trials Table on page 40-43.

The LATINA study (LACOG 0615), LACOG is conducting the most comprehensive breast cancer prospective registry in Latin America. The study has already enrolled more than 1,600 patients from a planned 4,500, at 35 sites in 11 countries. “The LATINA study will for the first time provide detailed information on socio-economic, clinical pathological characteristics and outcomes of breast cancer in Latin America. It may help identify gaps for optimal breast cancer care on our continent”, said Dr Gustavo Werutsky, study PI.

At the San Antonio Breast Cancer Symposium (virtual SABCS 2020, 8-12 December, 2020), the LACOG Breast group and GRECAM presented the analysis of the AMAZONA III study and the socio-economic impact of breast cancer in Brazil. The results of the study showed that around 10% of patients do not return to work, get divorced or end their partner relationship within 1-year of their breast cancer diagnosis. Nonetheless, personal income and surgery type were associated with higher risk of not returning to work, whereas no specific variable was related to marital status change. The main message of this analysis is that governments’ social support, specifically to help people get back to work, remains critical for breast cancer patients, especially shortly after they have been diagnosed with the disease.

Another study presented at SABCS 2020 is LACOG 1218, which evaluated the influence of physicians’ lifestyle on prescribing healthy habits to their breast cancer patients. It has already been demonstrated that a healthy lifestyle has a positive impact on quality of life and outcomes of breast cancer. Physicians play an important role in encouraging their patients to modify their lifestyles. Nonetheless, little was known about physicians’ lifestyles and the impact this could have on the healthy habits recommended to their breast cancer patients. The LACOG 1218 study, led by Dr Renata Cangussu, showed that the majority of physicians treating breast cancer patients do have a healthy lifestyle. Physicians who regularly practise physical activity or who are older than 50 were more inclined to advise lifestyle changes. Only half of the physicians treated obesity or referred these patients to specialists. This may have an impact on patient outcome.

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

Current activities and clinical trials
The Project Group Breast Cancer of the Swiss Group for Clinical Cancer Research (SAKK) is a clinical research network gathering 48 hospitals and oncolgic practices. In 2020, the group recruited 560 patients to participate in clinical trials. Out of these, 436 came from the Swiss centres and the remaining 124 from the foreign members. SAKK’s goal is to investigate loco-regional, systemic, or quality-of-life interventions. Below are some ongoing examples:

TAXIS (SAKK 23/16) is a unique large phase III trial randomising 1,500 patients with axillary lymph node involvement. By comparing standard axillary lymph node dissection to limited axillary surgery, the trial aims to contribute significantly to de-escalation of axilla surgery. Thanks to an international effort bringing together Switzerland, Hungary, Germany, Austria and Lithuania, the recruitment is proceeding as planned, with currently 400 randomised patients.

Another successfully recruited trial is WISE (SAKK 95/17), aiming to improve quality of life. This phase III study assessed the impact of a 24-week activity programme (monitored by a tracking device) on arthralgia induced by aromatase inhibitors. The target recruitment of 350 patients was reached more than one year ahead of schedule.

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SAKK Project Group Breast Cancer is a long-term member of IBCTSG and BIG and is proud to have contributed actively to some major practice-changing trials conducted by these two collaborative groups.

References:
1. TAXIS (SAKK 23/16)
2. WISE (SAKK 95/17)
Although nowadays most breast cancers can be cured, a significant proportion of patients suffer from metastases and face an incurable disease. That is why on 22 October 2020, the SOLTI Breast Cancer Research Group launched HOPE, the first patient-led study for the genomic analysis of metastatic breast cancer.

The main objective of this study, led by Dr Aleix Prat (President of SOLTI and Head of the Medical Oncology Service at Hospital Clinic in Barcelona) and Dr Ana Casas (Medical Oncologist, Honorary Member of the SOLTI Governing Board, and President of Fundación Actitud Frente al Cáncer), is to empower patients suffering from metastatic breast cancer by giving them information and collecting real-time molecular data at the same time.

Through a mobile application (app), patients included in the study provide information about their medical history and the treatments they receive and have received. They are also encouraged to give the opportunity to the oncologist that has been following them during their whole journey to include his or her participation and follow-up in the study. In parallel, a tissue and blood sample are analysed to obtain the molecular profile of their metastatic tumours. Bringing together all these different pieces of information allows an experts’ committee (Molecular Advisory Board) to evaluate the results and to give a personalised recommendation for each patient, including the possibility to be enrolled in a clinical trial. In addition, the collection of patient information will be stored in an anonymised database that can contribute to the generation of new research hypotheses.

