BREAST-PREDICT SIX YEARS OF COLLABORATIVE RESEARCH







Foreword Robert O'Connor, PhD, Head of Research, Irish Cancer Society

The Irish Cancer Society has a proud history of investing in cancer research. Thanks to the amazing generosity of our donors, we've supported hundreds of researchers in their work to find ways to help prevent, detect and treat cancer, and ensure more people live well long after diagnosis and treatment.

But cancer is complex. It won't be stopped by one scientist in one lab. It needs continued investment by people working together with a singular focus on the disease.

This is the premise for the Irish Cancer Society's decision to begin investing in Collaborative Cancer Research Centres. Brought about by the energy and passion of Prof John Fitzpatrick, the visionary Irish Cancer Society Head of Research who passed away in May 2014, these centres were envisaged as transformational – a new way for researchers to work together. By pooling resources and expertise, the aim was for this collaborative effort to have an impact on cancer research that was even greater than the sum of its parts, because together is better.

After a highly competitive process, BREAST-PREDICT was chosen as the Society's first such centre. A major €7.5 million investment, it sought to focus our minds on a key problem. While research has driven enormous improvements in breast cancer outcome for many women, we still lose too many patients to variations of this disease.

For BREAST-PREDICT this posed the question: how can we better predict which treatments are best for each patient, thus giving all women affected the best possible chance at a long and healthy life?

Six years on, I'm proud to say that BREAST-PREDICT has had a major impact. The stories and achievements you'll read about in this booklet are just a small glimpse into the great work that has taken place.

This has only been possible through the actions of the centre's dedicated researchers, their superb management team, passionate academic and clinical staff, selfless patients who volunteered to give information, samples or participate in clinical trials, and the thousands of individuals and companies (large and small) who have donated and raised money for this incredible cause.

At the heart of this great work has always been the patient. Treatment for breast cancer is often a long and difficult journey. BREAST-PREDICT has striven to make this journey a little bit easier for those who will find themselves on this path in future years.

Robert J' Connon

DR ROBERT O'CONNOR

From population to patient: Towards personalised breast cancer medicine

Established in October 2013, BREAST-PREDICT was created as a unique multi-disciplinary centre, funded by the Irish Cancer Society, which united different breast cancer experts across the country to work towards a common goal. It involved six leading academic centres across Ireland: UCD, TCD, RCSI, DCU, NUIG and UCC, as well as the nationwide clinical trials group, Cancer Trials Ireland.

Over the past six years, the BREAST-PREDICT team has collected information and tumour samples from nearly every breast cancer patient in the country, with their consent. Using these valuable resources, we have now improved our understanding of how this disease can spread and become resistant to treatment. This information is vital in order to generate new and improved treatments and diagnostics.

Our vision is that each breast cancer patient in Ireland should have their treatment plan tailored for their individual cancer. Most women diagnosed with breast cancer now survive, due to earlier diagnosis and improved treatments. Our goal is to better predict which treatments are best for each patient, thus giving all breast cancer patients the best possible chance at a long and healthy life.



Thanks to funding of €7.5 million from the Irish Cancer Society over the past six years, our team of more than 50 BREAST-PREDICT researchers have carried out vital work that has the potential to benefit breast cancer patients for generations to come. We have also secured independent funding to support our research in the future.

Thank you for your support.

The BREAST-PREDICT Team



Professor Michael Joe Duffy St. Vincent's University Hospital & University College Dublin

Professor Lorraine O'Driscoll Trinity College Dublin

Professor Annette Byrne Royal College of Surgeons in Ireland

Dr Roisin Dwyer National University of Ireland, Galway

Professor Adrian Bracken Trinity College Dublin

Dr Verena Amberger-Murphy Cancer Trials Ireland

Professor Darran O'Connor Royal College of Surgeons in Ireland

Dr Simon Furney Royal College of Surgeons in Ireland

Dr Alex Eustace Dublin City University





Key Goals Towards Personalised Breast Cancer Treatment

Keeping patients at the heart of what we do

Our vision is for each breast cancer patient in Ireland to have their treatment plan personalised for their individual cancer



Create a National Breast Cancer Biobank and Database

We have collected samples of tumour tissue from breast cancer patients in Ireland, with their consent, along with information on their cancer.



Look at how previous medications affect breast cancer outcomes

We have also looked at the medical history of breast cancer patients in Ireland. We want to understand how certain medications, like aspirins or statins, can affect a patient's breast cancer.

Investigate how breast tumour cells can change over time

We have studied how and why tumour cells change over time, leading to cancers becoming resistant to treatments or developing the ability to spread to other areas in the body.



