

facilitating breast cancer research internationally

ANNUAL REPORT 2008

Breast International Group (BIG)-aisbl



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Facilitating breast cancer research internationally

The Breast International Group (BIG) is an international non-profit umbrella organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Founded by leading European opinion leaders in 1996, BIG now constitutes a network of over 44 groups based in Europe, Canada, Latin America, and the Asia- Pacific region. These research entities are, in turn, tied to approximately 3000 specialised hospitals and research centres worldwide. More than 30 clinical trials are run under the BIG umbrella, accounting for the recruitment of well over 76 000 patients.

BIG also collaborates with the U.S. National Cancer Institute (NCI) and North American collaborative groups, with BIG and the North Americans together representing an impressive integrating force in the breast cancer research arena.

To make significant scientific advances in breast cancer research, reduce the wasteful duplication of effort, and optimally serve those affected by the disease, large-scale cooperation is crucial. Therefore **BIG's mission is to facilitate breast cancer research at international level**, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

BIG'S CONTRIBUTION TO ADVANCING INTERNATIONAL BREAST CANCER RESEARCH

International collaboration makes it possible to conduct studies that would not be possible for a single research group to carry out on its own, especially as treatments become increasingly targeted. Combining efforts makes it possible to quickly enrol large numbers of patients and efficiently answer important scientific questions. Faster results mean faster direct benefits to patients.

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Message from the Chair and the Vice-Chair

We are delighted to present our Annual Report for 2008, which describes a year of evolution and changes, fruitful international collaboration and new undertakings for BIG.

Research conducted under the BIG umbrella continued to be productive, with more than 30 trials in various phases of activity. This has led to numerous publications in peer-reviewed journals as well as presentations at major European and North American conferences. The neoadjuvant Neo-ALTTO trial randomised the first patient in January 2008 and continuously increased its accrual rate, gathering momentum in the second half of the year.

TRANSBIG also continued to receive recognition, both as a BIG-managed consortium and for the MINDACT trial. Not only did its independent review again receive the highest ratings, but it was also selected by the European Commission as one of its Framework Programme 6 “success stories”.

Tremendous energies and efforts were put into setting the stage for the launch, in late 2009, of NeoBIG. This is an exciting multi-year research programme in early breast cancer, the aim of which is to accelerate biomarker research and new drug development by selecting the most promising targeted therapies for specific molecular breast cancer subpopulations. Features will include novel translational research conducted through an innovative platform integrating specialised academic centres from around the world, bio-banking, data-sharing and harmonisation of technical and other procedures. While the focus will be on neo-adjuvant trials initially, these are expected to generate some of the most important adjuvant trials of the future.

Moving in a completely new direction, BIG, jointly with ESMO, began planning in earnest for the very first edition of IMPAKT, a breast cancer conference focusing on latest developments in cutting-edge translational research, as well as training opportunities for early-career oncologists. It will be held 7 to 9 May 2009.

We are also pleased to announce that three new research groups (from Greece, India and the Asia-Pacific region) joined our network in June 2008, bringing BIG’s total membership to 44.

To create a stronger internal structure for the development and the implementation of BIG trials and related activities and to better support the growing BIG network, our Headquarters were restructured along three main pillars: research, communications, and finance/legal/human resources. This is part of a wider BIG strategic plan for 2008-2011, endorsed by the General Assembly in May 2008.

Finally, BIG reports a positive 2008 financial year and outlook for 2009.



Martine J Piccart, MD, PhD
BIG Chair



Aron Goldhirsch, MD, PhD
BIG Vice-Chair



Translational Research: an Important Component of BIG studies



The Neo-ALTTO trial, coordinated by the BIG member group SOLTI, evaluates the effectiveness of neoadjuvant lapatinib, trastuzumab and their combination plus paclitaxel in women with HER2/ErbB2 positive primary breast cancer.

Coordinated by the BIG member group SOLTI, this trial randomised the first patient in January 2008 and its accrual rate has taken on great momentum ever since. The trial recruited 173 patients in 2008 and it is expected to complete its recruitment of 450 patients by the end of 2009.

Neo-ALTTO provides an unprecedented opportunity to gain an early signal of efficacy from lapatinib, trastuzumab and their combination, to identify biomarkers with predictive value and allow the design of tailored treatments based on the observed response, and to enable the comprehensive collection of multiple biological samples.

The strength of the trial lies in how the translational research will be performed using fresh and paraffin embedded tumour samples, as well as frozen serum and plasma. The trial encompasses gene expression profiling, research on circulating tumour cells and analysis of FG-PET/CT imaging.

BIG Clinical Trials

Evolution of trials in 2008

ACTIVATED / RE-OPENED

- **BIG 3-02 TEXT**

The International Breast Cancer Study Group (IBCSG) has decided to re-open the study's recruitment to 600 additional patients in order to ensure that the primary trial question is reported with adequate power. The group's intention is also to include translational investigations to characterise molecular and histopathological features of the tumour and the patients that are predictive of differential responsiveness to available endocrine therapies.

- **BIG 1-02 Loco-regional relapse**

Due to the difficulty to increase the recruitment rate, the Data and Safety Monitoring Committee (DSMC) has decided in May 2008 to change the target accrual from 977 to 265.

CLOSED

- **BIG 3-98 Young patients** was closed in January 2008 as it reached target accrual
- **BIG 4-04 ICE** was also closed in July 2008 as target accrual was completed
- **BIG 2-05 ACTION** was prematurely closed in November 2008 due to difficult recruitment

SOON-TO-START

No new BIG studies opened in 2008 but considerable effort was invested in developing new trials such as BIG 3-07 DCIS and BIG 2-07 Male Breast Cancer.

- **BIG 2-07 Male Breast Cancer**

This project is divided in three parts. Part I is a retrospective joint analysis of all male breast patients diagnosed and treated in the participating centres within the last 20 years, with retrospective collection of tumour blocks and analysis of tumour biology.

A grant to support the retrospective part of the project was obtained from the Breast Cancer Research Foundation (BCRF). Thanks to this grant the central pathological assessment of available male breast cancer tumours specimens will be performed. The European Organisation for Research and Treatment of Cancer (EORTC) will be in charge of the collection of material and data, which is likely to start at the beginning of 2009.

Part II is a prospective, international registry of all male breast cancer patients treated at the participating institutions for a period of one year with the collection of data including demographic information, diagnostic and biological characteristics, treatment administered, and outcome of male

breast cancer, along with virtual collection of biological material such as tumour and blood. The main objective is to have an estimate of the number of patients that could be pooled by the groups involved over a period of three years. This male breast cancer registry would provide the background for setting up a prospective international clinical trial. For the prospective registry, a grant (European Breast Cancer Conference Type 2 grant) was also awarded and, although it will not cover all expenses, it will make it possible to start developing the database for recording clinical (and pathological data). Depending on the number of patients registered during the one-year period, one or several international, prospective randomised trials could be proposed in a Part III of the programme.

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

This trial is currently open to sites in Australia and New Zealand and is funded by an Australia National Health and Medical Research Council (NHMRC) grant to recruit 610 patients. The Trans-Tasman Radiation Oncology Group (TROG)'s application for an NHMRC grant for international activation was unsuccessful. However, the NHMRC approved the first grant to support international recruitment. Discussions within the DCIS trial development task force took place on whether to open BIG 3-07 internationally with a target accrual of 610 patients as an interim measure. If strong accrual is achieved over the following 12 months, the study would likely to be well positioned for a successful NHMRC grant application in 2010. BIG 3-07 could then be activated internationally via a protocol amendment in 2011.

- **The TROG RT in older women**

This study is a randomised phase III study of the effects of radiotherapy on older women with endocrine-responsive stage I breast cancer. The proposal for this study was presented by Dr Boon Chua (TROG lead investigator) to the BIG community during the BIG scientific meetings at the EBCC in Berlin in April and at ESMO in Stockholm in September. It was agreed that a task force would be convened to further develop the proposal and that Dr Chua had been nominated to lead the task force under BIG.

