Breast Cancer Research in East Asia: challenges and opportunities

“All in one and one for all” must remain the spirit of academic clinical research
A gripping conversation with Prof Aron Goldhirsch.

Expanding the network and its Executive Board
Get to know BIG’s new Executive Board members and the four research groups just joining the network.
SUBSCRIBE NOW

to keep up to date with trending topics in the world of breast cancer and BIG Member Group academic research.

Receive your FREE bi-annual PDF copy of «BIG Research in Focus» directly in your inbox!

Simply scan the QR code with your smartphone or type in the link to be directed to the sign-up form.

www.BIGagainståastbreastcancer.org/resources/publications
Contents

Note from the Editor .................................................. 4
Breast cancer research in East Asia - challenges and opportunities ................. 5-12
«All for one and one for all» must remain the spirit of academic clinical research .... 13-15
Expanding BIG Executive Board ..................................... 16-20
Welcoming new Member Groups .................................... 21-27
Member activities .......................................................... 28-35
Trial updates .................................................................. 36-41
BIG Groups .................................................................... 42
Note from the Editor

In the Feature section of this newsletter, the floor is given to BIG’s representatives based in East Asian countries, who share their views about the current situation of cancer research in their region, the various challenges faced with the conduct of clinical trials, and the specific needs of Asian patients. They also highlight their achievements, as well as the many opportunities they see for the future of international breast cancer research.

Cancer experts from China, Hong Kong, Thailand, Japan, Taiwan, South Korea and Singapore look forward to increasing the involvement of Asian research groups as participants in international studies, but also in developing and running them. We are convinced that our joining efforts in international collaboration is the way forward to advance research more rapidly and efficiently and, most importantly, help more women and men affected by the disease, wherever they live.

To fight efficiently such formidable an adversary as the cancer problem, we need to be able to tackle common global challenges, while being aware of the specific needs of each population and using all the expertise, knowledge and resources available to us.

BIG represents a large international and inclusive network of breast cancer professionals, which is exactly the platform needed to think globally and foster research collaborations to help patients worldwide. The organisation recently initiated an important shift, not only by welcoming new academic research groups – based in Georgia and Asia –, but also by adapting its governance structure with an Executive Board that better reflects the geographical extent of the organisation, as well as the broad range of expertise among its members.

The various interviews and profiles depicted hereafter will help you get to know our new Executive Board Members, as well as the Voting Representatives of the four member groups that recently joined BIG.

Since June 2017, BIG consists of 59 collaborative member groups, which represent an impressive network of more than 10,000 breast cancer experts present across the six continents. The following pages will give you a peek at BIG members’ activities, and will highlight both BIG trials and other trials conducted by the groups.

I hope you will find an intriguing read in this edition of BIG Research in Focus.

Shinji Ohno, MD, PhD
Center Chief of Breast Oncology Center, Cancer Institute Hospital, Tokyo, Japan
Representative Director of the Japan Breast Cancer Research Group (JBCRG)
BIG Executive Board member

Subscription
BIG Research in Focus is available in PDF format for download on www.BIGagainstbreastcancer.org/resources/publications. If you wish to receive a free print copy of BIG Research in Focus or to be informed by email when the next issue will be available for download on the BIG website, please write to communications@BIGagainstbc.org
Breast cancer research in East Asia – challenges and opportunities

In June 2017, BIG welcomed into its network four new academic research groups, including organisations based in South Korea, Thailand and China, and looks forward to increased Asian input in the development and conduct of future international studies. As breast cancer incidence in East Asia moves ever closer to that in western populations, science writer Jenny Bryan asks clinicians about the specific needs of patients in the region and the opportunities and challenges of research.

Forty per cent of women with breast cancer live in Asia, and the growing interest in research by breast cancer specialists across the region has the potential to speed up advances in treatment for patients at both local and global levels. In the 20 years since BIG was established, Asian researchers have more than tripled their contribution to the organisation’s registration studies, from nine to 30% of participants, and there is a strong commitment to increased participation in purely academic studies too.

“‘This is very good news for women with breast cancer because when these studies produce results that change clinical practice, we know that their findings are as meaningful for those living in Asian countries as in other parts of the world,’ explains BIG Chair, Professor Martine Piccart.

She highlights the advantages of the very high quality of data from South Korean and other Asian researchers, and the potential of greater input from Chinese investigators:

“‘Providing us with rigorously collected and robust data is greatly appreciated because it significantly reduces the bureaucratic burden of running a large international trial. We’re looking forward to working with our new Chinese members, in particular for the opportunities that their advanced technologies can bring to translational research.’
Recently elected to the Executive Board of BIG, Dr Shinji Ohno, from The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan, hopes to encourage greater involvement in clinical trial design and development from Asian countries:

"Until now, we've collaborated in clinical trials but we haven't taken a leadership role in choosing which studies are carried out. If good ideas come from Asian researchers, I'd like to see more of them going forward for collaborative studies. I would also like to see our young investigators building stronger relationships with researchers in Europe and North America so they can play a bigger role in international studies."

Professor Seock-Ah Im, from the Cancer Research Institute at Seoul National University College of Medicine, South Korea, highlights the need for more international support for investigator-led trials in Asia:

"In Korea, we have some of the top-recruiting investigators for clinical trials sponsored by pharmaceutical companies but we find it very hard to get funding for investigator-led trials. We are often advised to join similar studies in Europe or the US and we are very happy to collaborate, but we would also like to secure funding directly so we can initiate some of these studies ourselves."

Although there is, as yet, no pan-Asian breast cancer research network, there is extensive collaboration between research groups in East Asian countries, such as Hong Kong, South Korea, Thailand, Japan, Singapore and Taiwan. Each year, breast cancer specialists from across the region meet at the Global Breast Cancer Conference in South Korea to present results and discuss the management of Asian trials. In addition, BIG and European and North American cancer organisations such as the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO), are partnering with Asian cancer organisations in educational and other initiatives.

Dr Janice Tsang, Founding Convenor of the Hong Kong Breast Oncology Group (HKBOG), believes that she and colleagues can learn a lot from such organisations, not least about fundraising and maintaining momentum.

"By coming to our clinical meetings in Asia, representatives of BIG and other international organisations also help to show the value of being part of such a group and being able to share and discuss our issues and limitations," she says.

Professor Im agrees the value of sharing experiences particularly with European colleagues:

"The economic status and scientific background of European countries are very varied – just as in Asian countries. We can discover how Europe has developed software and friendship networks to aid collaboration and fundraising, and we can learn from those lessons to harmonise our own ways of working across Asia."

"Until now, we've collaborated in clinical trials but we haven't taken a leadership role in choosing which studies are carried out. If good ideas come from Asian researchers, I'd like to see more of them going forward for collaborative studies.

Dr Shinji Ohno
Prioritising Asian needs for breast cancer research

As approximately half of the women who get breast cancer in Asian countries are premenopausal, researchers such as Professor Chiun-Sheng Huang, Director of the Breast Care Center at the National Taiwan University Hospital, are urging that more trials are carried out in this group of women. He points out that recent studies of new CDK4/6 inhibitors in women with oestrogen receptor-positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) breast cancer were conducted in postmenopausal women and results cannot therefore automatically be applied to large numbers of patients in Taiwan and elsewhere in Asia.

“We need another study of CDK4/6 inhibitors in premenopausal women because, if we use the new drugs with different hormone treatment from that used in the studies of postmenopausal women, we won’t know if we can achieve the same efficacy,” says Professor Huang.

He adds that greater participation of Asian countries in the small number of studies of premenopausal breast cancer that are done in western countries would speed up enrolment and results.

Professor Huang makes the point that he would like to see more international clinical trials designed to de-escalate treatments, which is especially important for countries and people with fewer resources.

The need to ‘translate’ advances made in European and US studies for clinical practice in Asia extends to other areas of research. Professor Jiandong Wang, from the General Hospital of People’s Liberation Army (301 Hospital), China, explains that differences in breast density between western and Asian women mean that B-type ultrasound is more sensitive than the X rays typically used for screening in the west, and this needs to be recognised in national guidelines in China.

“The second dilemma relates to gene research. Commercial products such as Oncotype Dx, Pam 50 and Mammaprint were developed based on western populations, and some are now integrated into our breast cancer guidelines. But how well do they work for Chinese patients? We need to validate these tests or develop new gene panels that we can apply to clinical practice in Asia,” says Professor Wang.

He points to progress being made by Chinese researchers into the mechanisms of metastasis, proliferation and drug resistance, as well as therapies for difficult-to-treat breast cancer subtypes, such as triple negative breast cancer, but there are additional targets:

“We need clinical trials based on breast surgery and gene researches in order to advance clinical practice for women in China.”

Professor Jiandong Wang

Professor Jiandong Wang would therefore like to see more cost-effectiveness research for approved drugs to guide the most appropriate use of limited resources. Research to enable the most appropriate patients to receive more intensive treatment is also high on his list of priorities.

“Identifying patients most likely to benefit from different treatment approaches will be important for development of treatment guidelines and health policy in Thailand,” he says.

Until now, breast cancer research in Thailand has been fragmented, with individual academic centres conducting their own research with few collaborations. With the recent creation of the TSCO’s breast cancer group, Professor Sriranpong hopes that this will change. By stimulating
In Taiwan, we’ve been very active in clinical trials for many years and have a lot of experience in producing good quality data. So I hope that more study groups in many countries will consider including Asian patients in their studies, especially premenopausal women with breast cancer.

Prof Chiun-Sheng Huang

In collaboration between the various centres, he aims to gradually overcome issues such as small sample size and reliability and applicability, and to improve the treatment of patients in his region.

“We are currently setting up a breast cancer registry which will help give us the big picture on which we can build our future research initiatives,” says Professor Sriuranpong.

For Dr Tsang, another important issue for breast cancer research in Asia is the ageing population. She explains that Hong Kong has become the city with the greatest longevity in the world, and that older Chinese people tend not to seek help when they are ill because they do not want to be a burden to their families, as reflected by a recent review from the Hong Kong Breast Cancer Registry. In addition, oncologists may fail to offer more intensive treatments to older patients, even when they are otherwise fit and healthy, with age being the usual factor determining the intensity of standard treatment. Yet, research has shown that older women are more likely to accept chemotherapy if molecular profiling and other tests suggest that they have a high-risk breast tumour.

“We need to engage elderly patients so that they will present early, instead of hiding from doctors or their family members, and ensure that they get information about their tumour that will help them make appropriate treatment decisions. This could get around the problem of under treatment of elderly patients, which is common in Asia,” she says.

Taiwan: a small country with a big track record of breast cancer research

For a small country (population 23.5 million), Taiwan punches well above its weight when it comes to breast cancer research. Professor Huang is rightly proud of Taiwan’s contribution to major studies, such as BIG’s HERA and NeoALTTO trials:

“We’ve enrolled many patients in BIG and other breast cancer trials, especially in those for early breast cancer and neoadjuvant therapy. Most of our patients are treated in large medical centres and, our surgeons, who often lead the multidisciplinary teams, stay up to date with trials and results and have a good enrolment record,” he says.

Patients are also keen to take part, he says, partly because this entitles them to reimbursement for newer breast cancer drugs through Taiwan’s national health insurance scheme, which they may not get in clinical practice. While results of international studies are sufficient to gain approval of new medicines in Taiwan, the government carries out a cost/benefit analysis to determine whether costs can be reimbursed through national insurance or patients will have to pay or have additional private insurance. For example, many drugs are reimbursed only for node positive disease, whereas pertuzumab and T-DM1 are not reimbursed even for patients with metastatic disease.

“For most diseases the national insurance scheme works very well, but there have been so many expensive new drugs for cancer that the government cannot afford them. Unless a cancer drug has shown superior overall survival over previous treatment, it is unlikely to get reimbursed, even if the indication has been approved on the basis of prolonged progression-free survival,” explains Professor Huang.

Like many Asian countries, Taiwan is seeing a rapid rise in cases of breast cancer thanks, in part, to government subsidised screening for women aged over 45. This has resulted in more women being seen with early stage breast cancer and the start of a shift in peak age at diagnosis from 45 to 50 or older.

Taiwan has good infrastructure for clinical trial participation and makes a significant contribution to studies with pharmaceutical industry funding. However, breast cancer researchers have struggled to get funding for purely academic studies – as is the case in so many countries.
“Many hospitals haven’t supported peer-initiated clinical trials because of the problem of insurance. It has been difficult to get insurance, raising questions about who is responsible if adverse events occur during a trial. Things are now improving and we’re seeing insurance companies getting involved in this area,” says Professor Huang.

The Taiwanese government has also encouraged greater involvement in clinical trials with an efficient system for regulatory approval of protocols, and the Taiwan Breast Cancer Consortium has been established to support more sites being included. However, heavy clinical workloads mean that clinicians do not have much time to participate in clinical trial activities, and efforts are being made to provide more support for them in terms of additional study nurses and young principal investigators.

“In Taiwan, we’ve been very active in clinical trials for many years and have a lot of experience in producing good quality data. So I hope that more study groups in many countries will consider including Asian patients in their studies, especially premenopausal women with breast cancer, and I look forward to some exciting future collaborations,” concludes Professor Huang.

Where East meets West: breast cancer research in Hong Kong

Greater involvement in international breast cancer trials, centralised Institutional Review Board (IRB) approval of trial protocols and expanded participation in phase I studies are all high on the research wish list for Dr Tsang.

“We already have a vibrant environment for breast cancer research, and have been involved in many local and regional studies over the past decade, as well as international trials such as BIG’s APHINITY trial. But my dream is for all our centres to participate in clinical trials for all investigators in Hong Kong, under the umbrella of the Hong Kong Breast Oncology Group, and to collaborate with BIG and North American centres,” she says.

The HKBOG facilitates academic breast cancer research, especially in clinical and translational trials, and is involved in updating local guidelines and enhancing knowledge exchange activities within the community. It also strengthens links with regional and international breast oncology research groups.

Hong Kong licenses new medicines, usually within two to three years of US Food and Drug Administration (FDA) approval, without additional local registration studies. This has helped to incentivise breast cancer specialists in Hong Kong to become active researchers, especially as most patients have to pay for many medicines, such as adjuvant trastuzumab, unless they take part in a clinical trial.

“By conducting clinical trials, we can offer free of charge access to state-of-the-art drugs, and that has helped to raise awareness about the importance of breast cancer research,” explains Dr Tsang.

Indeed, with two of the seven academic institutions in Hong Kong that carry out breast cancer research recently accredited by the China Food and Drug Administration, data from studies carried out in the semi-autonomous territory are already being used to help fast-track regulatory approvals in China. However, the need for each research centre in Hong Kong to gain IRB approval for trial protocols is currently causing delays in recruiting patients into international trials.

“Recruiting patients to these studies is very competitive and the IRB system makes it hard to catch up. But a recent external review suggested that, since Hong Kong is so small, we should have a centralised IRB system and that could make a big difference to our ability to contribute to international research,” says Dr Tsang.

