cancer trials ireland

Together, we're finding answers to cancer.

The

Report

arising from Ireland's inaugural

Cancer Retreat 21.05.21

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Executive summary

Ahead of a significant change to the public funding environment in 2022 (new 5-year HRB grant cycle), and amid the pandemic, and the HSE Ransomware attack, Cancer Trials Ireland hosted Ireland's inaugural Cancer Retreat, as part of its annual celebration of International Clinical Trials Day 'Just Ask' campaign.

This day-long virtual conference was opened by An Taoiseach Micheál Martin TD. It featured 30 contributors from Europe and North America across 16 sessions (plenaries, panels, & breakout groups). It was attended by 250+ members of Ireland's cancer clinical trials community with a view to exploring:

- How do we choose which trials to open in Ireland?
- How do we fund these trials – and how do we properly support the careers of the doctors, investigators, and research staff who run them?
- How do we bring more trials to a country with a small population?
- How can we make running trials more efficient?

The day opened with one key message that became the theme for the day: collaboration is the engine of change. But if that is so, what then are the changes the cancer trials community identified at the Cancer Retreat?

First and foremost, that **clinical research must be embedded into wider healthcare planning**. Several other points discussed at the Retreat fit under this heading (including protected time for researchers, and clearly defined careers, and career paths for research nurses), but a number of contributors recognised that protected time and defined careers would only emerge if the health system formally plans and resources cancer (and other) clinical research as part of its core mission.

The second major issue identified at the Retreat concerned the l**ack of clarity around how translational research will be funded** in Ireland, in light of the HRB's changing grant system. As with the question of embedding health research in planning, panellists addressing this question raised the need for a long-term view, and to move away from the idea that science and medicine are siloed. Panellists made a robust case for the impact of translational research. Prof Liam Gallagher cited the positive example of BREAST-PREDICT, while Prof Mark Lawler referenced evidence that unequivocally shows that patients treated in research-active institutions have better outcomes.

Meanwhile, **Public & Patient Involvement (PPI)** emerged as another example of collaborative change in cancer trials. Judy Needham, chair of patient relations for the Canadian Clinical Trials Group (CCTG) delivered a very compelling presentation about the impact of properly structured PPI, leading to increases in trial accrual, retention, and even funding.

Under the heading of '**communication**', the Retreat gave the community a platform to express dissatisfaction with the bureaucracy and quite variable logistical problems they encounter – even as new measures like the Office for National Research Ethics Committees and the Clinical Trials Regulation come into operation. Communication around the progress (or lack thereof) on trial feasibilities was a particular bugbear, as Prof Joe Eustace of the National Clinical Trials Office noted.

The final over-arching point that arose repeatedly at the Retreat was **the pandemic, and its projected effects on cancer diagnosis in the coming years**. Many contributors expressed concerns that the existing Cancer Strategy will be challenged by COVID.

There is no escaping the scale of the questions outlined above, and no point pretending they have simple answers. Nevertheless, we can take heart in the inclusive and useful discussions that happened on the day. It was our hope to galvanise an embattled and exhausted community of healthcare professionals and researchers by bringing them together to talk about what matters to them. It was deeply encouraging to see more than 250 people make the effort to attend on the day, with more than half of these re-registering in the aftermath of the Ransomware attack.

It was a wonderful demonstration of the passion and appetite this group has to run more and better clinical trials in Ireland, irrespective of the challenges that beset them, and their contributions will inform the new Cancer Trials Ireland Strategy for the coming five years.

Prof Seamus O'Reilly
Vice-Clinical Lead

Ms Eibhlin Mulroe
CEO, Cancer Trials Ireland

Building a shared vision for the next five years

The first Cancer Trials Ireland Retreat took place on May 21 2021. Bringing together a host of different stakeholders in the field of cancer clinical research, the overarching goal of the virtual all-day meeting was to reflect on the achievements and learnings of the past two decades of cancer research in Ireland and work together to build a shared vision for the next five years.