- **BIG 1-08 MA.30 Faslodex**

This study, presented already at several BIG scientific meetings, is a 6000 patient trial involving a randomisation to either anastrozole or anastrozole + Faslodex as adjuvant endocrine therapy for postmenopausal women. The collaboration between the NCIC Clinical Trials Group (NCIC CTG)—sponsor and coordinator of the Canadian and US groups—and the IBCSG—the lead group for the rest of the world—was set up during 2008 and the related logistics were discussed during several meetings with Astra Zeneca. The BIG expression of interest form, carried out at the beginning of the year, showed a good level of response from the BIG member groups, thus confirming a significant level of interest in the trial. The Go/No-Go decision to proceed with the BIG 1-08 MA30 study was put on hold until the results of the FACT trial are available, expected towards the end of 2009.

Trials summary table by status

BIG OPEN TRIALS (open to recruitment on 31 December 2008)

BIG Trial	Coord. Group	Question Asked	Target N° of patients	Accrual at 31/12/08	Pharma Partners	Start Date
BIG 1-02 IBCSG 27-02 Loco-regional relapse	IBCSG	Benefit of adjuvant chemotherapy for radically resected loco-regional relapse of breast cancer?	265	141	NA	Aug 2003
BIG 2-02 IBCSG 24-02 SOFT	IBCSG	Benefits of ovarian suppression given in addition to tamoxifen in estrogen receptor positive pts who receive chemotherapy and regain premenopausal estradiol afterwards?	3000	2139	Pfizer	Dec 2003
BIG 3-02 IBCSG 25-02 TEXT	IBCSG	Benefit of tamoxifen vs. aromatase inhibitor for ER+ patients receiving GnRH analogue?	1845	2039	Pfizer	Re-opened Oct 2008
BIG 5-02 IBCSG 31-03 IBIS II	IBIS	Effectiveness of anastrozole vs placebo in preventing breast cancer in healthy, high-risk post-menopausal women "at risk" and comparison of tamoxifen and anastrozole in post menopausal women with ductal carcinoma in situ (DCIS)?	10 000 (Prevent.: 6000 DCIS: 4000)	4200 (Prevent.: 2408 DCIS: 1792)	Astra Zeneca (partial support)	Feb 2003
BIG 1-03 ICGC C/20/01 GBG 27 REACT	ICCG / GBG	Benefit of 2 yrs of adjuvant therapy with celecoxib compared with placebo in primary breast cancer patients?	2590	286	Pfizer	Jan 2007
BIG 2-03 GBG 29 Pregnancy study	GBG	What can we learn about the diagnosis, treatment and maternal/foetal outcome of pts w/breast cancer during pregnancy? (prospective register study)	1500	206	NA	Apr 2003
BIG 2-04 SUPREMO	ACCOG / CCTT	What is the role of adjuvant chest wall irradiation in "intermediate risk" operable breast cancer following mastectomy and axillary clearance?	3700	302	NA	June 2006
BIG 3-04 EORTC 10041 MINDACT	EORTC	Will gene profile signature be a better prognostic tool to help in adjuvant decision-making than traditional clinical/pathological factors in node negative breast cancer patients?	6000	982	Novartis / Hoffmann – La Roche / Sanofi-Aventis	Feb 2007
BIG 1-06 EGF 106903 Neo-ALTTO	BrEAST / SOLTI	Benefit of neoadjuvant lapatinib, trastuzumab and their combination plus paclitaxel in women with HER2+ primary breast cancer?	450	173	GSK	Dec 2007
BIG 2-06 N063D EGF 106708 ALTTO	BrEAST	Benefit of lapatinib (L) vs. trastuzumab (H) vs. L+H vs. L before H following anthracycline-based CT +/- RT; and L vs. H vs. L+H vs. L before H with concomitant weekly paclitaxel +/- RT, following anthracycline-based CT?	8000	3577	GSK	June 2007
BIG 1-07 IBCSG 35-07 SOLE	IBCSG	Optimal duration of letrozole (continuous vs. intermittent over a 5 yr period), for postmenopausal women, disease-free following 4-6 years adjuvant endocrine therapy with SERM and/or AI for endocrine-responsive, node-positive operable breast cancer?	4800	319	Novartis	Nov 2007

BIG TRIALS IN FOLLOW UP (on 31 December 2008)

BIG Trial	Coord. Group	Question Asked	Target N° of patients	Final Accrual	Reason for Closure	Pharma Partners
BIG 1-97 MA.17	NCIC CTG	Tamoxifen (5y) ⇔ letrozole (5y) superior to tamoxifen (5y) alone?	4800	5187	Reached target accrual	Novartis
BIG 2-97 C/13/96 IES	ICCG	Tamoxifen exemestane: superior to tamoxifen alone?	4740	4743	Reached target accrual	Pharmacia
BIG 3-97 HABITS	SBG	Hormone replacement therapy: safe after radically treated in situ, stage I or stage II breast cancer (<4+ nodes)?	1300	447	Following IDMC recommendations	NA
BIG 1-98 IBCSG 18-98	IBCSG	Sequencing of tamoxifen / letrozole or letrozole / tamoxifen superior to agent alone?	8000	8028	Reached target accrual	Novartis
BIG 2-98 TAX 315	BrEAST	Incorporation of docetaxel in sequence or combination with doxorubicin: benefits to patients?	2730	2887	Reached target accrual	Aventis
BIG 1-00 EORTC 10994 P53	EORTC	Is there a relationship between p53 status and response to anthracyclines or taxanes?	1850	1856	Reached target accrual	Sanofi-Aventis / Pfizer
BIG 1-01 BO 16348 HERA	BrEAST	Benefit of 1 year vs. 2 years vs. no trastuzumab in women with HER2+ primary breast cancer who have completed adjuvant chemotherapy?	3192	5102	Reached target accrual	Hoffmann-La Roche
BIG 4-02 IBCSG 26-02 PERCHE	IBCSG	Is chemotherapy necessary for low risk premenopausal endocrine responsive patients?	1750	29	Low accrual	Pfizer
BIG 1-04 AZURE	NCRI, BCSG, U Sheffield, CTRU	Benefit of zoledronic acid in (neo) adjuvant chemotherapy for improving bone metastasis and overall DFS in stage II/III breast cancer patients?	3300	3360	Reached target accrual	Novartis
BIG 4-04 GBG 32 ICE	GBG	What is the role of ibandronate with or without capecitabine in elderly pts with early breast cancer?	1394	1409	Reached target accrual	Hoffmann– La Roche / AstraZeneca
BIG 1-05 IBCSG 32-05 CASA	IBCSG	Role of adjuvant pegylated liposomal doxorubicin (PLD) for women (age 66 or older) with endocrine nonresponsive breast cancer NOT suitable for "standard" CT?	1296	77	Low accrual	Schering-Plough
BIG 2-05 ACTION	ICR-CTSU	Benefit of CT vs. no CT for older ER negative / poor pts (aged >70)?	1000	4	Low accrual	NA
BIG 3-05 GBG 26 TBP	GBG	Benefit of capecitabine with trastuzumab in patients with HER2+ metastatic breast cancer and progression after previous trastuzumab treatment?	482	156	Low accrual	Hoffmann-La Roche

BIG CLOSED TRIALS (on 31 December 2008)

BIG Trial	Coord. Group	Question Asked	Target N° of patients	Final Accrual	Reason for Closure	Pharma Partners
BIG 3-98 EORTC 10002 Young Patients	EORTC	What is the attitude toward risk of loss of fertility related to adjuvant therapies in young patients (<35) with early breast cancer?	400	400	Reached target accrual	NA
BIG 4-98 EORTC 10963 PEAT	EORTC	Inhibitory effect of perioperative fulvestrant on development of metastasis, measured by disease free survival (DFS) and overall survival (OS)?	3500	20	Low accrual	Astra Zeneca
BIG 2-00 EORTC 10974 LAMANOVA	EORTC	Benefit of conservative local therapy (vs. mastectomy) in locally advanced breast cancer?	1210	23	Low accrual	NA