Develop new treatments for breast cancer patients

We focus on finding 'weak spots' in breast cancers that can be targeted with new drugs, or with better combinations of existing drugs.



Predict which treatment is best for each patient

We are developing new tests for breast cancer patients, to predict how likely a patient is to respond to a specific drug, or predict the risk of their cancer recurring.

A Message from Prof William Gallagher, Director of BREAST-PREDICT

BREAST-PREDICT has been a truly collaborative centre. It has united the fragmented strands of Irish breast cancer research, and provided excellent training and research opportunities for our up-andcoming researchers.

While the BREAST-PREDICT research programme officially concludes in 2019, the work it has begun will continue to develop and evolve to the benefit of breast cancer patients. BREAST-PREDICT was pivotal, together with other key entities, in the launch of a new Irish bioresource. The National Breast Cancer Resource contains tissue, blood, DNA and RNA samples from more than 3,000 breast cancer patients. This has really transformed how breast cancer research can be carried out in Ireland. These samples will prove invaluable for researchers for years to come.

BREAST-PREDICT has played a vital role in training and inspiring a new generation of patient-focused cancer researchers. Through attending international conferences, publishing in high-impact academic journals and learning how to communicate their research, supported by a strong network of expert scientists, BREAST-PREDICT researchers are now among the best-trained in Ireland. I have great pride and high hopes in particular for our PhD students and postdoctoral fellows, now scattered all over the world from the National Institutes of Health to Harvard and beyond, whom act as our strongest ambassadors. Together, they will underpin a new ambition to further the progress BREAST-PREDICT has already made.

We're also working to ensure that this ambition will continue long after the Irish Cancer Society's initial

investment. Millions of euros in additional funding have been leveraged from other sources in academia, industry, and state and EU grants.

A critical feature of the BREAST-PREDICT journey was the growing input of the patient voice in cancer research. Centre investigators benefited considerably from close engagement with patient advocates and other stakeholders. In addition, BREAST-PREDICT held multiple patient-oriented seminars throughout the course of the programme, which were extremely well received. Accordingly, an increasing shift towards a richer level of patient involvement in guiding research priorities has been recognised, as is the role of a centre of this scale in providing a forum for two-way dialogue.

We envisage that the impact of BREAST-PREDICT on our knowledge base of cancer and on cancer patients themselves will continue to be seen in the years to come. Our researchers have made huge strides in cutting-edge areas such as examining the impact of prior exposure to aspirin on breast cancer outcome, systems modelling of therapeutic resistance, liquid biopsies as a novel diagnostic solution, and new therapies targeted at Her2 and p53, with the majority of studies being translational in nature.

BREAST-PREDICT has left a lasting legacy in providing a model of how world leading cancer research can be performed in a multi-institutional and truly collaborative manner, for the benefit of patients in Ireland and beyond.

William Gallagher

PROF WILLIAM GALLAGHER

The Value of Cancer Research: A letter to Ireland's breast cancer researchers

Dear Breast Cancer Researchers of Ireland,

My name is Ciara Devine and I volunteer as a breast cancer patient advocate with Europa Donna Ireland.

Four years ago, I developed early stage breast cancer at the age of 36. My daughter was two years old at the time. To say that my diagnosis was a shock is somewhat of an understatement: I liken it to a scene from an action movie, where a car is driving along a quiet street, the lights are green, and suddenly a huge juggernaut smashes into the side of the car and pushes it off the road.

Yet here I am. And I am here today not because of a positive attitude or an amount of prayer (though my parents tried that too) but as the result of hard work.

That hard work took shape in unrelenting family and community support, and in grit that I never knew I had as I dragged myself through treatment and recovery. That hard work took shape in a dedicated and expert multi-disciplinary team working in a specialist breast unit under a national cancer strategy. That hard work also took shape in decades of painstaking, high-quality research. We all worked together to get me to this point and I will always be grateful. I know how lucky I am. Research has made a concrete difference to my life: I had breast-conserving surgery instead of a mastectomy, thanks to randomised trials that showed that lumpectomy plus radiation is at least as good as mastectomy, with less burden to the woman. I had a sentinel-node biopsy, drastically reducing my risk of developing lymphoedema. The radiotherapy treatment I received minimised toxicity and long-term side effects to healthy tissues and organs. I had a genomic test to help me to make an informed decision about whether or not to have chemotherapy. (It was still a difficult decision as I fell into that unhelpfully large grey area of medium risk. I had the chemotherapy.) My hormonal therapy was extended from five years to ten following data from several large-scale international trials.

Of course, things have moved on even since 2013. Survival rates and quality of life for cancer patients are improving as medicine takes leaps forward, but medicine cannot do that without research.