Another differentiating objective of the study is to reinforce the empowerment of patients with advanced breast cancer, by providing them with information that allows them to make decisions, together with their reference oncologist, and remain active during their illness. For that reason, HOPE also offers a training programme, that includes educational videos on precision oncology and a series of webinars addressing topics such as the basics of breast cancer, clinical research, precision oncology and aspects related to the quality of life.

For this challenging study, SOLTI can count on the collaboration of the associations CMM (Cancer de Mama Metastásico), Fundación Actitud Frente al Cáncer and SARAY, who provided financial donations and contributed to the launch of this project.

The study is also supported by Novartis Spain, Guardant Health, and Roche Pharmaceuticals (through Foundation Medicine), which have provided their technologies for molecular analysis. Guardant-360 is a liquid biopsy test that involves the analysis of a blood sample and allows a comprehensive panel of 74 genes to be evaluated. The analysis of the tumour tissue is done with the FoundationOne CDx® test, from Roche Pharmaceuticals, a diagnostic system based on the sequencing of 324 genes, as well as the determination of biomarkers that include microsatellite instability and mutational load using a tumour biopsy.

Dr Aleix Prat points out the following: “HOPE has funding to include 600 patients. However, since there are more than 15,000 patients with metastatic breast cancer in Spain, it is necessary to expand this number as soon as possible. The study is pioneering in the world and applicable in the future to other types of advanced cancer”.

The SOLTI Group intends to increase these numbers in the future and to contribute to a better understanding and management of metastatic breast cancer.

For more information: www.soltilope.com (content written in Spanish)
Between May 2012 and September 2019, 5,625 patients were registered to the ADAPT HR+/HER2- trial from 81 centres in Germany. RS testing in the core biopsy was feasible in 94% of the cases, and post-therapeutic Ki67 evaluation in patients with baseline Ki67 > 10% was routinely available, with Spearman correlation of local (n=4322) and central (n=3955) Ki67 baseline measurements of 0.628.

Professor Nadia Harbeck and Professor Sherko Könnüel presented pioneering and practice-changing results from the ADAPT HR+/HER2- study for 2,356 patients receiving endocrine therapy only, and for 2,335 patients allocated to the chemotherapy trial. For the ADAPT only endocrine trial, pN0-1 patients entered control arm if RS<11 and experimental arm if RS12-25 with ET-response (Ki67post<=10%). The primary endpoint was non-inferiority (NI) of 5-year invasive disease-free survival (5y-DFS): <3.3% one-sided 95% confidence limit for experimental vs. control arm. Secondary endpoints included distant DFS (dDFS), overall survival (OS). The Intention To Treat (ITT) population comprised 2,290 patients (n=1,422 experimental vs. n=868 control arm). 26.3% vs. 34.6% were pre-menopausal, 27.4% vs. 24.0% pN1. The pre-specified N1-definition was met (p=0.05): 5y-DFS was 92.6% (95%-CI: [90.8% to 94.0%]) in the experimental vs. 93.9% (95%-CI: [91.8% to 95.4%]) in the control arm; 5y-DFS was 95.6% vs. 96.3%, and 5y-OS 93.7% vs. 98.0%. Similar relative outcome was seen in age and nodal subgroups.

In summary about half of the 5,000 patients in the study population (all candidates for chemotherapy by conventional criteria) could be spared chemotherapy. Extrapolated to the situation in Germany, it can be assumed, according to Prof Harbeck, this information concerns 10,000 to 15,000 patients a year.

Like the American TAILORx and RsPONDER trials, ADAPT HR+/HER2- represents another landmark study evaluating the role of genomic signatures in guiding adjuvant chemotherapy. Beyond the knowledge already gained from TAILORx and RsPONDER, ADAPT HR+/HER2- has generated important information, in particular for pre-menopausal women. In endocrine-responsive tumours, age-dependent effects in the low and intermediate risk RS populations in patients with pN0-1 disease could not be detected. Survival data for these patients are excellent, so it is unlikely that they will have a clinically meaningful benefit from chemotherapy.

All other HR+/HER2- patients (pN0-1/RS 12.25-25) were randomised to a chemotherapy trial comparing two different taxanes within a dose-dense regimen incorporating 4x sequential EC to a chemotherapy trial comparing two different taxanes. Among other HR+/HER2- patients (pN0-1/RS >25) and tumour size were independent predictors of pCR.

