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Western Europe
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Note from the editors

As we are approaching the end of the year, it is a good time to reflect on 2021. We are undoubtedly experiencing challenges never before imagined but there is reason for optimism and hope with the arrival of the COVID-19 vaccines. Despite all the challenges that the pandemic poses, BIG has continued its efforts to advance breast cancer research.

This edition of BIG Research in Focus highlights breast cancer research in Western Europe. Breast cancer research groups in Western Europe were among the first to join BIG when it was founded in 1999. Today, they recognise the advantages of a major international research organisation in reducing fragmentation of effort and avoiding duplication. However, escalating clinical trial costs, slower access to novel therapies, COVID-19 and even a major cyber-attack on a national healthcare computer system have been among recent challenges reported by leading oncologists from these groups. For the full article, see as of page 5.

With the themed article on Western Europe, we are closing the series “Fighting Breast Cancer Around the Globe”. We have now covered all the regions represented by BIG member groups. BIG would like to thank everyone who accepted to be interviewed in the last five years, about 50 breast cancer experts from the BIG network, representing nearly 40 countries, have shared with us their valuable insights into major developments in breast cancer care and research that are improving the outlook for patients around the world. See as of page 15.

The section “BIG Network” provides an overview of activities carried out by BIG Headquarters (HQ) and includes news from BIG members. At the virtual General Assembly of last June, two new academic cancer research groups were accepted as members of BIG. We are pleased to welcome the European Breast Cancer Research Association of Surgical Trialists (EUBREAST) Network, which consists of the German association EUBREAST e.V. and its Italian counterpart EUBREAST ETS. Other news: On 11 June, the newly elected Executive Board was presented to BIG’s General Assembly. See as of page 20.

BIG against breast cancer, BIG’s dedicated philanthropy unit within BIG HQ, 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. See as of page 32.

In the section “Clinical Trials and Activities”, we include an interview of Professor Martine Piccart and Dr Philippe Arimotis, who provide us with their insights and an update on the AURORA programme on metastatic breast cancer. We also include an update on the OlympiA clinical trial. See as of page 36.

The section “Other trials and activities by BIG Member Groups” gives a peek at BIG member’s research and related activities around the world. See as of page 41.

Finally, you will find the “Overview of the current clinical studies run within the BIG network” as of page 50.

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

Together, we will cure breast cancer

BIG’s Editorial Team

Breast cancer research groups in Western Europe were among the first to join BIG when it was founded in 1999. Today, they recognise the advantages of a major international research organisation in reducing fragmentation of effort and avoiding duplication. However, escalating clinical trial costs, slower access to novel therapies, COVID-19 and even a major cyber-attack on a national healthcare computer system have been among recent challenges reported by leading oncologists in Western Europe to medical journalist, Jenny Bryan.

In the late 1990s, when Professor Hervé Bonnefoi, Professor of Medical Oncology at the University of Bordeaux, and medical oncologist at the Bergonié Cancer Institute, France, began to attend US cancer congresses as a young doctor, there were very few presentations by researchers outside the USA. Two decades later, practice-changing breast cancer trials are reported from all around the world—many of them run by the BIG network of academic research groups that reaches across over 70 countries on six continents.

“BIG’s trials show international academic research at its best, and studies such as HERA, SOFT, MINDACT and, most recently, OLYMPIA, are having a huge impact on breast cancer care for patients,” says Bonnefoi. “Even when BIG trials are not practice changing, they are important because they carry a label of excellence. Moreover, BIG can help to guide development of new drugs in areas or niches that are important to clinicians but are not always a priority for our partners,” he adds.

Dr Evandro de Azambuja, Head of the Medical Support Team at the Institut Jules Bordet, Clinical Trials Support Unit (FJB / CTSE), Brussels, Belgium, agrees that the scientific leadership of BIG means that studies are carried out that answer important questions for clinicians and patients.

“If there was no BIG, it would be difficult to carry out trials with the thousands of patients needed to answer important questions and there would be a risk that by the time we had the answers, the questions would be irrelevant. Previously we might have had the same trials carried out in Europe and the USA so there was a lot of duplication, but now we can get answers with one large international trial,” says de Azambuja.

Large, increasingly complex national and international breast cancer trials cannot be done cheaply, and they have brought an increased administrative and financial burden for researchers across Western Europe, as in other parts of the world.

Professor Michael Grant, Professor of Surgery at the University of Vienna, and President of the Austrian Breast & Colorectal Cancer Study Group (ABCSG) explains that in the 1990s, one of the first trials in which he was involved had a budget of approximately €3 million for 3,000 patients.
The main aims of this survivorship research are to identify patients who are at risk of deteriorating quality of life after breast cancer treatment, owing to long-term drug toxicities or other reasons, and to develop innovative, personalised, multi-modal, digital and in-person support," explains medical oncologist, Dr Ines Vaz Luis, from Institut Gustave Roussy, Villejuif, France.

In the CANceT0oxicities (CANTO) study of chronic treatment toxicity, over 12,000 patients with localised breast cancer are being followed up over 10 years from diagnosis, with collection of a wide range of clinical, laboratory, biological (‘omic), social and psychological data.1-4

“We have clearly identified the main issues that affect the lives of patients after cancer, and we are starting to build predictive models for patients who are likely to develop these issues, initially based on clinical data but also now including biological data, so that in the future we can stratify patients according to the support they are likely to need,” says Vaz Luis.

Progress is also being made in developing multi-modal interventions, with a study due to start that will investigate intensive, tailored support for patients struggling with hormone therapy. In addition, through a national WeShare grant, French and other researchers, starting with young investigators, will have access to digital tools to accelerate quality of life studies.

French researchers are also leading the European My Personal Breast Screening (MyPBeS) initiative that is comparing a personalised risk-based screening strategy (based on an individual woman’s risk of developing breast cancer) to standard screening. Vaz Luis explains that risk-based strategies are also being used in ongoing treatment studies, including the PADA-1 trial of hormone switching in patients with metastatic oestrogen receptor positive, HER2-negative breast cancer with an ESR mutation in sequential ctDNA analysis. Iterative ctDNA screening is also being used in the TRAKER study (in collaboration with researchers at the Royal Marsden Hospital, London) to detect resistance mutations in patients with high-risk localised cancer so that early therapeutic intervention can be started. For patients with HER2-positive metastatic breast cancer with isolated brain progressions, the INTERCEPT study is investigating triple therapy with trastuzumab, pertuzumab, and naxitumab to try to significantly delay further progression.

Integrated breast cancer care and research in the UK

For Professor Judith Bliss, Director of the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU), London, UK, the practice-changing UK trials that showed the benefits of hypofractionated radiotherapy after primary surgery for early breast cancer are among the most important advances for UK patients of the last two decades.1-4

“By the 2000s, that had increased to €30-35 million and, most recently, one needs a budget of €300+ million for 5,000 patients. That’s a 10-fold increase almost every decade, which is surely something that cannot continue,” he says.

Rising costs are not only affecting trial budgets in Western Europe, they are also starting to impede access to new treatments in some countries. Bonnefoi explains that, in the past, the French government was among the first to grant access to new treatments where supportive evidence was strong (for example trastuzumab in the adjuvant setting) but access to new treatments is becoming more difficult, particularly when health authorities consider the benefit to be modest.

Grant is also seeing a trend towards reduced access to latest breast cancer treatments. “Access to novel cancer treatments in Austria is still among the best in Europe, but we are starting to feel economic pressures, made worse by the COVID-19 pandemic. We still have to act reasonably and, at the same time, decisively because some of these drugs are really very expensive – we try to interact with payers to prevent future problems,” he says.

In Switzerland and The Netherlands, professional advisory groups assess the evidence supporting novel agents, and their recommendations are proving helpful for reimbursement discussions.

“For the most expensive new drugs, there may be problems with reimbursement and the Ministry of Health has to get involved in negotiations with companies, which can delay access for patients,” says Vincent Dezentié, medical oncologist at the Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

Reimbursement negotiations after European Medicines Agency (EMA) approval of new cancer medicines can also cause bottlenecks in Germany, adds Professor Christoph Thomssen, gynaecological oncologist from Martin Luther University Halle-Wittenberg, Halle (Saale), Germany.

“There is a two-step procedure, which means that we have good access in the year after EMA approval, but the Federal Commission for Reimbursement may then question the benefit of a drug and want to negotiate over price. This may deter some physicians from prescribing the drug until the price has been agreed,” he says.

Shortage of oncologists threatens French breast cancer research

As the incidence of breast cancer continues to rise in France, there is growing concern that a shortage of trained oncologists and pathologists will put pressure on services and limit time for research.

“The workload for oncologists is increasing and it is tough to find time for research. The health system does not appear to recognise the importance of research and, while it is good that we are training more oncology nurses, we are not training enough oncologists,” says Bonnefoi.

“We also need biopathologists who can help drive molecular diagnosis of cancer as part of our move towards precision medicine. It makes me concerned not only for the health of our patients but also for our overworked doctors,” he adds.

Under France’s new National Cancer Plan agreed in February 2021, the government has committed €1.74 billion to improving cancer services. However, Bonnefoi explains that the emphasis is on reducing mortality from preventable cancers, such as stopping smoking and reducing alcohol intake, and also on rare tumours, such as pancreatic cancer, with high mortality where there has been little progress in treatment.

“This decision obviously makes sense but breast cancer does not fit well into these categories, though we may get some support for research into triple negative breast cancer. But that overlooks the fact that 12,000 people are still dying from breast cancer each year in France,” says Bonnefoi.

For the Unicancer Breast Group (UCBG) in France, the focus of research is on early diagnosis and personalised treatment, not only at the level of molecular biology but also for patient care, with a strong emphasis on regaining quality of life for cancer survivors.

For Professor Judith Bliss, Director of the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU), London, UK, the practice-changing UK trials that showed the benefits of hypofractionated radiotherapy after primary surgery for early breast cancer are among the most important advances for UK patients of the last two decades.1-4

“These seminal trials have changed the international standard for how radiotherapy is given – from 25 fractions requiring 25 visits to hospital for patients, down to 15 and, most recently, to five, without affecting treatment outcomes,” she explains.

Five-year data from the FAST-Forward trial in April 2020 confirming the non-inferiority of five fractions over one week compared to 15 fractions over 3 weeks could not have come at a better time for hard-pressed clinicians working in the midst of the COVID-19 pandemic.6

“There was phenomenal interest right from the start about how five fractions could be safely delivered, and the necessary technical protocols were rapidly shared, and recommendations included in relevant guidelines. The majority of patients in the UK – with the exception of those who need nodal as well as breast radiotherapy – are now given the much shorter course of treatment,” says Bliss.