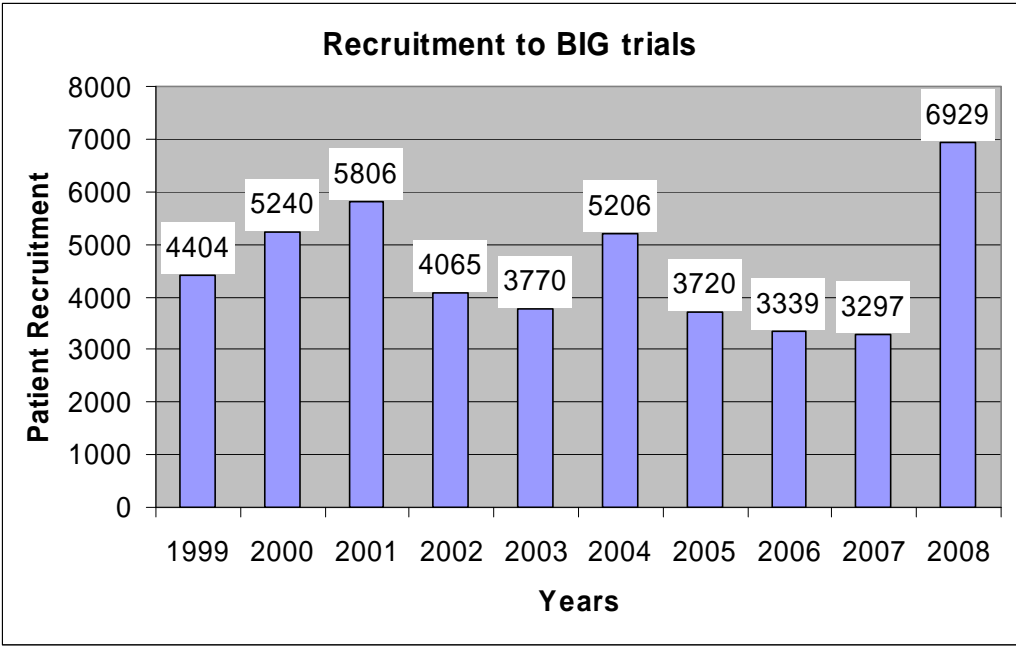
BIG TRIALS IN DEVELOPMENT (on 31 December 2008)

BIG Trial	Coord. Group	Question Asked	Target N° of patients	Pharma Partners	Comments
BIG 2-07 Male Breast Cancer	EORTC	Part 1 - Retrospective analysis of male BC pts w/ retrospective collection of tumor blocks and analysis of tumor biology; Part 2 - Prospective registration of all male BC cases, with simultaneous collection of biological material; Part 3 - possible adjuvant endocrine therapy trial.	TBC	None	Retrospective study ready to start
BIG 3-07 DCIS	TROG	A randomized phase III study of radiation doses and fractionation schedules for DCIS of the breast.	610	None	Final activation under discussion

Recruitment to BIG trials over time 1999-2008

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
BIG 1-97 / MA.17	771	1280	1830	1216						
BIG 2-97 / IES	1349	1632	1253	103	406					
BIG 3-97 / HABITS	78	76	81	76	136					
BIG 1-98 / Letrozole	1563	910	1847	1703	558					
BIG 2-98 / TAX 315	643	1342	735							
BIG 3-98 /Young pts					39	68	95	101	9	6
BIG 4-98 / PEAT			20							
BIG 1-00 / P53			57	257	446	500	205	250		
BIG 2-00 / Lamanoma			0	18	5					
BIG 1-01 / HERA			3	692	2028	2354	25			
BIG 1-02 / Locoreg.					4	15	26	34	37	25
BIG 2-02 / SOFT					2	134	285	498	595	625
BIG 3-02 / TEXT					6	278	403	630	722	0*
BIG 4-02 / PERCHE					0	0	15	14		
BIG 5-02 / IBIS II					93	442	800	884	855	1042
BIG 1-03 / REACT						0	0	0	73	213
BIG 2-03 / Pregnancy					9	26	23	13	55	80
BIG 1-04 / AZURE					38	1279	1553	430		
BIG 2-04 / SUPREMO							0	12	103	179
BIG 3-04 / MINDACT									83	826
BIG 4-04 / ICE						110	288	440	369	202
BIG 1-05 / CASA							2	33	41	
BIG 2-05 / ACTION									1	3
BIG 3-05 / TBP						53	45	44	13	
BIG 1-06 / Neo-ALTTO									1	173
BIG 2-06 / ALTTO									333	3244
BIG 1-07 / SOLE									7	312
Totals	4404	5240	5826	4065	3770	5259	3765	3383	3297	6929

* BIG 3-02 / TEXT was closed in November 2007 and was re-opened in October 2008.



The annual accrual rate to BIG trials more than doubled in 2008. This is mainly because BIG's ambitious trial ALTTO was fully open in this period. An important contribution to the overall recruitment was also given by studies like IBIS II, MINDACT, Neo-ALTTO, SOLE and REACT.

TRANSBIG

TRANSBIG is a translational research network, managed by the BIG Headquarters, involving 40 partners in 22 countries. It receives funding from the European Commission under Framework Programme VI and other sources such as the Breast Cancer Research Foundation, Susan G. Komen for the Cure, Fondation Contre le Cancer. More information about the TRANSBIG network's activities and structure is available on pages 31 – 33.

MINDACT

The first project launched under the network is the MINDACT trial, which compares a genomic prognostic test (Mammaprint®) developed with micro-array technology to traditional clinical-pathological methods for assessing the risk of breast cancer recurring in women with lymph node negative or 1 to 3 node positive disease. It is hypothesised that using the genomic test in addition to traditional methods will result in more accurate risk assessment and ultimately help physicians and patients make better decisions about who can safely avoid chemotherapy and its potential side effects.

With 63 centres participating in 9 countries and recruiting about 120 patients per month, accrual reached the first milestone of 800 patients (end of the pilot phase) in November 2008. The preliminary results of this pilot phase demonstrate that the trial is both feasible from the logistical point of view and scientifically relevant. These outcomes also demonstrate that multidisciplinary team collaboration on a large-scale is feasible.

In parallel to this, the TRANSBIG network implemented the first amendment to the study protocol. This amendment was primarily made to allow patients with 1-3 positive lymph nodes to participate in MINDACT and to allow the collection of the whole blood.

Main 2008 achievements include:

- analysis of MINDACT pilot phase,
- implementation of the first amendment to the MINDACT protocol,
- statistical assessment of the impact of new eligibility criteria on enrolled population and study results,
- ongoing selection of centres for participation in the MINDACT trial,
- first samples stored in the TRANSBIG biobank,
- evaluation of the first project proposals using MINDACT samples and data.

Beyond MINDACT, TRANSBIG's uniqueness lies in its emphasis on communications and on education for scientists, physicians, patients, and patient advocates, made possible by working closely with the European CanCer Organisation and Europa Donna.

Sample collection and other projects

TRANSBIG collects whole blood, fresh frozen tumour tissue, tumour paraffin blocks and serum from MINDACT patients. These samples are stored in an independent biological materials bank (“biobank”) under the governance of the TRANSBIG Steering Committee and are—together with the associated microarray raw—available for future research. The development and the management of this unique “biobank” and related database required pioneer work. TRANSBIG has for example created a specific tool To ensure the traceability of the samples a special management tool was created; this complements the previously developed policy for the selection of the research projects that will gain access to MINDACT samples and related data. During the fifth year of project, covering most of 2008, three research proposals were submitted to the Consortium for evaluation.