But, research is expensive and time-consuming. To have the most benefit, to get the most value for money, your research must strive to be relevant and impactful.

So how will you know if you are asking the right research questions? You must ask patients. We will tell you what matters because we are the frontline. Not only are we patients, we are people with wideranging skills and expertise. We are journalists, lawyers, carers, teachers, artists and some of us are scientists and doctors too. We have a lot to bring to the table and can also help to communicate complex ideas to different audiences. It is amazing what one can learn about molecular biology and signaling pathways with a laptop and plenty of motivation.

Patient and public involvement in research is evolving and many patients fully support this changing paradigm. For instance, the public outreach initiatives at UCD cancer research institutes, from open labs to the 'Patient Voice in Cancer Research' scoping exercises, have been instrumental in opening conversations between individual patients and patient groups and researchers. Increasingly, the Irish Cancer Society and Europa Donna Ireland collaborates on research proposals with Irish researchers, ensuring the relevance of proposed research to patients. We are experiencing a tangible willingness from your research community to share and engage with patients and we welcome that.

We would also like to point out that we patients – the diverse bunch that we are – can be your best advocates. We can call for more funding for research We can rally support for prioritising research on the national political agenda. Sometimes we just need to be asked. Sometimes we need to make ourselves heard.

It is a strange feeling to know that if I had been born a few generations earlier, then I probably wouldn't have survived breast cancer – this far. I believe that research and its careful application saved my life and I want the work to continue, to save the lives of others, to reduce the burden of breast cancer and its treatment on women and on their families and on society. Lastly, I would also like to say that research makes a difference to my life in another way, a less concrete but equally important way: it gives me hope. To know that excellent, focused research is happening in this country, to think that even I might be able to contribute to the success of this work, even to imagine that my daughter might grow up without fear of breast cancer – this gives me enormous hope.

For this, thank you. Yours sincerely,

Gava Derine

CIARA DEVINE Volunteer Patient Advocate Europa Donna Ireland – The Irish Breast Cancer Campaign

Adapted from a talk <u>delivered</u> to <u>BREAST-PREDICT</u> Oversight Committee Review Meeting on 19 October 2017 at UCD Conway Institute, Dublin.



Research Breakthroughs

Our team of over 50 BREAST-PREDICT researchers have carried out vital work that has the potential to benefit breast cancer patients for generations to come. Over the next few pages, you'll find a selection of the world-class research your donations have funded.



Potential therapeutic options for breast cancer patients with brain metastases

Research carried out by BREAST-PREDICT researchers in collaboration with scientists from the University of Pittsburgh examined molecular changes that happen in breast cancer cells that have spread to the brain. Breast cancer brain metastases occur in 10% - 30% of the patients with advanced breast cancer, offering few therapeutic options which are often limited to radiation and surgery. Brain metastases therefore represent an unmet medical need, leading to various neurological conditions that significantly decrease the quality of life of patients.

The ground-breaking research completed by Prof Leonie Young and Dr Damir Varešlija in RCSI, has revealed that breast cancer cells adapt and switch on and off various genes when spreading to the brain. By analysing levels of gene expression across 21 cases of primary breast tumours and their associated brain metastases, significant alterations were discovered. One of the most important changes is represented by the switch of HER2-negative primary tumours to HER2-positive brain metastases in 20% of cases, which could make these secondary tumours treatable with targeted HER2 therapies. These findings were published in the Journal of the National Cancer Institute.

Dr Varešlija is excited about this recent breakthrough: "This preclinical study indicates that brain metastases acquire enhanced survival capabilities, through genetic changes, as they spread from the primary tumour site. A better tailored, more efficient treatment can therefore be designed for those patients with advanced breast cancer that has spread to the brain, many of whom have exhausted all other treatment options".

Irish research sheds light on the effects of aspirin and vitamin D on breast cancer

BREAST-PREDICT researcher Prof Kathleen Bennett. based in the Royal College of Surgeons in Ireland, leads a team of scientists investigating the effects of various medicines and supplements taken by breast cancer patients, either prior to or following their diagnosis.

In 2014, they discovered that women who had been prescribed aspirin regularly before being diagnosed with breast cancer are less likely to have that cancer spread to the lymph-nodes than women who were not on prescription aspirin. These women are also less likely to die from their breast cancer.

