HOW THE BIG NETWORK ADDRESSED THE COVID-19 CHALLENGES

HOW THE BIG NETWORK ADDRESSES THE COVID-19 PANDEMIC, DEMONSTRATING RESILIENCE AND PERSISTENCE

Long-term resilience and persistence are needed in academic research

Research is the only way to understand breast cancer, how and why it progresses, and how it can ultimately be stopped. For over 20 years, BIG has been conducting global breast cancer clinical trials and research programmes. By engaging its network to rapidly enrol large numbers of patients into complex international clinical trials, and by sharing best practices, expertise, and data in pursuit of answers to important scientific questions, BIG has the ability to achieve faster results and greater patient benefits. BIG trials also follow patients long after the experimental treatment ends, with the aim to detect long-term side effects, improve treatment therapies and patients' quality of life. **This requires resilience and persistence at every stage, from planning to completion, as well as sufficient funding.**

Over the years, breast cancer has been classified into multiple sub-types, each requiring different approaches to treatment. To test new treatments on enough patients within a sub-group, and to be confident about the results, most research cannot be limited to one institution or even to one country. **Large-scale international cooperation** is crucial to make significant advances in treating breast cancer, reduce the wasteful duplication of efforts, and best serve those affected by the disease.

Over 30 international clinical trials or research programmes are being run or are under development under the BIG umbrella at any one time. Since 1999, more than 97,000 patients have participated in BIG's studies.

Much of BIG's research is considered landmark, introducing particularly innovative designs, contributing to significant breakthroughs, or paving the way towards more personalised treatment of the disease.

"NONE OF BIG'S ACHIEVEMENTS WOULD BE POSSIBLE WITHOUT THE WILLINGNESS TO WORK TOGETHER. DESPITE THE COVID-19 PANDEMIC AND ALL THE CHALLENGES IT POSES, BIG'S NETWORK HAS CONTINUED ITS EFFORTS TO ADVANCE BREAST CANCER RESEARCH, DEMONSTRATING GREAT **RESILIENCE** AND **PERSISTENCE**"

Below are a few examples of how BIG member groups addressed the challenges of COVID-19.

HOW SOUTHERN EUROPE LED THE WAY: SOLTI & GOIRC

With high levels of COVID-19 in many parts of Southern Europe during the early stages of the pandemic, clinicians such as **Professor Aleix Prat, President of the SOLTI Breast Cancer Research Group (Spain)** and **Professor Gabriele Zoppoli, member of the Board of Directors of the Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC),** were concerned about its impact on breast cancer research.

"In Spain, trial recruitment fell and research facilities closed but, by the Summer, things were back to normal. I am optimistic that, unless there is a change in the next few months, clinical, translational and basic research will not be hugely impacted overall," says Prat.

His main concern is that the huge investment being made in COVID-19 prevention and patient care will affect resources for treatment of patients with cancer.

"It is understandable that COVID-19 was the priority, but we now need to catch up with breast cancer screening because of the risk of delayed diagnosis and the potential for worsening mortality a few years down the line," he says.

In Italy, which was the first European country to be hit by COVID-19, telemedicine played an important part in supporting patient care and, in Lombardy and Emilia Romagna – two of the worst hit regions of Italy – huge efforts were made to deliver cancer treatment in patients' homes and ensure continuation of clinical trials.

"Lombardy and Veneto were the hotspots of the pandemic in Italy but, in several centres, they actually managed to increase accrual of new patients in clinical trials through a structured parallel care pathway for those with cancer," recalls Zoppoli. "I think we can be very proud of how Italian centres dealt with the crisis and cared for patients," he adds.

Professor Aleix Prat

Professor Gabriele Zoppoli

ABCSG

Carrying on in challenging times

What to learn from the unexpected in clinical research? The COVID-19 pandemic had far-reaching consequences for daily clinical research routines. Best practice examples can be identified in countries and individual centres, but how the situation will develop over time and what implications this will have for clinical routine, research, translational work and study groups remains to be seen.