The TRANSBIG Proteomics Working Group, consisting of a team based at Imperial College of London, the University of Edinburgh and at the German Research Centre for Environmental Health in Munich, has also made important progress. The working group developed a range of molecular pathology protocols for the detection of protein-protein interactions and kinomic activation of proteins in situ. Further studies will be carried out using cohorts of early breast cancers representative of the patient profile for the MINDACT trial. Samples will be obtained from the local tumour cohorts (Wales Cancer Bank) until material from the MINDACT trial becomes available.

TRANSBIG is also taking part in the Collaborative Oncological Gene-environment Study (COGS) project. This Consortium, supported by the European Commission Framework Programme VII, will perform germline single nucleotide polymorphism (SNP) profiling on the MINDACT patient blood samples for 1536 SNPs (either general-BCAC or hereditary-CIMBA/IBCCS — it may be expanded to genome-wide analysis based upon budgetary considerations) that will be derived from breast cancer susceptibility screens including approximately 100 000 cancer cases and 100 000 controls. Assessed SNP profiles of the MINDACT patients will be evaluated for breast cancer susceptibility, and then correlated with the corresponding clinical and microarray data (70-gene signature profile).

TRANSBIG traineeship programme

In 2006 the TRANSBIG network launched an annual traineeship programme, entirely supported by the European Commission, for young scientists and researchers to acquire or develop knowledge and skills in the field of translational breast cancer research and the latest “omic” technologies. In 2008 the TRANSBIG network started preparing the launch of the 2009-2010 traineeship programme. Two young researchers will be selected and will have the opportunity to choose amongst five research positions available at TRANSBIG institutions.

TRANSBIG patients' workshop

As part of its educational activities TRANSBIG hosted a workshop at the European Breast Cancer Conference (EBCC-6) in Berlin, in April 2008, through the Spreading of Excellence Committee—the body responsible for disseminating TRANSBIG knowledge to the wider scientific community.

Bringing together experts and patients, the aim of this workshop was to address some of the difficulties experienced in integrating translational and overall research into the routine of patient care. During the first part of the workshop, dedicated to the conference participants, representatives from a multidisciplinary research team—oncologist, pathologist, surgeon, nurse, and patient advocate—illustrated the challenges of implementing multi-disciplinarity in research and patient care.

The second part, open to the public, involved patient representatives and scientists who examined progress in understanding breast cancer biology and the development of new drugs, as well as more general topics such as breast cancer screening and patient follow-up. An evaluation conducted after the workshop revealed that the about 50 participants appreciated this “open forum” formula, allowing them to pose questions on breast cancer related issues directly to a panel of experts. The most valued aspects of this session were the appropriate selection of topics, the understandable terminology and, last but not least, presentations delivered in German.

NeoBIG

NeoBIG is a new 5-year research programme in early breast cancer that will be launched in late 2009, with the aim to:

- set up a series of neoadjuvant trials selecting the most promising targeted therapies for specific molecular breast cancer subpopulations,
- utilise the pre-operative settings where valuable opportunities for correlative translational research will exist,
- use short-term surrogate endpoints to help detect early signals of drug activity or inactivity,
- integrate and accelerate drug development and predictive biomarker research.

NeoBIG platform

2008 was a year of intensive platform-building for the NeoBIG team to set the scene for the conduct of these innovative trials. Alongside the ongoing discussions with potential pharmaceutical partners to identify the most promising drugs, much energy was directed towards strengthening the various pillars that would support this platform. In particular, identifying the academic centres to participate in NeoBIG has been a particularly detailed process. Centres – or in some cases networks – will join NeoBIG either as part of a “core” consortium, constituting the backbone of NeoBIG, or on an ad hoc basis.

Core institutions, participating centres and networks

The NeoBIG core institutions are individual centres of cancer research excellence that will:

- participate in at least one NeoBIG trial,
- have the necessary infrastructure and expertise to run neoadjuvant trials,
- receive privileged access to biospecimen collected during NeoBIG trials for translational research purposes,
- have access to raw data from standard arms, shared by all partners in the network.

The pre-selection of core institutions was carried out through a questionnaire sent to all members of BIG, scientific partners of TRANSBIG, and to individual NeoALTTO sites. Up to 120 sites worldwide answered the questionnaire and expressed interest in the programme.

Based on the potential for patient recruitment, translational research and imaging, a short list of centres was selected, in consultation with BIG scientific leadership. The centres are mainly European, but a few leading centres are being identified outside Europe.

Additional centres will join NeoBIG on a per trial basis to augment patient recruitment. The follow-up of this initial selection process is being planned for early 2009. Parallel contacts have also been initiated with existing neo-adjuvant networks in Germany and the UK.

Legal aspects

Much time and effort have been dedicated to building the legal structure that will govern the interaction between BIG and the partners within NeoBIG. Each core institution will be legally bound to BIG through the NeoBIG Consortium Agreement. Additionally, individual Study Agreements will govern the collaboration between BIG and individual biopharmaceutical companies involved in any specific trial within NeoBIG. Contracts with the core institutions, participating centres and other partners will be a focus in 2009.

Data sharing

The concept of data sharing embedded in the NeoBIG research programme is an innovative principle whereby raw data from the “standard of care” arms from each NeoBIG study will be shared by NeoBIG partners. In order to set up the needed structure, contacts have been established with European informatics networks offering the technological infrastructure for biomedical data management. Follow-up meetings are planned to move discussions forward and try to bring the concept to reality in 2009.

Contacts with potential partners

Pharmaceutical companies

Discussions with several biopharmaceutical companies took place throughout 2008. These focused on exploring potential compounds in the companies' pipeline as candidates for NeoBIG trials. At more advanced stages, the discussions were held as day-long brainstorming sessions for possible study designs. Discussions with Merck were the most advanced, with a detailed study proposal developed jointly by scientific teams from BIG, the Jules Bordet Institute (JIB), the Breast European Adjuvant Studies Team (BrEAST) and Merck. The study will target the luminal high proliferative breast cancer sub-population. The Merck protocol is expected to be launched late 2009 as the first NeoBIG trial.

Small and Medium Enterprises (SMEs)

To set up the needed logistics and operational aspects of the project, contacts were also sought with potential SME partners in the areas of bio-diagnostics and transport. The specific details of these collaborations will be determined according to the protocols for each individual NeoBIG study.

Imaging

Contacts were established with several imaging companies and renowned imaging experts worldwide, in order to explore potential collaboration and assess the best ways to integrate imaging in the platform. Companies such as Phillips, GE Healthcare and Siemens were approached, and discussions will continue in 2009, especially as the needs and expectations related to particular studies are defined.

Contacts with imaging experts led to the constitution of the NeoBIG Imaging Experts Group, which includes:

- Dr Christiane Kuhl, Bonn University, Germany
- David Mankoff, University of Washington, USA
- Rodney Hicks, Peter MacCallum Cancer Centre, Australia
- Patrick Flamen, Jules Bordet Institute, Belgium

The input of these experts was sought for example during the development of the study concept elaborated with Merck. Their expertise regarding the imaging modalities as endpoints in other trials, as well as during discussions with imaging companies, remains indispensable.

A **global discussion** on breast cancer research

In 2005 BIG initiated a global discussion on breast cancer research with US-based research groups: the Canadian NCIC Clinical Trials Group (NCIC CTG, which has been a member of BIG from its early years), The Breast Cancer Intergroup of North America (TBCI), National Surgical Adjuvant Breast and Bowel Project (NSABP), Radiation Therapy Oncology Group (RTOG) and the National Cancer Institute (NCI).

This collaboration has since continued to grow. Its aim is to bring into focus and discuss breast cancer research areas of mutual concern to **find solutions**.

The BIG-NCI-North American groups collaboration comprises approximately 70% of breast cancer specialists world-wide: this allows to run truly global trials facilitating rapid patient recruitment, even in relatively rare patient populations, with obvious advantages for both patients and society.