One of the lead authors. Dr Ian Barron, said "Our findings suggest that aspirin could play a role in reducing mortality from breast cancer by preventing the cancer spreading to nearby lymph nodes, We analysed data from 2,796 women with stage I-III breast cancer. We found that those women prescribed aspirin in the years immediately prior to their breast cancer diagnosis were statistically significantly less likely to present with a lymph node-positive breast cancer than nonusers. The association was strongest among women prescribed aspirin regularly and women prescribed higher aspirin doses. We now need to establish how and why this is the case'.

Prof Kathleen Bennett adds a word of caution: "Our study was observational and these results do not mean that women should start taking aspirin as a precautionary measure. Aspirin can have serious side effects."

In 2018, the group published a further study which showed that women who take vitamin D after being diagnosed with breast cancer may have an increased chance of survival.

This study, led by RCSI researcher Dr Jamie Madden under the supervision of Prof Kathleen Bennett, analysed data from almost 5,500 breast cancer patients, and found that taking vitamin D supplements after diagnosis was associated with an increased relative survival of 20% compared to those who did not take it.

Prof Bennett said: "Previous studies have found that higher blood levels of vitamin D, which can come from our diet, sunlight or supplements, is associated with increased breast cancer survival. Our study suggests that vitamin D supplementation might be useful for women diagnosed with breast cancer. Large clinical trials are already underway overseas to look into this further "

However, both studies show an association, and not a causal link. Women with breast cancer should talk to their medical team if they are thinking of taking aspirin or vitamin D supplements.

Both of these studies analysed data gathered by the National Cancer Registry of Ireland.

11%

reduction in spread to lymph nodes in women who took aspirin prior to their breast cancer diagnosis

Prof Kathleen Bennett



Avoiding unnecessary treatment for 'low risk' breast cancer patients

BREAST-PREDICT researchers have developed a new test which may mean fewer women with breast cancer having to undergo chemotherapy.

For the majority of women with early-stage breast cancer, standard treatment involves surgery to remove the tumour, followed by a harrowing chemotherapy regime to prevent cancer recurrence. However, it is estimated that approximately 70% of women with early-stage breast cancer do not need chemotherapy. Yet oncologists still recommend chemotherapy to the majority, as tests to measure its effectiveness often give inconclusive responses.

OncoMasTR is a new test developed by BREAST-PREDICT researchers Prof William Gallagher, UCD, and Prof Adrian Bracken, TCD, which aims to overcome this limitation by better predicting which women can forego chemotherapy.

The researchers have shown that *OncoMasTR* offers improved performance over existing tests by classifying 67% of patients as low-risk and 33% as high-risk, closely paralleling clinically observed recurrence rates.

Additional funding has been obtained from both the EU Horizon 2020 programme and Science Foundation Ireland to drive the development of this test towards clinical use, in collaboration with the Irish SME, OncoMark. A further study, which included more than 1000 breast cancer samples, confirmed the original result.

Prof William Gallagher is excited about where this may lead, and says: "We have shown that the OncoMasTR test can accurately identify low-risk patients with early-stage breast cancer who can safely forgo chemotherapy as part of their treatment. This will allow these patients to improve their quality of life, and reduce overall healthcare costs."

70% of women with

early-stage breast cancer do not need chemotherapy

67% Patients classified as low risk by OncoMasTR tests

BREAST-PREDICT scientists find new hope in overcomina potentially deadly form of breast cancer

Irish scientists have found a potential new way to treat one of the most aggressive and difficult to treat forms of breast cancer.

Researchers from BREAST-PREDICT have shown that a new drug – COTI-2 – can prevent the growth of triple-negative breast cancer cells. If found to be successful in clinical trials. COTI-2 has the potential to save lives for patients with a form of breast cancer which is currently difficult to treat.

More than 250 people in Ireland are diagnosed with triple-negative breast cancer each year. The subtype accounts for approximately one in six breast cancer cases globally. Triple-negative breast cancer is often aggressive, difficult to treat and tends to be more common in younger women.

This work, led by Dr Naoise Synnott, Prof Joe Duffy, and Prof John Crown, focused on p53, a gene which is altered in almost all cases of triple-negative breast cancer. P53 is a gene which normally prevents people from getting cancer, but when p53 is mutated or altered, it can drive cancer cells to grow out of control.

The researchers found that the drug COTI-2 is effective at stopping this gene and killing these cancer cells. Together with further studies in the US, results proved positive enough for an early-stage clinical trial to begin. This trial, due to start later this year, will test COTI-2 in combination with a chemotherapy drug, eribulin, in patients with advanced chemo-resistant triple negative breast cancer.

According to Dr Naoise Synnott, the only form of treatment currently available to patients with this type of cancer is chemotherapy. "While this will work well for some patients, others may find that their cancer cells don't respond as well as might be hoped to chemo, leading to patients suffering the side effects of this treatment without any of the desired outcomes. I hope that this work will be a big step in providing hope and better treatment options to future triplenegative breast cancer patients."