She also stresses the continuing need for pan-Asian studies to gain an ethnic perspective on the use of novel breast cancer drugs because of potential toxicity differences compared to western populations. For example, in the EMILIA study of TDM-1 versus capecitabine and lapatinib in women with HER2+ locally advanced or metastatic breast cancer, there was an increased incidence of thrombocytopenia in Asian patients. In contrast, recent Asian sub-analyses of the MONALEESA-2 and PALOMA-2 trials of CDK4/6 inhibitors in women with advanced or metastatic ER+, HER2- breast cancer showed efficacy and safety profiles consistent with those seen in the overall population.2,3

“As well as contributing to international breast cancer studies of new treatments, we need to offer expert input and opinion on potential toxicity or efficacy differences from patients in this part of the world,” says Dr Tsang.

Looking ahead, she would like to see Hong Kong catch up with Singapore in making a greater contribution to phase I studies, as this could have significant benefits for patients as well as for establishing research platforms for clinicians. Like breast cancer specialists in the West, she would
also like to be involved in more research to identify women with less aggressive tumours who could be spared the most intensive treatment.

‘At present, we don’t have the budget for the technologies to investigate tumours in this way, but there is evidence suggesting that even some premenopausal women with breast cancer could avoid the need for chemotherapy,” says Dr Tsang.

However, she is realistic in recognising the limitations on what Hong Kong can currently contribute, in terms of its size, infrastructure and funding:

“We’re a very small city and oncologists in Hong Kong don’t have official ‘protected time’ for research and continuing education – as colleagues in many countries do – and it can be hard to do research at the end of a long working day when many of us have family and other calls on our time.”

Japanese breast cancer research impacts worldwide practice

When positive efficacy data from the CREATE-X trial were first presented at the San Antonio Breast Cancer Symposium in 2015, the findings were predicted to change clinical practice for women with residual invasive disease after preoperative chemotherapy and surgery for HER2- breast cancer. The study, carried out by clinicians in Japan and South Korea, and recently published in the New England Journal of Medicine, showed that adjuvant capecitabine prolonged disease-free survival and overall survival Hong Kong marks the 20th anniversary of its handover to her motherland of China, it in this difficult-to-treat group of women, with particularly impressive results in those with triple negative breast cancer.

“We’re very proud that CREATE-X has addressed an unmet need for improved breast cancer treatment, not just for women in Japan and Korea, but for women worldwide. I hope that this success will encourage more doctors in Japan to get involved in breast cancer clinical trials,” says Dr Ohno.

In Japan, breast cancer surgeons, such as Dr Ohno, oversee all aspects of care for most women with breast cancer, including radiotherapy, hormonal and chemotherapy, as there is a shortage of medical oncologists. This means there is limited time for clinical trials, though there is a growing culture of research.

The Japan Breast Cancer Research Group (JBCRG) has members in 280 institutions, and most of the approximately 90,000 women diagnosed with breast cancer in Japan each year are treated at these centres. In addition, the Organisation for Oncology and Translational Research (OOTR), originally established in Hong Kong and now run jointly from Hong Kong and Japan, is carrying out several important clinical trials across the region in order to optimise treatment strategies, particularly for patients with breast cancer.

“Translational research is very important for helping us to find good biomarkers to help identify which patients will respond best to capecitabine and other treatments for breast cancer. This is a priority not just for Asian countries, but for researchers worldwide and, with better collaboration, we can get answers more quickly,” says Dr Ohno.

However, clinical trial funding, especially for translational research and studies of supportive therapies, has become more difficult since greater restrictions were introduced on pharmaceutical industry grants, forcing Dr Ohno and colleagues to look further afield:

“We’ve been able to get money for clinical trials from a cosmetics company and through crowdfunding. There is growing public awareness about breast cancer and the importance of clinical trials, so I hope that in the future we will receive more donations to enable us to complete important clinical trials in breast cancer.”

South Korea: a reputation for excellence in clinical research

In less than 20 years, breast cancer researchers in South Korea have developed a strong presence in the scientific literature and an impressive portfolio of ongoing clinical trials, though there are still a number of hurdles to overcome.

“When I started clinical trials in 2000, there was no activity at all so we have come a long way, but
our government funding is limited and we need to develop more infrastructure including research nurses, research managers and biostatisticians,” says Professor Im.

South Korea has approximately 25 institutions involved in breast cancer clinical trials but, like other countries in East Asia, these are mainly sponsored by pharmaceutical companies. Clinicians consider it the duty of well organised institutions to participate in research but expansion of investigator-led trials is hampered by limited funding and poor availability of newer drugs. In contrast to Japan for example, South Korea does not have its own pharmaceutical companies to discover and develop new cancer drugs and is reliant on the drug pipelines of western companies.

Professor Im explains that healthcare is almost fully government-funded in South Korea and, thanks to nationwide ultrasound screening for the largely premenopausal women at risk, 70% of those diagnosed with breast cancer have stage I/II disease. However, regulatory approval of new cancer drugs is slow, and there can be further delays before enough pharmacoeconomic data become available to support government reimbursement.

“If patients have the opportunity to get into clinical trials, they will have a good chance of receiving new drugs several years before they become generally available, and this may be in both the active and standard of care arms of a study. Research has shown that public understanding of clinical trials is improving, and patients are happy to participate, especially in studies of metastatic breast cancer,” says Professor Im.

Despite some limitations on breast cancer research, she remains optimistic about future opportunities. Professor Im would particularly like to see more translational research in South Korea, and believes that being part of the BIG network is an advantage for such initiatives:

“We have medical and clinical oncologists who are committed to clinical research and we have many basic scientists, but we need a bridge from basic science to clinical research. BIG has a strong infrastructure for translational research to connect basic research and clinical trials, and I hope that this will enable us to play a bigger role in future, in this area of breast cancer research.”

Breast cancer: not just a ‘western’ disease

In Asia Pacific countries, at least 400,000 women are diagnosed with breast cancer each year. and the disease accounts for nearly one in five cases of cancer in the region. But, as Dr Yoon-Sim Yap, from the National Cancer Centre and Cancer Therapeutics Research Group (CTRGI), Singapore explains, breast cancer has traditionally been regarded as a ‘western’ disease, with greater research priority given to ‘Asian’ cancers such as hepatocellular carcinoma, gastric cancer, T-cell lymphoma, nasopharyngeal carcinoma and lung adenocarcinoma.

“There is increasing awareness that breast cancer is now a major health problem in Asia and, here in Singapore, it comprises 30% of all cancers in women. Indeed, we have the highest breast cancer incidence in Asia,” says Dr Yap.

In 2012, breast cancer was responsible for nine per cent of cancer deaths in East Asia, making it the fourth most common cause of cancer mortality, behind lung, liver and stomach cancers.

Although breast cancer rates in East Asia are less than half those seen in Europe and North America, there was a significant rise in incidence between 1980 and 2010. The greatest increase was in South Korea, where the incidence rose by 47.5% from 1999 to 2010.1 This compared with a 30.8% increase in China (including Hong Kong and Shanghai) between 1988 and 2002, and a 12% rise in Japan between 1983 and 2002.1

“The reasons for the dramatic rise in breast cancer incidence in several East Asian countries, including Singapore, are still unclear, although this is often attributed to ‘westernisation’ of diet, and lifestyle changes,” points out Dr Yap.

Large studies have shown that breast cancer occurs at a younger age in many parts of Asia, with a median age at diagnosis of 49-50 years in South Korea, Singapore, Malaysia, Hong Kong, China, and India, compared to 57 years in Japan.1

“The incidence among younger women in Singapore is surpassing that in the US and this has led to greater emphasis and interest in understanding the epidemiology and biology of Asian breast cancers,” says Dr Yap.

Globally, an estimated one in three women with breast cancer are diagnosed under the age of 50, compared to 42% throughout the Asia-Pacific region and 47% in South-East Asia, rising as high as 55% in South Korea. Genetic and other risk factors have been proposed to account for the different age at diagnosis, and different genetic polymorphisms have been reported between Asian and Caucasian women with breast cancer.

Venturing into the region

Most East Asian women are diagnosed with breast cancer at an early stage. As a result, chemotherapy and hormone therapy, which have been shown to improve outcomes, are less commonly used in practice. However, there are some promising developments:“...makes it the fourth most common cause of cancer mortality, behind lung, liver and stomach cancers.”

Dr Yoon-Sim Yap
but more data are needed, especially in relation to BRCA1/2 prevalence.

Treatment of breast cancer is similar in East Asia to that in Europe and North America, though breast cancer mortality in East Asia is below the world average. However, mortality rates increased steadily in Korea, Japan, and Taiwan between 1975 and 2006.1 Data reported in the late 1990s showed that, at over 80%, five-year survival for breast cancer was highest in Hong Kong and Tianjin in China, Korea, and Japan, followed by Taiwan, Singapore and Shanghai (75-80%).

“We need to prioritise breast cancer research in all three areas of prevention, early detection and treatment;” concludes Dr Yap. “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. We also need new therapeutic targets for more effective systemic treatments. We are encouraged by progress in targeting treatment at the mutations in epidermal growth factor receptor that occur in a high proportion of non-small cell lung tumours in Asian patients. Now, we need comparable advances to transform the lives of Asian women with breast cancer.”

References
3. Im S, Mukai H, Park IH et al. Palbociclib (PAI) plus letrozole (L) as first-line [IL] therapy (tx) in postmenopausal Asian women with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2–) metastatic breast cancer (mBC). Annals of Oncology 2016; 27 (suppl 9): i335, abstract 1160
"All for one and one for all" must remain the spirit of academic clinical research

In the run-up to elections to expand BIG’s Executive Board (EB) and BIG’s last General Assembly held in Chicago last June, Prof Aron Goldhirsch, co-founder and until recently vice-chair of the organisation, announced his decision to step down from BIG’s Executive Board (EB) after nearly 20 years of commitment.

In a wide-ranging interview with BIG Headquarters, Prof Goldhirsch looks back on the early days of international research and what has been achieved so far through the collaboration of academic research groups, sharing his vision of the future of breast cancer research.

In the early 1990s, while breast cancer research in Europe was highly fragmented, with academic groups running many similar trials and consequently duplicating efforts, and wasting time and resources, two European oncologists shared a different vision for the future.

Prof Aron Goldhirsch, who was at the time Head of Division of Medical Oncology in Bellinzona, Switzerland, and Prof Martine Piccart, medical oncologist at the Jules Bordet Institute in Brussels, Belgium, strongly believed that large-scale cooperation was crucial. They felt that this was the only way forward to make significant advances in breast cancer research and moving more rapidly and innovatively towards better treatments and cures.

In 1996 Dr Goldhirsch and Dr Piccart, together with other opinion leaders in breast cancer research, created the Breast International Group (BIG), with the aim of bringing together academic research groups to debate the latest research findings, share ideas for new clinical trials, and work in harmony to conduct those trials together.

Now, nearly 20 years later, BIG is considered as a leading force in the breast cancer research arena.

Among your many achievements both with the International Breast Cancer Study Group (IBCSG) and within the BIG network, which make you feel the most proud? To you, which clinical study or research project was particularly landmark?

Being a founding member of both the IBCSG and BIG, there are several decades of research activities to screen. Each period of clinical trials in the field of adjuvant therapies for women with operated breast cancer has its own context of standard of care and of desire for innovation. This explains the fact that for each period there are trials to be proud of. It is impossible to declare one or two trials as winners of the hit parade of trials. I therefore find it more appropriate to mention chronologically some of the most relevant trials of the IBCSG and later of BIG, which were important for patient care (which, after all, is the reason to be proud):

• IBCSG Trial III: the first trial that indicated the need for targeted therapy for endocrine responsive disease (and that adjuvant chemotherapy might not be needed for all).
• IBCSG Trial IV: the first (and only) trial that evaluated an adjuvant systemic therapy for the elderly with long term follow-up.
• IBCSG 13-93: the first randomised trial for endocrine responsive disease in premenopausal women that demonstrated the high efficacy of tamoxifen after adjuvant chemotherapy.

A conversation with Prof Aron Goldhirsch  
Co-founder of the Breast International Group (BIG)

...a multidisciplinary approach across groups and institutions, working together with the spirit of “all for one and one for all”, is the most powerful attitude to improve results.
An environment for clinical research must be created, which is driven by academic investigators who receive significant legitimacy, as important as that of bringing a new drug to the market...

- HERA: the trial that demonstrated the efficacy of adjuvant anti-HER2 therapy with trastuzumab in terms of disease-free and overall survival, indicating also that one year of exposure to the drug is sufficient (and prolonging treatment to two years does not further benefit the treated patients).
- BIG 1-98: this demonstrated the best adjuvant endocrine therapeutic strategy for postmenopausal women with endocrine responsive disease.
- SOFT & TEXT: these sister trials were the first to prove the important role of ovarian function suppression and of adjuvant exemestane for endocrine-responsive disease in premenopausal women.
- SOLE: this trial recently demonstrated the efficacy of extended adjuvant letrozole, despite periods of temporary treatment interruption (included into the treatment plan to improve tolerance).

These trials, among others important as well, illustrate the flavour of the studies carried out by the IBCSG and BIG to move from investigations about the BEST THERAPY on average to personalised adjuvant therapies for individual patients.

The most significant episode in BIG’s early days, which makes me the most proud of the Group, was however the story of HERA. Roche wanted to conduct a two-arm trial to investigate standard treatment compared to standard treatment plus trastuzumab. The various groups that formed the BIG network at that time decided to insist, all together, on conducting a three-arm trial to incorporate an additional question about optimal treatment duration. Sticking all together made the pharmaceutical company accept the design we insisted on.

The interaction with Martine Piccart was particularly intensive and fruitful. Much of the powerful collaboration characterising BIG has been due to her tenacious sticking to the rules of global international collaboration.

About 20 years have passed since you, together with Martine Piccart and other cancer experts, had the idea to create the Breast International Group. At the time, you and your peers shared a strong vision of the future of breast cancer research.

The vision behind the strong desire to work together in the field of breast cancer had several aspects:
- To work together with other groups across the world to answer pertinent therapeutic questions rapidly and efficiently.
- To provide an academic platform for formulating relevant questions for improved patient care and for increasing scientific knowledge.
- The chance to more successfully negotiate with pharmaceutical companies on trials and related research.
- To stimulate clinical research across the world with a genuine multidisciplinary approach.
- To educate clinical researchers to conduct trials across the world, together with others who share the same clinical and scientific interests, obtaining results which none of them would have reached if not through genuine collaboration.

What challenges do you perceive for the younger generation of breast cancer experts? If you had to give one piece of advice to the young generation, what would it be?

Clinical research in the field of breast cancer needs to maintain two features to achieve further progress:
- The recognition that the disease is heterogeneous and thus requires several types of therapies to become part of one patient’s treatment programme.
- The recognition that a multidisciplinary approach across groups and institutions, working together with the spirit of “all for one and one for all” is the most powerful attitude to improve results.

What has changed, compared to 20 years ago, in the realm of breast cancer research? What are the biggest challenges currently faced by all stakeholders and how do you think BIG can play a significant role in this context?