In parallel with the hypofractionation studies, partial breast radiotherapy research in the UK has also yielded practice-changing results, with some women with early breast cancer now able to avoid whole-breast radiotherapy.7
Thomssen highlights a series of studies that have improved our understanding of optimal regimens in different breast cancer types, including the German Breast Group's (GBG) recently reported GEPARNuevo study showing that neoadjuvant durvalumab improves long-term outcome in TNBC when added to anthracycline/taxane-based chemotherapy. Other recent reported data – from the ADAPT trial carried out by the West West German Study Group (WSG) – showed excellent pCR and survival in patients receiving de-escalated neoadjuvant chemotherapy and dual HER2 blockade in HR-negative, HER2-positive breast cancer. Early pCR after 12 weeks was strongly associated with improved outcomes and has potential as a predictive marker for further de-escalation.

With regard to luminal breast cancer, WSG's ADAPT program showed the predictive impact of Ki-67 drop after a short period of endocrine therapy in order to reduce the need of adjuvant chemotherapy in these patients. The main challenges still facing us are risk estimation for reducing chemotherapy in all breast cancer types and better individualisation of neoadjuvant treatment according to subgroups. We also need to explore the relationship between pCR and disease-free survival, how to improve pCR rates with neoadjuvant therapy, and what should be offered to those who do not get a pCR,” says Thomssen.

“In 5 or 10 years’ time, I hope there will be less surgical intervention – even though I am a surgeon. If we can reduce the rate of false negative biopsy results after neoadjuvant therapy, we may be able to reduce the need for surgery or at least reduce the need for chemotherapy. I am also looking forward to regimens that are as effective as the taxanes but without their neurotoxic effects. All these advances would have an important impact on the quality of life of our patients,” concludes Thomssen.

Treatment de-escalation is a priority in the Netherlands

Celebrating two decades of the Dutch Breast Cancer Research Group (Borstkanker Onderzoek Groep (BOOG)) studies this year, Dutch breast cancer researchers are rightly proud of the impact that multiple trials have had on patient care in The Netherlands since the organisation was established.

“Since 2001, we have recruited over 30,000 patients in The Netherlands to breast cancer trials and, as BOOG is now the most important breast cancer research platform in The Netherlands and nearly all breast cancer oncologists are members; BOOG research has helped to standardise clinical practice in hospitals across the country,” says Vincent Dezentjé, medical oncologist at the Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

He explains that the TRAIN trials have been important in establishing neoadjuvant therapy as standard of care for patients with HER2-positive breast cancer. After promising data from an initial single-arm Phase 2 study, TRAIN 2 showed that, in the presence of dual HER2 blockade, non-anthracycline and anthracycline-containing regimens were equally effective but the former was less toxic.

“Neoadjuvant therapy was previously thought to be logistically complex and disliked by patients, but the TRAIN studies showed the value of this approach, and that anthracycline-free treatment could reduce toxicity,” explains Dezentjé.

TRAIN 3, another single arm, Phase II study is now evaluating the efficacy of image-guided de-escalating neoadjuvant treatment with paclitaxel, carboplatin and dual HER2 blockade in stage II-III HER2-positive breast cancer.

“A key part of the BOOG research strategy is treatment de-escalation and the aim of TRAIN 3 is to see whether, in patients who have a radiological complete response, three or six courses of neoadjuvant treatment will be as effective as nine courses before breast cancer surgery,” explains Dezentjé.

Recruitment is almost complete to the SONIA trial, which is investigating the optimal place of CDK4/6 inhibitors, either as first line treatment with aromatase inhibitors or second line with fulvestrant in patients with hormone receptor positive advanced breast cancer.

“We very much hope to show that giving CDK4/6 inhibitors as second line will be non-inferior to first line, as this will mean fewer hospital visits and potentially better quality of life for patients and more cost-effective treatment,” Dezentjé points out. “SONIA is seen as such an important study in The Netherlands that it has government funding.”

Currently at the planning stage is the SEQUEL-Breast study, which is hoped to provide further insights into optimal endocrine sequencing in patients with advanced breast cancer. This Phase 2 study will investigate the combination of fulvestrant and alpelisib in patients with PIK3CA-mutated, hormone receptor-positive, HER2-negative advanced breast cancer, following progression on fulvestrant as second line therapy.
Imagine arriving at work to find that a major cyber-attack has paralysed your country’s health service and you have no access to patient records, appointments, or research data. That was the scenario facing the 18,000 doctors working in Ireland earlier this year, including Professor Seamus O’Reilly, Consultant Medical oncologist at Cork-Mercy and South Infirmary Victoria University Hospitals, Ireland.

“It happened when we were trying to clear the backlog after COVID-19, so the timing was dreadful, and I would recommend that anyone reading this should ask their hospitals how susceptible they are to cyber-attack and what steps they should take to prepare for it. COVID-19 was a ‘speed bump in the road’ compared to ‘the mountain on the motorway’ resulting from our cyber-attack,” he says.

Setting aside recent events, Ireland has seen major improvements in breast cancer survival over the last 20 years – thanks to substantial improvements in treatment and greater integration of care. Patients now receive care through well-defined pathways from primary care to eight large cancer centres across Ireland instead of the previous 30 less specialist hospitals. In parallel, a less well-known benefit of the 1998 Belfast/Good Friday agreement that brought an end to conflict in Northern Ireland was to result in the development of the Irish Cancer Society, which worked with the Department of Health to establish BreastCheck, a breast cancer screening programme.

This agreement has been transformative for breast cancer research because it sanctioned government funding for cancer trials in cancer centres throughout the country. It really turbocharged research because we were able to build infrastructure and recruit staff, and develop cross-border synergies, education, training, and career development on an all-Ireland landscape,” says O’Reilly.

He adds that a reorganisation of Ireland’s hospitals into clusters attached to universities with links to the national clinical research organisation, Cancer Trials Ireland (CT-IRE), aims to increase the footprint of clinical cancer research and build stronger links between cancer research units and universities.

“We recognise that many of us can’t work harder but many of us can work better, so we need to decide how to work together and adapt career pathways to the reality of modern working patterns, where doctors don’t just get a job and stay in it for ever as used to be the case,” says O’Reilly.

CT-IRE’s workstreams are currently focused mainly on improving survival and quality of life in early breast cancer through better drug selection, and at reducing side effects of hormone treatment.

“Hormones are one of the key challenges of breast cancer medicine. They are pivotal for treating the disease, but the cost in terms of side effects for patients can be considerable. There is a disparity between clinical reality and patient reality for many of these side effects, and these issues can lead to non-compliance with treatment and worse outcomes. Most of the conversations I have with patients about side effects are not about chemotherapy but about hormone therapy,” says O’Reilly.

Among the trials to which CT-Ireland members are contributing are BIG’s EXPERT trial of personalised radiotherapy in early breast cancer and to the German Breast Group’s SASCIA study of post neoadjuvant treatment with the antibody-drug conjugate sacituzumab govitecan in women with HER2-negative breast cancer and a high risk of relapse after standard neoadjuvant treatment. They are also recruiting for the KEYNOTE-756 study of pembrolizumab and the CA299-7FL study of nivolumab – both in combination with neoadjuvant or adjuvant hormone treatment in high-risk early-stage ER-positive, HER2-negative breast cancer – and for the KEYLYNK-009 study of olaparib and pembrolizumab in triple negative breast cancer.

Belgian research: helping to change the international treatment landscape

Over the last 20 years, the Institut Jules Bordet/Clincial Trials Support Unit (IJB/CTSU), Brussels, Belgium, has made a major contribution to practice-changing breast cancer research, including BIG’s HERA and APHINITY trials in early stage HER2-positive breast cancer. IJB also recruited many patients to the MINDACT trial of genomic risk to help identify patients with early breast cancer who can potentially avoid chemotherapy.

“We are very privileged to have been involved in many clinical trials and to be able to rapidly contribute significant numbers of patients to studies of trastuzumab, pertuzumab, CDK4/6 inhibitors and others that have changed the treatment landscape,” says Dr Evandro de Azambuja, Head of the Medical Support Team at the Institut Jules Bordet, Clinical Trials Support Unit (IJB / CTSU), Brussels.

Among current research priorities is an investigation into risk factors for brain metastases in patients with breast and other solid tumours, using the clinical research platform BrainStorm, carried out with researchers in the Oncodistinct network under the supervision of Dr Nuria Kotecki. Clinical and biological data are being collected to identify risk factors for central nervous system (CNS) metastases and better understand the biology of CNS metastases (brain and leptomeningeal). de Azambuja explains that it is hoped that this will lead to the development of new treatment targets and help to intensify the multidisciplinary approach for the management of CNS metastases. The translational part of the programme will include the use of cerebrospinal fluid circulating tumour DNA (CSF-ctDNA) as a surrogate for CNS metastases in order to characterise its molecular landscape.

In Belgium, there is also a strong focus on triple negative breast cancer (TNBC), with IJB/CTSU researchers working closely with BIG on the use of immunotherapy and chemotherapy in the adjuvant setting. IJB is also conducting a trial testing combination immunotherapy and chemotherapy as first line treatment in patients with metastatic TNBC. In addition, there is an initiative looking at whether neoadjuvant immunotherapy and radiotherapy can boost response to chemotherapy in patients with luminal breast cancer.
The impact of COVID-19

No country in Western Europe has been untouched by the COVID-19 pandemic, with adverse effects on both breast cancer care and research. In general, breast cancer screening has been the biggest victim of the pandemic, with programmes reduced or halted for many weeks or months.

Breast cancer trials in the UK were probably amongst the worst hit in Western Europe owing to the integrated nature of research within the country’s National Health Service. Bliss explains that, during the worst periods of the pandemic, we are much more adept at helping patients with COVID-19 in intensive therapy units, so it was difficult to keep trials going at their usual pace.

“Before COVID, the picture for breast cancer research in the UK was bright because we have a lot of coordinated, multidisciplinary teams of enthusiastic researchers working with a network of clinical trials units,” Bliss explains. “During the pandemic, we managed to keep some trials going and saw patients online, but not trials that needed biomarker testing in labs that were closed. Now that trials are re-opening, there is a priority to get studies finished rather than start new ones, so the picture is very mixed.”

France was also badly hit during the pandemic, with all recruitment to trials stopped for at least four months and accrual still low in June 2021. In Ireland, trial recruitment dropped by 40% partly due to safety concerns of getting patients into trials and, as in the UK, the loss of research nurses to COVID-19 patient care. In Belgium, breast cancer care and research were most affected during the first wave of infections, and no new patients went into trials. The situation was disrupted.

Despite the adverse effects of the pandemic, many clinicians have reported positive effects arising from limitations on healthcare systems. “There have been delays in Austria and we halted recruitment to one trial for four weeks, but the regulators have been flexible and allowed longer gaps between patient check-ups, together with video and telephone consultations. This would previously have been unthinkable, but I certainly hope it will continue after the pandemic,” says Grant.

Future goals

In the years ahead, personalisation and de-escalation of treatment are important goals for breast cancer specialists in Western Europe, along with continued reductions in mortality and better treatment options for TNBC.

“In Austria, breast cancer mortality has gone down by 30% in the last 20 years, but we cannot rest. Despite our achievements, we are still not good at treating late recurrences of hormone dependent breast cancer,” says Grant.