>250

people in Ireland are diagnosed with triple negative breast cancer each year





Tackling resistance to treatment in advanced HER2-positive breast cancer

Women whose breast cancer is resistant to current drugs may in the future have access to personalised, more effective treatments.

BREAST-PREDICT researchers Dr Sinead Toomey, Dr Alex Eustace and Prof Bryan Hennessy, based in RCSI and DCU, have looked for ways to tackle therapy resistance in HER2-positive breast cancer, a form of the disease which affects around 500 women in Ireland each year.

HER2-positive breast cancer is a type of breast cancer in which cancer cells are mutated so they produce high amounts of human epidermal growth factor receptor 2 (HER2), which promotes growth of cancer cells and makes them more aggressive.

Even though treatment of HER2-positive breast cancer improved with the arrival of anti-HER2 drugs such as trastuzumab, at least 20% of HER2-positive breast cancer patients have cancers that become resistant to these new treatments.

Prof Bryan Hennessy

Prof Hennessy said: 'It is known that HER2+ breast cancer can become resistant to current HER2 therapy. We are now learning how this happens. The switching on of a pathway called the PI3K pathway in cancer cells is often responsible. One of the possible ways this happens is through mutations (changes) that occur in a gene called PIK3CA. Research studies that we have carried out at the laboratory level have suggested that blocking the abnormal activity of the PI3K pathway in cancer cells, may help to reverse the resistance of some HER2+ breast cancers to HER2 treatments including trastuzumab'.

The team discovered that copanlisib, a new drug targeting the PI3K pathway, added to trastuzumab could reverse anti-HER2 treatment resistance in some breast cancers. This exciting discovery was confirmed by preclinical tests and has progressed the new therapeutic scheme to a clinical trial, called PantHER.

Prof Hennessy comments: 'Copanlisib blocks the abnormal activity in the PI3K pathway and it is currently being tested in a variety of cancers. By combining copanlisib and trastuzumab, this trial hopes copanlisib will block the abnormal activity of the PI3K pathway and allow trastuzumab to work effectively.' The PantHER trial is being run by Cancer Trials Ireland, and is expected to be completed in 2020.

20% of Her2+ patients develop resistance to targeted therapy

BREAST-PREDICT Achievements





€7.5 million

initial investment from the Irish Cancer Society

Over €55 million

extra funding leveraged



9 clinical studies across 15 hospitals



>3,400 patients accrued on clinical studies



17 novel therapeutics in testing some reaching clinical trial phase



breast cancer diagnostic tests in development

original papers published

and 40 review papers

250+ speakers invited to conferences organised



100+ collaborations initiated with industry partners and other

academic researchers

Researcher Training

The first rung of the ladder of a career in cancer research is completing a PhD. The BREAST-PREDICT research programme funded 13 PhD students on a four-year structured PhD training programme, at universities around Ireland.

All of our PhD students have successfully defended their PhD theses and moved on to varied careers within or outside of academia. Aside from their research work, many students gave generously of their time to organise fundraising activities for Irish Cancer Society campaigns such as Daffodil Day and Cups Against Breast Cancer. In their final years with the programme, our students presented their work in front of expert audiences at international conferences around the globe. Their work led to original research articles being published in high-ranking academic journals, and new breast cancer treatments being tested in clinical trials. We couldn't be more proud of them!





"Cancer research is like a puzzle, and all the pieces must come together for it to be solved. My research focuses on the potential links between statins (cholesterol-lowering medications) and improved breast cancer survival. I hope that my work has added to the knowledge base and, collectively, that we will make a difference to the lives of those living with cancer."

Dr Amelia Smith

Former BREAST-PREDICT PhD student, now a Postdoctoral Research Fellow and Data Analyst at the Medicines Management Programme at St. James' Hospital.



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"Completing a PhD gave me the confidence to present and defend my data. It gave me the critical eye to analyse and interpret data. It gave me the resilience to accept failed experiments and to thoughtfully plan out my next one. It also gave me the determination to see a project through until its end, no matter how frustrating that may be."

Dr Killian O'Brien

Former BREAST-PREDICT PhD student, now a Postdoctoral Research Fellow at Massachusetts General Hospital and Harvard Medical School.



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"Having watched someone I love battle through breast cancer, I knew I wanted to make a contribution to understanding and treating this complex disease. Combined with my love of science, a PhD with BREAST-PREDICT was the perfect option for me. Having the opportunity to discuss my research with fellow students, senior academics and clinicians on a regular basis was invaluable to the progression of my work."