The impressively high cost of anticancer drugs, the degree of control which pharmaceutical companies exert on clinical trials design, and the favorable attitude of regulatory agencies towards pharmaceutical oriented clinical trials (less incentive for academic research) are all important challenges for current and future research.

An environment for clinical research must be created that is driven by academic investigators who receive significant legitimacy, as important as that of bringing a new drug to the market. It is important to note that having an effective drug does not mean that it is to be used for every individual patient!

BIG should continue to remain compact and effective, maintaining the spirit of academic research, which includes better care for patients and better knowledge for advancing science, both derived from clinical trials.
Could you please cite three elements that you find critical for the continued success of BIG in the next decade? This is a very personal view:

- Maintain the agenda of BIG as broad as possible to favor all its group participants.
- Increase the participation of groups in the governing structure of BIG, to allow a more effective collaboration with the spirit of “all for one and one for all”.
- BIG’s help and support should be effectively given to member groups and institutions to provide incentives for BIG-related collaboration. It should be easier to conduct a trial within the BIG network than within your own institution.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

Improvement of patient care has been observed, as a result of hard work, in each of the last four decades. There is no reason for this trend to stop! Our current degree of knowledge will increase and, with it, improve practice.

What is your hope for the next 10 years of research?

I realistically think that improvement will occur for the treatment of all patients with endocrine responsive disease, whether premenopausal or postmenopausal age. Understanding of triple negative disease will lead to differential treatment programmes for each tumour subtype within this group of patients. Finally, advances in the understanding of HER2 overexpressed disease will lead to improving targeted therapies for those who also have hormone receptors co-expressed in the tumour. Drugs that potentiate existing treatments will be the challenge for the next trials.

As BIG co-founder and a member of the BIG EB since its creation, as well as being a leader in the IBCSG, you have played a key role in shaping the international breast cancer research agenda, while dealing with heavy responsibilities at two major cancer institutions, and contributing to the advancement of research in your country. How did you balance your national with your international activities?

Having a major responsibility in institutions with predominant clinical responsibilities is a condition sine qua non for understanding the essence and the leadership role of clinical research. Leaders of groups devoted to clinical research must be experts in patient care in order to understand the various facets of caring for individuals with breast cancer.

We would like to know more about you. When you are not in the clinic or in the office, what are your hobbies?

Photography has been one of my favorite hobbies. I have enjoyed traveling and meeting with friends throughout the world. I am lucky to have friends in many countries and continents, with whom I enjoy very much the contact despite traveling less than before.

A family of friends whom I particularly enjoy are the Gelbers (Rich & Shari) from Boston, who make the most touching efforts to maintain friendly contacts despite the distance.

A particular pillar of my life is my family, my wife Francesca and my children, Tommy, Lea and Nina, whose presence in my life keep it very interesting and active. They have always allowed me to remain actively involved in my profession, for which I am very grateful to them.

A strong national and international commitment against breast cancer

Prof Goldhirsch is recognised as a world leading expert and opinion leader in the field of breast cancer. His main areas of research include new treatments for breast cancer, definition of biological features that predict responsiveness or resistance to anti-cancer treatments, and quality-of-life-oriented approaches.

He is the founder of the International Breast Cancer Study Group (IBCSG) – where he still serves as the Co-Chairman of the Scientific Committee –, an internationally renowned academic research group based in Switzerland that is active in several countries and has conducted 40 Trials over the years. The IBCSG has been part of the BIG network from the beginning. From 1994 to 2004 Prof Goldhirsch also held the position of Chairman for the Swiss Group for Clinical Cancer Research (SAKK), another research group that joined BIG in 2000.

Prof Goldhirsch, among other duties, currently serves as Director of the Clinical Research Platform at the European Institute of Oncology (IEO), Milan, Italy, and Senior Consultant for Senology in Switzerland. He is also Emeritus Professor of Medical Oncology at the University of Bern, Switzerland. Over the years he has been bestowed with numerous prestigious honours for his work, and has been a prodigious writer and editor of oncology publications.

During the years spent with BIG, and together with the other members of the Executive Board, he has shaped BIG’s research strategy and objectives, always keeping patients’ interests at the heart.

Sharing a spirit of openness and collaboration, Prof Goldhirsch’s contribution and unfailing commitment to international cooperation have been key to the development and extension of what is now considered to be the largest international academic network of collaborative groups dedicated to breast cancer research.
Expanding BIG Executive Board

Following a governance review and elections held during the first half of 2017, BIG was proud to announce the appointment of seven new Executive Board (EB) members during the General Assembly held last June in Chicago: Judith Bliss, Boon Chua, Marco Colleoni, Barbro Linderholm, Shinji Ohno, Aleix Prat and Ander Urruticoechea assumed their new roles on 1 July 2017.

They joined Fabrice André, José Baselga, David Cameron, Angelo Di Leo, Karen Gelmon, Michael Gnant, Sibylle Loibl and Martine Piccart, who had been previously elected for the 2014 – 2018 mandate.

Together, they represent the new leadership and the main scientific and decision-making authority of the organisation. This expanded EB better reflects not only the geographical extent of the network, but also the broad range of expertise among its members.

BIG is delighted to introduce you to the new members of the EB.

“I’ve been involved in BIG since the early days and seen its role grow in depth and diversity.”

Interview with Judith Bliss

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

I’ve been involved with BIG since the early days and seen its role grow in depth and diversity. I therefore welcome the opportunity to help shape its future.

What particular expertise do you think you can bring to the BIG EB?

As a statistician and Director of an academic Clinical Trials Unit (CTU [at the Institute of Cancer Research, ICR, London - Ed.]), I bring complementary expertise to that of my clinical colleagues. That will relate to the scientific research methodology associated with proposed and ongoing trials and also to the research governance and management arrangements required for large scale multi-national and multi-disciplinary projects.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

Scientific ambition, pragmatic collaboration, and research integrity.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

A major challenge is the length and scale of trials required to provide definitive practice changing evidence. Another is overcoming the obstacles to enable the conduct of robust but scientifically efficient trials, and the incorporation of pragmatic solutions.

BIG can assist – to listen, to learn – how international groups can best work together, recognising the different working practices and infrastructures surrounding trial conduct in each country – brokering collaborations both between groups and with pharmaceutical company partners to enable cutting-edge contemporary trials to be expedited.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

- The definition of better biomarker selection for preferential targeting of therapies
- The discovery and validation of novel endpoints (e.g., biomarkers, ctDNA positivity) to enable both tracking of disease progression and to provide an earlier read out for large adjuvant trials.
Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

The rationale underpinning the vision and mission of BIG to accelerate translation of science to cure through global, multidisciplinary collaboration in breast cancer research makes complete sense to me. The global reach of BIG and the power of team science are critical to realising our vision — no one succeeds as an island.

The vision of BIG aligns with my professional commitment to provide every patient with the best possible care, irrespective of geography and socio-economic status. It is my privilege to serve the BIG community and, above all, our patients.

What particular expertise do you think you can bring to the BIG EB?

I will contribute to the scientific agenda of the BIG EB not purely as a radiation oncologist but more broadly, with a clear recognition of the importance of genuine multidisciplinary collaboration.

My knowledge and experience in healthcare leadership (e.g. within the BIG member groups ANZBCTG (the Australia & New Zealand Breast Cancer Trials Group) and TROG (the Trans-Tasman Radiation Oncology Group) - Ed.) would enable me to contribute methodically and effectively to the strategic positioning, organisational design, communication strategies, performance management and growth of BIG as a complex and dynamic global organisation.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

- A clear strategic position in the evolving and competitive landscape of cancer research
- Effective engagement of our members including early career researchers to cultivate an organisational culture and scientific vibrancy necessary for collective successes
- A sound governance, operational and business model that is aligned with our strategic directions.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

There have been substantial investments from the pharmaceutical industry and funding bodies in clinical evaluation of precision oncology and precision diagnostics. Many institutions are pursuing independent research in these fields. However, research of limited scale will likely generate limited successes in part due to limited access to targeted agents and diagnostics and tumour specimens for analysis. This is enormously costly, and perhaps wasteful. With its global network, BIG is strongly positioned to evaluate precision oncology in scientifically rigorous collaborative programmes, ensure independence from the industry, and enable more effective and efficient translation of research into clinical practice to optimally serve the needs of our patients.

Another major challenge is the viability of non-industry sponsored academic research that addresses questions of significance and relevance to the patients and healthcare systems. BIG can provide the global leadership and collaborative framework to collectively optimise the use of limited resources and enable its successful conduct.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

I am cautiously optimistic that we will, particularly through scientifically rigorous academic research that focuses on patient outcomes and adds value to the healthcare systems. This is typically amongst the most challenging research to conduct in many parts of the world due to funding and resource constraints. However, it is also amongst the most meaningful research to the diverse stakeholders in healthcare, none more so than the patients.

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

BIG represents the best opportunity to preserve the academic freedom of clinical investigations focusing on new therapies for patients with breast cancer. My experience as Chair of the Executive of the Scientific Committee of the International Breast Cancer Study Group (IBCSG), as well as the opportunities I have had to coordinate research activities across different countries, have persuaded me that global collaboration is crucial to make progress. Despite the special challenges of cross-cultural collaboration, the goal to improve patient care is imperative. Promoting BIG’s Principles of Research Conduct is an indispensable component of this work. I am convinced that the membership on the BIG Executive Board will give me the chance to contribute optimally to BIG’s mission.

What particular expertise do you think you can bring to the BIG EB?

Serving as Chair for several international collaborative studies, I have the experience of negotiating with pharmaceutical partners as well as fostering cooperation among group members to provide a united front in seeking pharmaceutical industry partnerships. I have also been actively

"Research is my hobby, curiosity is hard-wired into my DNA"

Interview with Dr Boon Chua

"Global collaboration is crucial to make progress."

Interview with Dr Marco Colleoni
involved in the development of innovative clinical trials of promising treatments, with emphasis on translational research that will lead to more personalised patient care. I will use these experiences as well as my management knowledge to contribute to the deliberations of the Executive Board.

Please cite three elements that you find critical for the continued success of BIG in the next decade?
Caring for women and men with breast cancer, scientific integrity and independent thinking, respect for the various cultural and ethnic environments in which we work.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?
BIG played a significant role in advancing science and breast cancer patient care by addressing questions important to patients and reflecting the spirit that guides a worldwide collaboration with the goal of serving women and men with breast cancer. Several large phase III trials have matured in recent years, leading to numerous clinical trial reports with a major impact on the care of patients with breast cancer. However, at the same time, major collaborative groups have been experiencing difficulties to initiate new large clinical trials. The evolution of research on new drugs in the field of breast cancer has been focused on selection of niches rather than large groups of patients. The current reality is that the majority of the patients from member institutions of large cooperative groups are typically treated outside clinical trials. With large phase III trials now quite rare, we have to adapt and shift our efforts towards developing and launching smaller trials with selected groups of patients. The programme for the next future is looking to prioritise genomics and biomarker-based research, improve the design, review, and operation of translational research, reduce time from initial study concept to final approval, and increase partnership with Industries. BIG as an organisation is in the best position to translate these concepts into reality.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?
I would expect new important information about endocrine therapies, both in premenopausal and postmenopausal patients. In particular, I think we will identify new agents able to induce adequate ovarian function suppression as well as new combinations of endocrine and targeted agents.

“I’m highly motivated for patient and academic work, especially clinical trials”

Dr Barbro Linderholm

Dr Linderholm is a medical oncologist based in Sweden and working actively both in the clinic and on research programmes and trials. She currently serves as Senior Associate Professor and Head of the Clinical Trial Unit at the Department of Oncology of the Sahlgrenska University Hospital, Göteborg, Sweden. She is also affiliated to the Department of Oncology/Pathology at the Karolinska Institutet in Stockholm.

When joining BIG, Dr Linderholm said: “I… we believe in the necessity of large cooperative groups to achieve results from clinical trials within shorter time periods, thus improving breast cancer therapy faster. Taking into account the further subdivision of breast cancer into several molecular subgroups, we do not believe that single research groups can solve relevant issues in an effective way anymore. We consider BIG, acting as umbrella organisation for many academic groups, to have an invaluable qualification to discuss and conduct studies aiming to answer several aspects of breast cancer care.”

About her recent election to the BIG Executive Board, Dr Linderholm said she is very motivated to participate in high quality translational research and to function as a BIG ambassador with the ultimate vision to increase the cure of breast cancer.

“I hope to enhance the collaboration between BIG and the Asian groups.”

Interview with Dr Shinji Ohno

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?
I believe that the mission of the breast cancer clinical trial groups is to contribute to conquering breast cancer, as well as making state of the art treatment strategies and suitable care for each individual patient. As the incidence of breast cancer is...
In order to conquer breast cancer, we have to prevent breast cancer occurrence and cure patients affected by the disease. In order to treat patients optimally, good biomarkers to predict the effect of drugs are essential. Translational research associated with our clinical trials should clarify the significance of specific biomarkers, as well as help us define new clinical strategies to improve patient survival. BIG plays an important role as the biggest worldwide research network working to conquer breast cancer.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

Precision medicine will be achieved by basic research, translational research and clinical trials. As well as producing new drugs, de-escalating breast cancer therapies will be improved in early breast cancer without sacrificing outcomes.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

Personally, time and money are the most important elements. We have to support young investigators to grow to act globally and consider good ideas to resolve the clinical questions and unmet needs.

Optimal design is necessary for the completion of clinical trials, and we have to enroll patients as quickly as possible. Innovative clinical trial designs are needed to demonstrate a drug’s efficacy and validate biomarkers of response in a short period of time.

While continuing to be strict about safeguarding our independence from pharmaceutical companies, we have to get enough funding to manage clinical trials and to make translational research happen.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

I try to achieve this first, as an oncologist treating patients and conducting clinical trials in my hospital, then, as part of a collaborative network such as SOLTI. The next natural step is to serve at the international level, and what better platform than BIG. It is an honor that the General Assembly has considered me to occupy such an important position.

What particular expertise do you think you can bring to the BIG EB? As an oncologist with vast translational research training, I intend to provide all my expertise to continue developing precision medicine trials through the BIG network.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

I certainly hope so. It’s up to us to make sure we design and conduct the best possible trials in order to achieve this.

“Unity is the source of our strength as academics.”

Interview with Dr Aleix Prat

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

My main motivation to serve on the BIG Executive Board is to make the biggest possible impact in the advancement of breast cancer research, changing paradigms and accelerating the development of therapeutic strategies for our patients.

In order to conquer breast cancer, we have to prevent breast cancer occurrence and cure patients affected by the disease. In order to treat patients optimally, good biomarkers to predict the effect of drugs are essential. Translational research associated with our clinical trials should clarify the significance of specific biomarkers, as well as help us define new clinical strategies to improve patient survival. BIG plays an important role as the biggest worldwide research network working to conquer breast cancer.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

Personally, time and money are the most important elements. We have to support young investigators to grow to act globally and consider good ideas to resolve the clinical questions and unmet needs.

