Cancer Retreat Report 2022

cancer trials ireland

Together, we're finding answers to cancer.

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Executive Summary: Prof Seamus O'Reilly

The second Cancer Trials Ireland Cancer Retreat took place on May 20 2022, appropriately on what is International Clinical Trials Day. Building on the success of the inaugural event which was wholly virtual, this year's iteration was a hybrid affair, with a warmly-welcomed audience in situ, as well as a large number of online attendees logging on.

The goal of the Retreat was once again to outline the vision for clinical trials infrastructure in Ireland and the steps that must be taken to achieve the ambitious goals relating to patient participation in clinical trials.

"Cancer research saves lives"

Outlining the developments since the first Retreat in 2021 was CTI clinical leader and consultant medical oncologist Professor Seamus O'Reilly. The professor explained that the discourse at last year's Retreat had clearly identified a number of pivotal issues, from recruitment retention, to logistics, to international competitiveness and patient participation and involvement as issues to address in bringing more trials to Ireland. Furthermore, in an environment where access to healthcare has been impacted by a global pandemic as well as a devastating cyber attack, the cancer trials community has faced significant challenges in terms of delivering its clinical trial work, although Prof O'Reilly noted that this has thankfully already begun to recover.

In preparation for this year's retreat, CTI surveyed investigators and other clinical trial staff on barriers to trial conduct, and assessed their relative importance. It was found that respondents believed that protocol review - road testing a trial - and trial logistics were the key determinants to successful trial conduct. This year's meeting seeks to uncover how these limiting factors can be optimised.

Advances in cancer research have been staggering, but they must now be more evenly spread across all disease focuses, Prof O'Reilly stated. Trial accrual in haematological malignancies has risen significantly in recent years because of access to clinical trials in this portfolio; "we want to extend that dramatic increase to all cancers."

Indeed, significant challenges remain. Not all units were successful in the last funding round, with two cancer centres in the West and Northwest missing out. CTI are committed to national equity of access and the Retreat will explore how this can be achieved. And like all areas of the health service, the cancer trials workforce was fragile even before the pandemic and this will be an ongoing problem. Ireland must also learn from its successful clinical trials and use these learnings going forward

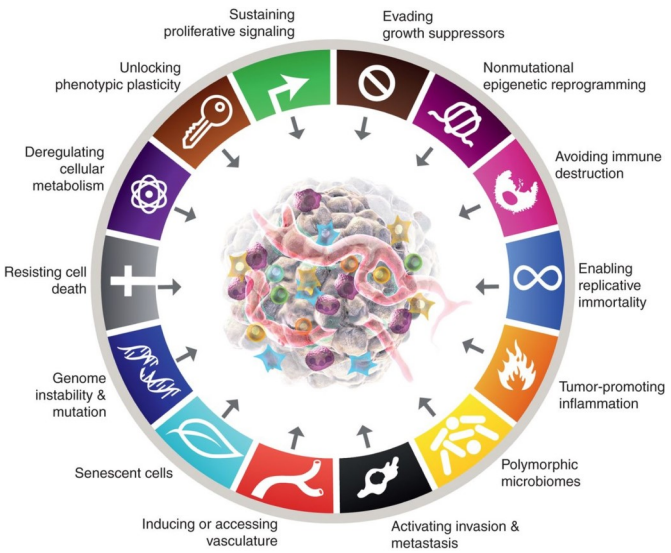
as it seeks to build the infrastructure needed, the professor added.

According to Prof O'Reilly, the "most important paper in cancer medicine this year" was published in Cancer Discovery in January. Entitled "Hallmarks of Cancer", it outlined the advances in identifying targets for treatments for cancer for the next decade.

"Cancer research saves lives. Today's meeting is about building harmony between researchers, patients, and risk management so that our society can benefit from the discoveries outlined in 'Hallmarks of Cancer'."

Prof Seamus O'Reilly
Clinical Leadership

Hallmarks of Cancer



Deirdre Somers, Chair, Cancer Trials Ireland

A landmark event

The Chair of Cancer Trials Ireland, Deirdre Somers, called the 2022 Cancer Retreat "a landmark event", which allows stakeholders in cancer clinical research a forum in which to determine the "priorities, possibilities and challenges in the fight against this terrible disease".

CTI does not lack ambition, and it is aiming for cancer trials to be indispensable, to be a recognised hub for cancer trials and to be globally recognised for its excellence governance and innovation in clinical research, she said. CTI has a five year plan that will address many of the deficits and challenges already highlighted, and this includes clear goals and metrics, including specific "achievable but ambitious targets".

"We want every cancer patient on the entire island of Ireland to have optimal access to, utmost confidence in, and the best outcomes from cancer trials," said Ms Somers. "Everyone in this room and online is crucial to achieving that success."

Keynote: **Dr Doug Lowy, Acting Director, NCI, America**

With the longstanding Memorandum of Understanding between the NCI and Ireland and Northern Ireland having recently been renewed, Dr Lowy told the audience that he looks forward to working even more closely than before with those involved in cancer clinical trials in Ireland, both North and South.

Covid had a devastating impact across healthcare but a silver lining was to be found in the adoption of telemedicine and the importance of "bringing medication to patients rather than patients to medication," Dr Lowy said. This has allowed the NCI to reboot its clinical trial structure and further enhance patient accrual.