In Belgium, de Azambuja hopes for better understanding of the reasons why breast cancer incidence and mortality are among the highest in Western Europe.

“We have a large screening programme with good uptake so cases are detected early, but we still have higher mortality than we would expect, considering the good availability of treatment. The Belgian Cancer Agency is looking into possible causes, and we hope we will soon have some answers,” he says.

In France, Vaz Luis hopes that progress with earlier diagnosis and treatment of breast cancer will mean less longer-term impact on quality of life and that routine stratification and support for those at greatest risk will reduce disparities of care.

“In 10-years’ time, I hope that our efforts to personalise all aspects of breast cancer care will have become a reality and that preventive strategies based on individual risk will enable us to prevent more cases,” she says.

However, Bonnefoi remains very concerned about the potential negative impact of a continuing shortage of oncologists in France on cancer research.

O’Reilly also looks forward to more personalised treatment for patients in Ireland, taking account of the diversity of the population.

“Ireland now has a significant immigrant community who are less likely to present for screening and may respond differently to treatment, with different side effect profiles leading to differences in compliance. By being part of the BIG collective, we can be more aware of these nuances between ethnic groups and in those with rarer types of breast cancer so that, in the future, we are not only improving survival for patients in Ireland, we are improving the quality of their survival,” he concludes.
References

From Latin America to Australasia
In Latin America, where 115,000 patients are diagnosed with breast cancer each year, experts described a series of initiatives aimed at reducing regulatory delays, training clinicians, improving infrastructure, and boosting funding. Through a growing network of cancer organisations across the region, a new culture of research was being built that predicted to have a major impact in the years ahead.

“Research and innovation are integral parts of development in any society. We will only evolve if we can generate credible scientific information with high quality research,” said Professor Carlos Barrios, Founder of the Latin American Cooperative Oncology Group (LACOG).

For the growing number of breast cancer specialists working across the Middle East, key priorities include establishing breast cancer registries, improving mammographic and BRCA screening, and achieving earlier diagnosis. They are also working to expand treatment options, reduce mortality, and create opportunities for contributing to worldwide clinical trials.

“We have plenty of ideas and we are expanding and integrating our research infrastructure, but it will only be possible to get the full flavour of breast cancer worldwide if countries of the Middle East take part in international studies,” said Professor Hesham El Ghazaly, Ain Shams University, Cairo, Egypt.

Raising awareness of breast cancer and improving access to care are also priorities for clinicians across South Asia. Through research focused on local needs, they are identifying affordable diagnostic and treatment options to improve outcomes for patients who often live many miles from specialist cancer centres. In addition, they are building support services to enhance survivorship. At the same time, some are moving ahead with basic breast cancer research and making a growing contribution to international clinical trials.

“We need to educate both women and men in rural areas that this is a curable disease in the early stages, so that men understand the importance of taking their wives and other female relatives to hospital,” explained Dr Mazhar Ali shah, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
For breast cancer specialists in East Asia, there is an urgent need to ‘translate’ treatment advances made in European and US studies to local clinical practice and a strong desire to play a leadership role in collaborative research. Although breast cancer rates are less than half those seen in western countries, levels are rising, and approximately half of women who get breast cancer in Asian countries are premenopausal.

“We need a better understanding of the aetiology and predisposing factors in order to prevent breast cancer, and there is room for improvement of early detection by improving awareness and minimising barriers to seeking treatment in the region,” pointed out Dr Yoon-Sim Yap, National Cancer Centre, Singapore.

Despite their relatively small populations spread over large and often remote areas, Australia and New Zealand have played an important part in many practice-changing breast cancer trials. However, faced with some of the highest incidence rates for breast cancer in the world, clinicians are all too aware of the need to implement research findings so that patients receive the highest standards of care – whatever their cultural background and wherever they live.

“It's very important to understand where we come from in terms of research that has been carried out in Australia and New Zealand over the last 40 years, so that we can implement our findings in daily practice, and plan for the future,” stressed Dr Prue Francis, Peter MacCallum Cancer Centre, Melbourne, Australia.

**A transatlantic partnership**

With the National Clinical Trials Network (NCTN) – a network of major US and Canada-based research groups – BIG is collaborating on important clinical trials including POSITIVE and AURORA, and research exploiting the place of immunotherapy. In addition, the collaboration has helped to standardise Ki67 assessment for predicting breast cancer progression and determining clinical management, and development of endpoints in adjuvant and neoadjuvant trials. The partnership has also led to a much-needed research initiative in male breast cancer.

“The ultimate goal is to see a truly international collaboration in which researchers from across the world contribute data from great many patients in one study to answer one question. In that way, instead of answering questions in years, we will be able to answer them in months,” said Dr Larry Norton, Founding Scientific Director of the Breast Cancer Research Foundation, which provides funding for the BIG-NCTN collaboration.

**Europe – a continent of similarities and contrasts**

We ended our breast cancer journey of discovery by talking to researchers across Europe – a continent that includes some of the earliest and some of the newest members of BIG. Although breast cancer is less common in Central and Eastern Europe than in other parts of Europe, delayed diagnosis and limited access to newer treatments have resulted in poorer outcomes in many parts of the region. For breast cancer specialists in Central and Eastern Europe, shaping future services, wider availability of breast screening, better access to genomic testing and targeted therapies, and more specialist breast cancer centres are high on the agenda.

“I hope that we will be able to close the gap in breast cancer care between Western and Central and Eastern Europe, and we are working hard to convince governments to prioritise cancer because it is not just an expense but a good investment. I remain optimistic!” said Professor Jacek Jassem, Chair of the Central and East European Oncology Group (CEEOG).

Southern Europe has seen major improvements in breast cancer care over the last 20 years, despite the heterogeneity of healthcare systems and research infrastructure of Mediterranean countries. Promising initiatives are underway to reduce inequalities of care, build and extend cooperative research groups, encourage academic research and, most recently, to address the challenges of COVID-19.

“It is extremely rewarding to see Southern Europe so well represented in these and other collaborative trials and it is a measure of the success of current care and research in a region that may previously have been thought to be a little behind other parts of Europe,” commented the late Dr Angelo Di Leo, from the Istituto Toscana Tumori, Italy.

The countries of Northern Europe have often been at the forefront of breast cancer research that has shaped worldwide clinical practice and helped reduce mortality, though current delays in approval of novel therapies are frustrating clinicians. As in many countries, treatment de-escalation and improved quality of life for patients are key goals for further advances in care and research.

“For many years we added more and more treatments for patients without really understanding tumour biology. Now, this is changing as molecular sub-typing is leading to more precision medicine, and treatment de-escalation may become possible in selected patients,” explained Dr Barbro Linderholm, Chair of the Swedish Association of Breast Oncologists (SABO).

Breast cancer researchers in Western Europe recognise the advantages of a major international research organisation, such as BIG, in reducing fragmentation of effort and avoiding duplication. However, escalating clinical trial costs, slower access to novel therapies, COVID-19, and even a major cyber-attack on a national healthcare computer system, have been among recent challenges reported by leading oncologists in Western Europe.

“BIG’s trials show international academic research at its best, and studies such as HERA, SOFT, MINDACT and, most recently, OLYMPIA, are having a huge impact on breast cancer care for patients. Even when BIG trials are not practice changing, they are important because they carry a label of excellence. Moreover, BIG can help to guide development of new drugs in areas or niches that are important to clinicians but are not always a priority for our pharma partners,” concluded Professor Hervé Bonnefoi, University of Bordeaux, and medical oncologist at the Bergonié Cancer Institute, France.
Meet the experts

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Michael Grant, MD, FACS, EBSQhon
Professor of Surgery at the Medical University of Vienna, Austria
President of the Austrian Breast & Colorectal Cancer Study Group (ABCSG)
Co-chair of the St. Gallen International Breast Cancer Conference
Vienna, Austria

Seamus O’Reilly, MD, PhD
Consultant Medical Oncologist at Cork University Hospital and Professor at University College Cork, Ireland
Co-National Director in Medical Oncology at the Royal College of Physicians of Ireland
Vice Clinical Lead of CT-IRE (Cancer Trials Ireland)
Member of BIG’s Executive Board
Cork, Ireland

Manuela Rabaglio, MD
Medical oncologist at the Inselspital (University Hospital Bern), Universitätsklinik für Medizinische Onkologie, Switzerland
Member of SAKK (Swiss Group for Clinical Cancer Research)
Bern, Switzerland

Christoph Thomssen, MD, PhD
Doctor of Medicine, Professor in Gynaecology and Obstetrics
Director of the Clinic and Polyclinic for Gynaecology, Martin Luther University Halle-Wittenberg, MLU - Clinic for Gynaecology, Germany
Member of AGO-B (Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group)
Halle, Germany

Ines Vaz Luis, MD, MSc, PhD
Medical oncologist
Director of Breast Cancer Survivorship Research Group, Institut Gustave Roussy, France
Member of UCBG (Unicancer Breast Group, France)
Member of BIG’s Executive Board
Villejuif, France

Khalil Zaman, MD, PhD
Medical oncologist
Medical Director of the Breast Center, Department of Oncology, Lausanne University Hospital CHUV, Switzerland
Member of SAKK (Swiss Group for Clinical Cancer Research)
Lausanne, Switzerland
BIG's new Executive Board

On 11 June, the newly elected Executive Board was presented to BIG's General Assembly. Below is an overview of the 14 Executive Board members, as well as an outline of the Executive Board's role, BIG's mission and vision, and BIG's strategy statement.

BIG is constantly striving to be at the forefront of breast cancer research, adapting to new situations, further professionalising and enlarging its network of breast cancer experts. Let us not forget that we started small more than 20 years ago … and now we are BIG, the largest global network of academic research groups dedicated to finding cures for breast cancer. The two co-founders of BIG, Martine Piccart and the late Arno Goldhirsch made this possible. Global collaboration is key if we want to eradicate breast cancer.

BIG's Executive Board represents the leadership of the organisation, reporting to the General Assembly of all member groups. It is primarily responsible for proposing, shaping, and reviewing BIG’s strategies and related objectives, and for ensuring the long-term viability of the association.

Today it consists of 14 individuals chosen from amongst its member groups and embodies a range of cancer expertise such as medical oncology, radiation oncology, medical statistics and clinical trials methodology, and translational research.

As per BIG’s statutes, the General Assembly elected 4 individuals from among the candidates (Boon Chua, Judith Bliss, Sherene Loi, Shigehira Saji) and the BIG EB appointed the remaining 10 (Ines Vaz-Luís, Seamus O'Reilly, Evangelia Razis, Barbro Linderholm) to join the EB members whose terms were continuing (Philippe Bedard, Etienne Brain, David Cameron, Eva Carrasco, Angelo di Leo, Ander Urruticoechea). Tragically, we were informed of the death of Angelo di Leo the day after the General Assembly; his term would have continued to 2023.