The results of the ADAPT HR+/HER2- study are pioneering and practice-changing. Nevertheless, further questions remain to be answered in relation to women with HR-positive/HER2-negative breast cancer. For example, what can be offered to women who have high tumour burden, but “good biology”? What about women with a high RS >25, a good endocrine therapy-response but a poor chemotherapy-response? Could these groups potentially benefit from “intensified endocrine therapy”? These issues are currently being examined in the ADAPT cycle study and WSG will report on them in due course.

De-escalation strategies for the other early breast cancer subtypes HR-/HER2+, HR+/HER2- (triple positive), HR-/HER2- (triple negative) and for early breast cancer in elderly patients have been addressed in the sub-trials of ADAPT. An overview of the presentations on the primary results from these studies can be found in the table below.

### Table 1: ADAPT subtrials main publications

<table>
<thead>
<tr>
<th>Subtrials</th>
<th>Title</th>
<th>Population</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2+/HER2-</td>
<td>De-escalation Strategies in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Early Breast Cancer (BC): Final Analysis of the West German Study Group Adjunctive Adjuvant Monotherapy Trial Optimizing Risk Assessment and Therapy Response Prediction in Early BC: HER2-Positive Endocrine Therapy (ET) Versus Combination Therapy (CT)</td>
<td>2,335 patients were allocated to ADAPT, 8 courses of weekly nab-paclitaxel were compared to 4x sequential EC. 2,335 patients were randomised to ET (n=1,168) or CT (n=1,167).</td>
<td>doi: 10.1200/JCO.2019.85.9393</td>
</tr>
<tr>
<td>HER2-/HER2-</td>
<td>De-escalation Strategies in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Early Breast Cancer (BC): Final Analysis of the West German Study Group Adjunctive Adjuvant Monotherapy Trial Optimizing Risk Assessment and Therapy Response Prediction in Early BC: HER2-Positive Endocrine Therapy (ET) Versus Combination Therapy (CT)</td>
<td>5,625 patients were registered to the ADAPT HR+/HER2- trial from 81 centres in Germany. RS testing in the core biopsy was feasible in 94% of the cases, and post-therapeutic Ki67 evaluation in patients with baseline Ki67 &gt; 10% was routinely available, with Spearman correlation of local (n=4322) and central (n=3955) Ki67 baseline measurements of 0.628.</td>
<td>doi: 10.1200/JCO.2019.85.9393</td>
</tr>
<tr>
<td>TN</td>
<td>Comparison of Noninvasive Nab-Paclitaxel, Gemcitabine, and Docetaxel vs. Noninvasive Nab-Paclitaxel, Docetaxel, and GA-ADAPT TN Trial Results.</td>
<td>2,335 patients were allocated to ADAPT HR+/HER2- chemotherapy trial. Prof Könnüel reported pCR data from 427 patients in the nab-paclitaxel arm and 437 in the paclitaxel arm who received neoadjuvant treatment. PCR was significantly higher in the nab-paclitaxel arm (25.4% vs. 12.9%) and 7.2% versus 16.1% in the RS &gt; 25 group. RS &gt; 25 and tumour size were independent predictors of PCR. Patients with high RS &gt; 25 but endocrine response had a low rate of PCR (5.6%).</td>
<td>doi: 10.1093/jnci/djx258.8</td>
</tr>
<tr>
<td>Endocrine Endocrine</td>
<td>Effect of response- and toxicity-guided neoadjuvant chemotherapy in elderly early breast cancer patients results of WSG ADAPT Elderly sub-trial.</td>
<td>5,625 patients were registered to the ADAPT HR+/HER2- trial from 81 centres in Germany. RS testing in the core biopsy was feasible in 94% of the cases, and post-therapeutic Ki67 evaluation in patients with baseline Ki67 &gt; 10% was routinely available, with Spearman correlation of local (n=4322) and central (n=3955) Ki67 baseline measurements of 0.628.</td>
<td>doi: 10.1093/jnci/djx258.8</td>
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**Presentation of primary survival outcome data at SABCS 2020**

The ADAPT HR+/HER2- study was conducted by the West German Study Group (WSG), and 5 year survival data were presented orally at the San Antonio Breast Cancer Symposium (virtual S-ABCS 2020, 8-12 December, 2020).

Within ADAPT HR+/HER2- adjuvant treatment decision-making was guided by a predefined algorithm combining information from the 21-gene expression assay (Recurrent Score, RS) and Ki-67 response to 3-week pre-operative endocrine therapy. The prognostic and predictive value of endocrine responsiveness has been extensively evaluated by Mitch Dowsett and Ian Smith (IMPACT and POETIC trials), but this early information up to now has been used only to investigate next generation endocrine therapies after a short window of treatment (PALLET trial).