Advances in precision medicine are underlining the crucial role of cancer clinical trials, he notes. "Clinical trials have been very important but in the future they will be even more important when it comes to getting more drugs to more patients at the right time." Increasing clinical trials accrual is critical so that it can be determined more quickly whether new interventions are working - they can then be made the standard of care so that more patients can benefit. "The investment in the necessary infrastructure will be worth the effort."

This must be achieved not only for common cancers but more uncommon cancers, and clinical trials must progress towards being more representative; Dr Lowy noted that NCI endeavours have seen the numbers of black and Hispanic patients entering clinical trials increase significantly.

The MoU has always opened up opportunities, and Dr Lowy said he hopes to see more Irish patients on clinical trials happening in the US, while also helping clinical trials in Ireland accrue more patients.

See Dr Lowy's address here.

Increasing clinical trials accrual is critical so that it can be determined more quickly whether new interventions are working - they can then be made the standard of care so that more patients can benefit.

- Dr Doug Lowy, NCI

CEO: Eibhlin Mulroe - Cancer Trials Ireland 2022-2027

Cancer Trials Ireland CEO, Eibhlin Mulroe, outlined the findings of market research recently conducted on behalf of the organisation to ascertain public attitudes towards clinical trials. The survey found three out of five people said they would take part in a clinical trial, with 85% agreeing and 44% strongly agreeing that clinical trials provide patients with access to treatments that would not otherwise be available. Some 26% said they would participate in a trial to access a treatment not otherwise available and 16% know someone who has taken part in a trial.

These findings are "very powerful information", said Ms Mulroe. "This shift has happened because of Covid and the recognition of the importance of clinical research" According to the survey, 78% agree the pandemic has highlighted the importance of clinical trials.

The cancer clinical trials community has come a long way since last year's inaugural retreat, noted Ms Mulroe. The HRB Cancer Clinical Trials Network has become a reality and the Irish Cancer Society contributed €1 million towards research in 2022, which was gratefully received. There have been 23 peer reviewed documents since last year. Cancer Trials Ireland is now set to take over the Molecular Tumour Board, while the Pancreatic Cancer Trials portfolio is expanding thanks to the generosity of late jockey Pat Smullen and his family.

Cancer Trials Ireland also has a new chair and board, and a whole complement of new staff. When devising its five-year 2022-2027 strategy, Ms Mulroe explained that they spent time speaking to stakeholders so that they could clearly define its mission, vision and values. Its key strategic objectives are:

STRATEGIC OBJECTIVES:

- **Maximise contribution to National Cancer Strategy**
- **Optimal, stable and scalable talent to serve growth**
- **Position clinical research as a integral part of cancer care through thought leadership, advocacy, and influence**
- **Deliver a compelling "All-Ireland" cancer trial proposition**
- **Financially sustainable and funded for growth**

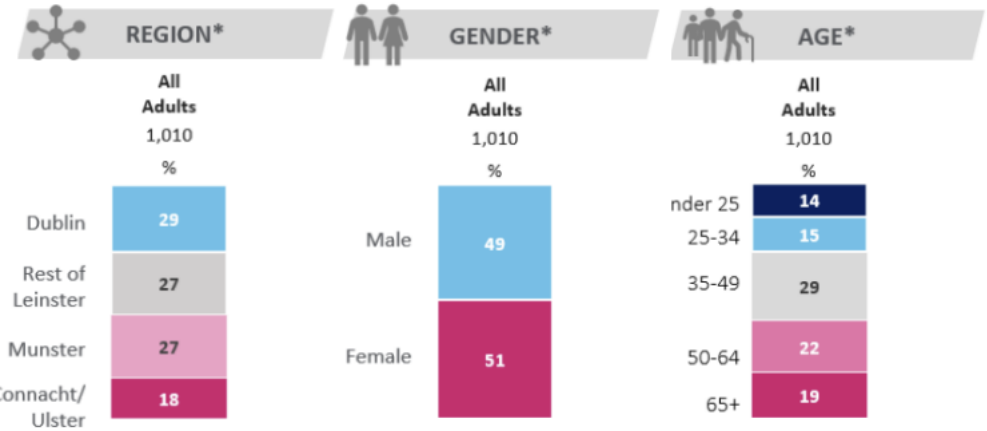
Survey highlights

- **3 in 5 people in Ireland (60%) would participate in a clinical trial**
- **85% agree (and 44% strongly agree) that Clinical trials provide patients with access to treatments not otherwise available**
- **26% would participate in a trial to access treatments not otherwise available**
- **16% know someone who has taken part in a trial**
- **78% agree pandemic has highlighted the importance of clinical trials**

Sample:

1,010 people in Ireland taking an online survey in April 2022

Figure 2:



Vision for clinical trials infrastructure for the future

PANEL 1

The discussion was facilitated by CTI's Eibhlin Mulroe, who was joined by Dr Heather Burns, Specialist in Public Health Medicine, working with the National Cancer Control Programme, Oonagh Ward, Head of Research and Innovation Infrastructures with the Health Research Board, Professor Leonie Young, Associate Professor at the RCSI, a Cancer Trials Ireland host institution, and Professor Martina Hennessy, Director of the Wellcome HRB CRF at St James's Hospital, Trinity College Dublin.

Opening the discussion, Ms Ward noted the HRB has been in this space since 2002, beginning with ICORG, which evolved to Cancer Trials Ireland. The original ambition was to build capacity and that has grown in recent years, she asserted. International evidence supports the need for clinical trials and what they can do, not only for patients but the entire healthcare system and the wider economy. But how they are funded and resourced has changed; "so they are becoming more complex and thus demanding and intensive".