We wish to extend our sincere gratitude to the leaving EB members who have devoted their time to BIG in the past and have contributed to the organisation’s growth and global breast cancer research. A BIG Thank You to Sibylle Loibl, Marco Colleoni, Shinji Ohno, and Aleix Prat. We wish them luck in all their future endeavours!

BIG’s leadership authority

BIG’s Executive Board is chaired by Professor David Cameron and supported by BIG Headquarters in Brussels.

As of 11 June 2021, the BIG Executive Board comprises the following world-class breast cancer specialists:

- Carlos Barrios, medical oncologist, Brazil – LACOG (Latin American Cooperative Oncology Group, www.lacog.org.br)
- Philippe Bedard, medical oncologist, Canada – CCGT (Canadian Cancer Trials Group, www.ccgta.queensu.ca)
- Eva Carrasco, medical oncologist, Spain – GEICAM (Spanish Breast Cancer Group, www.geicam.org)
- Barbro Linderholm, medical oncologist, Sweden – SABO (Swedish Association of Breast Oncologists, www.onkologii.org)
- Seamus O'Reilly, medical oncologist, Ireland – CT- IRE (Cancer Trials Ireland, www.cancertrials.ie)
- Evangelia Razis, medical oncologist, Greece – HeCoG (Hellenic Cooperative Oncology Group, www.hecog.gr)
- Ander Urruticoechea, BIG Treasurer, medical oncologist, Spain – GEICAM (Spanish Breast Cancer Group, www.geicam.org)

Two new research groups joined BIG: the EUbreast Network (Germany/Italy)

At the virtual General Assembly of last June, two new academic cancer research groups joined the BIG network, further enlarging its international reach.

We are pleased to welcome the European Breast Cancer Research Association of Surgical Trialists (EUbreast) Network, which consists of the German association EUbreast e.V. and its Italian counterpart EUbreast ETS.

The European Breast Cancer Research Association of Surgical Trialists (EUbreast) Network was founded by a group of European breast surgeons in 2018. The two not-for-profit EUbreast associations in the network are chaired by Professor Dr Thorsten Kuehn (Germany) and Dr Oreste Gentilini (Italy).

“BIG and EUbreast share the same objective and mission. We are happy and honoured to contribute to the BIG family with our focus on breast surgical research, as this partnership will increase and improve international scientific cooperation, which is the ultimate goal of both organisations.” – Professor Dr Thorsten Kuehn and Dr Oreste Gentilini.

EUBREAST promotes national and international research projects with the goal of developing less-invasive techniques for breast cancer surgery in order to improve affected patients’ quality of life. Several trials are currently underway, with more than 20 countries represented.

For further information: https://www.eubreast.com

BIG now represents 56 like-minded research groups from around the world and reaches across more than 70 countries on 6 continents.

Through its network of groups, BIG connects 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.

For information: https://www.eubreast.com
BIG as a network designs and conducts its own research. The role of the BIG Executive Board is critical to ensure that all clinical trials and programmes carried out under the BIG umbrella are run according to BIG’s mission and principles of research conduct and that they fall within BIG’s strategy.

These principles aim to eliminate bias from the research process, protect academic freedom, and maintain integrity vis-à-vis patients, both when working with the pharmaceutical partners or when working alone. Particularly important is that BIG commits to prioritising research that otherwise would not be possible and cannot be done by one research group alone. Within this framework, BIG conducts research to advance treatments that make a real difference to women and men with breast cancer.

**Professor David Cameron, BIG Chair:** “BIG recognises that the ‘global cancer problem’ has particularities in each region and country. I’m delighted by the composition of the new Executive Board – I’m confident that this talented, multi-national and multi-disciplinary group of people will further develop the important advances already set into motion in recent years. In the years to come, the BIG network aims to continue to play an important role in international breast cancer research, allowing for the most efficient conduct of clinical trials and always keeping patients’ interests at the heart of its activities. Further collaboration with research groups in countries where research is scarcer and availability of innovative trials is rarer could be a significant step towards improving treatment and care for women and men with breast cancer, wherever they live.”

And he continues: “Finally, I would like to take this moment to make a special mention of Professor Angelo Di Leo (Head of the Sandro Priglani Medical Oncology Department at the Hospital of Prato, Italy) who tragically passed away on 12 June, 2021. Professor Di Leo was a true defender of academic research and international collaboration. He will be missed by all of us, his family and patients.”

In 1999, BIG was founded by Dr Martine Piccart and Dr Aron Goldhirsch with the aim to address fragmentation in European breast cancer research. Research groups from other parts of the world rapidly expressed interest in joining BIG and, more than two decades later, BIG constitutes a network of 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.

Since its foundation in 1999, BIG has run over 50 clinical trials under its umbrella, many of which are considered practice-changing landmark studies, such as the HERA (BIG 1-01) and MINDACT (BIG 3-04) studies. HERA’s main results have been published in prestigious journals such as the *New England Journal of Medicine* (2005) and *The Lancet* (2017). The primary results of MINDACT were published in the *New England Journal of Medicine* (2016). More recently, the OlympeA (BIG 6-13) study reported significant results associated with olaparib to prevent cancer recurrence in women with hereditary breast cancer triggered by the BRCA1 and 2 genes, which was also published in the *New England Journal of Medicine* (2021).

More than 30 clinical trials are run or are under development under the BIG umbrella at any time.

In 1999, BIG was founded by Dr Martine Piccart and Dr Aron Goldhirsch with the aim to address fragmentation in European breast cancer research. Research groups from other parts of the world rapidly expressed interest in joining BIG and, more than two decades later, BIG constitutes a network of 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.

As a member of BIG since the beginning, and of BIG’s Executive Board since 2010, he contributed to many of BIG’s major trials and research programmes. He also served as a key member of the Scientific and Executive Committee of the International Breast Cancer Study Group (IBCSG). Professor Di Leo was a true defender of academic research and international collaboration. He will be missed by all of us, his family and patients.”

**Professor Sherene Loi, an Academy Fellow and medical oncologist at the Peter MacCallum Cancer Centre (Melbourne, Australia), is one of this year’s recipients. Sherene, who recently joined BIG’s Executive Board, is also a member of the IBCSG and BCT-ANZ (International Breast Cancer Study Group and Breast Cancer Trials Australia and New Zealand).**

Professor Loi challenged the dogma that immunotherapy was not possible with breast cancer and has led a series of treatment trials that are already changing the lives of her patients.

She was also the first to show that immune cell infiltration of breast tumour tissue strongly predicts improved survival in some types of breast cancer and led the development and standardisation of this unique biomarker – to where it is now routine in the pathology work-up of breast cancers.

**The Australian Academy of Health and Medical Sciences’ Jian Zhou Medal**

The medal is awarded annually to up to two individuals who are making an impact in translational medical science, honouring cervical cancer vaccine co-inventor Professor Jian Zhou.
In Memoriam

The first half of 2021 brought us great sadness with the successive deaths of five of our longstanding and loyal friends and colleagues: Dr Ashis Mukhopadhyaya, Dr José Baselga, Dr Gouri Bhattacharyya, Dr Bella Kaufman and Dr Angelo Di Leo. They were all exceptional oncologists and had been involved in the BIG network for many years. Their friendship, advice, expertise, and passion for breast cancer research will be truly missed by their colleagues, and especially also by their patients. They were examples for many of us, and their legacies will live on forever. We offer our heartfelt condolences to their families, colleagues, friends, and relatives.

Dr Ashis Mukhopadhyaya, † January 26, 2021

Dr Ashis Mukhopadhyaya, a renowned Indian oncologist, had a great heart and was very appreciated by his colleagues and patients. He practised at Netaji Subhas Chandra Bose Cancer Hospital, Kolkata (India), of which he was the founder and medical director. He started the centre 16 years ago with the mission to help poor and middle-class cancer patients by offering world-class and modern facilities at an affordable cost and in a professional and compassionate manner. Today, the hospital renders therapeutic service for all types of cancer and blood disorders, has a well-equipped and modern cancer diagnostics unit, and conducts nuclear medicine and research in the fields of molecular biology, stem cell biology and biochemistry. A true legacy.

Dr Ashis’ research interests included hematologic oncology and the use of nanoparticles and nanomaterial in the formulation and drug therapy of solid tumours. He had published many research articles in national and international journals and was the representative for the Breast Intergroup of Eastern India (BIEI), a member of the BIG network. Sadly, Dr Mukhopadhyaya himself succumbed to advanced cholangiocarcinoma (advanced bile duct cancer).

Photographs: source & copyrights by "Netaji Subhas Chandra Bose Cancer Hospital, Kolkata (India)"

BIG’s vision and mission statement

The Breast International Group (BIG) is an independent, international not-for-profit umbrella organisation for academic breast cancer research groups from around the world. We expect our members to share the principle of conducting breast cancer research that is scientifically independent and not motivated by personal profit, meaning that any surplus from BIG’s or its member groups’ research must be reinvested into breast cancer research. BIG’s vision is to cure breast cancer through global research and collaboration; its mission is to facilitate breast cancer research internationally.

BIG provides a forum for its member groups to:
- combine resources and expertise to conduct research to advance knowledge of the disease and to optimally serve patients;
- establish clinical and translational research priorities;
- reduce the unnecessary duplication of efforts;
- obtain study results quickly;
- collaborate with other scientific networks;
- develop models of collaboration with the pharmaceutical and biotechnology industry that preserve scientific independence.

BIG’s strategy statement

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 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 biosamples and data collected in the context of BIG’s 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 conduct research to advance treatments that make a difference to women and men with breast cancer.
Professor José Baselga was a world-renowned Spanish oncologist and researcher. Throughout his career, he 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-HER2 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 Weill 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.

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.

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

Professor José Baselga, † March 21, 2021

Professor Gouri Shankar Bhattacharrya was a recognised and eminent medical oncologist and researcher based in Kolkata, India. He succumbed to Covid-19. With this sudden demise, the international oncology community lost one of its most admired and valuable members. He will be greatly missed.

Throughout his career, Professor Bhattacharrya made significant contributions to breast cancer treatment in his region. Together with his colleagues, he was fighting the limited access to cancer diagnosis procedures and treatments in South Asia and the lack of awareness about breast cancer in some segments of the population. One can only applaud and honour his relentless commitment and efforts to improve uniformity of care, develop education campaigns, and prioritise research to better address patients’ needs.

His main interests included gastro-intestinal, breast and lung cancer, and in particular palliative care and geriatric oncology. In addition, to address the difficulty of getting access to novel treatments in his region, he was exploring ways to repurpose inexpensive and widely available drugs that are established in other areas of medicine.

Professor Bhattacharrya was also very active at the international level. As a founding member of the Indian Co-Operative Oncology Network (ICON ARO) and official representative of the group within the BIG network since 2009, he contributed to India’s involvement in large clinical trials, such as ALTTO and NeoALTTO. Despite the challenges, he was confident that South Asia could play a bigger role in global breast cancer research in the near future.