Figure 1 shows the trial design, which we refer to as comprising two trials, one with endocrine therapy only, the other including chemotherapy. Based on nodal status, RS (recurrence score), and ET response (endocrine therapy), NO-3 HR+/HER2- early breast cancer patients were allocated to ET alone ("ADAPT endocrine trial") or to chemotherapy-ET ("ADAPT chemotherapy trial"). Baseline and post-endocrine Ki67 shows the trial design, which we refer to as window of treatment (investigate next generation endocrine therapies after a short but this early information up to now has been used only to investigate next generation endocrine therapies after a short window of treatment (PALLET trial).

Figure 1: ADAPT HR+/HER2- trial design

- Female patients >18 years
- ER and/or PR positive (>1%)
- HER2-negative unilateral EBC
- cT1-4c, cN0-3
- Candidates for adjuvant chemotherapy by conventional prognostic criteria: cT2 or G3 or Ki67>15% or <35 years old or cN+
### Open trials / Research programmes

<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>
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<tbody>
<tr>
<td>ALEXANDRA / IMpassion 030</td>
<td>BIG 16-05</td>
<td>A randomised phase III trial comparing standard chemotherapy vs. chemotherapy alone as adjuvant treatment in patients with operable TNBC - NCT01340176</td>
<td>M. Ignatiadis, H. McArthur, S. Saji</td>
<td>Lead trial (Co-Leading partners: BIG HQ / IBJ-CTSU / EORTC / FSTRF and AFT) Pharma partner: Roche / Genentech (sponsor) Funding: Roche / Genentech</td>
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<tr>
<td>APPALACHES</td>
<td>BIG 16-01</td>
<td>A Phase II study of Adjuvant Paclitaxel as an Alternative to Chemotherapy in Elderly patients with high-risk ER+/HER2- early breast cancer - NCT03609047</td>
<td>H. Wilders, E. Braun, K. Panic</td>
<td>Supporter trial Coordinating group: EORTC (sponsor) Pharma partner: Pfizer</td>
</tr>
<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>P. Hajduš and M. Oliveira</td>
<td>BIG-sponsored programme (Co-Leading partners: BIG HQ / IBJ-CTSU / FSS Pharma partner: N/A Funding: Breast Cancer Research Foundation (BCRF) as the main funder, Foundation Cancer (Luxembourg), Foundation Cancer (Belgium), Barbie and Dana Webb, Foundation NIF; National Lottery Belgium, Think Pink Belgium (SMART Fund), and many individual donors. AURORA has also been supported by the Fund Friends of BIG, managed by the King Baudouin Foundation.</td>
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### Breast Cancer in Pregnancy

<table>
<thead>
<tr>
<th>BIG Number</th>
<th>Short description</th>
<th>Principal Investigator(s)</th>
<th>Trial model &amp; partners</th>
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<tbody>
<tr>
<td>BIG 2-03</td>
<td>Prospective registry of women treated for breast cancer while pregnant - NCT00196833</td>
<td>S. Loibl, G. von Minckwitz</td>
<td>Supporter study (Co-Leading partner: GBG (sponsor) Pharma partner: N/A Funding: GBG, Deutsches Konsortium für Translationale Krebsforschung</td>
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### Expert (BIG Radio Tuning)

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<tr>
<th>BIG Number</th>
<th>Short description</th>
<th>Principal Investigator(s)</th>
<th>Trial model &amp; partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIG 16-02</td>
<td>A randomised phase III trial of adjuvant radiation therapy vs observation after breast conserving surgery for patients with molecularly characterised low-risk luminal A early breast cancer - NCT02589874</td>
<td>B. Chua, G. Graber</td>
<td>Co-lead trial (Co-Leading partners: BCT-ANZ (sponsor)</td>
</tr>
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### POLAR

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<tr>
<th>BIG Number</th>
<th>Short description</th>
<th>Principal Investigator(s)</th>
<th>Trial model &amp; partners</th>
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<tbody>
<tr>
<td>BIG 18-02</td>
<td>Pembrolizumab for HR+ isolated local or regional recurrence of breast cancer - NCT03201850</td>
<td>E. Manzoni, S. Aald</td>
<td>Supporter trial Coordinating group: IBG (sponsor) Pharma partner: Pfizer</td>
</tr>
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</table>