Robust clinical trials infrastructure and support is necessary and the HRB has recognised this and made a strategic investment over the years.

This growth meant that in 2018, a decision was made to change the approach to funding, altering the funding structure and bringing in partnerships with the universities while expanding funding opportunities with the HSE.

"By working together in that collaborative environment, synergies happen and duplication is avoided," Ms Ward said. This restructuring and remodelling is their attempt to reach the ambitious target of 6% of patients on trials. "The more evidence we have around performance we can build the case for additional funds and supports. We need to be innovative and support innovation."

Pictured (L-R): Oonagh Ward, Health Research Board; Dr Heather Burns, Specialist in Public Health Medicine, NCCP; Prof Martina Hennessy (Wellcome-HRB CRF at St James's / TCD)

Dr Burns then discussed the role of the NCCP in building clinical trials infrastructure. The NCCP has committed €20 million to services in 2021 and a further €20 million in 2022; this funding has been used to support delivery of the National Cancer Strategy, building resilience in existing services and adding new services, she explained. This includes 400 new posts in 2021 and 2022; of the first 200 posts, two-thirds have been filled. This included seven consultant medical oncologist posts, five consultant haematologist posts and 44 nursing posts, including 26 acute oncology Clinical Nurse Specialist posts.

The HSE has recently constituted a National Genetics and Genomics Steering Group, who are tasked with developing a National Genetic and Genomic Strategy for Ireland by the end of this year. The NCCP is represented on this group by Professor Risteard O'Laoide, National Director, and Dr Triona McCarthy, Consultant in Public Health Medicine. The NCCP is also constituting its own advisory group on future cancer genetic and genomic services. Ms Mulroe suggested that a CTI representative would be a great addition to one of those committees.

Professor Young discussed RCSI's investment in cancer research and its ambition in this respect - "we are not short on ambition." The establishment of the RCSI Beaumont Cancer Centre was done with the objective of improving not only outcomes for cancer patients but also their quality of life through education and research, she explained. The university and hospital have also joined together to enable new appointments in oncology and surgery including lung cancer specialist Dr Jarushka Naidoo.

"International evidence supports the need for clinical trials... not only for patients but the entire healthcare system and the wider economy. But how they are funded and resourced has changed, so they are becoming more complex and thus demanding and intensive".

- Oonagh ward, Health Research Board

The RCSI is committed to a target over the next five years of having 75 open trials with 10% of its patient population either on interventional or observational trials and the professor acknowledged that its partnership with CTI has been "transformative". A new clinical trials education programme is also being rolled out by the RCSI in collaboration with the RCPI and CTI, which is not only aimed at medical oncology staff but all allied healthcare professionals. Prof Young also spoke of their desire to grow investigator initiated trials, which she said is impossible without the support of translational trials. An "innovation hub" is now being planned to put translational trials "on everybody's agenda".

Prof Hennessy spoke of capacity building within the Wellcome-HRB Clinical Research Facility at St James's Hospital, a centre of excellence for cancer care. Key players have been brought together at the facility, which sees St James's partnering with Trinity College Dublin; the professor spoke of this having facilitated unprecedented collaboration and a thriving culture of innovation. The CRF recently received OECI (Organisation of European Cancer Institutes) accreditation and is about offering a space where "the rigour of the trial becomes the central piece", she noted. With the Dublin -Midlands hospital group treating one in six of every patient in the country, the goal is to build a sustainable partnership that will facilitate excellent research. "Investigator-led work is where the systems are built for the future."

The ensuing discussion delved further into these insights, as the panel discussed capacity building and collaboration as the key determinant of that. Prof Young agreed that it is about playing as a team "rather than being competitors".

Ruth Barrington, former chief executive of the HRB, asked if the HRB would reconsider the decision not to fund translational studies. Ms Ward noted that the HRB support Investigator Led projects through its ILP scheme but as the only funder in Ireland with the resources to fund investigator-led trials the "focus at the moment is to support investigator-led trials". She cited that €3 million is available through the DIFA (Definitive Intervention and Feasibility Awards) scheme for cancer specific investigator-led trials. While the HRB funding pot is a relatively small one, efforts should be made to avail of European funding, she clarified.

Patient advocate Seamus Cotter asked if the HRB had disadvantaged cancer patients in the west of Ireland by not fully funding the cancer centres in this region. Ms Ward said there are complex reasons for that decision, however HRB remain committed to working together with the NCCP/DoH, Galway and Limerick hospitals to build capacity and capability to conduct investigator-led trials these regions. Both hospital sites are members of the CTI clinical executive and will have access to national cancer clinical trials. Ms Mulroe agreed it is complex but "we can't wait five years for the next grant call for those two sites". Dr Burns agreed that recruitment and retention is an issue in this region, as it is across the entire health service, and the goal is to increase capacity on a national basis.

The RCSI is committed to a target over the next five years of having 75 open trials with 10% of its patient population either on interventional or observational trials and the professor acknowledged that its partnership with Cancer Trials Ireland has been transformative.

- Prof Leonie Young, RCSI

A recurring theme throughout the Retreat was the availability of information on clinical trials for patients. One commented that there should be a national communication portal for this information. While the CTI website contains details of all available trials, it was agreed that there isn't necessarily a joined-up approach to this and the panel agreed that this could be easily achieved so that patients find it easier to find out about clinical trials and engage with them.