BIG-NCI-NoAm Meeting

In April 2008 representatives from BIG, the US National Cancer Institute (NCI) and several North American Breast Cancer Cooperative Groups (NoAm Groups) met in Bruges, Belgium, to discuss ongoing and future collaboration. This was the fourth time group representatives have met since the collaboration started in December 2005. On this occasion participants tried to understand whether the time is ripe to initiate clinical trials in the breast cancer population defined by biomarkers other than ER and HER2 overexpression, and had the opportunity to share their views on long-term follow-up in adjuvant trials as well as new challenges in global trials collaboration.



The outcome of the discussions was that more clarity is needed before undertaking any studies in the breast cancer population defined by other biomarkers. This and other considerations led to establishing **task forces** that became operative in 2008:

- a task force on classical lobular to determine the feasibility of data set collection and make recommendations for both retrospective and prospective actions;
- a task force on triple negative to develop a common terminology, including subdivisions, stratifications and a better definition of the trial population;
- a task force on immuno-vaccines to consider proposals for a vaccination study (e.g. basal-like), with ground work first being done by an already initiated BIG task force preparing an inventory of ongoing research and evaluating available vaccines.

The meeting also allowed participants to follow-up on previous collaborations and establish new directions to explore. An important achievement of the initial collaboration among the various groups was the publication in the *Journal of Clinical Oncology* of the “Recommendations for collection and handling of specimens from group breast cancer clinical trials, from onsite collection through shipping to the central bank”¹, which will be updated from time-to-time. The plan is for the networks on both sides of the Atlantic to adopt this guideline for all future studies involving translational research.

¹ Leyland-Jones B, Ambrosone C, Bartlett J M S, Ellis M, Enos R, Raji A, Pins M, Zujewski J A, Hewitt S M, Forbes J, Abramovitz M, Braga S, Cardoso F, Harbeck N, Denkert C, Jewell S. Recommendations for collection and handling of specimens from group breast cancer clinical trials, from onsite collection through shipping to the central bank. On behalf of the Blood, FFPE, and Fresh/Frozen Tissue Working Groups of the NCI Cooperative Group Banking Committee, Breast International Group, and the North American breast cancer Cooperative Groups. *Journal of Clinical Oncology* (2008). Published Ahead of Print on October 27, 2008 as 10.1200/JCO.2007.15.1712.

BIG Task Forces

Developing Regions

In August 2008, the BIG task force (TF) on Developing Regions was launched to help BIG develop a strategy to better serve the research efforts and related needs of its members around the world and, more specifically, in developing and underserved regions. The TF comprises a small group of individuals with knowledge of some key geographic areas, either by being from the region or having had extensive experience there. They all share a particular interest in supporting breast cancer research in developing countries.

The members of the TF are:

- Ian Kunkler, UK, Chair
- Clement Adebamowo Adebayo, Nigeria
- José Bines, Brazil
- Reena Nair, India
- Eva. Kantelhardt, Germany
- Tushar Vora, India – Belgium

The main objectives of this TF – in line with BIG's strategic plan for 2008 – 2011 – are to develop synergies with academic breast cancer research networks and groups, within and beyond BIG, and to recommend scientific research priorities and related educational support.

Based on the current conditions for breast cancer research in Brazil, India and Nigeria, the TF will draw up a strategy document for presentation and discussion at the BIG General Assembly in June 2009. The methodology adopted to achieve the objectives of the TF is a consensus approach developed through a series of teleconferences and reports from TF members describing the infrastructures for breast cancer trials in their countries, the barriers to participation and their respective priorities for research proposals. As a first step, TF members provided descriptions of the following: facilities available for screening, diagnosis, treatment and follow-up of breast cancer; trial infrastructures, including for ethical and other approval processes, and facilities for data management.

The final document will focus on the priorities of research questions in these areas, the resources required and the specific support and training needed to conduct studies. While the views expressed will represent those of individuals, the TF believes their detailed knowledge of breast cancer management and research is a valid expression of the situation 'on the ground' in these countries.

Immunovaccine

This TF consists of 5 members:

- Fabrice André (Chair)
- Christos Sotiriou
- Giuseppe Curigliano
- Peter Dubsy
- José Baselga

Over the last year, the TF has identified a need to have two programmes developed in parallel: the basic science / biomarker programme and the clinical programme. Meetings have taken place with pharmaceutical partners to firstly explore whether collaboration would be possible to better understand antigen expression. The main objective is to ultimately build upon the discoveries of the basic science programme to develop a phase II clinical study testing vaccines in breast cancer.

RT for elderly

Following a proposal for a randomised phase III study on the effects of radiotherapy in older women with endocrine-responsive stage I breast cancer by Dr Boon Chua (TROG lead investigator), a task force was established to determine the level of international interest in conducting a well-powered study and the following 3-arm design: whole breast irradiation, partial breast irradiation and no radiotherapy. Dr Chua was nominated to lead this task force under BIG. In view of a NHMRC grant application foreseen for February 2009, the conduct of an expression of interest survey of the BIG member groups was planned to be completed by end of January 2009.

Regulatory

The BIG Regulatory Coordinating Group (BIG-Reg)—bringing together primarily the BIG member groups' trial coordinators / regulatory experts—was called into being while the Clinical Trials Directive (CTD) was being implemented. At the time, there was a clear need for groups to understand how the CTD had been interpreted across Europe, as well as to identify appropriate contact people within groups as a resource for answering country-specific questions in the context of setting-up multi-national trials. Overall this information-sharing / networking objective was achieved and the last formal BIG-Reg meeting was held during St Gallen in 2007.

In 2008 this group met to review the objectives of their meetings and to determine the mission of and the need for the BIG-Reg on an ongoing basis.

Overall the BIG-Reg agrees that given lack of resources and heavy workloads, BIG's core business of developing trials (rather than lobbying) and the work being done by other organisations, it is difficult to currently justify holding regular meetings of the BIG-Reg group. Instead, it was decided to:

- Not to pursue regular activities / meetings for the time being; but consider re-instating the group on an ad hoc basis as needed in the future (e.g., if there is a new or substantial changes to the CTD);
- Endeavour to keep the list of key contact (clinical trials coordinators / regulatory experts) in the BIG member groups updated;
- Send any information (e.g., reports about CTD, BBMRI, etc.) that could be of interest to the BIG member groups to the BIG HQ for dissemination / posting to the BIG website.

Enriching the Network

Three new members joined the BIG network in 2008, bringing along their own local experience and further enriching our capabilities as an international network: BIEI, CTRG and HORG.

The **Breast Intergroup of Eastern India (BIEI)** was initiated in 2007 to develop activities for the effective treatment of breast cancer in Eastern India. BIEI brings together individuals from 6 institutions, and its members' varied backgrounds comprise all key aspects of medical oncology.

“There is no well-concerted inter-organisational effort in Eastern India to fight [breast cancer] effectively at epidemiological, molecular biological, clinical research or management levels. So we decided to join our hands so to speak to do relevant collaborative research in this part of India.”

(Dr Ashis Mukhopadhyay, BIEI voting representative)

The **Hellenic Oncology Research Group (HORG)** is a not-for-profit organisation started in 2000, but officially founded in 2002, that consists of 85 oncologists and cancer investigators working in 36 public or private oncology department units located all over Greece and Cyprus. HORG conducts clinical and laboratory-based research on patients with malignant neoplasms, and it aims in particular to promote clinical and applied research while improving the therapeutic approaches and systems for patient care and support.”

“We are ready to join an international research network such as BIG to participate and contribute our efforts to well-designed clinical trials aiming at changing the practice of oncology.”