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

<table>
<thead>
<tr>
<th>Study name</th>
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</tr>
</thead>
<tbody>
<tr>
<td>ALTTO</td>
<td>BIG 2-06</td>
<td>Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization; sequences and combination for patients with HER2+/ER+ positive primary breast cancer - NCT00490139</td>
<td>M. Piccart, A. Montero, S. Loibl, J. Binns</td>
<td>Lead trial (Co-Leading partners: BIG HQ / IBJ-CTSU / EORTC / FSTRF / Alliance (former NCCTG), sponsor for the US) Pharma partner: Novartis (global sponsor for all countries with the exception of US) Funding: GSK (past) / Novartis</td>
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<tr>
<td>APHINITY</td>
<td>BIG 4-11</td>
<td>Comparison of single-versus dual anti-HER2 therapy (trastuzumab, pamidronate) for patients with HER2-positive primary breast cancer - NCT0150877</td>
<td>M. Piccart, S. Loibl, J. Binns</td>
<td>Lead trial (Co-Leading partners: BIG HQ / IBJ-CTSU / FSTRF Pharma partner: Roche (sponsor) Funding: Roche</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 - NCT0190552</td>
<td>N. Turner, J. Balmaña, H. Cameron, J. Eifel</td>
<td>Co-lead trial (Co-Leading partners: EORTC / BIG HQ Pharma partner: Tesaro (sponsor) Funding: Tesaro</td>
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<tr>
<td>DCIS</td>
<td>BIG 5-07</td>
<td>Radiation doses and fractionation schedules for women with DCIS - NCT00470236</td>
<td>B. Chua</td>
<td>Supporter trial (Co-Leading partner: TBCG (sponsor) Pharma partner: N/A Funding: National Health &amp; Medical Research Council Project Grant, Susan G. Komen</td>
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<tr>
<td>Exceptional Responders</td>
<td>BIG 16-04</td>
<td>A global hunt for exceptional responders in the BIG network: aiming to identify breast cancer patients with a truly remarkable clinical response to anticancer treatments, and to characterise their tumour molecular</td>
<td>A. Irmhuber (coordinator)</td>
<td>BIG-sponsored programme (Co-Leading partner: BIG HQ Pharma partner: N/A Funding: Breast Cancer Research Foundation</td>
</tr>
<tr>
<td>FINESE</td>
<td>BIG 2-13</td>
<td>Oral lactulose for patients with FGFR1 ER+ metastatic breast cancer - NCT02853636</td>
<td>F. Andre, J. Coisne</td>
<td>Lead trial (Co-Leading partners: BIG HQ / EORTC / FSS Pharma partner: Servier (sponsor) Funding: Servier</td>
</tr>
<tr>
<td>IBIS-II</td>
<td>BIG 5-02</td>
<td>Prevention study of anastrozole for post-menopausal women at increased risk of breast cancer, and of effects of tamoxifen vs. anastrozole in postmenopausal women with DCIS - NCT0072462</td>
<td>J. Ganz, S. Cincotta</td>
<td>Supporter trial (Co-Leading partners: IBIS Pharma partner: Amgen Sponsor: Queen Mary University of London Funding: Cancer Research UK, Queen Mary University of London</td>
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<tr>
<td>International Male Breast Cancer Programme</td>
<td>BIG 2-07</td>
<td>Registration and biologic characterisation programme of breast cancer in men - NCT0101425</td>
<td>E. Candi, S. Giordano</td>
<td>Supporter programme (Co-Leading partners: EORTC (sponsor) / NABCG (US) Pharma partner: N/A Funding: Breast Cancer Research Foundation</td>
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<tbody>
<tr>
<td><strong>LORELEI</strong></td>
<td>BIG 3-13</td>
<td>Neoadjuvant letrozole plus ruxolitinib versus letrozole plus placebo in postmenopausal women with ER+ HER2- early-stage breast cancer - NCT02799737</td>
<td>C. Saura (Co-Lead), E. de Azambuja (Pharma partner: Genentech (sponser))</td>
<td>Co-lead trial (Co-Leading partners: ABCSG, SOLIT and BIG HQ) Funding: Genentech*</td>
</tr>
<tr>
<td><strong>MA.32</strong></td>
<td>BIG 5-11</td>
<td>Effect of metformin on recurrence and survival in early stage breast cancer - NCT01104138</td>
<td>P. J. Goodwin (Supporter)</td>
<td>Supporter trial (Co-Leading partners: CCGT (sponser), BIG HQ) Funding: NC/NIH grants, Cancer Research UK, Canadian Cancer Society, BCRF and Canadian Breast Cancer Foundation</td>
</tr>
<tr>
<td><strong>MINDACT</strong></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 (Co-Lead), E. Cardoso (Co-Leading partner): EORTC (sponser), M. Piccart (Co-Leading partner): BCRF (sponser)</td>
<td>Co-lead trial (Co-Leading partners: EORTC (sponser), BIG HQ) Commercial partners: Roche, Sanofi, Novartis and Agenaxis Funding: European Commission, Roche, Sanofi and Novartis grants, BCRF, Susan G. Komen for the Cure, Cancer Research UK, EORTC, Chatebille Trust, numerous national cancer societies and many other charitable grants*</td>
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<tr>
<td><strong>NEO-ALTTO</strong></td>
<td>BIG 1-06</td>
<td>Comparison of dual HER2 inhibition (lapatinib, transzumab) plus chemotherapy before surgery versus single HER2-targeted therapy - NCT00533308</td>
<td>C. Saura (Co-Lead), J. Hussher (Pharma partner: Novartis (global sponsor for all countries with the exception of US, where Alliance is the sponsor))</td>
<td>Co-lead trial (Co-Leading partners: EJB-CTSU (BrEAST) / FSSI / SOLIT / BIG HQ) Pharma partner: Novartis (global sponsor for all countries with the exception of US, where Alliance is the sponsor) Funding: GSK (past) / Novartis</td>