Consultant medical oncologist in St James's Hospital and St Luke's Hospital, Dublin, and ICORG co-founder Professor John Kennedy took the opportunity to highlight what he called the "danger of over regulation" when it comes to putting patients in clinical trials.

The large number of bodies involved in getting cancer clinical trials off the ground is problematic in itself and when new EU regulations are announced "we tend to adopt the most rigorous version", he commented. The interpretation of data protection at various sites can vary wildly and it is beginning to affect the feasibility of studies. "We need to try to get together and influence legislators and not throw the baby out with the bathwater every time there is a new regulatory edict from Brussels," said the professor, who added that these issues will come into "sharp focus" when trying to do collaborative studies with colleagues in Northern Ireland, which has different interpretations of the regulations.

Eibhlin Mulroe agreed that Ireland tends to apply a regulation and then not invest in the people required to achieve its requirements - what Prof Kennedy called an "unfunded mandate". She noted that NREC is not properly resourced and there are significant delays right now and bottlenecks in clinical trials around ethics.

Cancer Trials Ireland Clinical Leader Professor Ray McDermott facilitated this session, which explored the factors that result in a successful clinical trial that is well accrued. He was joined by Professor Elizabeth Vandenberghe, consultant haematologist in St James's Hospital, Dr Paul Kelly, DSSG co-chair genitourinary, and radiation oncologist at the Bons Secours Cork, and Dr Jarushka Naidoo, DSSG chair for lung and consultant medical oncologist at Beaumont Hospital.

Prof Vandenberghe explained that about 500 new patients are diagnosed with chronic lymphocytic leukaemia (CLL) in Ireland each year, and of these 160-170 patients will be treated each year. These patients are mostly in their 60s and more men than women and most will have a normal life expectancy .

The **CLL-17 study** was outlined by Prof Vandenberghe. A phase II, international study, with 64 patients accrued since 2021, it has far surpassed its original target of 40. "This study ticks all the elements for me, it is a good quality study and recruitment has surpassed what was expected," she said, noting that St James's was the second biggest accruer of patients globally for the study. One reason for this is that it is an "incredibly inclusive study", said the professor, who added that most phase II studies tend to be niche, especially in haematology and increasingly in oncology. Yet all of her patients who require treatment for CLL succeeded in getting on the trial. She added that it is a very rational study and the data required for the study is very useful and applicable. An academically driven study, it compares a new immunotherapy to the standard of care, ibrutinib. While this is a targeted treatment, patients stay on it long-term - this can have disadvantages for the patient and also in an economic sense, Prof Vandenberghe noted. The promise of the trial is not cure but the hope is to defer the time until patients begin chemo-immunotherapy. This is a "powerful promise for patients", who avail of state of the art treatment and may avoid treatment for a significant period of time. "I know my patients are on a pathway that I can really stand over." Prof Vandenberghe said she believed a consultant with an interest in this area should be identified, who could then attend international meetings and build up the necessary connections to bring trials like this to Ireland - she cited the work done by consultant haematologist Prof Patrick Thornton in this regard.

Cancer trials go beyond drugs and radiation and surgical oncology must also be considered in this domain, said Dr Kelly, who noted that without available funding from pharmaceutical companies, funding radiotherapy trials can be challenging; "hence why we need additional funding and support". He has been involved in the **PACE-C trial (Prostate Advances in Comparative Evidence)**, which is a large Phase III radiation study in prostate cancer organised by the Institute of Cancer Research in the UK. The major advantage of the UK system, Dr Kelly said, is that they carry out very inclusive trials that "answer the big questions in radiotherapy and put large numbers on studies".

Prostate radiation is one of the curative treatments for localised prostate cancer. Traditionally that is delivered in small doses each day over six to eight weeks, which represents a significant patient burden and has major implications in terms of a patient's ability to work and carry on a normal life. The PACE-C study asks whether stereotactic radiation delivered over five days can be as or more effective. "This study is particularly attractive to patients because if randomised to the stereotactic treatment, they manage to complete it within a week."

This is a critical success factor, Dr Kelly noted. "In my experience of trials in Ireland, patients are never the barrier, they always want clinical trials and a very practical one like this is attractive." He added that the protocol is not particularly onerous and the criteria for the trial are not restrictive, including a broad population of intermediate risk prostate cancer patients.

Clinical trials are critically important in an era where radiation technology is improving rapidly and there is a lag in the evidence to support the newer technologies, said Dr Kelly.

"It is really important that we do these trials to copper fasten the role of more advanced technologies, which have major advantages of sparing patients side effects and limiting the duration of treatment and the impact on their lives." A reduced treatment burden also has the benefit of freeing up resources in radiotherapy departments, and ultimately means more patients can be treated.

Dr Naidoo then spoke of her efforts to move the **lung cancer portfolio** forward. Having worked in Memorial Sloan Kettering Hospital and Johns Hopkins in the US, she said she had learned many lessons "from observing some of the best people in the world", the three main ones she shared with the audience at the Retreat.

Firstly. Dr Naidoo said, oncologists must understand their study population and tailor and structure a clinical trials portfolio that deals with the patients they see on a daily basis, as those are the patients that will stand to benefit. "In Ireland, we have a smaller population in lung cancer that has fewer oncogenic driver mutations and therefore bring-

Panel (L-R): Paul Kelly, DSSG Co-Chair, GU trials & Bon Secours Cork (PACE-C); Prof Elisabeth Vandenberghe, St James's Hospital (CLL17); Jarushka Naidoo, DSSG Chair for lung, Beaumont Hospital (Lung Portfolio going forward)

ing clinical trials that are focused on immunotherapy and certain targeted therapies may serve our population better," she said.