Optimal design is necessary for the completion of clinical trials, and we have to enroll patients as quickly as possible. Innovative clinical trial designs are needed to demonstrate a drug’s efficacy and validate biomarkers of response in a short period of time.

While continuing to be strict about safeguarding our independence from pharmaceutical companies, we have to get enough funding to manage clinical trials and to make translational research happen.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

I try to achieve this first, as an oncologist treating patients and conducting clinical trials in my hospital, then, as part of a collaborative network such as SOLTI. The next natural step is to serve at the international level, and what better platform than BIG. It is an honor that the General Assembly has considered me to occupy such an important position.

What particular expertise do you think you can bring to the BIG EB? As an oncologist with vast translational research training, I intend to provide all my expertise to continue developing precision medicine trials through the BIG network.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

Personally, time and money are the most important elements. We have to support young investigators to grow to act globally and consider good ideas to resolve the clinical questions and unmet needs.

Optimal design is necessary for the completion of clinical trials, and we have to enroll patients as quickly as possible. Innovative clinical trial designs are needed to demonstrate a drug’s efficacy and validate biomarkers of response in a short period of time.

While continuing to be strict about safeguarding our independence from pharmaceutical companies, we have to get enough funding to manage clinical trials and to make translational research happen.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?
Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

In the current scenario of cancer research, where the academic lead of innovation is deeply handicapped by the constraints of research regulation, the role of large cooperative groups is of paramount importance.

Large transnational academic consortia are one of the only means to get relevant answers to a substantial number of the most urgent questions that patients and physicians face daily in the clinic.

I am deeply convinced of the importance of clinical research for optimal patient care. As a matter of fact, I have made it my personal commitment to make research my main focus in work; so being part of BIG Executive Board is a fantastic opportunity, and a personal challenge, to meet some of these own goals.

What particular expertise do you think you can bring to the BIG EB?

My contribution to the BIG EB will stream from three areas of expertise:

- Team group management: I currently serve as the scientific and general manager in a cancer hospital where my main focus, beyond patient care, is leading team work of health professionals towards research and development.
- My own scientific expertise in breast cancer biology, in particular in endocrine resistance and new therapies in this area.
- My expertise on early clinical trials organisation from a cooperative perspective, a task that I carried out at GEICAM, the Spanish Group of Breast Cancer.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

As I see it, the future success of BIG in changing breast cancer patients’ futures through research depends on its ability to adapt to a novel paradigm of research in cancer:

- BIG is currently experiencing the transition from a group for large phase III adjuvant trials to a network of investigators working together to design and perform complex trials in early phases with highly demanding patient stratification. Projects such as AURORA or OPTIMISM need to be boosted as priorities for the group.
- BIG needs to incorporate extensive knowledge into translational medicine in order to co-lead, alongside the other stakeholders, biologically sound research from an academic perspective.
- BIG needs to adapt its governance policy to allow being viewed by breast cancer investigators of all disciplines as their primary professional partner for research development. We need to follow our current progress regarding transparency and to open the group further to all areas/agents of research beyond medical oncology, including basic and value-based medicine researchers.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

I would anticipate that the major challenge to all breast cancer investigators is to delineate novel forms of clinical research that:

- go beyond traditional clinical trial design in order to speed-up the arrival of solutions to clinical practice;
- adapt research to the molecularly defined scenarios in the context of precision medicine;
- allow a larger number of patients to be part of research;
- allow the use of patient reported outcomes as major goals of novel developments, and
- contribute to healthcare systems’ sustainability.

In order to achieve these goals, cooperative research in BIG, further and beyond the traditional, highly motivated individual-based research, has a potential major role as THE key agent for breast cancer.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

Yes, we will soon see better outcomes with less toxicity from therapies through optimal patient stratification. We will see some patients being cured without surgery, and we will see blood-based patient screening and clinical follow-up. We will see chemotherapy progressively disappearing from most clinical instances… and much more.

I’ve made it my personal commitment to make research my main focus in work

Network

Interview with Dr Ander Urruticoechea

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

In the current scenario of cancer research, where the academic lead of innovation is deeply handicapped by the constraints of research regulation, the role of large cooperative groups is of paramount importance.

Large transnational academic consortia are one of the only means to get relevant answers to a substantial number of the most urgent questions that patients and physicians face daily in the clinic.

I am deeply convinced of the importance of clinical research for optimal patient care. As a matter of fact, I have made it my personal commitment to make research my main focus in work; so being part of BIG Executive Board is a fantast

What particular expertise do you think you can bring to the BIG EB?

My contribution to the BIG EB will stream from three areas of expertise:

- Team group management: I currently serve as the scientific and general manager in a cancer hospital where my main focus, beyond patient care, is leading team work of health professionals towards research and development.
- My own scientific expertise in breast cancer biology, in particular in endocrine resistance and new therapies in this area.
- My expertise on early clinical trials organisation from a cooperative perspective, a task that I carried out at GEICAM, the Spanish Group of Breast Cancer.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

As I see it, the future success of BIG in changing breast cancer patients’ futures through research depends on its ability to adapt to a novel paradigm of research in cancer:

- BIG is currently experiencing the transition from a group for large phase III adjuvant trials to a network of investigators working together to design and perform complex trials in early phases with highly demanding patient stratification. Projects such as AURORA or OPTIMISM need to be boosted as priorities for the group.
- BIG needs to incorporate extensive knowledge into translational medicine in order to co-lead, alongside the other stakeholders, biologically sound research from an academic perspective.
- BIG needs to adapt its governance policy to allow being viewed by breast cancer investigators of all disciplines as their primary professional partner for research development. We need to follow our current progress regarding transparency and to open the group further to all areas/agents of research beyond medical oncology, including basic and value-based medicine researchers.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

I would anticipate that the major challenge to all breast cancer investigators is to delineate novel forms of clinical research that:

- go beyond traditional clinical trial design in order to speed-up the arrival of solutions to clinical practice;
- adapt research to the molecularly defined scenarios in the context of precision medicine;
- allow a larger number of patients to be part of research;
- allow the use of patient reported outcomes as major goals of novel developments, and
- contribute to healthcare systems’ sustainability.

In order to achieve these goals, cooperative research in BIG, further and beyond the traditional, highly motivated individual-based research, has a potential major role as THE key agent for breast cancer.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

Yes, we will soon see better outcomes with less toxicity from therapies through optimal patient stratification. We will see some patients being cured without surgery, and we will see blood-based patient screening and clinical follow-up. We will see chemotherapy progressively disappearing from most clinical instances… and much more.

Interview with Dr Ander Urruticoechea

Could you please explain what motivated you to apply and serve on the BIG Executive Board (EB)?

In the current scenario of cancer research, where the academic lead of innovation is deeply handicapped by the constraints of research regulation, the role of large cooperative groups is of paramount importance.

Large transnational academic consortia are one of the only means to get relevant answers to a substantial number of the most urgent questions that patients and physicians face daily in the clinic.

I am deeply convinced of the importance of clinical research for optimal patient care. As a matter of fact, I have made it my personal commitment to make research my main focus in work; so being part of BIG Executive Board is a fantastic opportunity, to meet some of these own goals.

What particular expertise do you think you can bring to the BIG EB?

My contribution to the BIG EB will stream from three areas of expertise:

- Team group management: I currently serve as the scientific and general manager in a cancer hospital where my main focus, beyond patient care, is leading team work of health professionals towards research and development.
- My own scientific expertise in breast cancer biology, in particular in endocrine resistance and new therapies in this area.
- My expertise on early clinical trials organisation from a cooperative perspective, a task that I carried out at GEICAM, the Spanish Group of Breast Cancer.

Please cite three elements that you find critical for the continued success of BIG in the next decade?

As I see it, the future success of BIG in changing breast cancer patients’ futures through research depends on its ability to adapt to a novel paradigm of research in cancer:

- BIG is currently experiencing the transition from a group for large phase III adjuvant trials to a network of investigators working together to design and perform complex trials in early phases with highly demanding patient stratification. Projects such as AURORA or OPTIMISM need to be boosted as priorities for the group.
- BIG needs to incorporate extensive knowledge into translational medicine in order to co-lead, alongside the other stakeholders, biologically sound research from an academic perspective.
- BIG needs to adapt its governance policy to allow being viewed by breast cancer investigators of all disciplines as their primary professional partner for research development. We need to follow our current progress regarding transparency and to open the group further to all areas/agents of research beyond medical oncology, including basic and value-based medicine researchers.

What are the biggest challenges currently faced by all stakeholders of the breast cancer research area? How do you think BIG can play a significant role in this context?

I would anticipate that the major challenge to all breast cancer investigators is to delineate novel forms of clinical research that:

- go beyond traditional clinical trial design in order to speed-up the arrival of solutions to clinical practice;
- adapt research to the molecularly defined scenarios in the context of precision medicine;
- allow a larger number of patients to be part of research;
- allow the use of patient reported outcomes as major goals of novel developments, and
- contribute to healthcare systems’ sustainability.

In order to achieve these goals, cooperative research in BIG, further and beyond the traditional, highly motivated individual-based research, has a potential major role as THE key agent for breast cancer.

Do you think we will see practice-changing results from breast cancer research in the next decade? Which ones?

Yes, we will soon see better outcomes with less toxicity from therapies through optimal patient stratification. We will see some patients being cured without surgery, and we will see blood-based patient screening and clinical follow-up. We will see chemotherapy progressively disappearing from most clinical instances… and much more.
Welcoming new Member Groups

Since June 2017 BIG encompasses **59 members worldwide**.

**Four new members** have recently joined BIG, bringing along their own local experience and further enlarging BIG’s international network reach:

- **Georgian Cancer Study Group (GCSG), Georgia**
- **Breast Disease Professional Committee of CMEA (BDPCC), China**
- **Korean Cancer Study Group (KCSG), South Korea**
- **Thai Society of Clinical Oncology (TSCO), Thailand**

The voting representatives of these new members introduce their respective groups, sharing their expectations and challenges.
Why did your group join the BIG network? What do you expect from this affiliation?

GCSG is a not-for-profit organisation focused on cancer research in Georgia. Since the establishment of the group in 2006, we have been working in several directions to improve breast cancer treatment standards, public awareness and scientific research. Joining BIG will help us to take the academic research environment to the next level, improve existing programmes and deliver better treatment to patients.

What are the biggest challenges for your group? Do you think that these are likely to be shared with other BIG member groups?

Despite making huge improvements both in scientific and clinical directions, Georgia still has more to achieve. GCSG has been actively involved in changing the general approach to cancer research and treatment in Georgia by working both with the public and private sectors. Improving treatment standards and the research environment as well as reducing talent drain still are major challenges to overcome.

How are clinical trials run at the GCSG? In which clinical trials or research programmes is your group currently involved?

Georgia has been endorsed by the clinical research industry, becoming one of the most promising countries in the region. Since the late 1990s, clinical research has been steadily growing thanks to the transparent and straightforward regulatory environment, investigators’ dedication to quality, and extremely positive feedback from the global pharmaceutical industry and regulators. GCSG members have participated in hundreds of clinical trials so far. Georgia is always on the list of the top recruiting countries while maintaining the quality of data.

In the different cancer centres affiliated with GCSG, the following interesting clinical trials are currently open:

- A randomised, multicentre, open-label trial, comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab emtansine plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer (Roche)
- A randomised phase II study of fulvestrant in combination with either the dual mTOR inhibitor AZD2014 or everolimus, or fulvestrant alone in ER-positive metastatic breast cancer (Astra Zeneca)
- A phase II, randomised, placebo-controlled study of the AKT inhibitor AZD5363 in combination with paclitaxel in triple-negative advanced or metastatic breast cancer (Astra Zeneca)
- A multicentre, double-blind, randomised, parallel-group, phase III study to compare the efficacy and safety of epirubicin versus trastuzumab in patients with HER2+ metastatic breast cancer (Mylan)
- A phase III, double-blind, randomised, parallel-group, active-controlled study to compare the efficacy and safety of CT-P6 and trastuzumab as neoadjuvant and adjuvant treatment in patients with HER2-positive early breast cancer (Celltrion)

What does the breast cancer scenario look like today in Georgia and how do you think it will evolve in the next decade?

Breast cancer research and treatment have significantly improved in the last decade. Major challenges have been overcome. Several years ago there were no major screening or treatment programmes, academic research was halted and one of the most significant factors in contemporary cancer treatment – multidisciplinary approach to cancer treatment – was non-existent. In 2008, the breast cancer screening programme was launched, which was one of the most important steps forward. The patient advocacy group Europa Donna Georgia was established, as well as several treatment programmes funded by the government. The local oncology society endorsed a multidisciplinary approach to breast cancer treatment, and a new generation of medical oncologists has entered the scene. All of these factors have translated into better patient care, as well as increased life expectancy and quality of life. GCSG has been part of every major change so far and continues to be the leading group behind future development of the cancer research environment in Georgia.

Finally, what do you consider to be your group’s main achievements so far?

We are happy to be the major group behind the aforementioned positive changes happening in Georgia. Although more still has to be done, we are proud of the work we have done for the search and education of young talent, promotion of breast cancer research, and improvement of treatment standards.

www.gcsg.ge
The China Medicine Education Association (CMEA) is a national level, academic non-profit organisation. The Breast Disease Professional Committee of CMEA (BDPCC) is a secondary branch of the CMEA, which was established on 30 January 2015. The BDPCC has 415 members, most of whom are breast surgeons, oncologists and pathologists. Our members come from over 300 hospitals, spread over 30 provinces in China.

The main activities of the BDPCC are to
1) offer continuing education to community physicians with the purpose to train them in breast disease treatment
2) hold the Breast Disease Multidisciplinary Symposium and the Great Wall Breast Cancer Conference every year
3) launch a multicentre prospective observational study, with the purpose of collecting breast cancer tissue samples for further sequencing and analysis
4) play a leading role in multicentre clinical trials in China and participate actively in international clinical trials.

BDPCC’s researchers believe that the collaboration with BIG will expedite international research and its impact on patients’ lives. Bringing local experience and knowledge, the BDPCC will contribute to better serve breast cancer physicians and patients, both in China and beyond.

Why did your group join the BIG network? What do you expect from this affiliation?

The vision of BDPCC is in accord with that of BIG: “We will find a cure for breast cancer through global research and collaboration”. What we are doing is pushing forward breast cancer therapy in China. We aim to communicate and enhance coordination with the international community on scientific research and clinical trials.

Joining the BIG network, BDPCC is ready to collaborate with all the excellent investigators and outstanding institutions all over the world. We can work together to solve clinical problems and promote improved breast cancer therapy.

What are the biggest challenges for your group? Do you think that these are likely to be shared with other BIG member groups?

Chinese research institutes are playing more and more important roles at the international level. Meanwhile, the China Food and Drug Administration (CFDA) has already announced the “Fast-Track-Application” of new drugs. With BDPCC’s involvement in international research, we aim to reach a win-win situation for BIG and the trial sponsors.

By becoming a member of BIG, we would like to bond with other member groups and cooperate together in seeking further progress in breast cancer research and therapy.