"A watershed moment"

Vice clinical lead of Cancer Trials Ireland Professor Seamus O'Reilly introduced the day's proceedings. If more than 30,000 people have taken part in cancer trials in Ireland over the last two decades, then why is a "retreat" required? Prof O'Reilly outlined the four main reasons:

- Changes in funding structure: The initial mechanism linked CTI with cancer centres, whereas the new mechanism will link CTI with health sciences universities, with the cancer centres now contained within clusters with these universities and the HRB units such as TMRN and CRCI. The enterprise emphasises the need for patient participation and inclusion. These changes will enlarge the ecosystem of clinical cancer research in Ireland. The reality is that patients needed these changes - despite progress in cancer care, "the era of discovery", the number of people diagnosed with cancer in Ireland each year has doubled in the past three decades.
- Launch of European Beating Cancer Plan: The new Plan, launched in February 2021, offers an opportunity to reflect on the activity of cancer trials and cancer centres.
- Human capital: This is "our greatest resource" and the efforts to attract, recruit and retain this talent has become more difficult. A linear career path has been replaced by a "braided river". Diversity needs to be harnessed, as this accelerates innovation - this is a priority for CTI.
- Covid-19 Pandemic: This has been "medicine's longest year" and has reduced cancer clinical trials activity in the US by 40%. Even with vaccination disruption, the effects of the pandemic will linger into 2022. Now is a time to reflect on what has been achieved and what the future holds.

"Collaboration is the engine of change," said Prof O'Reilly.

An Taoiseach

In his opening address, An Taoiseach Micheál Martin spoke of the positive impact of research activity including clinical trials on the care of patients is "universally accepted" and the National Cancer Strategy aims to develop a culture in the cancer system that values research to the benefit of patients and is supportive of those who engage in research. The Taoiseach thanked CTI for their endeavours to increase patient participation in cancer trials across Ireland. He also highlighted the value of all-Island cooperation in cancer research.

"The positive impact of research activity including clinical trials on the care of patients is universally accepted." An Taoiseach, Micheál Martin, TD

"I have no doubt that Cancer Trials Ireland will continue to build on the important work you have done to date, and make a significant contribution in the coming years."

The Patient Voice

The patient voice was delivered by Patrick Kivlehan, who is chair of the patient consultants committee (PCC) of CTI. For a board to establish a subcommittee of consumers and allow them access to the inner workings of the organisation is highly unusual, he noted; " but it gives a sense of how seriously the board of CTI and the management take the patient voice and ensuring that voice is heard."

The objectives of the PCC are wide-ranging; not only does it ensure the patient voice is heard, it advises the DSSGs [Disease Specific Sub Groups) and also has a public communications and raising awareness role. The PCC is "not just a talking shop" but a body that can have a real impact on all facets of cancer research. Mr Kivlehan issued a "call to arms" for patients to become involved in the Committee. "Clinical trials save and extend patient lives so having the patient voice involved in that process is very important."

Cancer Trials Ireland Strategy for the next five years

The Cancer Trials Ireland strategy for the next five years and its building blocks were then outlined by its chief executive Eibhlín Mulroe. She highlighted the core support offered by the Health Research Board and Irish Cancer Society. The target of placing 6% of newly diagnosed cancer patients on a clinical trial is an ambitious one - it is currently at 2% - but this core funding support will help make it a reality.

Global collaboration is another pillar, as is the growth in investigator-led trials - these are intrinsically linked, noted Ms Mulroe. The mix of trials is critical and the recent Memorandum of Understanding signed with the US National Cancer Institute focuses on what Ireland, north and south, can achieve by working together with US sites.

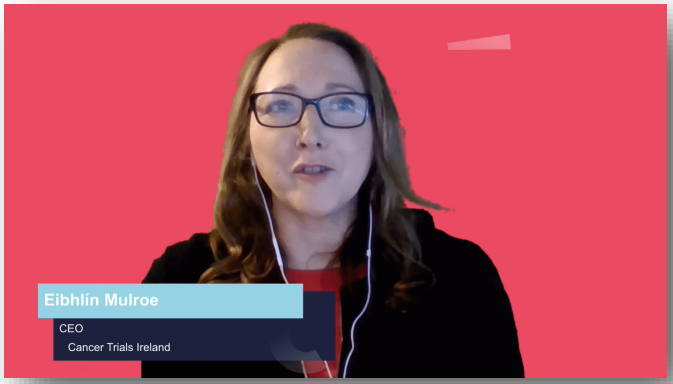
A strategy for biobanking in Ireland is necessary and this will be a critical step towards personalised medicine in cancer care. Attracting more pharma-sponsored trials to Ireland will also increase the number of trial opportunities for Irish patients. The power of collaboration was elegantly demonstrated in the context of new treatments and vaccines for Covid-19; "that's how you find answers to cancer and that's where you get hope."