Her second lesson is to keep questions close to the patient as this is what will drive success. Researchers need a balanced clinical practice where they see patients and they understand and listen to their questions, she said. "Working with patient advocacy partner Seamus Cotter and listening to my patients is the best thing in order to tailor the questions to their needs." For example, this means bringing liquid biopsies - a blood-based test - to lung cancer patients, will in a practical sense help to understand the biology of the tumour in seven days as opposed to 21 days; "this is the median time for tissue genotyping and represents a significant delay for our patients."

The third lesson, the most important, is maintaining connectivity between the PIs. "That is the secret sauce to making a clinical trial portfolio work," Dr Naidoo asserted. Despite its small size, Ireland can be geographically quite disparate with clinicians working within very different systems. Dr Naidoo has now established the Irish Lung Cancer Alliance which meets every four to six weeks and helps to maintain and build relationships between the investigators working in this space.

"A common theme is relatively straightforward trial design with broad eligibility," said Prof McDermott. But as well as factors for success, the panel explored the reasons for failure, noting that "extra layers of bureaucracy" can hamper a trial opening on time and make it lose valuable accrual time. Timelines are critical, they said, and the whole process must be streamlined to make Ireland more attractive for clinical trials.

A persistent theme during the retreat was the paucity of protected time for clinician researchers. National and international collaboration is key and does happen but again one of the main barriers is the lack of protected clinical research time, as many clinicians are simply too busy to develop and maximise those relationships, Vandenberghe noted. "People are doing this in their spare time - every job should have a small amount of time protected for research," noted an audience member. While clinicians may have enthusiasm, they are lacking the critical bandwidth that allows them to foster relationships and collaboration.

Prof Seamus O'Reilly spoke of the sustainability of the workforce in clinical research and the issue of burnout among his colleagues: "Research is incredibly rewarding at a personal level but it is exhausting and studies have shown it is directly related to burnout." He also expressed his concern at the current stalemate in consultant contract talks, although he noted the NCCP is sanctioning jobs "at a fantastic rate". Prof McDermott also noted the "huge workload" involved in placing patients on clinical trials, and Dr Dearbhaile Collins commented that giving clinicians more time to focus on trials will increase accruals: "Ireland is a small country and we should be able to recruit across all centres but we are not doing that too well." Prof Vandenberghe acknowledged that trial recruitment had fundamentally been improved by the change in the HRB grant system and the building of networks across the system.

The Molecular Tumour Board (MTB) PANEL 3

Cancer Trials Ireland & Roche Ireland recently announced a new partnership to deliver the first nationally accessible educational Molecular Tumour Board (MTB) in Ireland, following a successful pilot programme. The MTB is aimed at improving patients' lives by identifying the most appropriate treatment options for oncology patients, including innovative new cancer trials both here in Ireland and internationally. Facilitated again by Professor Ray McDermott, he was joined by Deirdre Poretti, Personalised Healthcare Partner with Roche, Dr Dearbhaile Collins, Clinical Lead of the MTB and consultant medical oncologist at Cork University Hospital, and Dr Verena Murphy, Head of Research & Business Development at Cancer Trials Ireland.

Cancer is no longer viewed as a single disease, and is continually being narrowed down into "lots and lots of niches", commented Prof McDermott. "We are moving away from saying a patient has lung cancer and instead we are saying a patient has an NTRK fusion positive lung cancer."

Ms Poretti explained that Roche is committed to the area of precision oncology as it relates to delivering more personalised healthcare in Ireland and around the world. The advent of technology in delivering advanced early accurate diagnosis, not just in genomics but also areas such as digital pathology is supporting robust clinical decision-making across healthcare. Key to this is harnessing the data and gaining insight through real world evidence, she said. As part of efforts by Roche to support the appropriate use of genomic sequencing and decision-making, the Molecular Tumour Board was born. Involving a broad range of stakeholders, including a patient representative, "allegiances were left at the door" as they worked together to determine what needed to happen at a national level to make this a reality.

Incorporating a national molecular tumour board and registry, a bespoke solution for Ireland was devised and the first meeting took place in November 2020. "Irish physicians could bring their most difficult cases to discuss in front of national and international experts," explained Ms Poretti. The pilot programme was very successful and has even led to a publication at ASCO this year. Cancer Trials Ireland have now come on board to bring the initiative to the next level; "they have the power to scale and adapt and enhance the functionality of the MTB."

Dr Collins explained that her involvement with the MTB came about as when she returned to Ireland, she felt that sequencing was becoming part of standard of care yet there was nowhere to go to discuss the findings. Oncologists were forced to make decisions based on genomic testing in isolation, while others had connections to other international

Prof Ray McDermott, Clinical Leadership, Cancer Trials Ireland

MTBs. Dr Collins and colleagues felt a national MTB would be the ideal forum for this discussion and Roche provided the "driving force" in establishing it.

The fact that it will be taken over by CTI will make it a truly national accessible MTB, she noted. "We want it to benefit our patients and be available to them so that we can make decisions on sequencing that will ultimately benefit patient care," she said. 'Sometimes mutations are found that are not significant and patients can be given particular treatments that ultimately will not benefit them, which wastes their time and gives false hope."