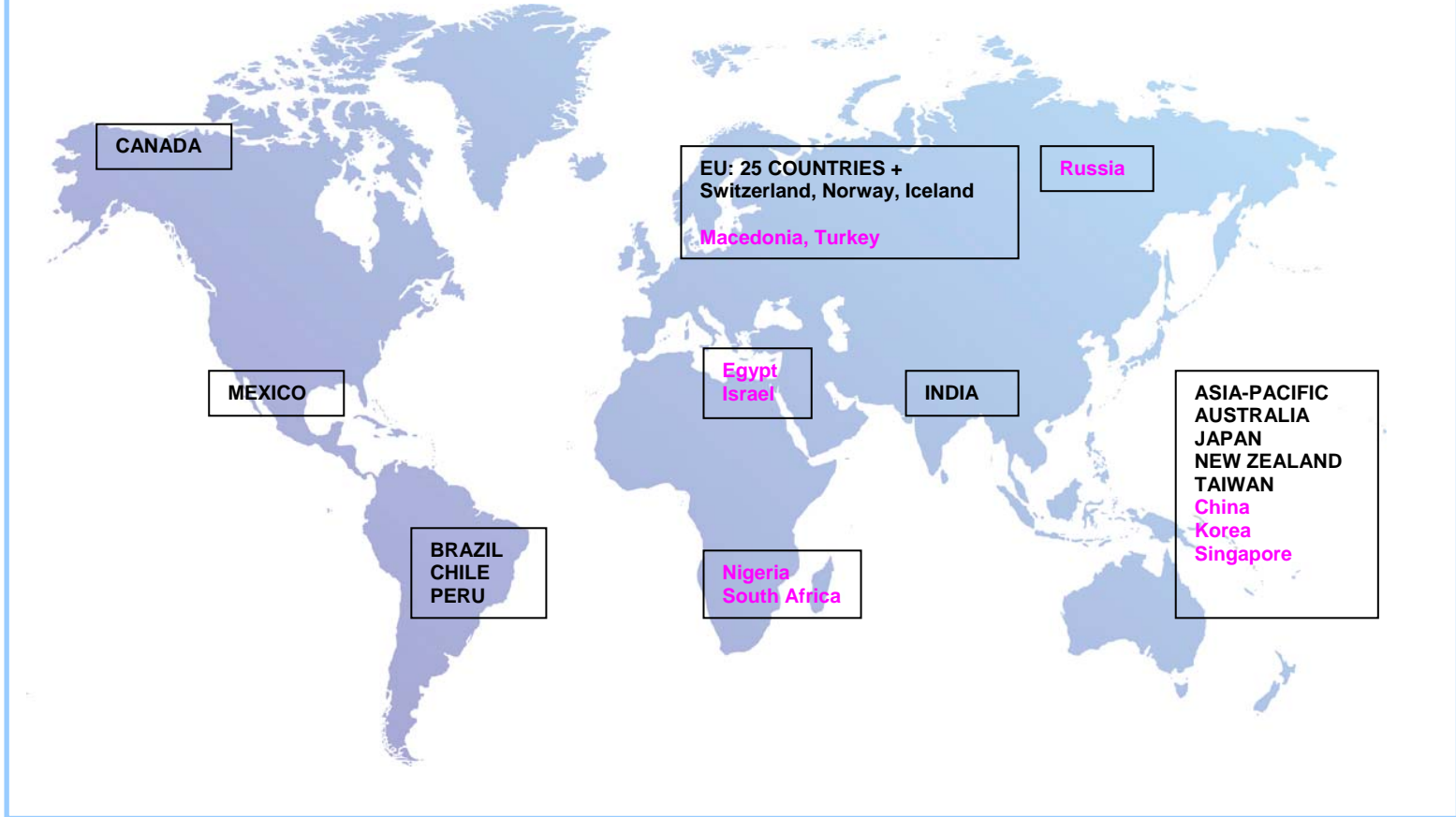
(Dr Dimitris Mavroudis, HORG voting representative)

The **Cancer Therapeutics Research Group (CTRG)** was formed in 1997 by Prof John Wong (Singapore) and Prof James Bishop (Sydney, Australia) to develop new therapeutic strategies for cancers common to Asia-Pacific. This resulted in a joint research group that performs clinical trials on new anti-cancer drugs in Asia-Pacific, and aims to be the equivalent of oncology cooperative groups in the USA.

List of members and geographical distribution

Acronym	Name of the group	BIG voting representative
ABCSG	Austrian Breast & Colorectal Cancer Study Group	Michael Gnant
ABS at BASO	Association of Breast Surgery at British Association of Surgical Oncology	Nigel Bundred
ACCOG	Anglo Celtic Cooperative Oncology Group	Robert C F Leonard
ANZ BCTG	Australian New Zealand Breast Cancer Trials Group	John F Forbes
BIEI	Breast Intergroup of Eastern India	Ashis Mukhopadhyay
BOOG	Borstkanker Onderzoek groep	Hans Nortier
BREAST	Breast European Adjuvant Studies Team	Martine Piccart
CEEOG	Central and East European Oncology Group	Jacek Jassem
CTRG	Cancer Therapeutics Research Group	Winnie Yeo
DBCG	Danish Breast Cancer Cooperative Group	Henning T Mouridsen
EORTC BCG	European Organisation for Research and Treatment of Cancer, Breast Cancer Group	Hervé Bonnefoi
FBCG	Finnish Breast Cancer Group	Minna Tanner
FBSG	French Breast Study Group	Henri Roché Thierry Delozier (alternating)
GBG	German Breast Group	Gunter von Minckwitz
GBOC	Grupo Brasileiro Cooperativo de Pesquisa em Oncologia Clinica	André Márcio Murad
GBECAM	Brazilian Breast Cancer Study Group	Sergio Simon
GECO	Grupo de Estudios Clinicos Oncologicos Peruano	Henry Gomez
GEICAM	Grupo Español de Investigación en Cáncer de Mama	Pedro Sanchez Rovira
GOCCHI	Chilean Cooperative Group for Oncologic Research	Jorge Gutierrez
GOIRC	Gruppo Oncologico Italiano di Ricerca Clinica	Rodolfo Passalacqua
GONO	Gruppo Oncologico del Nord Ovest	Lucia Del Mastro
HBSS	Hellenic Breast Surgeons Society	Christos Markopoulos
HORG	Hellenic Oncology Research Group	Dimitris Mavroudis
IBCG	Icelandic Breast Cancer Group	Oskar Johannsson
IBCSG	International Breast Cancer Study Group	Aron Goldhirsch
IBIS	International Breast Cancer Intervention Study	Jack Cuzick
ICCG	International Collaborative Cancer Group	R. Charles Coombes Pierre Hupperets (alternating)
ICORG	The All Ireland Co-operative Oncology Research Group	John Crown
ICR-CTSU	Institute of Cancer Research - Clinical Trials & Statistics Unit	Judith Bliss
IOSG	Indian Oncology Study Group	Reena Nair
ITMO	Italian Trials in Medical Oncology	Emilio Bajetta
JBCRG	Japan Breast Cancer Research Group	Masakazu Toi
MOSG	Mexican Oncology Study Group	Laura Torrecillas Torres
NBCG	Norwegian Breast Cancer Group	Erik Wist
NCIC CTG	NCIC Clinical Trials Group	Karen Gelmon Timothy Whelan (alternating)
NCRI	National Cancer Research Institute, Breast Cancer Study Group	Robert Coleman
SAKK	Swiss Group for Clinical Cancer Research	Olivia Pagani
SBCG	Swedish Breast Cancer Group	Jonas Bergh
SOLTI	Grupo Español de Estudio, Tratamiento y Otras Estrategias Experimentales en Tumores Sólidos	José Baselga
TCOG	Taiwan Cooperative Oncology Group	Jacqueline Whang-Peng
TROG	Trans-Tasman Radiation Oncology Group	Boon Chua
WSG	Westdeutsche Studiengruppe	Ulrike Nitz
WMBG	West Midlands Breast Group	Christopher J. Poole
YBCRG	Yorkshire Breast Cancer Research Group	David Dodwell

44 MEMBERS WORLDWIDE



National or international GROUPS or *centres* involved in large multinational trials.