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<td><strong>PALLAS</strong></td>
<td>BIG 14-03</td>
<td>Palbociclib-Glucantive Adjuvant Study: palbociclib with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for HR+ / HER2-negative early stage breast cancer - NCT01213094</td>
<td>E. Mayer (Co-Lead), M. Gnun (Co-Leading partner): ABCSG (RoW), A. de Michele (Co-Leading partner): BCRF (sponser)</td>
<td>Co-Lead trial (Co-Leading partners: ABCSG (RoW), AFT (US) (sponser)) and BIG HQ Pharma partner: Pfizer Funding: Pfizer grant</td>
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<td><strong>PENELOPE-B</strong></td>
<td>BIG 1-13</td>
<td>Post-neoadjuvant palbociclib for patients with HR+, HER2-negative breast cancer with high risk of recurrence after neoadjuvant chemotherapy - NCT01064746</td>
<td>S. Lohit (Co-Lead), S. Piccart (Pharma partner: Pfizer)</td>
<td>Co-Lead trial (Co-Leading partners: BCG (sponser), BIG HQ) Pharma partner: Pfizer Funding: Pfizer grant</td>
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<td><strong>POSITIVE (BIG Time for Baby)</strong></td>
<td>BIG 8-13</td>
<td>Endocrine therapy interruption to enable conception for young women with ER+ breast cancer - NCT012808885</td>
<td>O. Paganini (Co-Lead), A. Peat (Pharma partner: Pfizer)</td>
<td>Co-Lead trial (Co-Leading partners: BCSG (sponser), BIG HQ) Pharma partner: Pfizer Funding: Pfizer grant</td>
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<td><strong>PYTHIA</strong></td>
<td>BIG 14-04</td>
<td>Palbociclib plus fulvestrant for premenopausal patients with ER+ / HER2: metastatic breast cancer - NCT01256742</td>
<td>L. Makrini (Co-Lead)</td>
<td>Co-lead trial (Co-Leading partners: ABCSG (sponser) and BIG HQ Pharma partner: Pfizer Funding: Pfizer grant</td>
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<tr>
<td><strong>SNAP</strong></td>
<td>BIG 2-12</td>
<td>Schedules of nab-Paclitaxel evaluation of different schedules of nab-pacli for metastatic breast cancer - NCT01746225</td>
<td>A. Gennari (Co-Leader)</td>
<td>Supporter trial (Co-Leading partner: BCSG (sponser) Pharma partner: Celgene Funding: Celgene grant</td>
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<td><strong>SOFT</strong></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 - NCT00966905</td>
<td>P. Francis (Co-Leader)</td>
<td>Supporter trial (Co-Leading partner: BCSG (sponser) Pharma partner: Pfizer Funding: Grant support from Pfizer, Ipsen, US NCI, BCRF and many participating collaborative academic groups, BCRF) as well as various charities</td>
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<td><strong>SOLE</strong></td>
<td>BIG 1-07</td>
<td>A phase III trial evaluating the role of continuous letrozole versus intermittent letrozole following 4 to 5 years of prior adjuvant endocrine therapy for postmenopausal women with hormone-receptor positive, node positive early stage breast cancer (SOLiD - Study Of Letrozole Extension) - NCT00553410</td>
<td>M. Collonii (Co-Leader), P. Parietti (Pharma partner: Novartis)</td>
<td>Supporter trial (Co-Leading partners: ABCSG (RoW), BCSG Pharma partner: Novartis Funding: Novartis</td>
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<tr>
<td><strong>SUPREMO</strong></td>
<td>BIG 2-04</td>
<td>Selective Use of Postoperative Radiotherapy After Macroscopic Axillary node involvement wall irradiation for LocoMetastatic risk: breast cancer following mastectomy - NCT00966888</td>
<td>I. Kallikter (Co-Leader)</td>
<td>Supporter trial (Co-Leading partner: SPECTB Pharma partner: U.K. Medical Research Council Pharma partner: N/A Funding: U.K. Medical Research Council, EORTC, Cancer Australia, William and Elizabeth Davies Charitable Trust, Peter Chan Jo Yat Foundation, Yeung Ying Yin and Mr. Yeung Yizong Foundation</td>
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<tr>
<td><strong>TEXT</strong></td>
<td>BIG 3-02</td>
<td>Tansoxifen and Exemestone Trial: evaluation of exemestane plus GnrH analogue for premenopausal women with endocrine responsive breast cancer - NCT00966705</td>
<td>O. Paganini (Co-Leader)</td>
<td>Supporter trial (Co-Leading partner: BCSG (sponser) Pharma partner: Pfizer Funding: Grant support from Pfizer, Ipsen, US NCI, BCRF and many participating collaborative academic groups, BCRF) as well as various charities</td>
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<tr>
<td><strong>TREAT-CTC</strong></td>
<td>BIG 1-12</td>
<td>Palbociclib in HER2-negative Early breast cancer as: Adjuvant Treatment for Circulating Tumor Cells (CTC) (TREAT-CTC Trial) - NCT01548677</td>
<td>M. Ignatius (Co-Leader), M. Picciari (Pharma partner: Pfizer)</td>
<td>Supporter trial (Co-Leading partner: EORTC, BGC, SUCCESS, UNCANCER Sponsor: EORTC Pharma partner: Roche, Janssen Diagnostics Funding: Roche educational grant / medication; Janssen test kits</td>
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<td><strong>ULTIMATE</strong></td>
<td>BIG 16-01</td>
<td>Immunomotherapy combined with standard endocrine therapy as neoadjuvant maximum for women with ER+/HER2-negative breast cancer - NCT02979795</td>
<td>F. Adami (Co-Leader)</td>
<td>Co-lead trial (Co-Leading partners: French Breast Cancer Intergroup Unicancer (UCBG) (sponser) and BIG HQ Pharma partner: AstraZeneca Funding: AstraZeneca</td>
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</tbody>
</table>