For the A**ustrian Breast and Colorectal Cancer Study Group (ABCSG)**, the implications of the pandemic are impacting daily operations as well as strategic scenarios. **Professor Michael Gnant, President of the ABCSG**, describes challenges, opportunities and lessons learned.

Professor Michael Gnant

INTERVIEW FROM DECEMBER 2020

How does the COVID-19 pandemic affect clinicians, and the study landscape? What are the learnings for ABCSG so far?

Professor Gnant: "The pandemic has hit us unexpectedly, like everybody else. Probably the biggest challenge for clinicians in late Winter 2019 and Spring 2020 was the uncertainty about how dramatic the impact on our health care systems would be. Like everybody else in Europe, I was greatly moved and concerned after the alarming reports from our brave colleagues in Northern Italy came in. Some countries suffered more than others (in terms of health care capacity), and obviously the reaction (times) by political leaders was difficult. Personally, I would have hoped for a bit more unity and solidarity between EU countries and globally, but obviously politics is not yet as mature as we have developed in international research collaboration. While hospital capacities were blocked by and/or for COVID-19 patients, "nonessential" patient visits were postponed in many environments, which clearly affected clinical trials. However, with a lot of spirit and dedication, the study teams were able to maintain "damage control", also supported by regulators and ethics committees, who helped in conquering the extraordinary situation.

In addition to the things you have mastered in your study activities with the ABCSG, what is your personal motivation to continue clinical breast cancer studies in these difficult times?

Professor Gnant: "Clinical research multiplies the creativity and dedication of caregivers. Developing ideas, discussing improvements in diagnosis and therapy, transforming exciting new achievements into clinical practice, mentoring young people – all of this keeps me going. In the last 30 years of clinical research, we have saved thousands of lives, achieved improvements in patient quality of life through modernisation and de-escalation, de-ciphered part of the enemies' code – and made important friendships around the globe. I am very grateful for all of that."

BCT-ANZ

Accelerating the digital

Staff at BCT-ANZ worked from home for a period of three months, returning to the office at the start of July 2020. But rather than allowing this disruptive environment to halt their activities in the research, fundraising, communications, and business departments, BCT-ANZ identified opportunities to streamline processes and create new ways to engage its stakeholders. These include system improvements such as implementing a Sharepoint portal to allow for real time collaboration of documents for multiple users from any location; implementation of initiatives to overcome source data verification difficulties associated with increased remote monitoring activities; enhancement of online training tools and conduct of site initiation meetings; virtual public workshops; and online fundraising events.

COVID-19 brought forward and expedited the development and implementation of an electronic patient-reported outcome-measures platform, known as **e-PROMs**, which was launched with the **BCT 2001 (Breast-MRI)** trial in July 2020. The e-PROMS platform now allows for important patient questionnaires to be completed by participants (at the appropriate time) electronically on a computer or smart device, including remotely away from the clinic, if necessary. Participants are provided a link via email as their next round of study questionnaires falls due, enabling them to complete the questionnaires in their own time. The system is completely customisable to all forms of questionnaires and usable on all platforms. Now that this has been successfully launched, BCT-ANZ will be utilising this e-platform for all future trials requiring PROMs completion.

Similarly, BCT-ANZ is developing a platform for providing a digital patient information and consent form, known as **e-CONSENT**, with the aim of patient consent forms being available for all future clinical trials in an electronic format. Patients will still be able to receive the traditional paper version of the consent materials. However, the digital version will provide the opportunity to present and explain the clinical trial in a more interactive way through the inclusion of video and animation. The e-CONSENT platform will also allow patients to remotely provide their consent from anywhere at any time. It is anticipated that this system will provide more condensed, intuitive, and easy-to-understand information about each clinical trial.

CCTG

The 2020 trial activity of the **Canadian Cancer Trials Group (CCTG)** (www.ctg.queensu.ca) focused on ensuring the continued development and safe conduct of cancer clinical trials during the COVID-19 pandemic in addition to the activation of new trials aimed at improving outcomes in patients with cancer.