A **strategic plan** for the BIG network

Following a survey of BIG members and discussions with the BIG Board of Directors and others at scientific meetings, the General Assembly endorsed a strategic plan for 2008-2011. More in particular, by 2011 BIG wants to:

- be recognised as a global leader in setting priorities for and facilitating international collaboration in breast cancer research,
- enhance the strength of BIG's collaborative member groups while improving synergies between them in order to function as a better "whole" in the clinical and translational breast cancer research community,
- achieve a better reduction in the duplication of research effort and obtain research results more quickly.

Concretely, this translates into a series of strategic goals and operational objectives, to be implemented and achieved by 2011.

STRATEGIC GOALS	OPERATIONAL OBJECTIVES
1. Develop a research programme to accelerate drug and biomarker development in early breast cancer	<ul style="list-style-type: none"> • Develop and launch a BIG neoadjuvant programme (NeoBIG), by building on the existing BIG-TRANSBIG structure, to generate both neoadjuvant trials and adjuvant trials
2. Systematically provide leadership development opportunities for young investigators and scientists from BIG groups in all BIG activities	<ul style="list-style-type: none"> • Create a young members committee (engaging also their supervisors/institutions) and launch this with IMPAKT • Involve young investigators in the NeoBIG programme; as co-PIs in BIG clinical trials; in IMPAKT
3. Improve multi-disciplinarity in the development of BIG research endeavours	<ul style="list-style-type: none"> • Create "consultancy groups" of experts from specific fields (e.g. pathology, surgery, imaging, cardiology...) for either hands-on or advisory involvement in BIG trials • Develop educational sessions (e.g. pathologists) • Appoint cross-disciplinary PIs in BIG clinical trials
4. Further develop synergies with academic breast cancer research networks and groups, within and beyond BIG, in particular in connection with developing or under-represented regions in BIG	<ul style="list-style-type: none"> • Create a task force to develop scientific research priorities and research related educational support for developing regions • Pursue relationships with other research networks
5. Develop more efficient collaborations with the pharmaceutical and biotechnology industry	<ul style="list-style-type: none"> • Develop BIG's "Conduct of Studies" policy (e.g. research models, financial guidelines, contracts...)
6. Create a stronger internal structure for the development and implementation of BIG trials and related activities	<ul style="list-style-type: none"> • Restructure Brussels office along three pillars: scientific, communications, financial/legal/HR • Refresh BIG's "look": logo, house style, "Secretariat"- "Headquarters" • Restructure BIG meetings (e.g. allow for task force reports, more opportunities for reporting on groups' own research, workshops...)

BIG Board of directors

The Board of Directors acts as BIG's administrative and advisory body. This group meets several times a year to see that decisions taken by the General Assembly are carried out and to ensure the smooth running of the association. Board members are elected every five years at the General Assembly. The Board consists of:



**Martine J Piccart, MD, PhD
CHAIR**



**Aron Goldhirsch, MD, PhD
VICE-CHAIR**



**Michael Gnant, MD, PhD
TREASURER**



**John Forbes, MS, FRACS, FRCS
VICE-TREASURER**



**Kathleen Pritchard, MD
NORTH AMERICAN LIAISON**



**Gunter von Minckwitz, MD, PhD
SECRETARY**



**Mitchell Dowsett, PhD
VICE-SECRETARY**

BIG Headquarters

The BIG Headquarters is located at the Jules Bordet Institute in Brussels, Belgium and works on behalf of the Board of Directors and the General Assembly to move BIG's research agenda forward.

In 2008 the BIG Secretariat was actually renamed to BIG Headquarters to better reflect not only the increasing scientific responsibility of the unit, but also its function as a central hub for BIG members and many research partners. To create a stronger internal structure for the development and implementation of BIG trials and related activities, and to better support the BIG expanding network, the Headquarters were reorganised around three main pillars: research, communications, finance/legal/human resources.



The Headquarters is responsible, among other things, for:

- providing support to BIG member groups and data centres that run BIG studies,
- developing and managing new research programmes, including aspects of the associated clinical trials (e.g., contracts, budgets, committees, policies ...),
- liaising with industry partners,
- managing the European Commission supported translational research consortium (TRANSBIG)
- leading communications activities (e.g. website, newsletter...),
- relating with members through meetings and other channels,
- managing association finances, contracts and Headquarters' human resources.



Established in 2004, TRANSBIG is a translational research network, managed by the BIG Headquarters, involving 40 partners in 22 countries. It receives funding from the European Commission under Framework Programme VI and other sources such as the Breast Cancer Research Foundation, Susan G. Komen for the Cure, Fondation Contre le Cancer.

Each participating organisation brings with it expertise that ranges from being specialised in cutting-edge biomedical technologies and cancer treatment programmes to lobbying governments on behalf of patient groups and supporting cancer societies.

The main objectives of this network are:

- to develop ways of individualising breast cancer treatment, so that treatment is tailored to the person receiving it,
- to integrate, strengthen and facilitate translational breast cancer research in Europe and internationally by linking it to an existing network for clinical breast cancer trials (BIG),
- to develop and run a major clinical trial aimed at validating the hypothesis that understanding the genomic make-up (signature) of a tumour can lead to improved tailoring of treatment.

The first project launched under the network is the MINDACT trial, which compares a genomic prognostic test (Mammaprint®) developed with micro-array technology, to traditional clinical-pathological methods for assessing the risk of breast cancer recurring in women with lymph node negative or 1 to 3 node positive disease. More details about this trial are available on page 14.

Beyond MINDACT, because TRANSBIG also emphasises education for scientists, physicians, patients, and patient advocates by working closely with cancer societies and patient groups, it brings a coherence and synergy to breast cancer research that has not previously existed.

The TRANSBIG consortium is governed by three entities: a) the TRANSBIG Steering Committee, composed of representatives from all the parties involved in the project; b) the TRANSBIG-MINDACT Executive Committee, responsible for the day-to-day management of both the MINDACT trial and the overall TRANSBIG project; and c) the BIG Headquarters, responsible for communications and the implementation of the project. This management scheme once again proved to be very efficient, with regular communication and face-to-face or teleconference meetings. It is worth mentioning the role of the recently created TRANSBIG Independent Review Committee, whose members are selected on a case-by-case basis to evaluate research proposals requesting to use samples and data from the MINDACT trial.

List of consortium partners:

- Breast International Group (BIG-aisbl), Brussels (International) – Central coordination
- Institut Jules Bordet / Jules Bordet Instituut, Brussels (Belgium)
- The Netherlands Cancer Institute, Amsterdam (Netherlands)
- Istituto Europeo di Oncologia - European Institute of Oncology (Italy)
- Karolinska Institutet, Stockholm (Sweden)
- The European Organization for the Research and Treatment of Cancer (EORTC), Brussels (International)
- Universitaet Wien, Vienna (Austria)
- Grupo Oncologico Cooperativo Chileno de Investigacion, Santiago (Chile)
- Bank of Cyprus Oncology Centre, Nicosia (Cyprus)
- Univerzita Karlova v Praze, Prague (Czech Republic)
- Finsen Centre - Rigshospitalet, Copenhagen (Denmark)
- Institut Gustave Roussy, Villejuif (France)
- West German Study Group, Universitaetsklinikum Duesseldorf, Duesseldorf (Germany)
- Klinikum der Johann Wolfgang von Goethe Universitaet, Frankfurt (Germany)
- Technische Universitaet Muenchen, Munich (Germany)
- National and Kapodistrian University of Athens, Athens (Greece)
- St Vincent's University Hospital, Dublin (Ireland)
- Gruppo Oncologico Italiano di Ricerca Clinica, Parma (Italy)
- Centre Hospitalier de Luxembourg (Luxembourg)
- Universiteit Maastricht, Maastricht, (Netherlands)
- Medical University of Gdansk, Gdansk (Poland)
- Portuguese Institute of Oncology Francisco Gentil, Porto (Portugal)
- N. N. Blokhin Cancer Research Centre, Moscow (Russia)
- Institute of Oncology, Ljubljana (Slovenia)
- Institute of Oncology of Southern Switzerland Mendrisio (Switzerland)
- Marmara University Medical School Hospital, Istanbul (Turkey)
- European CanCer Organisation, Brussels (International)
- Europa Donna – The European Breast Cancer Coalition, Milan (International)
- Instituto de Patologia e Imunologia Molecular da Universidade do Porto, Porto (Portugal)
- Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit und Umwelt/German Research Center for Environmental Health, Munich (Germany)
- Agendia, Amsterdam (the Netherlands)
- International Institute for Drug Development, Brussels (International)
- Fundacion Institut per la Recerca Vall d'Hebron, Barcelona (Spain)
- Grupo Español de Estudio, Tratamiento y otras Estrategias Experimentales en Tumores Sólidos, Madrid (Spain)
- Swiss Institute of Bioinformatics, Lausanne (Switzerland)