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**Legend**

- **ABCFS** Alliance Foundation Trials, LLC
- **BCRF** Breast Cancer Research Foundation
- **BIG** Breast International Group
- **CCG** Cancer Care Group
- **CCTG** Canadian Clinical Trials Group
- **CTAT** Companioning Trials Administering Therapeutics
- **CTSG** Canadian Trials Group
- **EORTC** European Organisation for the Research and Treatment of Cancer
- **FSTRF** Frontier Science and Technology Research Foundation
- **IJB-CTSU** Intergroup Unicancer (UCBG) (sponsor) / FSS / Co-lead trial / (Co)-Leading partners: IBCSG (sponser)
- **ICRD** International Cancer Research and Development Foundation
- **IBCSG** International Breast Cancer Surgical Group
- **IJBCTSU** Intergroup Unicancer (UCBG) (sponsor) / FSS / (Co)-Leading partners: IBCSG (sponser)
- **IJB-CTSU** Intergroup Unicancer (UCBG) (sponsor) / FSS / (Co)-Leading partners: IBCSG (sponser)
- **IJBCTSU** Intergroup Unicancer (UCBG) (sponsor) / FSS / (Co)-Leading partners: IBCSG (sponser)
- **NCT** National Cancer Institute
- **NCCTG** North Central Cancer Treatment Group
- **NRS** North Rhine Westphalia Research Foundation
- **SCTBG** Scottish Clinical Trials Breast Group
- **TBCC** Translational Breast Cancer Research Consortium
- **USNCI** US National Cancer Institute
- **FSS** Foundation of the Swiss Society for the Study of Breast Cancer
- **Y-Yie Foundation** Yeung Ying Yin and Mr. Yeung Yizong Foundation