Below are three COVID-19 trials that allow enrolment of patients with breast cancer:

CCTG IC.8 COV-IMMUNO – a randomised, phase III trial of Immunisation with IMM-101 versus Observation for the Prevention of Severe Respiratory and COVID-19 Related Infections in Cancer Patients at Increased Risk of Exposure (NCT04442048)

The purpose of the trial is to find out if immunisation with a new immune-stimulator will prevent or reduce severe respiratory and COVID-19 infections in cancer patients. A new type of immune stimulating therapy is being developed for the treatment of cancer. It works by activating the parts of your immune system involved with protecting against viral and bacterial infections. It has been studied in over 300 cancer patients who have also been receiving other cancer treatments and seems promising. But it is not yet clear if it can offer better results than not having the immunisation at all.

Cancer patients, while undergoing treatment, are at higher risk for COVID-19 because of a compromised immune system and the need for frequent visits to a cancer centre. The new immune stimulator also shows promise in tolerability for individuals with compromised immune systems.

CCTG ICC.1: NCI COVID-19 in Cancer Patients Study (N-CCaPS) – a Longitudinal Natural History Study of COVID-19 in people with cancer (NCT04387656)

In this study, researchers are following people and collecting medical and other information about them over time to learn more about how a disease and its symptoms develop and change. The knowledge gained through this study will help doctors better manage treatment for people with cancer and COVID-19 in the future.

As part of the N-CCaPS study, researchers will collect blood samples, medical information, and medical images from 2,000 people with cancer who also have COVID-19. Each person will be followed for up to 2 years to help doctors understand how cancer affects COVID-19 and COVID-19 affects cancer.

CCTG SC.27: Living with Cancer in the Time of COVID-19 - a Cohort Study of the Impact of the COVID-19 Pandemic on Cancer Patients During Treatment and Survivors

The goal of CCTG SC.27 is to examine the impact of the COVID-19 pandemic on the experience of Canadian cancer patients at all stages of treatment, focusing on self-reported emotional, social and physical symptoms, quality of life, changes in cancer care, satisfaction with care, and use of a variety of positive and negative coping strategies.

Drs Linda Carlson, University of Calgary, and Lynda Balneaves, University of Manitoba, with CCTG Senior Investigator, Dr Harriet Richardson, are leading the study team. They will be looking at the unique challenges and potential benefits of these changes in care during the current pandemic by conducting a series of online surveys over a 12-month period asking cancer patients and survivors about their experiences, including people currently receiving cancer treatment and up to 10 years post-treatment. Participants will complete online surveys and investigators will interview cancer patients, survivors and their caregivers to better understand their experiences during the pandemic and how they have coped and adjusted to changes to their care.

Investigators hope that the results of the trial will help to provide a better understanding of the nature of challenges encountered by cancer patients and that identifying potential solutions and developing appropriate supports that can be implemented and evaluated in future emergency planning and research will help to better support patients with cancer.

GAICO

COVID-19 recommendations for cancer patients

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

GEICAM

COVID-19 information for cancer patients

As other parts of the world, Spain was hit by the COVID-19 crisis in the first months of 2020 and a national lockdown was announced on 14 March. At that time, there was not a lot of information about the virus, but it was suspected that infected cancer patients could suffer from a larger number of complications than the healthy population. This is due to their cancer itself as well as to the immunosuppressive effect of its treatments. Cancer patients worried about their specific situation and demanded quality information about the relationship between cancer and COVID-19.

Via its website and social media, the **Spanish Breast Cancer Group (GEICAM)** decided it was critical to underline the importance of cancer patients, their families and their caregivers to be particularly careful when following the international guidelines for COVID-19 prevention. GEICAM added some nuances to the information provided by Spain's National Health System. In addition to these recommendations, GEICAM created a specific section on its website where it collected the latest information on the coronavirus and the risks for cancer patients. GEICAM also prepared a series of support documents and media of interest, including infographics on how breast cancer patients can exercise at home, a collection of frequent Q&A, and webinars hosted by experts in cancer treatment and psycho-oncology.