How are clinical trials run at the Breast Disease Professional Committee of CMEA? In which clinical trials or research programmes is your group currently involved?

BDPCC is a highly motivated group, affiliated with hospitals that have a high recruitment potential, which is crucial for the success of clinical trials. We have an extensive network of breast cancer investigators, with longstanding relationships between hospitals all over China. This allows quick access to principal investigators across a broad range of hospitals in China, and enables us to contribute to the successful recruitment of clinical trials.

BDPCC has the ability to sponsor trials with its member hospitals. We have already launched a prospective observational study with the objective to perform whole genome sequencing in patients with breast cancer. We also contract with other sponsors, such as pharmaceutical partners.

The BDPCC has recently launched the Chinese women gene signature screening programme. Could you tell us more about this programme and its objectives?

We launched the Chinese women gene signature screening programme on April 2016, which is a multicentre prospective observational study. The objectives of the study are to find the breast cancer related gene mutations in Chinese patients, as well as guide and support rapid development of individualised targeted drugs. We are aiming to enrol 20,000 Chinese patients with a primary diagnostic invasive ductal carcinoma of the breast, metastatic patients are excluded. Clinical data is collected at diagnosis, and patients are then followed-up for 10 years, with the aim to compare the primary tumour tissue with the para-tumour tissue and blood samples, which will be drawn before any treatment.

We are planning to do the whole genome and RNA sequencing on the breast tumour samples. This will provide us with detailed information about the somatic mutations (SNP, Rearrangement), copy number

www.cmea.org.cn
variations and neoantigen analysis. Our aim is to unveil the mask of the gene signature of Chinese women with breast cancer.

We have obtained Ethics Committee approval by The General Hospital of People's Liberation Army (301 Hospitals) and the protocol, ICF, eCRF are being developed. We have recruited 40 hospitals across China, covering more than 30 provinces. We are now working on the legal documents translation and registration on clinicaltrials.gov (not yet finished). There are no related publications yet.

Finally, what do you consider to be your group's main achievements so far?
The BDPCC has achieved some good results, in areas such as academic research and technical communication, continuing education and training in district and community hospitals of China. The launch of the breast cancer gene mutation screening programme in China will promote precision therapy for Chinese women.

Also important is the continuing education project of breast cancer diagnosis and treatment, “County education, China tour. This helps all BCPCCC members to stay up to date with research information.

Finally, individuals affiliated with the BDPCC have experience participating in international clinical trials with different sponsors, including major pharmaceutical companies.

A few examples of clinical trials involving hospitals affiliated with BDPCC.

A multicentre, randomised, double-blind phase 3 study of palbociclib (oral CDK 4/6 inhibitor) plus letrozole versus placebo plus letrozole for the treatment of previously untreated Asian postmenopausal women with ER+, HER2- advanced breast cancer (NCT02297438, recruiting)

A two-cohort, open-label, multicentre study of trastuzumab emtansine (TDM1) in HER2-positive locally advanced or metastatic breast cancer patients who have received prior anti-HER2 and chemotherapy-based treatment (NCT01702571, recruiting)

Double-blind, randomised, multicentre, phase 3 clinical study to compare the efficacy and to evaluate the safety and immunogenicity of trastuzumab biosimilar HLX02 and EU-sourced Herceptin® in HER2-positive, locally recurrent or previously untreated metastatic breast cancer (NCT03084237, recruiting)

A randomised, double-blind, placebo-controlled, phase 3 study to compare NSAI (anastrozole or letrozole) plus abemaciclib, a CDK4 and CDK6 inhibitor, or plus placebo, and to compare fulvestrant plus abemaciclib or plus placebo in postmenopausal women with hormone receptor-positive, HER2-negative, locally recurrent or metastatic breast cancer (NCT02763566, recruiting)

The study of goserelin plus fulvestrant comparing with goserelin plus anastrozole for advanced breast cancer (phase 2, NCT02072512)

A randomised, double-blind, parallel-group, multicentre, phase 3 study to compare the efficacy and tolerability of fulvestrant (FASLODEX) 500 mg with anastrozole (ARIMIDEX) 1 mg as hormonal treatment for postmenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer who have not previously been treated with any hormonal therapy (NCT01602380, active but not recruiting).
The Korean Cancer Study Group (KCSG) is a multicentre oncology clinical trials group representing Korea. It was established on 12 June 1998 and constantly attempts to advance oncology through collaborative cancer studies, presenting rational policy to improve anti-cancer therapies and clinical trial practices, with the ultimate goal of fostering and enhancing public health. We have 720 members from 110 institutes or hospitals in Korea, and most of our members are well-trained and highly motivated medical oncologists. KCSG consists of a protocol review committee, an IRB (Institutional Review Board), a planning committee, an education committee, an international relationship committee, a public relations committee, and 10 disease committees including the Breast Cancer Committee. KCSG has its own data centre. CRAs (Clinical Research Associates), data managers and biostatisticians from the data centre work on study coordination, regulatory affairs, monitoring and data management. We also hold meetings for education, such as the Clinical Research Methodology Workshop, the Clinical Trial Education Workshop, the Institutional Review Board Workshop, and Collaborative R & D (Research & Development) Symposia. Recently, an independent QC (Quality Control) committee was incorporated into the data centre to facilitate quality issues, which is outsourced. Our global partners for cooperative activities include ECOG (Eastern Cooperative Oncology Group), the EORTC (European Organisation for Research and Treatment of Cancer), AGITG (Australasian Gastro-Intestinal Trials Group), SWOG (South West Oncology Group) and TRIO (Translational Research in Oncology).

Why did your group join the BIG network? What do you expect from this affiliation?

BIG is an international organisation of academic breast cancer research groups from around the world. KCSG’s mission is similar to that of BIG – conducting clinical research and contributing to better patient outcomes – and we also know that international collaboration can make it happen so much more quickly and efficiently. This is why we joined the BIG network. With the BIG affiliation, many more Asian breast cancer patients can now be involved in global clinical trials, so they can have a chance of better outcomes with new drugs. At the same time, BIG research can get results that are more globally representative of various races or countries, especially for Asian breast cancer patients. Study groups, pharmaceutical companies and governments need a more globally representative set of trial results to share. As a growing clinical trials group, we think we can learn from BIG about the harmonisation of collaborative work through international collaboration, including translational research.

What are the biggest challenges for your group? Do you think that these are likely to be shared with other BIG member groups?

Although Korea has participated very actively in pharmaceutical sponsor-initiated clinical trials, there are many challenges in the real world, especially for investigator-initiated clinical trials. First, as time goes on, it is becoming very difficult to receive investigational agents from global pharmaceutical companies for investigator-initiated trial platforms. Second, we faced major challenges for appropriate government funding for clinical trials. Besides the overburdened role as an investigator, other challenges are limited human resources, including data management, operation and international relationships. A particular
Published articles of our KCSG Breast Cancer Committee

<table>
<thead>
<tr>
<th>No</th>
<th>Study type</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Metastatic</td>
<td>A multicentre, randomised phase II, 3-arm, open-label study of goserelin plus fulvestrant versus goserelin plus anastrozole versus goserelin alone for hormone receptor-positive, tamoxifen pre-treated, premenopausal women with recurrent or metastatic breast cancer [PROCEED]. KCSG-BR10-04</td>
</tr>
<tr>
<td>2</td>
<td>Metastatic</td>
<td>Phase III multicentre randomised open-label study of irinotecan plus capcitabine versus capcitabine in patients previously treated with anthracycline and taxane for HER2-negative metastatic breast cancer [PROCEED]. KCSG-BR11-01</td>
</tr>
<tr>
<td>3</td>
<td>Metastatic</td>
<td>Randomised phase II study of lapatinib plus vinorelbine versus vinorelbine in patients with HER2-positive metastatic breast cancer progressed after lapatinib and trastuzumab treatment. KCSG-BR11-06</td>
</tr>
<tr>
<td>4</td>
<td>Metastatic</td>
<td>A phase II, multicentre, randomised trial of eribulin plus gemcitabine (EG) vs. paclitaxel plus gemcitabine (PG) in patients with HER2-negative metastatic breast cancer as first-line chemotherapy. KCSG BR13-11</td>
</tr>
<tr>
<td>5</td>
<td>Metastatic</td>
<td>Prospective cohort and analysis of clinical outcomes of patients with metastatic or recurrent breast cancer. KCSG BR14-07</td>
</tr>
<tr>
<td>6</td>
<td>Adjuvant</td>
<td>A randomised, multicentre, open-label, phase II trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as neoadjuvant therapy in patients with early triple-negative breast cancer (PEART). KCSG BR 15-01</td>
</tr>
<tr>
<td>7</td>
<td>Metastatic</td>
<td>A phase II randomised study of palbociclib in combination with exemestane plus GnRH agonist versus capcitabine in premenopausal women with hormone receptor-positive metastatic breast cancer. KCSG BR 15-10</td>
</tr>
</tbody>
</table>

Ongoing IITs in KCSG Breast Cancer Committee

<table>
<thead>
<tr>
<th>No</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Docetaxel plus enrubacin as first-line chemotherapy in MBC (KCSG 01-10-05): phase II trial and the predictive values of circulating HER2 extracellular domain and vascular endothelial growth factor. KCSG-BR06-01.</td>
</tr>
<tr>
<td>2</td>
<td>Zoledronic acid prevents bone loss in premenopausal women with early breast cancer undergoing adjuvant chemotherapy: a phase II trial of the Korean Cancer Study Group (KCSG-BR06-01).</td>
</tr>
<tr>
<td>3</td>
<td>Phase II trial of paclitaxel, gemcitabine, and trastuzumab combination therapy in HER2 positive stage II/III breast cancer: the Korean Cancer Study Group [BR 07-01].</td>
</tr>
<tr>
<td>4</td>
<td>Multicentre phase II trial of bevacizumab combined with docetaxel-carboplatin for the neoadjuvant treatment of triple-negative breast cancer (KCSG BR-0905).</td>
</tr>
<tr>
<td>5</td>
<td>Phase II, multicentre, randomised trial of maintenance chemotherapy versus observation in patients with metastatic breast cancer after achieving disease control with six cycles of gemcitabine plus paclitaxel as first-line chemotherapy. KCSG-BR07-02.</td>
</tr>
<tr>
<td>6</td>
<td>A randomised, multicentre, open-label, phase II study of once-per-cycle DA-3031, a biosimilar pegylated G-CSF, compared with daily filgrastim in patients receiving TAC chemotherapy for early-stage breast cancer. KCSG BR10-03.</td>
</tr>
</tbody>
</table>

Collaboration is ongoing between our Breast Cancer Committee and the U.S. NCI (National Cancer Institute) for the RXPONDER trial (S1007), a phase III randomised clinical trial of standard adjuvant endocrine therapy +/- chemotherapy in patients with 1-3 positive nodes, hormone receptor-positive and HER2-negative breast cancer with recurrence score (RS) of 25 or less. Also, recently, we launched the ECOG-EPRIN (E2112) trial which compares the additional entinostat to exemestane in treating patients with recurrent hormone receptor-positive cancer that is locally advanced or metastatic.

Finally, what do you consider to be your group's main achievements so far?

For the past 10 years, KCSG focused on nation-wide collaborative clinical research throughout Korea, while also setting the stage for broad-scale, multicentre clinical research in order to become a truly representative study group of Korean medical oncologists. Therefore, we have established infrastructures for multicentre clinical trials, including fast regulatory controls and data management systems. Based on these achievements, we have not only contributed high-volume patient recruitment but also high-quality data in global collaborative studies, and we are now regularly invited to serve as advisory board member in various clinical trials. Recently we have increased our reach outside the nation and contribute to global collaborative clinical trials as part of a core group of Asian breast cancer research societies.
The Thai Society of Clinical Oncology (TSCO) is a non-profit organisation, founded in 1996, with the primary goals to educate medical oncologists through major cancer centres in university hospitals, and to improve cancer care along with other professional societies involved in treatment and prevention of cancer. Members include 219 registered medical oncologists practicing at various levels of cancer care throughout the country. In addition to advancing education of medical oncology, TSCO is committed to providing education for other disciplines to advance quality of cancer care in Thailand.

**Vision and Mission**

1. To promote education and medical research in the fields of oncology and related disciplines.
2. To establish/exchange academic experiences and research results among its members
3. To promote unity and mutual assistance among members of the society
4. To coordinate and share ideas with other medical associations and institutions, both locally and abroad
5. To promote and improve the condition of cancer care in Thailand, particularly for the public sector

**Why did your group join the BIG network? What do you expect from this affiliation?**

As BIG has been a very reputable organisation in breast cancer research, being able to join the BIG network is a golden opportunity not to be missed. Our group is very young and does not have much experience in collaborative-type clinical research. We hope that by having a chance to observe and work with BIG, we will be empowered to grow stronger and become a leader in breast cancer research in Thailand, which would help to improve breast cancer care for our people.

**What are the biggest challenges for your group? Do you think that these are likely to be shared among other BIG member groups?**

There are certainly many challenges that our group is facing. But, one of the biggest challenges is, in my opinion, individualisation, rather than collaboration. This could be considered as one of the Thai cultural attitudes from the past, which has to change, in particular during this time of rapid data exchange and globalisation. So what we are trying to do is to change this mindset so that we can work together and network for a better output which, I think, is very possible. We need to have data from our Thai patients, which are very sparse at present. With that, if those data become available, for example, it may come up that we may need a different approach to treating our patients. Of course, other challenges remain, including a need to improve infrastructure, and to address inadequate funding and manpower. But nevertheless, we are looking forward to building a new culture of research, which should have some impact in the near future.

**How are clinical trials run at TSCO? In which clinical trials or research programmes is your group currently involved?**

Most of our clinical trials are conducted mainly in academic centres across Thailand. The majority of these are pharmaceutical company sponsored-based trials. Examples include HERA, CLEOPATRA, MARIANNE, EMILIA, BOLERO 2/3, MONALEESA 2 and PALOMA 4. Currently, we are planning to conduct a breast cancer registry based on data from our members nationwide. This will be the first database for us and hopefully will spark some more ideas for future collaborative research.

**Finally, what do you consider to be your group’s main achievements so far?**

As we have just started the collaborative breast cancer group within TSCO, I think this would be considered the first achievement from our point of view. We have discussed this issue for quite some time and finally we could do it! And a big thank you to BIG for allowing us to join this prestigious network. We do hope that this will bring us a few steps forward towards a fruitful research collaboration.

**www.thethaicancer.com**
Member activities

Breast Cancer Trials - New Name for the ANZBCTG

By Anna Fitzgerald

For almost 40 years, the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG) has been committed to finding new and improved breast cancer treatments and prevention strategies for every patient. This has been supported by our fundraising department, the Breast Cancer Institute of Australia (BCIA), which has raised more than $80 million for our research programme in the last 20 years thanks to the generosity of Australian individuals and corporate supporters.

We have worked closely with our international collaborators over this time and, together, our work has improved the treatment of breast cancer, led to changes in the way breast cancer is managed, and saved millions of lives.