Professor Bhattacharrya was a member of numerous national associations. Among others, he was Past President of the Indian Society of Medical Paediatric Oncology (ISMPO) and a founding member of the Indian Association of Cancer Research (IACR) and of ICON Biorepository. He was also a member of the Task Force for Management of Cancer at the Indian Council for Medical Research (Government of India) and of the Planning Committee of the National Cancer Control Program.

At the international level, he was a member of the International Association for the Study of Lung Cancer (IASLC), the International Cardi-Oncological Society (ICOS) and of ESMO’s Global Policy Committee. He was part of the Governance Council of the International Society of Geriatric Oncology (SIOG), a member of the US NCI-NIH’s Task Force for Gastro-intestinal cancer and Hepato-biliary cancer and of the Global Advanced Breast Cancer Alliance. He was also part of the World Health Organisation Steering Committee for Oncology.

Professor Bhattacharrya authored more than 200 papers and was a member of various editorial boards, such as ESMO Open, the Journal of Thoracic Oncology (JTO), the Journal of Geriatric Oncology, Critical Reviews in Oncology / Hematology (CROH), Journal of Global Oncology–ASCO, Journal of Annals of Translational Medicine, the Asian Journal of Clinical Oncology Reviewer for International Journal of Gynecological Cancer (IJGC), the American Journal of Clinical Oncology, among others.

Professor Gouri Shankar Bhattacharrya, † May 1, 2021
Dr Bella Kaufman, † May 13, 2021

The breast cancer community has lost one of its leading researchers and most brilliant scientists. Cancer has stolen yet another amazing person.

Professor Kaufman was a renowned and exceptional Israeli oncologist, globally respected for her pioneering work in the field of breast cancer research and, more specifically, BRCA mutations and genetics. She was an investigator on many important clinical trials, some of which have been essential to the development of PARP inhibitors for the treatment of BRCA-related cancers.

As Chair of the Sheba Breast Collaborative Group (SBCG), which joined the BIG network in 2000, Professor Kaufman has been involved in international trials run in collaboration with BIG, such as the BRAVO and OlympiA clinical trials. Both studies focus on BRCA mutations. She was one of the principal investigators of the OlympiA study, the first results of which were recently presented.

David Cameron, BIG Chair: “The passing away of Professor Kaufman is another tremendous loss for the breast cancer community. Bella was a brilliant researcher and a compassionate doctor who will be greatly missed.”

An oncologist with over 25 years’ experience, Bella was diagnosed with metastatic breast cancer in 2013. Since then, she used her personal experience to tirelessly address breast cancer patients’ needs. With her powerful testimony and her deep sense of empathy and optimism, she touched and inspired countless people.

Bella’s condition triggered the launch of a compassionate programme for metastatic breast cancer patients in Israel called PALBOCICLIB, of which she was the first patient.

Professor Kaufman obtained her medical degree and completed her oncology training at the Hebrew University and Hadassah Hospital in Jerusalem. She was the founder and leader of the Israeli Consortium for Hereditary Breast Cancer and, in 2001, was appointed head of the Breast Cancer Unit at the Chaim Sheba Medical Center at Tel Hashomer, Israel, which is affiliated with the University of Tel Aviv.

An academic, she published widely and held positions as an expert on various committees, consulting and providing advice to the Ministry of Health and the Israeli parliament on key issues concerning oncology-related health policy. She was the former secretary of the Israeli Breast Group, bringing the group to BIG, and also member of the Israeli Cancer Association’s research and steering committees up to the time of her death.

In December 2020, Prof Kaufman was honoured with the eighth “Basser Global Prize”, which recognises a leading scientist in medical oncology from the University of Paris in 1992 and his European certification in medical oncology in 1996. He trained at the National Cancer Institute in Milan, Italy, where he worked for 7 years until 1996. It was during those years that he first met Professor Aron Goldhirsch.

As a member of BIG since the beginning, and of BIG’s Executive Board since 2010, he contributed to many of BIG’s major trials and research programmes, such as TAI-315, HERA, TRANSBIG and MINDACT, ALTTO and NeoALTTO, and AURORA, among others. He also served as a key member of the Scientific and Executive Committee of the International Breast Cancer Study Group (IBCSG).

Professor Di Leo graduated in medicine and surgery at the University of Palermo, Italy, in 1988. He received his postgraduate diploma in medical oncology from the University of Pavia in 1993 and his European certification in medical oncology in 1996. He trained at the National Cancer Institute in Milan, Italy, where he worked for 7 years until 1996. It was during those years that he first met Professor Aron Goldhirsch.

In 1996, Professor Di Leo and his wife, Dr Laura Biganzoli, moved to Brussels, where they both started to work at the Institut Jules Bordet with Dr Martine Piccart and Dr Christos Sotiriou, among others. This was the beginning of a long collaboration and precious friendships that were to last over 20 years. Professor Di Leo was appointed Senior Staff Member and Medical Director of the Breast European Adjuvant Studies Team (BrEAST, now known as the Institut Jules Bordet Clinical Trials Support Unit). Laura was also involved in the beginnings of BIG. They left Belgium to return to their beloved Italy in 2003.

Since 2003, Professor Di Leo was Head of the Sandro Pertiniani Medical Oncology Department at the Hospital of Pavia, Italy.

He was a true defender of academic research and international collaboration: “One of the first things I learned from Aron [Goldhirsch] was that it doesn’t matter where you work, you need to be part of an international network of high-quality researchers so that you can learn, grow and express yourself.” (Extract from an interview in 2020)

Something that he put in practice himself, as he also became a true and generous mentor and educator, supportive of younger oncologists.

“He was a wonderful physician and person, and he will be missed by all of us, his family and patients. For myself, I will miss his wise counsel – as a long-standing member and friend of BIG – and I will miss the opportunity to get his advice on difficult matters where his wisdom was always appreciated.” Prof David Cameron, BIG Chair

“Angelo was going to become my successor as BIG Chair, when he was diagnosed with an incurable disease… This shows how deeply I trusted this wonderful colleague and friend who, together with his wife Laura, helped me to ‘create’ the Breast International Group and to run its first large adjuvant trial focused on the role of taxanes. I will miss him enormously.” Prof Martine Piccart, President of BIG against breast cancer.

In 2019, Professor Di Leo received the prestigious ESMO Lifetime Achievement Award as recognition for his brilliant career and outstanding contributions to cancer research and treatment.

He authored numerous publications and was a member of the Early Breast Cancer Trials’ Cooperative Group (EBCTCG) Steering Committee, Chair of the Biological Protocol Working Group (BPWG) at IBCSG. He also served on the American Society of Clinical Oncology (ASCO) Grants Selection Committee (2006–2009), the ASCO Education Committee (2012–2014), and the Scientific Advisory Council of the Susan G. Komen for the Cure® (2010–2016).

Professor Di Leo was not only a world-renowned oncologist and researcher, but he was a wonderful person, too. His colleagues and friends describe him as approachable, always quiet, smiling, and helpful. He was a charismatic and elegant man, dedicated to his work, a loving husband and father, and an art enthusiast.

He and his wife Laura shared a passion for contemporary art and started a collection in the late nineties. Recently, they had opened a gallery in the south of Florence, where the pieces reflect their vision of a borderless world, combined with their curiosity for travelling and discovering. https://www.thestudiocollection.org/
PINK OCTOBER – TWO BIG/EORTC WEBINARS – REGISTER NOW

Free webinar for lay audience: 13 October 2021

For the third consecutive year, BIG and the EORTC Breast Cancer Group are combining their efforts and expertise by organising an annual Pink October webinar for the general public.

The one-hour webinar will take place on Wednesday 13 October 2021 from 13:00 to 14:00 CET. Registration is free but mandatory.

As 13 October is Metastatic Breast Cancer Awareness Day, what better time than to draw attention to this advanced disease, for which there still is no cure. The topic of the educational webinar therefore is “I have metastatic breast cancer: what is my future?”.

The objective is to create further awareness around metastatic breast cancer and to discuss and inform the general public of challenges and recent developments through the research conducted by BIG and the EORTC Breast Cancer Group. Our aim for this event is to reach patients and their families.

Speakers include breast cancer experts from the BIG and EORTC networks – Dr Fatima Cardoso (Portugal), Dr Philippe Aftimos (Belgium) and Dr Frederieke van Duijnhoven (The Netherlands) – who are joined by Eva Schumacher-Wulf (Germany). Eva is the editor-in-chief of the breast cancer magazine Mamma Mia! She has been involved in BIG’s patient advisory group, participating in recent BIG-NCTN (National Clinical Trials Network, former NABCG - North American Breast Cancer Group) meetings among other activities, and will give her precious perspective on how it is to live with metastatic breast cancer. The sessions will be presented in English.

For the programme and on-line registration form of the webinar, click on this link.

Free webinar for scientific audience: 26 October 2021

This webinar, organised by BIG and the EORTC Breast Cancer Group, will address the scientific community and will focus on adjuvant endocrine treatment in breast cancer.

The one-hour webinar will take place on Tuesday 26 October 2021 from 17:00 to 18:00 CET. Registration is free but mandatory.

Speakers from the EORTC and BIG network include Dr Michail Ignatiadis, Professor Aleix Prat and Professor Etienne Brain.

For the programme and on-line registration form of the webinar, click on this link.
Even from a distance: BIG AGAINST BREAST CANCER!

Musical "Enrique Granados, l’Artiste retrouvé"

Saturday 12 June was an important day for BIG against breast cancer. It marked the day of the first philanthropic event in over a year. On this day, in collaboration with the Cultural Centre of Uccle, BIG against breast cancer organised the "Enrique Granados, l’Artiste retrouvé" musical, which featured the soprano Julie Gebhart, daughter of Professor Martine Piccart. The influx of enthusiastic people showed that even after a difficult period, solidarity and motivation are still highly valued by the BIG against breast cancer community.

Move for BIG – fundraising initiatives

The same enthusiasm and motivation can also be seen in the personal fundraising initiatives that supporters of BIG against breast cancer’s community have launched via the MoveforBIG.org platform on BIG’s website, raising funds for BIG studies.

One example includes the challenge of running the 20 km of Brussels, an annual race through Brussels, with some 20,000 participants. 20 km amounts to approximately 28,800 steps … and €28,800 supports the participation of one patient for up to 10 years in the AURORA study (or the "BIG Metastatic Breast Cancer GPS" study, which is how it is referred to when we communicate with BIG’s lay audience). Numerous BIG Headquarters’ staff members and BIG supporters participating in the 20 km of Brussels use the MoveforBIG platform to create their personal fundraising project.

Another example is taking on a 230 km desert race to raise precious funds for the AURORA study. In order to increase awareness about metastatic breast cancer as well as raise funds, BIG’s communications manager Valerie Van der Veeken initiated the “Al Andalus Ultimate Trail” fundraising challenge on the MoveforBIG platform and called it “AAUT TRAIL IN ANDALUSIA - Research is needed to prevent breast cancer from becoming a rucksack that you carry for the rest of your life”. Together with her friend Joëlle Thils, who has been diagnosed with metastatic breast cancer, they both participated in this tough, semi self-sufficient five-day footrace taking place in Andalusia and covering 230 km of difficult rocky terrain with lots of altimeters, temperatures around 40°C during the day and dropping to 4°C at night, and no comfort (sleeping in small tents, on thin mattresses). In total, Valerie and Joëlle raised about €2,500 for the AURORA study.