Dr Lisa Dwane

Former BREAST-PREDICT PhD student, now a Postdoctoral Research Fellow at the Sanger Institute in Cambridge.



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"My most exciting scientific discovery was that the biomarker we studied was involved in the development of brain metastasis, and that we could prevent this with a treatment that we developed. This has obvious implications for the clinic, as the brain is seen as a 'sanctuary' site for breast cancer metastasis and can be difficult to treat."

Dr Ben Doherty

Former BREAST-PREDICT PhD student, now an Analytical Scientist at Pfizer.



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"There are many challenges when completing a PhD. Research can be slow and the results can sometimes be unexpected. You need to be resilient and have a lot of determination. One of the most enjoyable parts of my work was getting to meet patients and the public at various events and talks. I'm very grateful to everyone that wanted to chat and hear about my research."

Dr Michelle Lowry

Former BREAST-PREDICT PhD student, now Biomedical Research Coordinator within the Research Team in the Irish Cancer Society.



BREAST-PREDICT Highlights



Launch of BREAST-PREDICT



First Scientific Advisory Board meeting

BREAST-PREDICT holds its **first Scientific Advisory Board meeting**, with international experts providing crucial feedback on the developing research programme.



Patient Voice in Cancer Research

The **Patient Voice in Cancer Research** holds its inaugural event, with more than 100 cancer survivors and their families joining health care professionals, researchers, patient advocates, funding agencies and charity groups at an open forum in UCD. The discussion is focused on placing survivorship at the heart of the research agenda.



National Breast Cancer Bioresource and Database is established

The National Breast Cancer Bioresource and Database is established, which holds information on more than 3,000 patients. This resource is described as the 'jewel' of BREAST-PREDICT by their Scientific Advisory Board, and is expected to see significant use by researchers across the country.

Team of over 50 researchers recruited to the BREAST-PREDICT research programme



Test to assess risk of breast cancer recurrence

BREAST-PREDICT scientists develop **test to assess risk of breast cancer recurrence**. Prof William Gallagher (UCD) and Dr Adrian Bracken (TCD) develop the 'OncoMasTR' test, which can distinguish between low risk and high risk early-stage breast cancer patients, better than current approaches. This will help doctors and patients to make decisions about the best treatment options for each patient based on their particular tumour.



PantHER Clinical Trial

The PantHER Clinical Trial,

led by BREAST-PREDICT scientist Prof Bryan Hennessy, begins recruiting patients: this trial tests the PI3-Kinase inhibitor copanlisib in combination with trastuzumab in patients with recurrent or metastatic HER2-positive breast cancer. This will improve treatment options for late-stage cancer patients, many of whom have exhausted available treatments





Effects of aspirin on breast cancer

BREAST-PREDICT scientist Prof Kathleen Bennett is continuing to investigate the effects of aspirin on breast cancer, publishing new research focusing on end-of-life care. Their previous research found that women who had been prescribed aspirin regularly before being diagnosed with breast cancer are less likely to have that cancer spread to the lymph-nodes than women who were not on prescription aspirin. These women are also less likely to die from their breast cancer.





Cancer Stories & Choirs for Cancer

Cancer patients, advocates, survivors and family members gathered to share their personal cancer stories with cancer researchers and the public at the Cancer Stories & Choirs for Cancer event. This was followed by a concert featuring over 200 singers from 7 choirs across Ireland, in tribute to people whose lives have been touched by cancer.



94 original research articles and 40 review articles

To date, the BREAST-PREDICT team have published 94 original research articles and 40 review articles. Several of these articles describe key research advances likely to impact patient care.

Hope for patients with advanced breast cancer

A finding by BREAST-PREDICT researchers gives **hope for** patients with advanced breast cancer whose cancer has spread to the brain. Groundbreaking research carried out by Prof Leonie Young and Dr Damir Vareslija in RCSI reveals a novel approach to treat the spread of breast cancer to the brain.



July 2018

New treatment for triple negative breast cancer

BREAST-PREDICT scientists Prof Joe Duffy and Dr Naoise Synnott have been involved in testing a new treatment for triple negative breast cancer. Their work focuses on p53, a gene which is altered in almost all cases of triple-negative breast cancer. They found that the drug COTI-2 is effective at blocking this gene and killing cancer cells. This drug is now being tested in a clinical trial in women with advanced triple negative breast cancer.

Has the potential to benefit breast cancer patients for generations to come

BREAST-PREDICT researchers have carried out vital work that has the potential to benefit breast cancer patients for generations to come. The initial investment of the Irish Cancer Society in this pivotal research centre has paid off, and BREAST-PREDICT researchers have secured independent funding to continue their research into the future.