- The Chancellors, Masters and Scholars of the University of Oxford, Oxford (UK)
- The University of Edinburgh (UK)
- Martin Luther Universität Halle Wittenberg, Halle (Germany)
- The University of Dundee (UK)
- Imperial College London (UK)

The work of the TRANSBIG consortium for the 4th year of the project was evaluated as “excellent” according to the report of the European Commission’s independent review.

The report, covering the period 1 March 2007 – 29 February 2008, considered that the TRANSBIG group has fully achieved its objectives, planned milestones and deliverables to date.

As recommendations for the current phase of the project, the report suggested to accelerate the MINDACT trial accrual to obtain the required data and tissue samples in the timeframe of the project. A concept for the integration of the complex data sets (mRNA expression profiling, proteomics work, serum proteins and cell-free DNA) obtained from analyses of the samples of the MINDACT trial would also be desirable.

The TRANSBIG-MINDACT Executive Committee is confident that these issues can be addressed, in particular with recruitment expected to increase once the MINDACT trial is fully open also to patients with 1 to 3 positive nodes (amendment in process of being submitted to ethics committees at the time of this writing). Towards the end of 2008, monthly accrual figures had already begun to reflect this effect.



The European Commission published a catalogue² on “Framework programme 6 success stories”, which features – among others – the TRANSBIG project.

² European Union, Directorate-General for Research Communication Unit. Research for Europe. A selection of EU success stories. Luxembourg: Office for Official Publications of the European Communities, 2008. The publication is available from the EU Bookshop on <http://bookshop.europa.eu>

BIG Operating Mode

General Assembly and strategic plan 2008-2011

The General Assembly (GA) is held once a year to discuss and make decisions about issues of scientific and strategic importance, as well as operational issues. The assembly is attended by representatives with voting rights, designated by their member group, and requires a quorum of 50%.

In 2008 the GA was held during the 44th ASCO annual meeting in Chicago, IL, USA on 1 June 2008. Following a survey of BIG members and discussions with the BIG Board of Directors and at scientific meetings, the GA endorsed a strategic plan for 2008-2011. Details on this plan are on page 28.

Scientific meetings

Throughout the year two scientific meetings are held in conjunction with major European (breast) cancer conferences. The purpose of the scientific meetings is to discuss new and/or recent study proposals, ongoing studies, related task forces and any other relevant issues. These meetings are attended by both voting and non-voting representatives of BIG member groups and TRANSBIG partners. Two scientific meetings were held in 2008, on 15 April in Berlin, Germany (during EBCC-6) and on 12 September in Stockholm, Sweden (during the 33rd ESMO Congress).

Communications

In 2007 BIG overhauled some of its communications tools (e.g. newsletter, website) to better reflect its increased dynamism. This “rejuvenation” process continued in 2008, with the development of a new logo that conveys a fresher and more incisive image of BIG that was progressively integrated in all BIG materials.

Two editions of the BIG newsletter were issued in 2008, in print and electronically: the first one tackled breast cancer challenges of resource-limited countries while the second one focused on the role and the involvement of pathologists in clinical trials.

The BIG website was regularly updated. Plans for its reorganisation, to be achieved by end May 2009, started in the course of 2008.

Finally, since it is important that every element of the organisation, including communications, follows a well-concerted strategic plan in alignment with BIG’s mission and strategic goals, a communications strategy for 2009 was developed, to efficiently support the evolving and growing BIG network and its activities.

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THANK YOU

**For making international breast cancer research
collaboration possible...**

...and helping us to better serve patients!

- European Commission Framework Programme VI
- Breast Cancer Research Foundation
- Breast Cancer Working Group
- Fondation Contre le Cancer / Stichting tegen Kanker (Belgium)

BIG also partners with the pharmaceutical and biotechnology industry to develop and run clinical trials. All trials under the BIG umbrella adhere to the BIG Principles of Research Conduct, which ensure that scientific and academic independence is maintained in all collaborations with industry partners.

HOW CAN YOU ADVANCE INTERNATIONAL BREAST CANCER RESEARCH

By supporting BIG you can foster international research, and ultimately contribute to improving the lives of those affected by the disease.

If you wish to make a donation or discuss any other type of support opportunities, contact Ms Carolyn Straehle at BIG Headquarters by telephone at +32 2 541 3146 or by email at carolyn.straehle@bordet.be

Financial summary

Balance Sheet & Statement of Income and Expenses

Balance Sheet	31/12/2008	31/12/2007
<u>Assets</u>		
Fixed Assets	8.149,10	0
Tangible Assets		
Current Assets		
Receivables up to 1 year	3.503.761,43	2.535.684,10
Treasury investment	6.894.082,36	6.185.000,00
Cash at bank	408.550,24	401.275,74
Deferred charges and accrued income	227,48	16.613,96
Total Assets	10.814.770,61	9.138.573,80
<u>Liabilities</u>		
Unrestricted net assets	1.506.252,67	1.449.891,07
Provision for liabilities and charges	1.265.000,00	1.265.000,00
Debts:		
Amount payable up to 1 year	6.927.283,82	4.618.517,04
<i>Suppliers</i>	<i>6.802.517,37</i>	<i>4.525.488,87</i>
<i>Tax , remuneration & social security</i>	<i>124.766,45</i>	<i>93.028,17</i>
Accrued charges and deferred income	1.116.234,12	1.805.165,69
Total Liabilities	10.814.770,61	9.138.573,80
Income & Expenses Statement		
Operating income & expenses		
Turnover (research)	5.566.358,32	4.759.105,03
Other goods & services	-4.997.654,27	-4.102.556,23
Operating margin	568.704,05	656.548,80
Remuneration, social security and pension costs	-672.088,13	-477.712,87
Operating result	-103.384,08	178.835,93
Financial result	190.446,21	240.367,80
Extraordinary income (+)	400,27	33.896,54
Extraordinary expenses(-)	-31.100,80	-79.104,14
Result for the financial year	56.361,60	373.996,13

BIG's balance sheet and statement of income and expenses for 2008 provides a statement of BIG's financial position.

In 2008 BIG's total assets amounted to EUR 10.814.770,61. Its total income, derived mainly from the coordination of research activities, amounted to EUR 5.566.358,32, and total expenses were EUR 4.997,654,27. The 2008 fiscal year ended with a surplus of EUR 56.361,60.

In 2008 BIG continued its sound and prudent financial policy in order to consolidate its net assets structure. This will ensure BIG's long-term activity and provide BIG with the flexibility needed to adapt to annual fluctuations in its sources of income. Consequently an amount of EUR 50,000 will be set aside at the year end 2008 and will be incorporated into BIG's existing unrestricted net assets. On 31/12/2008 the net assets amounted to EUR 1.506.252, 67.

BIG's accounts are audited annually and conform with the standards for non-profit organisations as defined by Belgian law and the Belgian Institut des Réviseurs d'Entreprises (business auditors). An independent auditor from the Institut des Réviseurs d'Entreprises has reviewed and certified BIG's 2008 accounts without reservation. The audit certificate constitutes part of the Annual Financial Statement.