Doctors will also benefit from the educational aspect on many levels – we are working on CPD points for participation, while trainees in medical oncology and pathology are getting involved and using it as an educational platform. Translational research projects would also be able to avail of the MTB, and it could help advise the HSE and NCPE as they make decisions on drug access, Dr Collins added.

Dr Murphy then outlined how Cancer Trials Ireland is taking over the operation of the MTB by putting an effective structure in place and hiring staff. A core aspect is building a database; "we know it will be important to collect all this knowledge and have a database that can be accessed over time," she explained, adding that there are plans to link up with other European boards. "I am very positive that it will be a successful programme."

Panel (L-R): Verena Murphy, Head of Research and Business Development, Cancer Trials Ireland; Dearbhaile Collins, Clinical Lead, Molecular Tumour Board, Cork University Hospital; Deirdre Poretti, Personalised Healthcare Partner, PHC Ecosystems, Roche Ireland

Genomic and genetic testing services in Ireland are not perfect, acknowledged Prof McDermott. "This is one way of speeding up the process." Yet challenges can arise when a target is identified but the corresponding drug is not yet available in Ireland - explaining this to patients can be problematic, agreed Prof McDermott and Dr Collins. Poretti noted that other countries have specific guidelines linked to their molecular tumour boards and these may need to be produced.

It was also discussed how the results from genetic sequencing panels are simply a computer readout and expert interpretation of the reports is still needed; Dr Collins noted that often the Expert Board will not recommend an agent that has poor success rates, even if the sequencing panel points toward it as an option. She noted that she would like to see the MTB playing a role in helping with drug access, whether it is compassionate access programmes or clinical trials. "In the real world, we are not going to be able to get every drug, for every variant, for every case, but in individualised cases the MTB could work really well for drug access," she acknowledged.

AS CTI takes over the initiative, Prof McDermott pointed out that this will democratise and enhance the equality of access to the MTB but Professor John Kennedy cautioned there is a risk that it could become limited to patients who can afford to pay for genetic testing. "There is a difference between having a routine panel done in lung cancer and what some would say is a 'fishing expedition'. National support is needed for deciding who is eligible for these tests and making it equitable." The NCCP needs to ensure this is available in the right way for people and Dr Collins confirmed that these conversations are happening.

"We need to ensure that it doesn't come crashing down over red tape and legal obstruction," she said. "We need it to happen and then a lot of good things can flow from it."

Points made during the discussion included one from the Irish Cancer Society's Dr Robert O'Connor that this is an opportunity to develop standardised communication and education for patients surrounding genetic testing and genomic sequencing. In response to an online question as to whether the MTB had the potential to "overwhelm" Ireland's current genetic service, the panel commented that it was already overwhelmed but the value of the MTB would be to identify potential germline mutations and refer these

"The pilot programme was very successful and has even led to a publication at ASCO this year.

- Deirdre Poretti, PHC Ecosystems, Roche Ireland

Eibhlin Mulroe facilitated a discussion that illustrated how public and patient involvement (PPI) will help oncology researchers improve recruitment and meet HRB grant requirements. Joining Ms Mulroe on the panel were Dr Anne Cody, head of investigator-led grants at the Health Research Board, Dr Claire Kilty, research manager in the Irish Cancer Society, Dr Siobhan Gaynor, member of the Patient Consultants Committee with Cancer Trials Ireland and Noelle McAlinden, arts and human rights activist.

Dr Cody opened the discussion by explaining that as the HRB funds research from taxpayers money, it has an inherent obligation to make the best possible use of that money. They want to see that grant applications are not only a good idea but are set up in the best possible way so that the resulting trial will be a success. "We are perfectly aware that every grant we give is a gamble, but we do want assurances that the investigators are looking to minimise the risk."

Involving patients in the decision making around a study makes it a lot more likely to be successful, said Dr Cody. Recruitment has always been a bugbear for those running clinical trials but there is now hard evidence that involving members of the public in the decision making increases recruitment. She cited a systematic review from 2018 to back this up, which included 26 trials. The authors extrapolated from the results that in a hypothetical sample of 1,000 patients where 100 enrol in a trial, a PPI intervention would lead to an average of 14 extra patients being recruited (view slides here). The authors of the systematic review noted that patient involvement in the included studies had typically only started when designing participant-facing materials and noted that had it happened at an earlier stage in trial design, the positive effect might be even greater. "This is an easy win," she said.

The Irish Cancer Society is the largest voluntary funder of cancer research in Ireland and the largest voluntary funder of cancer clinical trials in Ireland. "For us, the most important thing is that that research is patient-focused," said Dr Kilty. To do this, people affected by cancer must be involved at the earliest stage of the research process. PPI is to be welcomed but ultimately the Irish cancer society is seeking PPP - public and patient partnership. It makes for more relevant research, more impactful research and better quality research, Dr Kilty stated.

It is now mandatory in all Irish Cancer Society applications that PPI is embedded, ideally at the very earliest stage of defining and refining the research question. Her advice was that researchers should not be "cold calling" people with cancer; rather they should network with them like any other stakeholder they collaborate with and build up the connections in advance of any grant application. That said, best practice in PPI is still evolving and Dr Kilty noted that the Irish Cancer Society works closely with other bodies such as the HRB, IPPOSI and Health Research Charities Ireland, among others.