For the full story, visit their MoveforBIG fundraising page: https://donate.moveforbig.org/projects/aaut-trail-in-andalusia-research-is-needed-to-prevent-breast-cancer-from-becoming-a-rucksack-that-you-carry-for-the-rest-of-your-life

Joëlle and Valerie wearing the ‘BIG against breast cancer’ colors during the AAUT footrace in Andalusia

Stella (whose mother survived breast cancer) and Valerie wearing the ‘BIG against breast cancer’ colors during the AAUT footrace in Andalusia

Musical "Enrique Granados, l’Artiste retrouvé"

Soprano Julie Gebhart and her mother Professor Martine Piccart

20 km of Brussels: fundraising project on the MoveforBIG platform

Joëlle and Valerie raising funds for the AURORA study during the AAUT footrace in Andalusia
Online shopping just got “BIGger”

That’s right, from now on everyone who shops online can support BIG against breast cancer at the same time!

How? Thanks to Trooper, a website that allows you to support us with only one extra click when you shop online. The best part? This won’t cost you a single eurocent extra. A win-win shopping experience!

With just a few easy steps you make a BIG difference. How does Trooper work?
1. Need to do some online shopping? Go to our personal Trooper page: www.trooper.be/bigagainstbreastcancer.
2. Select the shop you wish to visit by clicking on their logo. This will redirect you to the online shop. The only difference is that by going via the Trooper platform, the shop will know that you want to support BIG against breast cancer.
3. Shop and pay like you always do.

A percentage of your purchase, with no cost to you, is then donated directly to BIG by the shop of your choice. On average 5 percent of your purchase amount is donated to our association.

As simple as that!

Trooper works together with over 600 web shops, ranging from electronics and books (Fnac, Coolblue, bol.com, …), make-up, perfumes, and fashion (Scotch & Soda, Ici Paris XL, …), web shops with fun weekends away (booking.com, Bongo, …) and many more. Discover all the shops Trooper has to offer: https://www.trooper.be/nl/trooperverenigingen/bigagainstbreastcancer

Make sure to add this easy step to your online shopping habits. We believe that every little bit helps to advance breast cancer research!

Big Together e-newsletter

2020 taught us to connect with our community in different ways. Through this challenging time, when closeness was hard to come by, we created, with the aim of togetherness and support, the “BIG Together” electronic newsletter. A tri-lingual (Dutch, English, and French) e-newsletter that gives BIG against breast cancer the opportunity to communicate openly and transparently with its community. The e-newsletter touches on subjects such as upcoming philanthropy activities, as well as the BIG Network at large and its research.

If you would also like to be kept up to date on upcoming fundraising activities, news from the network, and more, do not hesitate to sign-up here: www.BIGagainstbreastcancer.org/BIG-Together

Even from a distance, there are many ways to raise funds for BIG. Whether you live in Northern Europe, Asia or Australia, there is nothing more rewarding than starting original and fun initiatives together with friends, family or colleagues for a cause that matters to all of us: breast cancer research.

You can create a fundraiser for your birthday, organise solidarity dinners with your friends – where instead of bringing flowers or a bottle of wine, they can donate to your page – or why not even a puzzle challenge? The possibilities are limitless.
CLINICAL TRIALS AND ACTIVITIES

AURORA reveals new molecular insights into metastatic breast cancer

First results from the AURORA programme of metastatic breast cancer have identified driver gene mutations and copy number variations in metastatic samples that could guide future treatment strategies for patients. In addition, RNA sequencing has shown a change in intrinsic breast cancer subtype between primary and metastatic tumours in 36% of patients, usually towards a more aggressive form of disease, with possible implications for treatment.

The results, from the first 381 patients in the study, have been published in Cancer Discovery, a journal of the American Association for Cancer Research. Dr Philippe Aftimos, co-Principal Investigator of the programme and Clinical Trials Development Leader at the Institut Jules Bordet (Brussels, Belgium), explains that the AURORA study is unique in having matched pairs of primary and metastatic tumour samples from large numbers of patients with early metastatic breast cancer who have received minimal treatment.

"Between 10% and 30% of metastatic samples showed molecular changes, and about 50% of patients had alterations that were targetable with current therapies, as defined by the ESMO Scale of Clinical Actionability for molecular Targets. However, only 7% received matched treatment owing to variability of access to such therapies," he says.

Driver gene mutations were identified in GATA1 and MEN1, and increased clonality was seen in driver genes such as ERBB2 and RB1. Metastases were enriched in ESRR1, PTEN, CDH1, PIK3CA and RB1 mutations; MDM4, MYC amplifications; and ARID1A deletions. Analysis of changes in intrinsic breast cancer subtype showed that luminal A/B to HER2-Enriched (HER2-E) switching was associated with TP53 and/or PIK3CA mutations.

"The mutations we find in the metastatic lesions are very often present in the primary lesion but about one in three patients have these copy number aberrations and a better understanding of their biology may shed some light on future drug targets," she says.

"The mutations we find in the metastatic lesions are very often present in the primary lesion but about one in three patients have these copy number aberrations and a better understanding of their biology may shed some light on future drug targets," she says.

Another analysis of AURORA data highlighted the importance of tumour mutational burden (TMB). It showed that patients with hormone receptor-positive (HR+), HER2-negative breast cancer who also had a high TMB in their primary tumours had both shorter overall survival and shorter time to relapse, indicating that TMB is an independent factor for poor prognosis.

Piccart points out that drug registration trials have not previously looked at high TMB and survival in metastatic breast cancer, so the value of TMB as a biomarker was not known.

"We must now look at what treatment these patients had and what worked or didn’t work. My suspicion is that the treatments we usually give did not work well, or the patients would not have progressed so quickly – in less than two years," says Piccart.

She was also very interested in the unexpected finding that approximately one in three patients with metastatic disease had a genomic signature of homologous recombination deficiency (HRD), i.e., an impairment in DNA repair.

"First line treatment of metastatic breast cancer is a taxane but this finding about HRD means that these patients may do better with cytotoxic drugs, such as platinum or cyclophosphamide, which specifically target DNA. Our current treatment of metastatic breast cancer is extremely simplistic and that could well change with what AURORA can tell us. By looking at treatment from a new angle, we may be able to make better treatment choices in the future," says Piccart.

The AURORA data also showed a lower immune score and increased immune permissive cells in metastatic tissue samples compared with primary tumours. This and subsequent immune data can contribute to understanding of immune evasion and inform plans for future immunotherapy trials.

"These initial results are just the tip of the iceberg, and we can expect a lot more important information from the full trial population of 1,150 patients, including those with specific types of breast cancer and specific resistance to certain types of cancer treatment," says Aftimos.

AURORA: leading the way in metastatic breast cancer research

The AURORA trial is an academic study funded substantially by the Breast Cancer Research Foundation (BCRF) in the USA, and has received contributions from various other foundations, associations, companies, and individual donors. For over 15 years, BIG has collaborated closely with the (US) National Cancer Institute’s National Clinical Trials Network (NCTN) – a network of major US and Canada-based research groups. AURORA Europe and US are two of the most ambitious programmes ever carried out to improve understanding of metastatic breast cancer and have been established through the BIG-NCTN collaboration, funded by the BCRF as a result of the sale of the late Evelyn Lauder’s jewellery and clothing.

Launched in 2014, AURORA Europe has recruited patients in over 60 hospitals and cancer centres in 11 European countries.

Piccart explains that, before AURORA, BIG had focused on studies of adjuvant treatment for early breast cancer as metastatic disease was generally considered incurable, with patients mainly receiving palliative care. However, as attitudes changed and there was growing interest in treating oligometastatic breast cancer, Piccart felt the time was right for a major research programme in metastatic breast cancer.

"We knew so little about metastatic breast cancer – why it may spread quickly or remain confined to one area, and why some people die within a few months while others live for many years. In AURORA, we are not only comparing primary and metastatic tumour samples, we also have clinical longitudinal follow-up, so we hope for better understanding of disease progression," she says.

Piccart believes that it was BIG’s successful record in carrying out early breast cancer trials that helped gain BCRF’s tremendous support for AURORA.

"The Foundation placed great trust in us, and I still find it remarkable that an American charitable organisation was prepared to provide millions of dollars for a study to help women with breast cancer in Europe. I certainly hope that more European organisations will now be interested in helping to take the AURORA programme forward," says Piccart.
Applying latest technologies

Setting up a programme as ambitious as AURORA was a huge scientific and logistical challenge and multiple state-of-the-art technologies were needed. An IT platform was established that enabled investigators to track the status of patient samples at each step of the process, and a molecular advisory board of scientists from participating countries advised investigators about interpreting DNA and RNA results to guide subsequent treatment.

“The concept of a molecular advisory board was quite new. Oncologists were used to tumour boards, but this took multidisciplinary working to another level. Some institutions do now have molecular boards and there are some national networks, but AURORA is still unique in having an international board that works with clinicians in multiple countries,” Afrimos explains.

Following a pilot study at four centres, AURORA gradually opened up to centres across Europe to reflect the diversity of patients with metastatic breast cancer. At first, accrual was slow, partly because of the difficulty of getting consistently good quality tissue samples; some primary tumours had deteriorated as a result of being in storage for many years and some metastatic samples were difficult to obtain during biopsy procedures. As a result, the study design was modified to allow plasma samples to be used for ctDNA analysis when tissue samples were of poor quality or unavailable.

“Plasma samples from all patients entering the study were tested for mutations in approximately 25 important genes, such as PIK3CA, for which targeted therapies are available, so that patients could receive appropriate treatment, and this was very motivating for both clinicians and patients to participate,” says Piccart.

Alongside AURORA Europe, the US AURORA programme is also contributing valuable data. This started with a retrospective study sequencing samples from biopsy and autopsy material, and is being followed by a prospective study similar to AURORA Europe.

“The US study will have fewer patients but, while we look at a little over 400 genes in Europe, US investigators will do whole exome sequencing for a more complete molecular dissection. The later start time for the prospective part of the study will be very valuable because it will enable us to verify important findings from the European study,” says Piccart.

AURORA 2.0 future plans

Moving forward, plasma samples will be collected from the 1,150 patients in the AURORA programme every six months for ctDNA analysis, and at disease progression, in order to collect longitudinal data. These samples are currently being stored and will be analysed in the future to take advantage of likely improvements in assay technology.

“We are also introducing new technologies for the tumour analyses as they become available. We have top scientists working in the programme, and they are aware of all the latest developments, so any time there are advances we will do our best to introduce them. AURORA could not have been done without BIG, it would have been impossible to put all the scientists together and to recruit such a large number of patients. We have a fantastic collaboration which is benefiting not only scientific understanding of metastatic breast cancer but, at a human level, the patients who are participating in AURORA,” concludes Afrimos.