The four main objectives of CTI are:

1. Grow a diverse portfolio of cancer trials available to Irish cancer patients.
2. Provide governance and support for multicentre and HRB Cluster-led cancer clinical trials.
3. Develop an open and accessible National Cancer Clinical Trials Network
4. Embed Public/Patient engagement in all National Cancer Clinical Trials Network operations.

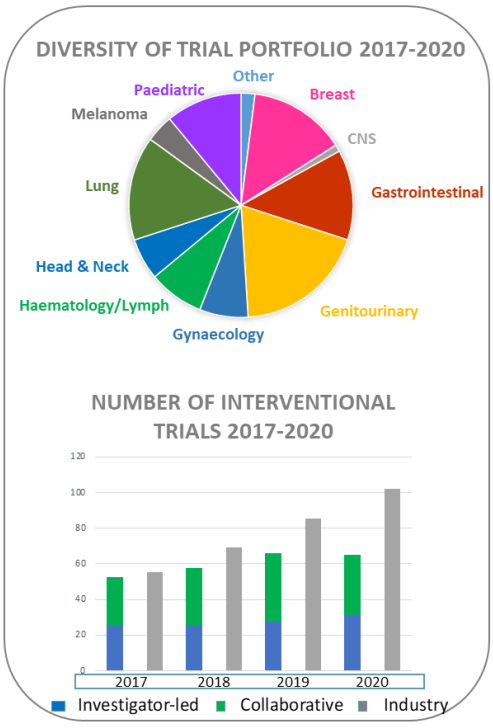
CTI has continued to diversify its trial portfolio and enhance patient participation since its inception but the next five years will see these efforts increased. Ms Mulroe noted that these targets could be set even higher if hospital sites were adequately resourced - but with just 40 medical oncologists in Ireland when there is a need for at least 100, this remains to be seen.

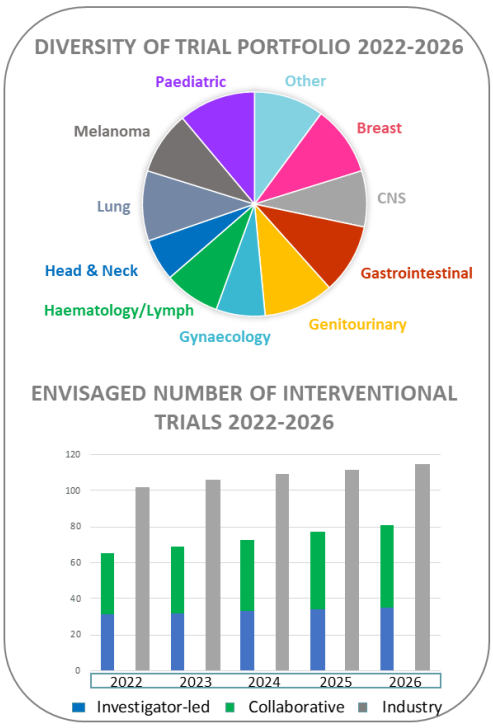
Ms Mulroe concluded by emphasising the commitment of CTI to fully embedding patient participation in all aspects of the clinical trial activity. The network together with the HRB-funded Cancer Clinical Trials Clusters will work as a strong team to deliver the target of 6% patients on trials. CTI's team of 50 experienced staff, led by the CEO, will enable study sponsorship, project management, pharmacovigilance, and data management and will maintain, grow and develop international partnerships.