Siobhan Gaynor, Patient Advocate, member of the Cancer Trials Ireland Patient Consultants Committee

Siobhan Gaynor gave her perspective as a clinical researcher and now a patient advocate. "Professionally and personally I have witnessed all sides of the discussion around PPI," she said. Operationalising PPI as it moves from strategy to reality has problems. 'Consulting one patient is just one opinion - this needs to be formalised," said Dr Gaynor.

A PPI coordinator is needed to ensure that meaningful partnership takes place and a flexible approach to PPI is needed for patients who are trying to juggle being a patient with all of their other responsibilities. "Patients can give the reality on the ground and highlight where the gaps are," she said.

Noelle McAlinden has been a patient and is now working closely with several groups in northern Ireland, which she said is "in a very different place" to the South of Ireland. The "dormant Stormont" has been damaging to all aspects of society including healthcare, she noted. By using education in the broadest sense, she has been working within the arts to raise awareness of critical issues. PPI offers patients a

chance to gain agency in the fight against their disease. She urged attendees to commit to "a culture of collaboration and culture of compassion".

In relation to operationalising PPI, Dr Cody noted that the HRB has been working on this since 2016, and has now moved from having PPI Ignite sites in five universities to a broader national network, which provides support across disease areas. "We are creating resources that can be used by many and building knowledge that transcends any one disease area." She added that the national PPI Network is now building its website, which will function as a fantastic resource.

For researchers, PPI is not always straightforward. Transparency is key in case of conflict further down the line, noted Dr Kilty. One audience member asked the panel how they should deal with a PPI request "diluting or negatively impacting the scientific integrity of the trial proposal". Patients may reject a monthly CT scan but that may be the only way to monitor tumour growth, for example. The need to compromise is key, said Dr Gaynor in response; "often investigators and patients will meet somewhere in the middle." Dr Kilty agreed, saying there is a need to manage expectations of both parties.

Consultant in adolescent and young adult cancer Dr Scheryll Alken said their mantra is "nothing about us without us". "This should be not at the protocol review stage but when setting the priorities for the research. They need to be there from the very beginning rather than trying to change things midstream."

Dr Anne Cody, Head of Investigator-Led Grants, Research Careers and Enablers at Health Research Board

PPI can be really hard, noted Avril Kennan of HRCI. "We can forget that it needs to be enjoyable and even fun if we want people to stick with it." Ms McAlinden agreed that researchers need to look at much more creative and innovative ways they can engage with patients. "Time is precious."

Dr Robert O'Connor said patients want not just enjoyment but empowerment in the interaction. People become involved in research because they want better for their children and grandchildren. "We are all patients and all will be patients."

Ms Mulroe commented that from the Cancer Trials Ireland perspective, they are "really seeing the fruits of the labour when it comes to patients being involved in research decisions and sitting at the table with researchers". "You begin to see other perspectives in a way you simply didn't see before." Ms McAlinden concluded by urging a culture of mutual respect as PPI continues to grow.

> **It is now mandatory in all Irish Cancer Society applications that PPI is embedded, ideally at the very earliest stage of defining and refining the research question.**
>
> - Claire Kilty, Research Manager, Irish Cancer Society

Public Webinar

As part of the Retreat, a one-hour public webinar was also held, aimed at members of the public who want to know more about clinical trials. On the panel for this session were:

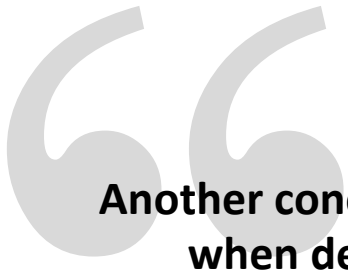
- ***Peter MacNamara, patient ambassador representing CTI's Patient Consultant Committee***
- ***Prof Seamus O'Reilly***
- ***Dr Robert O'Connor.***

Eibhlin Mulroe facilitated the webinar, saying the goal of the webinar was to help in demystifying clinical trials for those undergoing cancer treatment or family members and friends of someone with a cancer diagnosis.

Peter MacNamara outlined his cancer journey, beginning with his initial diagnosis in 2012. While the diagnosis came as a shock, he said he soon came to terms with it and began treatment. Peter underwent a radical prostatectomy and was placed on hormone treatment. In 2019 he learned that his PSA levels had once again begun to climb and he had begun to experience pain. At this stage, his consultant medical oncologist recommended that he begin chemotherapy but also suggested that he partake in a clinical trial.

Although Peter said he wasn't hugely daunted by the thought of entering a clinical trial, the panel acknowledged that this is not always the case. Prof O'Reilly admitted that the "guinea pig" misconception still persists, and constitutes a huge problem when trying to recruit patients for clinical trials. "In the medical community, we often underestimate how vulnerable people are when they are patients." He pointed out the impact that clinical trials had on ending the epidemic and acknowledged the bravery of those that partook in those vaccine clinical trials.

The practical implications of participating in a clinical trial may also deter potential participants. Peter explained that, contrary to some perceptions, there were no financial implications to taking part and he stated that the standard of care he was offered was "exceptional" - he even spoke with an oncology nurse daily. The treatment he received on the trial was an immunotherapy agent, which Prof O'Reilly explained has a very different side effect profile to chemotherapy, one that clinicians are getting better at managing. "Most people would find immunotherapy considerably easier to take than chemotherapy." Peter noted he had experienced blurred vision, for example, but this was a temporary side effect for him.