The AURORA programme is being led by BIG in collaboration with the Clinical Trials Support Unit of the Institut Jules Bordet (IJH-CTSU) and Frontier Science Foundation.

Funding

AURORA is a purely academic study made possible by generous contributions from the Breast Cancer Research Foundation® (BCRF), Fondation contre le Cancer (Belgium), Fondation Cancer (Luxembourg), National Lottery (Belgium), NIF Foundation, Barrie and Dena Webb, Candriam, Fondation Futur 21, Sogerim, Think Pink Belgium (SMART Fund) and many individual donors. AURORA has also been supported by the Fund Friends of BIG, managed by the King Baudouin Foundation.

References


11 countries are involved (Belgium, Germany, Iceland, Italy, Luxembourg, Portugal, Spain, Sweden, Switzerland, United Kingdom and Austria)

+60 hospitals are participating in the study

1,150 women and men with advanced (metastatic) breast cancer have already been enrolled in AURORA

About 30,000 blood and tumour tissue samples will be collected in total

411 genes are being analysed in primary tumours and in metastatic tumours
Olaparib (Lynparza) in the adjuvant treatment of patients with germline BRCA1/2 mutations and high-risk early breast cancer reduced the risk of cancer recurrence by 42% in Olympia Phase III trial.

The primary analysis conducted upon recommendation of the IDMC showed that olaparib (Lynparza) demonstrated a statistically significant and clinically meaningful improvement in invasive disease-free survival (iDFS) versus placebo in the trial population. Olaparib also demonstrated a statistically significant and clinically meaningful improvement in the key secondary endpoint of distant disease-free survival (DDFS).

At the time of this initial data cut-off, fewer deaths had occurred in patients receiving olaparib, but the difference in overall survival (OS) did not reach statistical significance. Safety data were consistent with known side effects of the treatment. The trial will continue to assess the key secondary endpoints of OS and distant disease-free survival.

ClinicalTrials.gov Identifier: NCT02032823.

OlympiaA (BIG 6-13) Results of the OlympiaA trial published

OlympiaA was a randomised study (1:1) of 2,321 postmenopausal women with hormone receptor-positive breast cancer to receive either 2 years of letrozole or 7 or 10 years of letrozole. The study included patients aged 50 years or older, with 30% of patients 70 years or older. The event size pre-defined to trigger the second interim analysis was 382 events. The trial was stopped early by the Steering Committee due to a significant reduction of invasive disease-free survival (iDFS) events in the letrozole arm (HR=0.73, 95% CI 0.61 to 0.88).

The median follow-up was 11.8 years in the 2-year group, 7.8 years in the 7-year group and 10.8 years in the 10-year group. The median duration of follow-up was 11.8 years in the 2-year group, 7.8 years in the 7-year group and 10.8 years in the 10-year group. The median duration of follow-up was 11.8 years in the 2-year group, 7.8 years in the 7-year group and 10.8 years in the 10-year group. The median duration of follow-up was 11.8 years in the 2-year group, 7.8 years in the 7-year group and 10.8 years in the 10-year group. The median duration of follow-up was 11.8 years in the 2-year group, 7.8 years in the 7-year group and 10.8 years in the 10-year group.

The results of the study have been published in The Lancet Oncology and the New England Journal of Medicine.

ClinicalTrials.gov Identifier: NCT01784485.

Final accrual: 1,836 patients from 546 sites in 23 countries worldwide. The following 20 BIG groups are participating: ABCSG, AGO-B, BCT-ANZ, BOOG, CCTG, CEEOOG, EORTC, GAICO, GEICAM, GOIRC, IBCCG, IBCSG, ICR-CTSU, IBRC, ICOR, SABO, SOIIT, SUCCESS, SueBCG, TCG, UCBG (FSRG).

ClinicalTrials.gov Identifier: NCT02032823.
Coordinating Investigator Professor Michael Grant concludes from these results of the ABCSG-16 study: “We managed to include almost 3,500 patients in this important study in a small country like Austria, which was a great achievement. With this large patient population, we were able to demonstrate that most postmenopausal patients with low and average-risk hormone receptor-positive breast cancer do not benefit from prolonged adjuvant hormone therapy with anastrozole beyond a total treatment duration of 7 years. They should therefore be spared the side effects and fracture risk associated with extending treatment beyond this duration.” The ABCSG and all partners involved in the study are delighted about this great publication success and this forward-looking achievement in the field of hormone receptor-positive breast cancer therapy – de-escalation is also feasible for endocrine therapy!

**References**


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**BCT-ANZ**

**Neoadjuvant Patient Decision Aid**

BCT-ANZ (Breast Cancer Trials Australia and New Zealand) has launched a new online platform designed to help women make informed decisions about their breast cancer treatment.

For many women recently diagnosed with breast cancer, the treatment process can be overwhelming and stressful. In certain situations, doctors may offer treatment with chemotherapy or hormonal therapy before surgery to the breast and lymph nodes (neoadjuvant).

BCT-ANZ has launched the online Neoadjuvant Patient Decision Aid to help women recently diagnosed with breast cancer decide if this is the right treatment choice for them.

The information provided in the online decision aid is tailored to each breast cancer patient and factors in what type of breast cancer they have been diagnosed with. The decision aid is not intended to change a patient’s mind about their treatment, rather to present an evidence-based view of their options and ensure their treatment choice is aligned with their particular circumstances. It informs breast cancer patients about their options for the timing of their treatment and surgery, why one might choose to have treatment before surgery and the pros and cons of having surgery first.

The Neoadjuvant Patient Decision Aid was created using the research findings from the DOMINO clinical trial and was led by BCT-ANZ’s medical advisor, researcher and medical oncologist, Dr Nick Zelenkowski.

To access the Neoadjuvant Patient Decision Aid, visit www.mynegoguide.com.

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**BGICS**

During 2021, and despite the global COVID pandemic, the Breast Gynaecological International Cancer Society (BGICS) continued its efforts in fighting breast cancer around the globe. Confirming the importance of the international collaboration and its value in fighting breast cancer, the BGICS was able to achieve a crucial milestone of its mission by publishing two important sets of consensus recommendations in breast cancer management.

The first was the “Breast Gynaecological International Cancer Conference (BGICC, the official conference of the BGICS) consensus and recommendations for breast cancer awareness, early detection and risk reduction in low- and middle income countries (LMICs) and the Middle East and North Africa (MENA) region” (February 2021, https://doi.org/10.1002/ijic.33506).

For this consensus, 26 experts from 7 countries worldwide met in Egypt during the 12th BGICC and established these consensus recommendations, which introduce a road map (Figure 1) for establishing breast cancer awareness and early detection programmes in areas with limited resources.

**42nd Annual Scientific Meeting**

BCT-ANZ held their 42nd Annual Scientific Meeting (ASM) as a virtual conference in July, attracting 250 delegates to the event. International speakers were Professor Fraser Symmans, Professor Eileen Rakowitch, Professor Frank A Vicini, Dr Lucy Yates and Professor Roberto Saltgato. Topics discussed during the three-day conference included early breast cancer, breast cancer in young women, translational research, as well as sessions on trial updates and new concepts, and a pathology workshop. The 43rd ASM will be held from 27-29 July 2022 in Auckland, New Zealand.

The consensus covered all the aspects of TNBC management with special coverage of areas of controversies. It also identified areas for future research in the management of TNBC, including the role of androgen-receptor targeted therapy, the predictive value of tumour infiltrating lymphocytes and Ki-67 and their role in tailoring treatment, the role of platinum-based chemotherapy in the neo-adjuvant setting, and the role of anti-PDL-1 treatment in management of early and advanced TNBC.

The second set was the “BGICC consensus and recommendations for the management of triple-negative breast cancer (TNBC),” published in the *Cancer Journal* in May 2021 (https://doi.org/10.3390/cancers13092262).

For this consensus, a panel of 35 breast cancer experts from 13 countries worldwide also met during the 12th BGICC and developed recommendations based on the latest data in the management of TNBC.
Activities and studies

In spite of the pandemic and a crippling ransomware attack on Ireland’s national health service (HSE), it has been a busy year to date for the cancer trials community in Ireland, and for us in Cancer Trials Ireland (CT-IRE).

In May we hosted Ireland’s inaugural "Cancer Retreat" a virtual event that brought together investigators, research staff, funders, and decision makers to capture a collective vision for cancer trials in Ireland for the coming five years.

In June we held our second series of Disease-Specific Sub-Group (DSSG) meetings, in which investigators, nurses, managers and other support staff collaborate nationally on existing and upcoming studies in a given disease area, e.g. breast, lung and genitourinary.

In the Breast DSSG, we discussed BIG’s DECRESCENDO study (CTRIAL-IE 20-23 / BIG 19-02), which will open at eight sites in Ireland. Five of the eight sites will also take part in the ‘Flexcare’ sub-study, which will investigate at home-based therapies. This is such an exciting trial to be a part of, given its potential to be practice-changing for HER2+ breast cancer. Studies of this kind obviously are not a natural fit for industry, so our collaboration with the BIG network is a huge win for patients in Ireland, where we might otherwise struggle to fund such a trial, and also identify a robust and eligible number of patients. DECRESCENDO brings treatment options to Ireland that otherwise would not exist here.

The same is true of the AMEERA study being developed under the BIG umbrella (BIG 20-01), for which Cancer Trials Ireland is currently undertaking a feasibility study. Here is a vital hormone therapy study (one in three patients is not completing the recommended course of treatment due to side effects) requiring 4,000 patients. That is an accrual target we could not hope to achieve in Ireland alone.

In terms of BIG studies already open in Ireland, the ALEXANDRA/IMpassion020 (CTRIAL-IE 17-15 / BIG 16-05) for patients with Stage II-III TNBC (Triple Negative Breast Cancer) is running in three Irish sites. To date it has recruited 15 patients, with a target of 28 in total. Meanwhile, PALLAS (CTRIAL-IE 15-17 / BIG 14-03) is in follow up, and the APHINITY study (CTRIAL-IE 11-25 / BIG 11-04) is closed.

Finally, with Professor Seamus O’Reilly (Vice-Clinical Lead for Cancer Trials Ireland) joining the Executive Board of BIG, we very much look forward to growing our collaboration with BIG and expanding treatment options for Irish patients through studies like HERA (BIG 01-01) and SOLE (BIG 07-01).
This study is sponsored by GEICAM and funded by Novartis. The study partners are IBCSG (International Breast Cancer Study Group) and BIG together with the following research groups from the BIG network: IBCSG (Austrian Breast & Colorectal Cancer Study Group), GOIRC (Gruppo Oncologico Italiano di Ricerca Clinica) and Fondazione MICHELANGELO.

With the ALPHABET study we want to explore the efficacy of a targeted “chemotherapy-free” therapy for HER2-positive ABC patients. The translational research project associated with the study will help us elucidate the biological mechanisms behind these different strategies.