Visit the "Breast cancer and COVID-19" section on GEICAM's website:

https://www.geicam.org/cancer-de-mama/coronavirus/informacion-para-pacientes-oncologicos

In this spirit, GEICAM started its podcast platform **GEICAM T-Habla** (which translates into **GEICAM speaks to you**), a space where experts and patients debate different topics related to breast cancer in a simple and rigorous way. The first podcast was about the benefits of physical exercise for cancer patients. After that, experts and collaborators covered topics such as lymphedema, metastatic cancer, psychology, the role of research in the development of new treatments, and male breast cancer.

GOIRC

The DOMONCOVID project (Italy): a homecare model for cancer patients during and after the COVID-19 pandemic

Cremona, a city in the Lombardy region in the north of Italy, was the Italian city with the 5th highest incidence of COVID-19. The pandemic added a significant strain on healthcare resources due to the sheer volume of patients presenting to emergency departments, often within a short space of time.

It became very difficult for cancer patients to be assisted and hospitalised. COVID-19-positive (COV-19+) cancer patients, even with mild symptoms, were hospitalised in COVID wards and completely isolated from their family members and from the treating oncologists themselves. Patients were faced with enormous stress and terror due to the risk of death in a situation of isolation and total abandonment.

In the middle of March 2020, during the crucial phase of the pandemic, the **Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC)**, decided to create a homecare project called **DOMONCOVID** with the aim of avoiding hospital admissions of cancer patients and their families, by following patients with mild to moderate symptoms at home and admitting only those with severe symptoms who needed invasive respiratory support.

Within a few days, and in agreement with the hospital management, a team composed of oncologists and nurses from the Oncology Division of Cremona Hospital was formed. It was supported by a secretary with a dedicated telephone number. The team worked for 6 days a week from 8 AM to 5 PM in collaboration with local operators and general practitioners. It assisted cancer patients at home with confirmed diagnosis or symptoms suggestive of COVID-19, without clear clinical or radiological criteria for hospitalisation.

The assistance was provided for residents living within a radius of 50 km from the hospital, from Monday to Saturday, 8 AM to 5 PM. Cancer patients and their cohabitants were tested with at least two nasopharyngeal swabs (NPS). Blood tests, medical examinations and vital parameters were performed.

All screened individuals were advised to follow the quarantine procedures and received an information leaflet. Oral/infusion treatments, including antiviral drugs, were administered.

From 23 March to 30 April 2020, 71 cancer patients were assisted at home, with a total of 191 visits. Of the 71 patients tested with NPS, 26 were COV-19+. Twelve COV-19+ cancer patients had mild symptoms, such as low-grade fever, cough, olfactory alterations and mild dyspnea. Seven patients showed clinical and radiological signs of initial pneumonia with stable parameters; they were successfully treated at home with hydroxychloroquine, antivirals and NSAIDs and did not require hospitalisation. Seven patients with severe symptoms were promptly hospitalised. Four of them died, two due to the infection and two due to disease progression. 52 cohabitants were screened with NPS, of which 28 lived with a COV-19+ cancer patient; in this subgroup, more than half (n = 16) were COV-19+ by NPS. Interestingly, most of them (n = 15) were totally asymptomatic. In Italy, NPS screening is not routinely performed, not even in cohabitants of COV-19+ patients.

This project demonstrated the feasibility of an innovative model based on homecare assistance for COV-19+ cancer patients with mild symptoms. This strategy, limiting hospital access for COV-19+ patients, might be useful to contain the spread of the infection. Further studies are needed to test this strategy in COV-19-negative cancer patients, and the plan is to implement this model of assistance in this population, who will receive oral therapy at home. Finally, this experience indicates a high probability of identifying asymptomatic COV-19+ individuals among cohabitants, and there is an urgent need to extend the screening to this population.

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The results of the DOMONCOVID Project were presented by Margherita Ratti as an oral presentation at the **ESMO Virtual Congress in September 2020**.