"The network together with the HRB-funded Cancer Clinical Trials Clusters will work as a strong team to deliver the target of 6% patients on trials. " Eibhlin Mulroe, CEO, Cancer Trials Ireland

Trial Diversification and Patient Participation 2022-2026





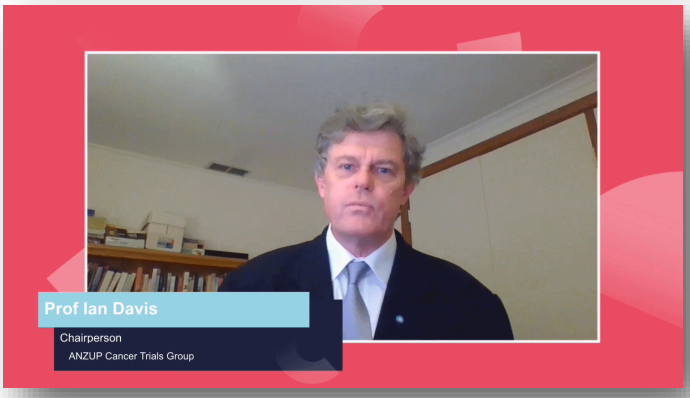
The first panel discussion was chaired by CTI Clinical Lead Professor Ray McDermott and focused on accruals, grant funding, and how to engage with industry and collaborative groups on funding. Panellists included Averil Power (CEO, Irish Cancer Society), Professor Ian Davis (Chair, ANZUP Cancer Trials Group), Dr Mairead O'Driscoll (CEO, Health Research Board), and Roisin Molloy, speaking on behalf of the Irish Pharmaceutical Healthcare Association (IPHA).

Prof Davis explained that ANZUP (the Australian and New Zealand Urogenital and Prostate cancer trials group) contacted CTI when seeking partners in Europe; "what we found was a group that was highly accomplished, that worked in a very similar way to us. It's worked out extremely well and we have done a number of trials together now and the relationship has been characterised by people willing to understand and communicate and be flexible."

Averil Power then outlined why the Irish Cancer Society is passionate about supporting clinical research and CTI, saying research means new discoveries and new therapies, and better odds on lives saved, "more birthdays, hugs, and precious moments". She pointed out that even just being treated for cancer in a research-linked institution is associated with a better outcome and better quality of care. With over 200,000 cancer survivors living in Ireland now, it is difficult to believe that just a generation ago, only three in every 10 people diagnosed with cancer would survive. Now six out of 10 will survive a cancer diagnosis, which is "incredible progress".

The pandemic-associated decline in clinical trial recruitment is part of the reason why the Society has doubled its funding towards CTI this year. Ms Power noted that a crucial part of their advocacy is making the case to politicians from all parties for much greater investment into basic cancer research infrastructure in Ireland; "it's not just about funding, it's about having the proper support."

Roisin Molloy is chair of the newly-formed cancer care project in IPHA. She explained that 18 pharmaceutical companies are now members of the project, which is geared at ensuring cancer patients gain access to ground breaking medicines in Ireland. One of the main avenues for this is via clinical trials and Ms Molloy noted the significant ongoing collaboration to ensure that industry-funded clinical trials come to Ireland in greater numbers. With the advent of immunotherapy and cell and gene therapies, it is a time of great excitement and there is significant commitment from industry to ensure Ireland is a key player in the research sphere, she said. Clear communication and partnership from the local entity on global clinical trials will also allow for a much smoother and hopefully quicker process in commencing clinical trials, she added.



Prof Ian Davis, Chair, ANZUP Cancer Trials Group

Dr Mairead O'Driscoll, CEO of the HRB, noted the Board's involvement in funding clinical research for almost two decades. The HRB will shortly announce its new round of funding, and this will be the first to take place under the updated funding model. This new model has two strands: the HRB will provide funding to between five and seven "clusters", which will see cancer centres and academic partners funded in unison, while there will also be one national cancer trials network which will provide oversight functions. Dr O'Driscoll said the overall ambition is to try and diversify, pool resources and work in as smart a way as possible, integrating healthcare and clinical trials seamlessly. A key goal is increasing the quality and quantity of investigator-led trials in Ireland and the HRB is committed to that. It is important for people to think about other sources of support, she added, noting the European Commission has identified cancer research as a priority.

Prof McDermott noted that Ireland is "stuck" at 2-3% when it comes to accrual, and he asked Prof Davis if Ireland could learn lessons from Australia in that respect. Prof Davis said

> **(Research means) more birthdays, hugs, and precious moments.**
>
> - Averil Power, Irish Cancer Society

some 5-6% of cancer patients in Australian hospitals will enter a clinical trial, but he echoed Dr O'Driscoll's point that it comes down to embedding clinical trials into routine cancer care. Australia is now making this part of its accreditations process, and hospital CEOs will be called on to provide evidence of what they are doing to enhance clinical trial recruitment. "Until that happens, we are not going to see substantial improvement."