Mav 2019

BREAST-PREDICT Clinical Trials

Cancer clinical trials aim to improve treatment options for patients and increase the quality of life. BREAST-PREDICT-affiliated clinical studies have offered access to innovative medicines and diagnostics to over 3,400 patients thus far, across 9 studies and 15 hospitals. All trials have been run by Cancer Trials Ireland.



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"One of the misconceptions that people have is that by going on a clinical trial, they are guinea pigs, and they might get a drug or treatment that is not tested. They are very well tested, for years, sometimes decades, before entering a trial. Medical developments in treating cancer have advanced significantly in the last decade."

Prof Bryan Hennessy is a Consultant Medical Oncologist based at the Royal College of Surgeons Ireland, a BREAST-PREDICT Principal Investigator and Clinical Lead with Cancer Trials Ireland.



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"For anyone who wants to start a trial, just ask your doctor and see what can be done. Give it a shot, take it one day at a time. I'm nearly a year on the trial now, my quality of life is great, I'm a busy mam with 3 kids."

Emma Corcoran is a breast cancer patient and participant in a clinical trial with Cancer Trials Ireland.



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"I manage the Translational and the Radiotherapy team in Cancer Trials Ireland and oversee the clinical and translational trial portfolio of both departments. Cancer Trials Ireland's involvement in BREAST-PREDICT was to support and enable access to clinical samples (blood and tissue) and data collected from patients who were enrolled on our studies. BREAST-PREDICT was an extremely fruitful collaboration between academic researchers and clinicians. Many research outputs achieved in this collaboration will have an influence on the development of new, more specific trials, which will help cancer patients to reach a better treatment outcome combined with a better quality of life.

Thank you for giving us the opportunity to be part of this program."

Dr Vereng Murphy is a BREAST-PREDICT Principal Investigator, Translational Research Leader in Cancer Trials Ireland, and part of the Leadership Team.



Elaine Kelly is one of the Irish Cancer Society's Living Life volunteers, who provide peer support to people with secondary cancer. Elaine was first diagnosed with inflammatory breast cancer aged 34. After initially successful treatment, her cancer returned more aggressively and spread to other parts of her body.

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"In February 2014 I was asked to take part in a clinical trial run by the Cancer Clinical Research Trust to measure the side effects of a targeted therapy drug called TDM1 (Kadcyla).

I felt privileged to be suitable for this trial and within months I saw the benefits. By June 2015 you could practically have called me an NED - No Evidence of Disease."

However, later that year Elaine discovered she had cancer in her brain. Intensive radiotherapy removed 95% of the tumour. Today, Elaine described herself as living well with cancer.



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Rhona Nally is a Living Life Volunteer with the Irish Cancer Society and lives with secondary breast cancer.

"Around 20 years ago a drug called Herceptin was approved for the treatment of HER2-positive breast cancer. It was an absolute game-changer for people with this form of breast cancer.

I quite literally owe my life to cancer research. Twenty years ago, women with HER2-positive disease had the poorest outcomes of all breast cancers. Today, thanks to Herceptin, they have one of the best."



Clinical Trials Supported by BREAST-PREDICT



15

major hospitals participating from Dublin, Cork, Limerick, Waterford, Galway and around the country (see map)



breast cancer clinical trials coordinated by Cancer Trials Ireland. Studies are designed for newly diagnosed, recurrent and Stage IV metastatic breast cancer patients

>3,400 patients accrued since the inception of BREAST-PREDICT





Closely monitored by a team of doctors and nurses With the purpose of finding better ways to

prevent, diagnose and treat breast cancer





Supporting Career Development

Following a PhD, early-career scientists generally undertake a postdoctoral fellowship under the mentorship of an experienced scientist, following which they aim to transition to an independent position, leading their own research group. This transition can be challenging and competitive, and only the most accomplished researchers succeed in establishing an independent career.

BREAST-PREDICT supported the transition of several of the brightest and best early-career researchers from postdoctoral positions to independent research positions during the programme, with many other promising scientists being well on their way to a successful research career.



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"My area of research is focused on understanding metastatic breast cancer. We have demonstrated that metastatic tumours are very different from the primary breast tumours from which they originated, and should be treated accordingly. My work has focused on patients that have the fewest treatment options and very poor prognosis. I hope that in the future my research can better drugs for those that need it most."

Dr Damir Vareslija

Research Fellow in the Royal College of Surgeons in Ireland.