The clinical trials landscape has changed markedly since the ANZBCTG formed some four decades ago, and we are operating in an increasingly competitive and disruptive research and not-for-profit environment in Australia and New Zealand. For this reason, the ANZBCTG embarked on a lengthy and extensive rebranding project over the last year with the aim of bringing our two brands, the Australia and New Zealand Breast Cancer Trials Group and the Breast Cancer Institute of Australia, together under one name.

Our new name is Breast Cancer Trials and it will be launched in September 2017. It clearly defines the research we conduct, which is our unique point of difference to other breast cancer and cancer charities. Our logo recognises our place in the world, with a map of Australia and New Zealand, and resembles a fingerprint that speaks to the tailoring of breast cancer treatments to every person and their unique set of circumstances.

So while our name has changed, our commitment to collaborative, high quality breast cancer clinical trials research has not. We are still the same group of world-class professionals based in Australia and New Zealand on a mission for people affected by breast cancer to live better, to live longer, and to never die from breast cancer.

Breast Cancer Trials is grounded and defined by one simple belief. We can and we will find new and better treatments and prevention strategies for every person affected by breast cancer that saves lives today, tomorrow and forever.

Retirement of Professor John Forbes AM from the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG)

Professor John Forbes AM has recently retired from his role as the Director of Research at Breast Cancer Trials (until recently known as the Australia and New Zealand Breast Cancer Trials Group or ANZBCTG), after almost 40 years with the group.

Prof Forbes was one of the founding members of the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG), an academic research group that has been involved in BIG from the very first days. As a former member of BIG’s Executive Board – BIG had the pleasure to have him on board as Vice-Treasurer from 2005 to 2010 – he has always played a key role in shaping the international breast cancer research agenda.

In his extraordinary career, Prof Forbes has made national and international contributions to the development and conduct of breast cancer clinical trials, which have improved survival rates and treatments available to women at risk or diagnosed with breast cancer.

His primary area of research was with large randomised trials that can produce reliable and definitive data, which can lead to improved outcomes for women. This encompassed prevention, systemic and local treatment of early breast cancer and treatment of advanced breast cancer.

Prof Forbes has definitely been an instrumental part of the success of the ANZBCTG’s research programme. He was the National Group Coordinator of the ANZBCTG from 1984-2008, was an ANZBCTG Board Director from 1991-2008 and 2013-2016, was the ANZBCTG’s
Director of Research from 2008-2016 and is a member of the ANZBCTG’s Scientific Advisory Committee.

Prof Forbes established the Breast Cancer Institute of Australia in 1994, to help fund the ANZBCTG’s research programme. He also established the first oncology consumer advisory group in Australia, the ANZBCTG’s Consumer Advisory Panel, to work with researchers in breast cancer trials. He has Chaired and Co-Chaired many international clinical trials including the IBIS-I and IBIS-II trials (International Breast Cancer Prevention Study), and the ATAC clinical trial.

Throughout his career, John Forbes has received numerous awards. In 2015 he received the New South Wales (NSW) Premier Award for Outstanding Cancer Research of the Year and, in 2012, he was awarded a Member of the Order of Australia for service to medicine in the field of breast cancer research, to the development of improved clinical practice standards and service to the community.

BIG would like to extend its heartfelt thanks and great admiration for Prof Forbes’s extraordinary work and precious contribution to breast cancer research in terms of treatment and prevention both in Australia and internationally.

In an interview with BIG in 2015 John Forbes confided that his particular concern was to achieve better outcomes for all women, with all stages of breast cancer, and for those women at risk of getting breast cancer.

Dr Soozy Smith, Chief Executive Officer of the ANZBCTG, has taken over Prof Forbes’s role as the Group’s Voting Representative within the BIG network.

More information about ANZBCTG’s activities can be found at www.bcia.org.au

Improve yourself at IMPROving ABCSG

By Nicole Scheiber and Michael Gnant

The Austrian Breast & Colorectal Cancer Study Group (ABCSG) created something completely new in advanced training – the advanced training course for physicians ‘IMPROving ABCSG’.

This event, which focuses on breast cancer, unites spontaneity, knowledge and interactivity. Three ABCSG experts present one case report each with fixed parameters on the one hand, and variable parameters on the other, e.g. patient’s age, Ki67-status, year of treatment. The audience can vote via iPad which of the mutable parameters shall be relevant for the notional patient and, together with the fixed parameters, you create a challenging case. Three or four volunteers from the audience then discuss this case together with the presenter in a separate room and devise an appropriate therapeutic strategy.

Meanwhile, the chairpersons discuss all the other parameters together with the remaining audience, so you can talk about treatment strategies for a variety of different patients in a short time. When the small group of volunteers has finished, one of them presents their suggested therapy to the audience and they discuss together whether it was a good choice (and why), which trials confirm their decision, and, of course, what they would have to change in their strategy if only one single parameter was different.

This challenging and enjoyable event took place for the first time in May this year in Vienna and Graz (Austria), organised by the ABCSG. IMPROving provides fascinating and unexpected case reports to be solved by the audience, a huge amount of interactivity and, of course, a high degree of fun for the attendees.

“We are glad that the participants enjoyed this advanced training course and also were able to learn a lot in a short time”, said ABCSG’s president Michael Gnant, MD, outlining the feedback. “It’s not easy to ‘invent’ something completely new which really works out as planned, but, actually, we did it!”

More information about ANZBCTG’s activities can be found at www.bcia.org.au
Clinical Trials Support Unit

By Marielle Sautois

The Breast Adjuvant Study Team (BrEAST) has joined the Institut Jules Bordet Clinical Trials Support Unit (CTSU).

The Breast Adjuvant Study Team (BrEAST) was established by Dr. Martine Piccart in 1997 at Belgium’s world-renowned cancer centre, Institut Jules Bordet (IJ). BrEAST was a specialised data centre conducting large, international phase III studies in breast cancer aiming to register new drugs. The unit set, coordinated and managed the data collected in these trials run in collaboration with pharmaceutical companies and the Breast International Group (BIG). BrEAST successfully managed several trials, such as the BIG 01-01 HERA trial, BIG 02-06/D063D ALTTO trial and BIG 04-11/BO25126/TOC4939G APHINITY trial.

In 2013 the IJ upper management decided to create an institutional structure to unite all the competencies, expertise and resources required to conduct high quality clinical research at the institute. To fulfill this objective, the Clinical Trials Support Unit (CTSU) was created to assist researchers in the conduct of clinical trials for all cancer types, for clinical trials phases I, II and III, for IJ-sponsored trials or for non-IJ-sponsored trials. BrEAST joined the CTSU as its data management unit. This unit is responsible for the data management activities implemented for all clinical trials managed by the CTSU.

The CTSU manages the operational activities both for investigator-initiated trials (sponsored by IJ) and for clinical trials sponsored by pharmaceutical companies, biotech companies or other academic institutions.

The CTSU expertise covers (cf. figure 1):

- **Project management**: coordination of various logistical aspects of clinical trials as per standard procedures/guidelines and clinical trial timelines
- **Regulatory affairs**: submission of clinical trials to competent authorities
- **Pharmacovigilance**: management of serious adverse events and safety reports
- **Data management**: case report form creation, data collection from sites, data cleaning for analysis
- **Monitoring**: oversight of trial conduct by participating sites, assessments of compliance with clinical trial protocol and Good Clinical Practice and applicable regulatory requirements
- **Central imaging review (Orilab)**: management of imaging data through standardisation and harmonisation of imaging data acquisition, analysis and storage
- **Translational research**: biological samples collection and analysis.

Moreover, the CTSU benefits from a close collaboration with the IJ medical team. Medical advisors and oncology fellows are involved in the review of adverse reactions and toxicities on a daily basis. This ensures that any global safety issues or trends are quickly identified and all necessary actions implemented.

The whole CTSU team is dedicated to effectively and efficiently answer the intended research question about the benefits and risks of a medical product or procedure while ensuring the protection of human subjects participating in clinical research.

Figure 1: Ub CTSU organisational units

Figure 2: New Institut Jules Bordet foreseen for 2020 (credit IJ)
The vibrant activity of the Italian Clinical Research Oncology Group (GOIRC) within the BIG network is exemplified not only by its active participation in BIG lead and co-lead trials, but also by its innovative and constantly frontline clinical investigations. GOIRC, one of the oldest Italian cooperative groups of its kind and co-founding Member of BIG, is a not-profit entity entirely led by physician scientists, clinical research coordinators, and other experts in the field of oncological research who devote part of their time to the Group. GOIRC’s mission is to bring forward clinical research in breast cancer (BC) and several cancer disease entities, as well as to promote free, independent, academia-driven studies amongst its affiliated centres.

Earlier this year, GOIRC was proud to have among its associated Investigators (Policlinico S. Martino from Genoa, Italy) one of the top three enrollers in the world for LORELEI, a phase II trial dedicated to exploring the activity of taselisib in combination with letrozole in the neoadjuvant setting. However, GOIRC is also a cradle of ideas in itself.

Two clinical and translational studies, conceived in one of the founding cities of GOIRC – Parma University Hospital – have advanced well: ERIGE, a phase II prospective trial aiming to explore the combination of eribulin and gemcitabine in first and second line metastatic triple negative BC, showed a clinical benefit rate of 49%, and was presented at ASCO earlier this year; ImmunHer is a phase II study assessing the immunological differences of two ways of administering trastuzumab (intravenous -iv- versus subcutaneous -sc-) in samples obtained from BC patients undergoing neoadjuvant treatment with a pertuzumab and trastuzumab iv or sc regimen.

Finally, from the Policlinico Hospital of Modena comes the coordination of a new proposal about a national registry for the follow-up of patients treated with palbociclib: since it is currently unclear which choice of treatment, and which response to such treatment HR+ patients will show after exposure to the first CDK4/6 inhibitor introduced in clinical practice, GOIRC will collect valuable information with the goal of optimising the sequence of therapies in this large subpopulation of BC patients.

In summary, after many years GOIRC remains one of the main Italian interfaces of BIG with Italian clinical centres involved in BC treatment, and showing more and more activity, involvement, and dedication in this field. The current GOIRC President is Prof Francesco Di Costanzo from University Hospital Careggi in Florence. More news about GOIRC can be obtained from our website, www.goirc.org.

Vibrant activity at GOIRC
By Gabriele Zoppoli
GEICAM has been keeping up with the times

By the GEICAM team

Biobanks are technological platforms that aim to provide researchers with access to high-quality biological sample collections and associated clinical data, particularly to support biomedical research projects of excellence.

The GEICAM Biobank or bGEICAM (www.geicam.org/en/medical-research-professionals/biobank) is a non-profit infrastructure for the management of a large number of valuable biological samples and clinical information, from both healthy donors and patients included in multi-centric clinical trials and other biomedical studies in breast cancer.

The main goal is to provide researchers with precious biological sample collections for the development of translational research of excellence, guaranteeing its rational, ethical and legal management and usage. Thus, bGEICAM fosters translational research aimed at improving the knowledge of the molecular basis and etiopathogenesis of breast cancer, the discovery of novel therapies, as well as the development of personalised medicine in this field. For this purpose, the biobank stimulates global translational collaborative research with other outstanding national and international breast cancer research groups and networks. It also supports oncology screening programmes, national registries and epidemiology initiatives.

All research projects applying to access samples from the biobank must be evaluated and approved by both the external scientific and ethical committees associated with the biobank before samples and related clinical data can be released. The committees include a multidisciplinary group of specialists in medical oncology, molecular pathology, radiotherapy and nuclear medicine, surgery, epidemiology, as well as members of patient advocacy organisations, lawyers and pharmacovigilance and regulatory experts in clinical trials.

Since 2015 bGEICAM has been part of the Spanish National Biobanks Network Platform of the National Institute of Health Carlos III (www.redbiobancos.es) as an associated member, specifically participating in the R&D and Innovation Group aiming to identify tissue quality markers and develop new procedures for tissue processing and storage.

**GEICAM Exercise-Oncology project**

The GEICAM Exercise-Oncology Project is based on the identified need to develop this area in Spain. Led by a research-experienced group, it aims to be a reference in Spain and Europe about exercise in oncology. The project focuses on three different pillars: build a professional network of researchers, educate new qualified professionals and inform both patients and society at large about the importance of being active.

All our research projects focus on breast cancer patients. At this time, we are running four studies, focused on achieving relevant clinical results. In this context, the effects of exercise on tumour and body physiology and the impact of exercise on patient outcomes are the main objectives of our studies.

**Educational programmes**

Educational programmes in the exercise-oncology area are being developed in collaboration with different universities. Our intention is to prepare specialised professionals who would be able to train patients with cancer and to create a network in Spain that may be involved in future research projects. The aim is also to educate other healthcare professionals about exercise-oncology.

**Information sessions**

Both patients and the general public attend information sessions developed by GEICAM. Upon request, the GEICAM Coordinator of Exercise Programmes in Oncology gives lectures in some hospitals to educate patients about exercise-oncology. Talks addressed to the general public are promoted by various companies from different fields and who are interested in breast cancer prevention.

With the GEICAM Exercise-Oncology Project, our Group wishes to respond to an increasing need with a comprehensive set of initiatives to become a reference partner in this area.

**Several awards received this year**

2017 has been a fruitful year for GEICAM (Spanish Breast Cancer Group), as it has been awarded various prizes that recognise its important contributions to the field of breast cancer. These include GEPAC's (Spanish Cancer patients Group) Albert Jovell Award in the Corporate and Social Responsibility category for the campaign “Little changes, big achievements”.

Member activities
XIV Women’s Run

The XIV Women’s Run, celebrated on 7 May in Madrid, raised more than €10,000 for GEICAM. This money will be invested in the group’s EfiK project, dedicated to the investigation of how physical exercise could benefit women with breast cancer by affecting the way the tumour evolves, reducing side effects or helping achieve well-being.

“Despite the evidence that exercise has an effect on how the tumour evolves, we still know little about its effect on tumour tissue”, says Dr Miguel Martín, President of GEICAM.

Women’s Run is the biggest sports event for women in Europe, gathering more than 130,000 participants.

GEPAC’s V Albert Jovell Awards

Dr Chacon, GEICAM’s board member, receives the V Alberto Jovell award. Behind, Begoña Barragán, GEPAC’s president and Dr. Julio Zarco (credit: GEPAC).

GEICAM received an award for its campaign Little changes, big achievements in the Corporate and Social Responsibility category of GEPAC’s (Spanish Cancer Patients Group) Albert Jovell Awards.

This campaign, in which GEICAM teamed up with Metro de Madrid and Renfe (National Network of Spanish Railways) with the sponsorship of Roche, aims to raise awareness of what leading a healthy lifestyle (healthy weight, balanced diet, active lifestyle) can do to prevent breast cancer. It also highlights the importance of scientific investigation to fight this disease.

The Albert Jovell Awards gets its name from the Spanish doctor Jovell and his contribution to protect patients’ rights. GEPAC dedicated its fifth awards edition to acknowledge the work done by those dedicated to improving medicine and the quality of life of cancer patients.