Another concern people have when deciding to go on a clinical trial is whether they will receive a placebo or not; it was once again emphasised that a trial participant will always receive the standard of care at the very least.

- Prof Seamus O'Reilly, Clinical Leadership, Cancer Trials Ireland

Another concern people have when deciding to go on a clinical trial is whether they will receive a placebo or not; it was once again emphasised that a trial participant will always receive the standard of care at the very least. Prof O'Reilly also explained that there are independent monitoring committees associated with a clinical trial, who will meet on a regular basis to review the data - if this is promising, then the trial could be stopped early to allow the patients in the placebo group to benefit.

Prof O'Reilly told the audience that according to Ireland's 2008 cancer strategy, "if we stopped all new developments in Ireland completely and just integrated what we already had, we could increase survival by 25%." This collaboration and working together is key to improving outcomes, he said, and he explained the benefit of the multidisciplinary team in devising the best treatment plan for a given patient. "This is hugely important because there are multiple insights and different nuances."

The broader societal importance of clinical trials was emphasised by Dr O'Connor, who noted that half of us will be directly diagnosed with an invasive cancer and face these difficult choices. "We want the best for our loved ones, our friends and families and it is only through clinical trials that that is made possible." He added that the international contribution that Ireland has made in this domain should not be underestimated.

PUBLIC WEBINAR ON CANCER CLINICAL TRIALS

Peter MacNamara | Eibhlín Mulroe | Dr Rob O'Connor | Prof Seamus O'Reilly

Cancer Trials Ireland has ambitious targets to increase the overall number of patients on clinical trials. But going from 2% of all cancer patients on clinical trials to the target of 6% will be challenging, the panel agreed. Prof O'Reilly commented that "we need more people… all working better together and a harmonisation of the regulatory processes." All of his treatment decisions are guided by historical clinical trials, he emphasised.

One of the major bottlenecks is having ample numbers working across this space, whether it is clinicians, researchers, oncology liaison nurses, etc. Having more researchers will bring more funding and ultimately more clinical trials to Ireland, meaning better care and better outcomes for patients. Cancer is suffering from the same recruitment and retention issues that are affecting the entire health service, in what is a global problem, said Dr O'Connor. "Everybody listening to this webinar today is going to be a patient so we all have a vested interest in addressing this."

The ongoing fallout from the pandemic was also addressed, and Dr O'Connor said he worries about the 33% extra cancer cases that are coming down the line, given that we are already struggling with capacity issues. "We need to think very cleverly about increasing capacity and look to the future. We learned how to box clever with Covid and we can bring across those learnings with cancer."

Yet communicating with patients regarding clinical trials presents a challenge, the panel agreed. It can be difficult for patients to find out about trials, while some patients may not understand why they are unsuitable for a particular trial they have come across; "managing expectations and explaining it can be difficult - it's very hard to navigate all of this for the patient."

All the currently open clinical trials in Ireland are listed on the Cancer Trials Ireland website, accompanied by lay summaries. Patients should look abroad (on clinicaltrials.gov) for clinical trials if a suitable one is not available in Ireland; however, access can be difficult and continuity of care is crucial, noted Prof O'Reilly.

And while participating in a clinical trial can bring individual benefit for the patient in terms of potential better outcomes, there is also the matter of the broader contribution to the field of cancer research and improving the standard of care - but the main hope for the patient is that they will do better, said Prof O'Reilly. "In medicine the core relationship is between the treater and the treated." Peter agreed that the motivation can be personal but there is also an awareness that it is a civic duty and a way of giving back to the broader health system.

Ireland is a highly regulated environment when it comes to clinical trials, something that is good for the potential participant but it can preclude us from taking part in some international trials and potentially earlier stage clinical trials. "Patients need access to the big clinical trials but also perhaps the more niche and nuanced ones, where investigations are perhaps at an earlier stage," said Dr Rob O'Connor.

CONCLUSIONS

- **In framing Ireland as an attractive clinical trials location, there are a number of challenges, many not unique to cancer as a research field.**
- **These include recruitment and retention of key staff including clinicians, and a lack of protected time for clinical research embedded within consultant contracts.**
- **Over-regulation is also a threat to trial success and Ireland risks suffering from this. A harmonisation of the regulatory process is necessary.**
- **The importance of collaboration and partnership was a persistent theme but clinicians must be supported in this as currently they lack the necessary bandwidth to develop and sustain these working relationships.**
- **Irish researchers must learn from their trial success stories. These are invariably trials which ask straightforward questions, are attractive to patients in terms of their protocol, and have broad eligibility criteria. Patients will vote with their feet when choosing to participate.**
- **Ireland must harness the benefits offered by the new targets in cancer treatment and clinical trials will be a key element of this.**
- **PPI is becoming mainstream in research and is now a key determinant when awarding funding grants. Patients are seeking empowerment through true partnership and should be consulted at the very earliest stages of defining the research question. This will help to ensure trial success.**

> **One thing that has come to the fore in 2022, whether through investigators, sites, funders, patients and even our own staff in Cancer Trials Ireland—it's the sheer level of ambition that everyone shares to open as many trials as possible to provide more and better treatment options for patients in Ireland.**
>
> - Eibhlin Mulroe, Cancer Trials Ireland





cancer trials ireland

Together, we're finding answers to cancer.

The Cancer Retreat was supported by the Cancer Trials Ireland's Just Ask campaign to raise awareness of clinical trials around International Clinical Trials Day, May 20th, 2021. The Just Ask campaign is supported by:

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