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"My research on a new type of drug called a PI3K inhibitor resulted in the initiation of a clinical trial. The trial has resulted in 13 women with advanced breast cancer being given the opportunity to receive this treatment, which we hope will improve their outcome. Ireland is such a small country that we should always look to share our resources and expertise. The collaborative approach of BREAST-PREDICT is really the template for how research should be performed."

Dr Alex Eustace

Scientific research lead for the Cancer Clinical Research Trust, and is based in Dublin City University. In 2019, he received a HRB Emerging Investigator Award to support his research.



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"Being part of the BREAST-PREDICT team gave me the opportunity to work with leading scientists. This provided me with a fantastic opportunity, at an early stage of my career, to build a network of academic and industry collaborators."

Dr Sinead Toomev

Lecturer and Translational Oncology Research Scientist at the Royal College of Surgeons in Ireland, based at Beaumont Hospital.



Patient Engagement and Involvement in Research

"Do nothing about me without me"

Until relatively recently, the role of patients in the research process was limited to their involvement as research subjects. The BREAST-PREDICT model aims to actively involve patients in the research process where possible, to ensure that the research that we carry out has the patient priorities at heart. This has included having patients attend our Scientific Advisory Board meetings, providing input on research funding applications, and helping to develop research questions at events such as the Patient Voice in Cancer Research. We also organise regular lay research seminars and engagement events to raise awareness of cancer research and the work of BREAST-PREDICT among patients and the public. "I helped form the patient advocate input for a BREAST-PREDICT team's grant application in 2017. Though the application was not successful, it was, for me, a fascinating insight into the process. I found it inspiring to meet so many dedicated researchers applying their considerable collective intellect to a problem that is directly relevant to me: how to 'catch' breast cancer cells before they metastasise to other organs in the body. I can't say that I followed all of the scientific discussion during our meetings, but I believe I helped to contextualise the research question for them, pointed out where plain English was needed and explained the priorities from a patient's point of view. I was made feel a genuinely welcome and crucial part of their team and I would happily get involved again."

Ciara Devine

Breast cancer survivor and patient advocate.

Roundtable discussion during a Patient Voice in Cancer Research event

Prof William Gallagher giving an overview of BREAST-PREDICT at a patient engagement event "In March 2018, I approached BREAST-PREDICT for support in relation to organising a public seminar on breast density. Together, we co-hosted the first Irish breast density seminar, 'Mammographic Breast Density: What Women Need to Know' on 10th June 2019. The event was hugely successful, an open discussion between patients, scientists, radiology experts and researchers. I can only say that organising this event would not have been possible without the organisational, administrative and research support of BREAST-PREDICT. They have mentored me and encouraged me to have a level of confidence and understanding in my ability to be a patient advocate."

Siobhan Freeney

Breast cancer survivor and patient advocate promoting awareness of breast density at www.beingdense.com.

"Being both a researcher and a patient is a strange intersection. I know a fair bit about the biology of cancer and can read the new cancer research papers and understand the stats. But now I am one of those stats. I am one of those data points on a survival curve. So I know all the scary stuff about how complex cancer is and the hard work that researchers do to understand it. But I also know that we don't even know how much we have yet to learn. And that is why I am so supportive of research. Because while we do have some great treatments that work for some people, there are still many people dying of cancer that need new treatments to be developed. The only way to get them is by supporting great researchers to come up with new ideas."

Dr Sarah McLoughlin

Biologist, breast cancer patient and patient advocate.

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Guest speaker Prof Paula Gordon being introduced by Siobhan Freeney at the 'Mammographic Breast Density: What Women Need to Know' event

lount Sion Choir at the 'Choirs fo Cancer 2019' event in UCD



Perspective of International Research Community

To ensure that BREAST-PREDICT research was scientifically excellent, an independent panel of international scientific experts was appointed to a Scientific Advisory Board. These experts attended the centre's end-of-year meetings to review the research, and received regular updates throughout the year. The Irish Cancer Society also had an independently appointed Oversight Committee of international scientists to monitor progress of the centre and provide an expert opinion on an ongoing basis.

This dual approach ensured that BREAST-PREDICT research was of the highest international standard.



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"We are unanimously impressed by the high calibre of the early-stage researchers in the programme, and feel that the level of training and development within the programme is exceptional." Scientific Advisory Board



"This has been an exceptional investment by the Irish Cancer Society that will impact patients, not only in Ireland, but globally." Oversight Committee

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"The research presented shows significant potential to have direct impact on the management of breast cancer for patients."

Scientific Advisory Board

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"It is my belief that the value of this work will last long after the expiry of funding and will be timeless." Oversight Committee

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"Overall, the whole is substantially greater than the sum of its parts." Scientific Advisory Board