GECOPERU: Education is key to improving research

In October 2016, with the support of the European Society for Medical Oncology (ESMO), GECOPERU held in Lima its second Workshop in Clinical Trial, focussing on young oncologists. The event attracted 30 participants from five different Latin American countries, and consisted of a three-day full immersion into the various aspects of clinical trials. The most important success is that the continuation of this course is guaranteed for 2017.

We believe that education is one of the most essential things to improve research in our region. To this end, we also organised the Best of the World Lung Cancer Conference in Lima, under the umbrella of IASLC (the International Association for the Study of Lung Cancer). The conference took place in February 2017 and gathered 150 oncologists from all over the country. It was the second time that we held it in Lima, and we plan to do it again in February 2018.

In August 2018 we will also organise the Multidisciplinary Cancer Management Courses (MCMC), with the support of ASCO.

GEICAM Estación de Metro Nuñez de Balboa (credit: GEICAM)
SOLTI seeds the future of breast cancer research by launching its Scientific Talent programme

By SOLTI

Expressing his gratitude for the opportunity, Dr Tomás Pascual explained, "It represents an excellent chance to complete my training as a medical oncologist and gain extensive clinical, translational and research knowledge in breast cancer. The final goal is to develop the ability to transform an idea from the laboratory into a clinical trial and, at the end, improve patients' treatment".

The purpose of this fellowship supported by the SOLTI Foundation is to enhance the career of a young oncologist or other professional in this field who is about to end his or her training as a physician. The Scientific Talent programme includes a part-time internship in one of the big research hospitals in Spain under the supervision of a mentor. In this case, Dr Pascual will be part of the team led by Dr Aleix Prat, who is SOLTI’s Scientific Coordinator, at the Hospital Clínic in Barcelona.

The programme is complemented by a period of practical training at SOLTI Headquarters, where Dr Pascual will give support to the development of clinical protocols, as well as participate in all clinical research activities led by the Scientific Department, from a scientific, strategic and operational point of view. Beneficiaries of the Scientific Talent grant may also participate in all the scientific events and medical training courses hosted by SOLTI, as well as attend an international congress.

This initiative has proven to be a great way to attract future investigators, get to know them, understand their motivations and start a collaboration. In the words of Dr Aleix Prat: "We need to make sure that young medical oncologists get involved into research because, if not, it is going to be difficult to move forward in this field".

As proof of SOLTI’s commitment to supporting early-career investigators, the academic research group has launched a new edition of its "Scientific Talent" grant, which is part of the Young Researchers Programme started in 2011. On this occasion, Dr Tomás Pascual was awarded this annual fellowship, which will give him the opportunity to benefit from a comprehensive training programme in clinical research.
Updates of Hong Kong Breast Oncology Group (HKBOG)

By Janice Tsang, Founding Convenor

The Hong Kong Breast Oncology Group (HKBOG) is a “young” member of the Breast International Group (BIG), a toddler, born in 2014 and admitted to BIG the same year. Being the third Asian member at that time just after Japan and Taiwan, HKBOG has been blessed with many supportive and passionate council members and members specialised in the treatment and care of breast cancer patients and survivors, sharing the same vision and mission for better care, research and education on breast oncology.

Over the past 12 months, HKBOG has had another busy year, starting with our Annual General Meeting and Scientific Dinner Symposium in July 2016, with Professor Yen-Shen LU from Taiwan speaking on hot off-the-press issues of treating breast cancer with brain metastases. This event was followed by several scientific conferences, including Molecular Genomic Profiling for Early Breast Cancer, and our very first consensus meeting with local delegates and members discussing hormone positive HER2-negative advanced breast cancer. The manuscript has been completed and is waiting publication. We also completed our first local real-practice review study led by our 2nd Vice President, Professor Winnie Yeo; the manuscript is currently under review. Our “Best of San Antonio Breast Cancer Symposium (SABCS)”, our iconic annual meeting, was held once again in January just after the Chinese New Year and welcomed by all our members and local delegates. This year, we invited Professor Ian Smith from the Royal Marsden Hospital and Professor Maggie Cheang from the Institute of Cancer Research, London, to speak. We further co-hosted the Asia Pacific Breast Cancer Summit Meeting in February in Hong Kong, in collaboration with the regional key opinion leaders, and also participated in the ESMO-ASIA meeting and the Global Breast Cancer Conference (GBCCI), connecting with our regional working partners and international key opinion leaders.

Looking forward, we are anticipating our upcoming Annual General Meeting and Scientific Dinner Symposium again, as well as our biannual Breast Cancer Conference hosted by The Chinese University of Hong Kong (CUHK) to be held on 11-12 November 2017 and led by Professor Winnie Yeo. Our Founding Convenor, Dr Janice Tsang, will co-chair the Breast Cancer Track at the upcoming ESMO-ASIA meeting with Professor Fatima Cardoso on 17-19 November 2017.

We look forward to meeting and greeting many more breast cancer professionals, especially members of the BIG network, either in Hong Kong or during any of BIG’s regional and international meetings, as well as through many more encounters in clinical trials and research programmes in breast oncology!
Trial updates

Clinical Trials

BIG clinical studies presented at ASCO 2017

The ASCO (American Society of Clinical Oncology) Annual Meeting brings together oncology professionals from around the world to discuss state-of-the-art treatment modalities, new therapies, and ongoing controversies in the field.

This year, the BIG network presented four of its clinical studies at ASCO: APHINITY, MINDACT, ALTTO & NeoALTTO, and SOLE. BIG HQ prepared newsfeeds about the results of these trials. These were published on the BIG website (scientific section) and were also shared via social media (Twitter). In collaboration with the respective study sponsors and study chairs, BIG HQ also prepared press releases which were sent to a mix of international and national media, targeting both medical/scientific and lay audiences.

Below is a summary of what was presented at ASCO:

APHINITY (BIG 4-11)
APHINITY (Adjuvant Pertuzumab and Herceptin IN Initial Therapy in Breast Cancer) is an international, phase III, randomised, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of pertuzumab plus trastuzumab and chemotherapy compared to trastuzumab and chemotherapy as adjuvant therapy in 4,805 people with operable HER2-positive early breast cancer.

- Phase III study confirms a benefit of the pertuzumab-based regimen over the current standard of care
- The study was positive in the overall population (risk reduction by 19%), with greatest risk reduction in patients with node-positive or hormone receptor-negative disease (risk reduction by 23% and 24%, respectively).
- Data will be submitted to global health authorities

Read the press release that we prepared with Roche, as well as further information about APHINITY on the BIG website, in the scientific section.

MINDACT (BIG 3-04)
MINDACT (Microarray In Node negative and 1 to 3 positive lymph node Disease may Avoid ChemoTherapy) is an international, prospective, randomised, phase III study to evaluate the added value of the 70 gene test (MammaPrint®) to the traditional method of assessing the likelihood of breast cancer recurrence for women with node-negative or 1-to-3 node positive breast cancer.

MINDACT’s primary results, published in the New England Journal of Medicine in August 2016, demonstrated that the use of MammaPrint could potentially reduce adjuvant chemotherapy of breast cancer patients by 46%, even in the presence of high risk clinical features. This means that nearly half of the early-stage breast cancer patients identified as high risk for recurrence based on traditional factors were identified as low risk when using the MammaPrint test. The data demonstrated that chemotherapy provided no clinically meaningful benefit for these patients: they could safely avoid chemotherapy.

At ASCO results of the chemotherapy randomisation that was part of the MINDACT study were presented.

The group of patients within the trial for whom chemotherapy was decided and who agreed to participate in an optional part of MINDACT aiming to compare two chemotherapy types were analysed: patients were randomly assigned to receive either standard anthracycline-based chemotherapy with or without taxanes (AT) or an experimental one without anthracyclines, using docetaxel plus capecitabine (DC). The study found that in all study endpoints, DC did not improve patient outcomes compared to AT, including those patients who were in the concordant group of clinical high risk (C-high)/genomic high risk (G-high, MammaPrint tested).

The aim of this randomisation was to prove the superiority of DC over anthracycline-based chemotherapy, which did not happen. Therefore, anthracyclines with or without taxanes remain the standard of care for early breast cancer, including those at the highest risk of relapse.

Future research using the study’s biological sample collection can also contribute to a much deeper understanding of breast cancer and how to continue to improve treatment in the future.
ALTTO (BIG 2-06) and NeoALTTO (BIG 1-06)

ALTTO (Adjuvant Lapatinib And/or Trastuzumab Treatment Optimisation) is a randomised trial comparing adjuvant (post-surgery) lapatinib with trastuzumab, given either alone, combined or sequentially, in patients with HER2-positive early breast cancer. The main aim of the study was to see whether treating this type of breast cancer with the two drugs trying to block HER2 (dual therapy or dual “blockade”) would be better than one.

The analysis looked at the participating patients’ chances of being free of cancer (disease-free survival or DFS) 5 years after being given a specific treatment. As such, DFS is a measure of treatment effectiveness. For the group of patients treated with lapatinib and trastuzumab combined, DFS was 85% compared with 82% in the group of patients treated with trastuzumab alone (hazard ratio [HR] of 0.86 [95% CI 0.74-1.00]).

The group of patients that was first treated with trastuzumab followed by lapatinib had a DFS of 84% (HR of 0.93 [95% CI 0.81-1.08]) compared to a DFS of 82% for those treated with trastuzumab alone. Although the DFS percentages were higher for the combination and sequential treatments than for trastuzumab alone, these differences were not statistically significant, and so the study’s main results remain unchanged: the evidence generated does not support adding lapatinib to trastuzumab as the standard of care for patients with HER2 positive early breast cancer.

NeoALTTO is a randomised clinical trial comparing lapatinib with trastuzumab in 454 patients with HER2-positive breast cancer in the neoadjuvant (pre-surgical) setting. The primary analysis of this study, published in 2012, showed that dual HER2-targeted therapy with lapatinib and trastuzumab resulted in more patients achieving a pathological complete response (pCR), meaning a disappearance of all visible signs of cancer, compared to a single HER2-targeted therapy (trastuzumab).

At ASCO, an updated analysis of NeoALTTO was presented. Patients had been followed for a median period of 6.7 years. The 6-year event free survival (EFS) (no signs of breast cancer returning) and overall survival (OS) were not significantly different between the two types of treatment, although the combination of trastuzumab with lapatinib showed numerically higher EFS compared to trastuzumab alone (74% vs 67%), especially in patients with hormone receptor negative disease (74% vs 63%). In addition, this analysis showed that patients who achieved a pCR had a significantly higher 6-year EFS and OS compared to those without pCR.

Follow-up for both studies will continue for at least ten years after enrolment. Exploratory (translational) research using the biological samples and data from these studies is ongoing.

SOLE (BIG 1-07)

SOLE (Study Of Letrozole Extension) is a phase III randomized clinical trial of continuous vs intermittent letrozole in postmenopausal women who have received 4 to 6 years of adjuvant endocrine therapy for lymph node-positive, early breast cancer.

SOLE’s results indicate that taking planned 3-month treatment breaks during long-term aromatase inhibitor treatment did not reduce the risk of recurrence of breast cancer compared with taking the aromatase inhibitor treatment continuously for 5 years for postmenopausal women with hormone-sensitive early breast cancer who had already completed 4 to 6 years of treatment for their breast cancer.

Read more information about BIG trials and programmes on BIG’s website.
BIG trial updates

IBCSG 48-14 / BIG 8-13 POSITIVE

A “BIG Time for Baby” for young women with breast cancer
By Monica Ruggeri

“In January 2015, it was ‘BIG Time for Baby’ for us – interrupt treatment and start planning a family. We were not sure whether we could succeed within the foreseen two years and whether the probability of a relapse would increase. Thanks to good medical care and participation in the study, we confidently jumped into the adventure. The decision was right. Lenny is now an eight-month-old, healthy and curious boy. And no, there has been no relapse yet.” said a young Swiss patient enrolled in the IBCSG 48-14/BIG 8-13 POSITIVE Trial, whose attempt to get pregnant was successful.

Young breast cancer patients often face the disease before having addressed their family planning: they may not have time to wait for 5 to 10 years of treatment completion before considering pregnancy. The best available evidence suggests that pregnancy after breast cancer therapy does not negatively impact disease outcome and is safe for the offspring. At the 2017 ASCO Annual Meeting, Lambertini et al presented the findings from a retrospective study of 1,200 women, which provide reassurance to breast cancer survivors who wish to attempt pregnancy.

A major focus of the study is the testing of biological correlates of pregnancy and disease outcome. In addition, a psycho-oncology companion study, which explores psychological distress, fertility concerns and decisional conflicts, is being activated in interested sites with the capacity to conduct it.

A total of 500 patients are planned to be recruited into the trial in approximately 4 years. To reach this accrual, the IBCSG brought together a consortium of more than 100 investigators from 23 countries worldwide.

As of 30 June 2017, the trial has been activated in 144 Centers from 18 countries and many BIG groups (Switzerland/SAKK, Australia, Italy, Belgium, Spain/SOLTIGEICAM, Greece/HORG, Slovenia, USA/Alliance, Canada/CTG, Japan/JBCRG, Portugal/SOLTIGEICAM, Greece/HORG, Slovenia, USA/Alliance, Canada/CTG, Japan/JBCRG, Portugal/SOLTIGEICAM, Greece/HORG, Slovenia, USA/Alliance, Canada/CTG, Japan/JBCRG, Portugal/SOLTIGEICAM, Greece/HORG, Slovenia, USA/Alliance, Canada/CTG, Japan/JBCRG).

The POSITIVE trial investigates endocrine therapy interruption to enable conception for young women between 18 and 42 years of age with endocrine responsive early breast cancer, who received adjuvant endocrine therapy for 18 to 30 months and wish to attempt pregnancy.

The acquisition of scientifically sound data for the benefit of young women with breast cancer requires a global effort and commitment by the scientific, patient and charitable communities.

Thanks to the successful efforts of Prof Martine Piccart and the team at BIG Headquarters, IBCSG received a substantial grant from the Baillet Latour Fund to support the POSITIVE Trial. This grant has enabled the IBCSG to provide some funding to help participating hospitals that are struggling to find financial support in their countries.

The main objectives are:
- To assess the risk of breast cancer relapse associated with temporary interruption of endocrine therapy to permit pregnancy
- To evaluate factors associated with pregnancy success after interruption of endocrine therapy.

ABCBSG 42 / BIG 14-03 PALLAS

Good progress in enrolment
By Nicole Scheiber and Michael Gnart

The international trial PALLAS (Palbociclib Collaborative Adjuvant Study) started in 2015 in Non-US-countries (through groups affiliated with the BIG network) with “first patient in” in Austria (October 28). Since then, the number of randomised patients increased to over 1,500* worldwide (target: 4,600). This randomised phase III trial compares the CDK4/6-inhibitor palbociclib given in combination with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for male and female patients with hormone receptor-positive (HR+) / human epidermal growth factor receptor 2 (HER2)-negative early breast cancer.