**NB:** This table does not include the studies in development and all closed trials. For more information please visit: www.BIGoscillatebreastcancer.org.
The breast cancer research groups of the BIG network

AFRICA
BIGCS Breast Gynaecological International Cancer Society
HGBS Hellenic Society of Breast Surgeons
HuCOG Hellenic Cooperative Oncology Group
HORG Hellenic Oncology Research Group
IBCSG Italian Breast Cancer Group
IBCSG International Breast Cancer Study Group
IBS International Breast Cancer Interventional Studies
ICCG International Collaborative Cancer Group
ICR-CTSU Institute of Cancer Research - Clinical Trials & Statistics Unit
IUB-CTSU Institute Jules Bordet / Clinical Trials Support Unit
MICHELANGIELO Fondazione Michela Figlin
NBCCG Norwegian Breast Cancer Group
NCR-BCSG National Cancer Research Institute - Breast Cancer Clinical Studies Group
SABO Swedish Association of Breast Oncologists
SARK Swiss Group for Clinical Cancer Research
SLG Société Luxembourgeoise d’Oncologie
SOCI Breast Cancer Research Group
SUCCESS Study Group
Swedish Breast Cancer Group
UCBG Uncancer Breast Group
WGo Westdeutsche Studeigruppe

ASIA
BBPCPC Breast Disease Professional Committee of China
BECI Breast Intergroup of Eastern India
CTRG Cancer Therapeutics Research Group
HKBDO Hong Kong Breast Oncology Group
ICON ARO Indian Co-operative Oncology Network
IOGC Indian Oncology Study Group
JBCRG Japan Breast Cancer Research Group
KCGS Korean Cancer Study Group
SKMHC & RC Shaukat Khanum Memorial Cancer Hospital & Research Centre
TCOG Taiwan Cooperative Oncology Group
TSCO Thai Society of Clinical Oncology

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

EUROPE
ABCSP Austrian Breast & Colorectal Cancer Study Group
AGO Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group
BOOOG Borstcancer Onderzoek Group
CEDOG Central and Eastern European Oncology Group
CS BR Cancer Trials Ireland
DBCOC Danish Breast Cancer Cooperative Group
EORTC-BCC European Organisation for Research and Treatment of Cancer - Breast Cancer Group
FFBC Finnish Breast Cancer Group
GCSG Finnish Georgian Cancer Study Group
GEICAM Spanish Breast Cancer Group
GORIC Gruppo Oncologico Italiano di Ricerca Clinica
HGBS Hellenic Society of Breast Surgeons
HuCOG Hellenic Cooperative Oncology Group
HORG Hellenic Oncology Research Group
IBCSG Italian Breast Cancer Group
IBCSG International Breast Cancer Study Group
IBS International Breast Cancer Interventional Studies
ICCG International Collaborative Cancer Group
ICR-CTSU Institute of Cancer Research - Clinical Trials & Statistics Unit
IUB-CTSU Institute Jules Bordet / Clinical Trials Support Unit
MICHELANGIELO Fondazione Michela Figlin
NBCCG Norwegian Breast Cancer Group
NCR-BCSG National Cancer Research Institute - Breast Cancer Clinical Studies Group
SABO Swedish Association of Breast Oncologists
SARK Swiss Group for Clinical Cancer Research
SLG Société Luxembourgeoise d’Oncologie
SOCI Breast Cancer Research Group
SUCCESS Study Group
Swedish Breast Cancer Group
UCBG Uncancer Breast Group
WGo Westdeutsche Studeigruppe

LATIN AMERICA
GAICO Grupo Argentino de Investigación Clinica en Oncología
GECO FERI Grupo de Estudios Clinicos Oncologicos Peruano
GCCCH Chilean Cooperative Group for Oncologic Research
GOCUR Grupo Oncologico Cooperativo Uruguaya
LACOG Latin American Cooperative Oncology Group

MIDDLE EAST
IBIO Israel Breast Group
ICRC Iranian Cancer Research Center
SBCG Sheba Breast Collaborative Group

NORTH AMERICA
CCTG Canadian Cancer Trials Group

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

In 1999, BIG was founded with the aim to address fragmentation in European breast cancer research. Research groups from other parts of the world rapidly expressed interest in joining BIG and, two decades later, BIG represents over 50 like-minded research groups from around the world and reaches across approximately 70 countries on 6 continents.

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

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

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

www.BIGagainstbreastcancer.org
Together, we make a difference

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or donate online:
www.BIGagainstbreastcancer.org/donate

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