Ireland's shortage of medical and radiation oncologists is an Achilles heel, and Prof McDermott noted that not all will be interested in clinical research regardless. When it comes to incentivising clinical research, Prof Davis said overall it comes down to time and its scarcity for doctors and all healthcare clinicians. People are "swallowed up" by clinical service provision and administrative tasks, and are pulled away from opportunities to do research. Protected time for clinicians is essential, and this is a problem not unique to Ireland or Australia but all around the world, he admitted.

The topic of patient participation is a hot one, and concrete efforts are being made to embed that at every stage of the process. Ms Power said patients should be educated on the potential benefits of entering a clinical trial at the earliest opportunity, and she reiterated the other speakers' points that care and research should be better integrated. It was noted that many patients are altruistic in their participation, understanding that clinical trials will not just hopefully help them, but have major benefits for future patients.

> **A Key goal is increasing the quality and quantity of investigator-led trials in Ireland**
>
> - Dr Mairead O'Driscoll, Health Research Board

Panel chair, Prof Ray McDermott (left) facilitates (clockwise from top left) Prof Ian Davis (Chair, ANZUP Cancer Trials Group); Averil Power (CEO, Irish Cancer Society); Dr Mairead O'Driscoll (CEO, Health Research Board), and Roisin Molloy, speaking on behalf of the Irish Pharmaceutical Healthcare Association (IPHA).

Creating careers in Cancer Clinical Trials **PANEL 2**

This lively discussion focused on education & training, hiring and retention of those working in the cancer clinical trials arena. Panellists included ***Professor Maeve Lowery*** *(TCD, St James's Hospital),* ***Prof Risteárd Ó Laoide*** *(NCCP),* ***Elizabeth Ness*** *(National Cancer Institute, USA),* ***Maureen O'Grady****, trial unit manager (University Hospital Limerick), and* ***Dr Teresa Maguire*** *of the HRB.*

Prof Ó Laoide began by saying the fundamental vision and objectives of the NCCP are based on the National Cancer Strategy, which was developed by a broad range of stakeholders (including patients) and endorsed by the Government. In the current environment, adaptability and flexibility must be shown but the learnings from the pandemic will be incorporated going forward. The NCCP and the cancer policy unit in the Department of Health devised an outline of the necessary staffing and funding to implement the National Cancer Strategy in 2017, and this serves as a blueprint for workforce planning.

The professor noted that the current workforce and projected future demands are subject to constant revision; any developments in technologies, guidelines, pathways and practices, as well as existing and projected skills supplies and skills mix, all influence the profile of resource requirements. A number of departments and national offices all work closely together on this issue of workforce planning, he added. Back in 2017, additional staffing for cancer care over the lifetime of the strategy was projected at over 1,000 positions; in the past four years the allocated funding allowed an additional 200 positions across cancer services funded by the NCCP. The significant additional funding given by the Department of Health this year has allowed a further 200-plus positions in 2021 alone. Despite this improvement, Prof Ó Laoide admitted they are cognisant of the significant capacity deficit in public cancer services but the hope is to build on this, year on year.

> **In 2017, additional staffing for cancer care over the lifetime of the strategy was projected at over 1,000 positions**
>
> - Prof Risteárd Ó Laoide, NCCP

Elizabeth Ness outlined the history of cancer nurses from both North and South training at the National Cancer Institute in the US, an initiative which began in 2002. She noted the similar challenges faced by research nurses on both sides of the Atlantic. Between 2002 and 2008 a total of 18 Irish nurses attended the programme, with overwhelmingly positive feedback from participants. And as they began to work with CTI (ICORG at the time), in a bid to meet the needs of unit managers, a cancer clinical trials leadership and management programme was later proposed as a complement to the existing programme. Five unit managers from Ireland attended in 2010 and a further three in 2011. However, this programme was beset with funding and time challenges. Ms Ness told the audience she would like to see this type of collaboration and training reinstated under the renewed MoU, and is keen to see more presentations and publications from Irish research nurses.