Research insights

The results of the following studies, for which Professor Musolino has served as PI, have either been published or presented, or are in preparation for publication.

The final results of the ERIGE trial have recently been published in the journal ESMO Ojs1. The combination of eribulin and gemcitabine showed promising activity and a moderate toxicity profile in metastatic triple negative BC (TNBC) with an ORR of 37% and a clinical benefit rate of 49%. 18% of the patients harboured germline BRCA1/2 mutations and 30% of the patients harboured a pathogenic variant of the breast cancer susceptibility genes BRCA1/2. The study results showed that gBRCA1/2 mutations confer worse prognosis in patients with HER2-negative BC.

At ABSCS 2020, Professor Musolino presented the preliminary results of a retrospective study investigating the prognostic role of gBRCA1/2 mutations in HER2-positive BC. The analysis, conducted on 120 patients, showed that gBRCA1/2 mutations confer worse prognosis in patients with HER2-positive BC.

Results of the IMMUNHER trial, a phase II, randomised, biomarker study exploring the immune-mediated mechanisms of action of neoadjuvant subcutaneous trastuzumab in early HER2-positive BC, will be published this year.

PEARL study Quality of Life Results

The PEARL study is a phase III trial (NCT02028507; EudraCT 2013-001710-27) comparing palbociclib plus endocrine therapy vs. capcitabine in postmenopausal advanced breast cancer patients who progressed on an aromatase inhibitor.


These results showed patients receiving palbociclib plus endocrine therapy experienced a significant delay in deterioration of global health status quality of life scores compared to capcitabine, which represents important additional evidence for the clinical practice.
HeCOG

For more than 30 years, the Hellenic Cooperative Oncology Group (HeCOG) has contributed to the global efforts to improve the clinical outcome of patients with breast cancer. HeCOG is a not-for-profit scientific organisation engaged in the design, development and conduct of cancer research characterised by high reliability. All studies are evaluated for their quality at all stages and result in the production of reliable scientific data. Numerous studies from the beginning of the early 1990s have been conducted under the umbrella of HeCOG, focusing on both clinical and translational research questions. HeCOG continues its long course of studying the different regimens in the neoadjuvant, adjuvant and metastatic settings. Last year, HeCOG published the results of a phase II clinical trial in which cabazitaxel was evaluated as second-line treatment in 88 patients with HER2-negative metastatic breast cancer previously treated with taxanes. In this study, the ORR (overall response rate) was 22.6% in the intent-to-treat population, with median progression-free survival (PFS) and overall survival (OS) being 3.7 months (95% CI 2.2–4.4) and 15.2 months (95% CI 11.3–19.4), respectively. Regarding toxicity, grade 3–4 neutropenia was reported in 22.6% and febrile neutropenia in 6% of the patients, respectively. Two fatal events (one febrile neutropenia and one sepsis) were reported as being related to study treatment. This study by Kourats et al showed that cabazitaxel is active as second-line treatment in taxane-pretreated patients with HER2-negative metastatic breast cancer, with manageable toxicity.

In another interesting study recently published by HeCOG, real-world clinical outcomes and toxicity, as well as treatment-related costs of treatment of patients with advanced breast cancer treated with cyclin-dependent kinase inhibitors (CDKIs) in combination with endocrine therapy, were evaluated. In this prospective, retrospective study, 365 women with advanced hormone receptor-positive, HER2-negative breast cancer who received a CDKI combined with endocrine therapy at any line of treatment were enrolled. In this cohort of Greek patients, CDKI administration was well tolerated, with a low drug discontinuation rate, providing survival benefit (PFS and OS). In particular, the median PFS for patients who received CDKI as first-line, second line and third-line treatment and beyond was 18.7, 12 and 7.4 months, respectively. The median OS since the initiation of CDKI treatment was 29.9 months (95% CI 23.0–not yet reached (NR)) (ESMO Open 2020;5:e000774. doi:10.1136/ esmoopen-2020-000774).

HeCOG also participated in a meta-analysis conducted by the Early Breast Cancer Trialsists’ Collaborative Group (EBCCG) that showed that the use of more dose-intensive schedules compared to standard schedules for adjuvant anthracycline and taxane further reduces the risk of breast cancer recurrence or death without increasing mortality from other causes (DOI:https://doi.org/10.1016/S0140-6736(18)33137-4).

For more information, visit: www.hecog.gr

References

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PhD candidates in Molecular Medicine, UNIPR 
EORTC Member of Young Breast Cancer Group 
ESMO Member of Practicing Oncology Working Group

BIG trials
GOIRC is participating in the following trials conducted under BIG’s umbrella:

Open trials
1. ALEXANDRA/ImPASSION030 (BIG 16-08)
2. EXPERT (BIG 16-02)
3. AURORA (BIG 14-01)
4. PYTHIA (BIG 14-04)

Trials in the pre-activation phase
1. AMEIRA-6 (BIG 20-01)
2. DECRESCENDI (BIG 19-02)
3. ALPHABET (BIG 16-05)
4. DIANIER (BIG 16-02)

The Brazilian Breast Cancer Conference 2021 – LACOG/GBECAM and Best of SABCS® Brazil

This online event had speakers from Brazil and elsewhere on its programme, dedicated to discussing the main developments in the diagnosis and treatment of breast cancer.

LACOG

The Brazilian Breast Cancer Conference 2021 – LACOG/GBECAM and Best of SABCS® Brazil

This event was organised by the Latin American American Cooperative Oncology Studies (LACOG) and the Brazilian Group for Breast Cancer Studies (GBECAM), two Brazilian organisations dedicated to education and research on breast cancer. This year’s event was held online. Experts from Brazil and elsewhere came together to debate the main developments in the diagnosis and treatment of breast cancer.

The first day of the event was dedicated to the Best of SABCS Brazil, during which the main highlights of the San Antonio Breast Cancer Symposium (Dec 2020, US) were presented to the participants. The main themes addressed at the meeting were introduced, and their relevance to Brazil was discussed. On the remaining days, different modules dedicated to the treatment of early and metastatic breast cancer were presented. These included some new ideas on the use of molecular and genetic tests for breast cancer, as well as some major advances in surgery, radiotherapy and systemic treatments, and their impact on clinical practice.

The conference involved 26 speakers, and 1,737 participants from various states in Brazil attended the three-day online programme.

AMAZONA III study presented at ASCO showed the reality of breast cancer in elderly women in Brazil

A sub-analysis of the AMAZONA III study was conducted by the Brazilian Breast Cancer Study Group (GBECAM) in partnership with LACOG.

This prospective cohort study, which took place from January 2016 to March 2018, included 2,950 women with recently diagnosed invasive breast cancer, sourced from 23 Brazilian centres. The sub-analysis presented at the annual ASCO congress only considered patients aged 65 years and older.

When assessed by subgroup, cohort patients > 75 years were more regularly diagnosed in advanced clinical stages and also presented the worst ECOG performance status in terms of the diagnosis. There was no significant statistically difference in the molecular subgroup, tumour grade and breast cancer detection method.

Using AMAZONA III data, investigators highlighted the importance of strategies to improve breast cancer tracing and educational programmes among the elderly population and to guarantee access to earlier diagnoses.

The study “Sociodemographic and clinicopathologic features of elderly breast cancer patients in Brazil: A sub-analysis of AMAZONA III study (GBCAM 0115)” was conducted by the Brazilian Breast Cancer Study Group (GBECAM) in partnership with LACOG.
## Open trials / Research programmes

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<td>BIG 16-05</td>
<td>A randomised phase III trial comparing ataxitinib (anti-PD-L1 inhibitor) given in combination with standard chemotherapy vs. chemotherapy alone as adjuvant treatment in patients with operable TNBC - NCT01409176</td>
<td>M. Ignatiadis, H. McArthur, S. Saji</td>
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<td>P. Pitzis-Falldis, C. Cinceticci, P. Riedel</td>
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<td>B. Chua, G. Graber</td>
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<td>Palbociclib for HR+ isolated local or regional recurrence of breast cancer - NCT03528350</td>
<td>E. Mutanen, S. Ahsa</td>
<td>Supporter study Coordinating group: IBCSG (sponsor) Pharma partner: Pfizer</td>
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## Follow-up or post-study activities, recently closed studies

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<td>Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization: sequence and combination for patients with HER2+ Breast cancer - NCT00490139</td>
<td>M. Piccart</td>
<td>Lead trial (Co-Leading partners: BIG HQ / IJB-CTSU / FSTRF / Alliance) Pharma partner: Novartis (global sponsor for all countries with the exception of US) Funding: GSK (past) / Novartis</td>
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<td>Lead trial (Co-Leading partners: BIG HQ / IJB-CTSU / FSTRF / Alliance) Pharma partner: Roche (sponsor) Funding: Roche</td>
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<td>Co-lead trial (Co-Leading partners: EORTC / BIG HQ / FSTRF Pharma partner: Tesaro (sponsor) Funding: Tesaro</td>
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<td>B. Chua</td>
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<td>A. Irthum (coordinator)</td>
<td>BIG-sponsored programme (Co-Leading partners: BIG HQ / FSTRF / Alliance) Pharma partner: Novartis (global sponsor for all countries with the exception of US) Funding: Breast Cancer Research Foundation</td>
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<td>F. Andre, J. Cornils</td>
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<td>J. Gauck</td>
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<td>F. Cardoso, 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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<td>C. Saara, E. de Azambuja</td>
<td>Co-led trial Co-lead partners: ABCSG, SOLITI and BIG HQ Pharma partner: Genentech (sponsor) Funding: Genentech</td>
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<td>E. Rutgers, F. Cardoso, M. Piccart</td>
<td>Co-led trial Co-lead partners: EORTC (sponsor) / BIG HQ Commercial partners: Roche, Sanofi, Novartis and Genentech Funding: European Commission, Roche, Sanofi and Novartis grants, BCRF, Susan G. Komen for the Cure, Cancer Research UK, EORTC, Charlotten Trust, numerous national cancer societies and many other charitable grants*</td>
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<td>A. Tutt, B. Kaufman † J. Garber, C. Geyer</td>
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<td>Co-Lead trial Co-lead partners: ABCSG (RoW), AFT (US) / SOLITI / BIG HQ Pharma partner: Pfizer Funding: Pfizer grant</td>
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<td>O. Paganu</td>
<td>Supporter trial Co-lead partners: ABCSG (sponsor) Pharma partner: N/A Funding: ABCSG, Boadback-Lawrie, national and local funding bodies, individual donors</td>
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* Full information available on the BIG website.
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’s National Clinical Trials Network (NCTN), 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.

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• To provide a platform for education, interaction and innovation
• To facilitate the breast cancer community to meet and discuss issues and challenges
• To update the community on recent results and concepts
• To promote academic skills in young specialists
• To critically review new information so that breast cancer specialists can integrate it into daily practice

Early Rate Registration Deadline:
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Abstract Submission Deadline:
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