The primary objective of PALLAS is to compare invasive disease-free survival...
for the combination of at least five years endocrine therapy and two-year palbociclib treatment versus at least five years endocrine therapy alone in patients with histologically confirmed HR+/HER2- invasive early breast cancer. Secondary objectives are invasive disease-free survival excluding second primary cancers of non-breast origin, distant recurrence-free survival, locoregional recurrence-free survival, and overall survival. Also, the safety of two years of palbociclib with adjuvant endocrine therapy versus adjuvant endocrine therapy alone shall be compared.

By now, 18* Non-US-countries have received full approval (ethical commission and competent authorities) to enroll patients in this academic trial, which means that 142 sites are activated and ready for enrolment. As the legal sponsor of this study, the Austrian Breast & Colorectal Cancer Study Group (ABCSG) is satisfied to see that site activation and enrolment are within schedule so far – about 42%* of the targeted sample size has already been randomised.

The global cap of 1,000 patients with breast cancer stage IIA will very likely be reached in the third quarter of the year – currently there are more than 750* patients with this tumour type enrolled – so for these patients the trial will be closed soon. In general, the enrolment is stronger than the revised projection, which is of course also due to the remarkable efforts of ABCSG’s partners worldwide. Spain and Austria are the most active countries in enrolling patients, followed by Australia and – by a long shot – Hungary.

“We are quite satisfied with the global progress of our PALLAS trial, although there is of course – as always in international studies – the need for improvement in some countries concerning various points”, says Michael Gnant, MD, Non-US Coordinating Investigator for PALLAS and president of the ABCSG. “But I’m convinced that ABCSG, together with our partners, will be able to achieve all goals in a timely and satisfactory way.”

ANZ 1601 / BIG 16-02

EXPERT – Personalising Radiation Therapy for Early Breast Cancer

By Boon Chua and Anna Fitzgerald

EXPERT (EXamining PErsonalised Radiation Therapy for low-risk early breast cancer) is a randomised phase III trial of adjuvant radiation therapy (RT) versus observation following breast conserving surgery and endocrine therapy in patients with molecularly characterised low-risk luminal A early breast cancer.

EXPERT is the first large-scale randomised trial that investigates the use of a multigene expression panel (PAM 50-based Prosigna® Assay) to enable safe and individualised de-escalation of adjuvant breast radiation in early breast cancer. Breast Cancer Trials (formerly known as the Australia and New Zealand Breast Cancer Trials Group or ANZBCTG) is the international academic research group coordinating the study together with the Breast International Group (BIG). About 1,170 patients will be recruited and randomised globally.

The primary objective of EXPERT is to determine if the omission of radiation therapy is not inferior to radiation therapy in terms of local recurrence free interval after breast conserving surgery in patients with stage I, luminal A early breast cancer who are planned to receive adjuvant endocrine therapy.

Radiation therapy after breast conserving surgery is the current standard of care for the majority of patients with early breast cancer. However, breast cancer is a heterogeneous disease, and the absolute benefit of radiation in individual patients varies substantially. Thus, a pressing priority in contemporary breast cancer management is to tailor the use of radiation therapy to the individual recurrence risks by identifying patients who are unlikely to benefit from radiation, thereby decreasing morbidity rates and the costs of over-treatment.

EXPERT is scheduled for activation in Australia and New Zealand in July 2017. Expression of interest for study participation will be sought from BIG member groups in the near future.

Breast cancer intrinsic subtypes distinguished by gene expression profiling are shown to be associated with distinct clinical outcomes. There is substantial evidence supporting the clinical validity of multigene assays, including the PAM50-based Prosigna Assay that identifies intrinsic subtypes and generates a Risk of Recurrence (ROR) score to quantify individual risks of distant relapse. Multigene assays are increasingly integrated into clinical practice to inform chemotherapy decisions, highlighting their substantial practice-changing potential in personalising the use of radiation therapy for early breast cancer.

A recent analysis of archived tumour specimens from 1,308 patients with early breast cancer has shown significant association between local recurrence risk and the PAM50-defined intrinsic subtypes and ROR score. EXPERT presents a unique opportunity of clinical and public health importance to optimise personalised local therapy for early breast cancer through precise, individualised quantification of local recurrence risk to identify low-risk patients for whom RT after breast conserving surgery could be safely omitted.

This international collaborative study lends itself to answering additional questions of clinical, research and public health importance. EXPERT will examine patient reported outcomes and health economic impact. Importantly, a biological resource bank will be curated to enable translational research that focuses on enhancing prognostic precision for individual local recurrence risk.

For more information on EXPERT, visit www.breastcancertrials.org.au. Professor Boon Chua, Lead Study Chair of the EXPERT clinical trial (credit ANZBCTG).
Other trials run by BIG Member Groups

**ABCSG 28/POSYTIVE**

**Surgery prior to systemic therapy does not improve treatment outcome for metastatic breast cancer**

*By Nicole Scheiber and Michael Gnant*

The first results of oncological outcomes in ABCSG’s multicentre trial POSYTIVE (ABCSG 28), conducted under the direction of Dr Florian Fitzal, were recently presented at the 2017 ASCO Annual Meeting in Chicago. The results indicated that women suffering from metastatic breast cancer do not benefit from surgery performed prior to drug treatment. This could cause a paradigm shift in the treatment of the disease.

A research team from the Austrian Breast & Colorectal Cancer Study Group (ABCSD) had explored whether immediate surgical removal of the breast cancer tissue prior to administration of systemic therapy influences the treatment outcome. During the last decade, this method was regarded as a possible strategy for treating primary metastatic breast cancer. The results of the POSYTIVE trial now show that surgery prior to systemic therapy does not improve the outcome over primary systemic therapy. These results tally with the findings of other international studies that have recently appeared.

“Our work shows that an operation does not offer patients any advantage in terms of survival”, Fitzal comments on the results. “This means that, in the interests of giving them a better quality of life, many of them could be spared this stressful procedure.”

**The Indian Oncology Study Group (IOSG) Studies**

*By Sudeep Gupta*

IOSG has a number of Indian oncologists as its members, one of the main constituents being the Tata Memorial Centre (TMC) in Mumbai, which is the largest cancer centre in India. The Breast Cancer Working Group at TMC has been conducting research with a particular focus on cost-effective treatments and the peri-operative window of opportunity. One important randomised study published by this group demonstrated that there was no improvement in overall survival of patients with metastatic breast cancer who received loco-regional therapy (surgery plus radiotherapy). This remains the most robust evidence on this controversial subject until now.

Another provocative study published by this group tested the hypothesis that creating a luteal environment during primary surgery for breast cancer by administering a single injection of hydroxy-progesterone might improve the outcome of patients with operable breast cancer. Although the hypothesis could not be proven in the overall study population, progesterone administration did seem to improve disease-free and overall survival in a predefined subgroup of node-positive patients. A follow-on multicentre Indian study is ongoing to specifically test this intervention in node-positive patients.

A number of other randomised studies are in various stages of progress by the TMC breast cancer group. One randomised controlled trial with a sample size of 1,600 (accrual until now: ~750) is evaluating the impact of yoga versus conventional exercises in women undergoing curative treatment. The primary endpoint of the study is disease-free survival and secondary endpoints include quality of life (QOL). The preliminary QOL results of this study were presented at the 2017 ASCO Annual Meeting. Although yoga did not show a significant improvement in global QOL, it did show a major benefit for fatigue, emotional score and pain compared to conventional exercise. Another important study being conducted by the TMC group is a randomised trial that tests the addition of weekly carboplatin to standard taxane-anthracycline neoadjuvant chemotherapy in patients with triple negative breast cancer. Unlike studies already presented or published on this question, this trial is powered for disease-free survival as its primary endpoint with a sample size of 720, of which 465 are already accrued.

A number of translational studies involving questions on the effect of acute surgical hypoxia on breast tumour characteristics, clonal evolution of triple negative breast cancers over multiple relapses in single patients, as well as multi-omics characterisation of endocrine resistance are also being undertaken by the TMC group.

**References**


New study looks at the need for regional radiotherapy after breast surgery

CCTG’s MA.39 breast cancer clinical trial receives green light from funding bodies

By Lisa Callahan

One of the most promising advances in cancer treatment is the use of biological markers or biomarkers to identify the therapies a particular cancer may or may not respond to. A new study undertaken by the Canadian Cancer Trials Group (CCTG) will look at whether additional radiation therapy is beneficial for patients with a specific subtype of breast cancer called luminal A.

“Studies have shown that radiotherapy to the chest wall and lymph-nodes following mastectomy, and radiotherapy to regional nodes after breast conserving surgery, reduces the risk of recurrence and breast cancer mortality in women with node-positive breast cancer,” explained Dr Wendy R. Parulekar, Senior Investigator at CCTG.

While these benefits are important, there is a large group of breast cancer patients who will likely not see the cancer come back and therefore would not benefit from regional radiotherapy.

Biomarkers are increasingly used to identify breast cancers that are likely to recur, or not respond to treatment. It is understood that the luminal A breast cancer subtype has a low risk of recurrence and is less likely to respond to chemotherapy and radiotherapy. This suggests that regional radiotherapy may not be necessary for these patients.

To answer this question, the MA.39 international multicentre randomised trial is underway to determine if regional radiotherapy could be safely omitted in women with 1 to 3 positive axillary lymph-nodes and luminal A breast cancer subtype.

The Principal Investigator of this clinical trial is Dr Tim Whelan, a radiation oncologist at the McMaster University Faculty of Health Sciences in Hamilton, Ontario. The rationale for the trial is based on observations arising from the CCTG’s MA.20 study of regional radiation therapy in early breast cancer (NCTNCT00005957).

The MA.39 trial will be supported by the Canadian Institute of Health Research, the Canadian Cancer Society Research Institute and the US National Cancer Institute. Recruitment into the study is anticipated to commence in Q3 or Q4 2017.

“The study concept has also been presented to the Breast International Group (BIG), which has expressed enthusiasm for this trial. BIG member groups will be surveyed for their interest and ability to participate in the trial,” said Dr Parulekar. Assuming that this initial interest is confirmed through the survey, the trial will be run by CCTG under the BIG umbrella.

The luminal A subtype of breast cancer accounts for up to 40% of patients with node positive breast cancer. If regional radiotherapy could be avoided in this group of patients, it would have substantial benefits, not only for women with breast cancer and their families, but also for the healthcare system at large.
Our vision: Together we will find a cure for breast cancer through global research and collaboration

The Breast International Group (BIG) is a not-for-profit organisation for academic breast cancer research groups from around the world.

Founded by leading European breast cancer experts in 1999, BIG now constitutes a network of 59 groups and data centres based in Europe, Canada, Latin America, the Middle East, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. About 30 clinical trials and several research programmes are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute and the North American Breast Cancer Group, so that together they act as a strong interacting force in the breast cancer research arena.

www.BIGagainstbreastcancer.org

The 59 breast cancer research groups of the BIG network

ABCSG
Austrian Breast & Colorectal Cancer Study Group

AGO-B
Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group

ARCAGY-GINECO
Association de Recherche dans les Cancers dont Gynécologiques – Groupe d’Investigateurs Nationaux pour l’Etude des Cancers Ovariens et du sein

BCT (formerly ANZBCCTG)
Breast Cancer Trials

BDPCC
Breast Disease Professional Committee of CMEA (China)

BGICS
Breast-Gynecological International Cancer Society

BRE!
Breast Intergroup of Eastern India

BOOG
Borstkanker Onderzoek Groep

CCTG
Canadian Cancer Trials Group

CEEOG
Central and East European Oncology Group

CT-IRE
Cancer Trials Ireland

CTRIG
Cancer Therapeutics Research Group

DBCQ
Danish Breast Cancer Cooperative Group

GCSG
Georgian Cancer Study Group

EORTC BCG
European Organisation for Research and Treatment of Cancer, Breast Cancer Group

FBCG
Finnish Breast Cancer Group / Suomen Rintasyöpäpäryhmä

FBI
Francilien Breast Intergroup

GAIICO
Grupo Argentino de Investigación Clínica en Oncología

GBD
German Breast Group

GECO PERU
Grupo de Estudios Clinicos Oncologicos Peruano

GECIAM
Spanish Breast Cancer Group

GOCHI
Chilean Cooperative Group for Oncologic Research

GOCUR
Grupo Oncologico Cooperativo Uruguayo

GORIC
Italian Oncology Group for Clinical Research

GONO
Gruppo Oncologico Nord-Ovest

HBSS
Hellenic Breast Surgical Society

HeCOG
Hellenic Cooperative Oncology Group

HKBOG
Hong Kong Breast Oncology Group

HORG
Hellenic Oncology Research Group

IBCG
Icelandic Breast Cancer Group

IBCSG
International Breast Cancer Study Group

IBG
Israel Breast Group

IBIS
International Breast Cancer Intervention Studies

ICCIG
International Collaborative Cancer Group

ICON ARO
Indian Co-Operative Oncology Network

ICRC
Iranian Cancer Research Center

ICR-CTSU
Institute of Cancer Research – Clinical Trials & Statistics Unit

IUB / IMS (formerly BrEAST)
Institut Jules Bordet / Clinical Trials Support Unit

IiOSG
Indian Oncology Study Group

ITMO
Italian Trials in Medical Oncology

JBCRG
Japan Breast Cancer Research Group

KCSG
Korean Cancer Study Group

LACOG
Latin American Cooperative Oncology Group

MICHELANGELO
Fondazione Michelangelo

NBCG
Norwegian Breast Cancer Group

NCRI-BCG
National Cancer Research Institute - Breast Cancer Clinical Studies Group

SABO
Swedish Association of Breast Oncologists

SARK
Swiss Group for Clinical Cancer Research

SBCG
Sheba Breast Collaborative Group

SweBCG
Swedish Breast Cancer Group

SKMCH & RC
Shaukat Khanum Memorial Cancer Hospital & Research Centre

SLO
Société Luxembourgeoise d’Oncologie

SOLTI
SUCCESS – Study Group

TCOG
Taiwan Cooperative Oncology Group

TROG
Trans Tasman Radiation Oncology Group

TSCO
Thai Society of Clinical Oncology

UCBG
Unicancer Breast Group

WGS
Westdeutsche Studiengruppe
Boobs Art is an itinerant exhibition of 50 to 200 themed posters articulated around the art of the breast, which has been an inexhaustible source of inspiration throughout history.

Showcasing the most significant works of creators, the exhibition also highlights remarkable postoperative tattoos and astounding awareness campaigns.

This expo is available to be hosted by companies wishing to show they care about their employees and their families all while supporting Breast Cancer awareness.

If you know of a company to contact, simply tell us:

Serge.Schmitz@BIGagainstBC.org
Hello. I’m Charly.

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

Evidence shows that younger women are increasingly being affected by breast cancer. Of the 1.7 million new cases diagnosed every year, one third are patients under the age of 50. We are on a mission to change that. Join us today.

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

Support breast cancer research today and help save lives.

Make a donation to our bank account

BE57 5230 8072 9135

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

www.BIGagainstbreastcancer.org/donate