Maureen O'Grady explained that her role is to encourage research at all levels of cancer nursing and avoid the "fear" people have when it comes to cancer clinical trials. She spoke glowingly of her working relationship with Ms Ness and a subsequent visit with NCI that provided inspiration for cancer nursing research here in Ireland. The role of the cancer research nurse should be aligned more with that of a clinical nurse specialist, given the speciality of what they do, said Ms O'Grady. "We care for our patients, we are the patient advocate, we are involved in the consent process and with the multidisciplinary teams. We are also very much holders of the protocol and this is very specialised - the research nurse has the best knowledge of that protocol." She added that nurses are striving to achieve the 6% accrual target into cancer clinical trials and said a defined career pathway and a standardised job description in cancer research nursing would help in terms of encouraging nurses into this area, as would proper education and training.

The path of the Irish medical oncologist often takes them to the US - some will return and some won't. Prof Maeve Lowery said, in her case, it was the specific role she was offered that brought her back to Ireland from time in Sloan-Kettering, with a 50/50 split between clinical practice and academic involvement. The ability to be able to continue doing lab-based translational research as well as being involved in and conducting clinical practice was a huge incentive to return. As a PI, she told the panel that the single most important thing when beginning her career was a culture of mentorship, sharing expertise and responsibility at an early stage and enabling networking and career develop-

Panel chair, Prof Seamus O'Reilly (left) facilitates (clockwise from top left) Professor Maeve Lowery (TCD, St James's Hospital), Prof Risteárd Ó Laoide (NCCP), Dr Teresa Maguire of the HRB, and Maureen O'Grady, trial unit manager (University Hospital Limerick).

ment. That type of mentorship is typically cross-institutional, which further facilitates partnership and collaboration in addition to training. Prof Lowery also echoed the need for a defined career pathway for cancer nurses in clinical research, saying it will ultimately enrich clinical trials programmes. Embedding patient involvement at both the individual and patient organisation level at the initial stages of trial development so that the patient is present throughout is also critical, she concluded.

The conversation around protected time has changed fundamentally in a decade, from discussing consultant contracts and individuals, to multidisciplinary teams and enabling research at a hospital level, said the HRB's Dr Teresa Maguire. Networked efforts at both national and international level must be supported. A key question is how we can move to a research-active health service where research staff are recognised as necessary and not optional, and are fully integrated into care delivery.

Building a critical mass of oncology clinicians will be necessary as the current complement will not be sufficient to deliver a broad and diverse portfolio of trials. A staffing framework that provides for clinical trial activity is essential to provide an enabling environment - protected time for clinicians in itself will not be enough and should not be seen as an "optional extra". Accountability mechanisms should be in place in hospitals to ensure that trials and trial metrics are discussed at board level. A formal forum with a "line of sight" right up to Government level will be crucial so that the price of carrying out research is seen as a valid and eligible cost of service delivery. "This investment needs to come from the health system and not be seen as a drain."

Panellists were enthused by Dr Maguire's comments and spoke of their hope for the future and the positive prospects for the next generation of graduates entering into a research career. Prof Ó'Laoide noted that the NCCP is bringing together all stakeholders including clinicians, funders, academic institutions and patients, in a bid to draw up a framework by which to undertake significant research. The NCCP is hoping to function as a coordination forum in this regard. Prof O'Reilly noted that the current crisis has only served to emphasise the health service's strengths in terms of its human capital. "There is a need to convey optimism after what has been a very difficult time."

A defined career pathway and a standardised job description in cancer research nursing would help in terms of encouraging nurses into this area, as would proper education and training

- Maureen O'Grady, UHL

The role of translational medicine, academic research and cross-border care **PANEL 3**

*Chaired by **Professor Bill Watson** (UCD), the final panel discussion of the first session focused on questions such as: 1) How will Ireland fund translational research going forward? 2) What are the opportunities on the island for cancer research, and treatment? Panellists included **Professor Liam Gallagher** (UCD), **Professor Mark Lawler** (QUB), **Dr Jarushka Naidoo** (Beaumont) and **Dr Robert O'Connor**, Irish Cancer Society.*

Setting the scene, Prof Watson explained that translational research involves bringing basic science concepts and findings into clinical utility - whether it is testing biomarkers or samples collected as part of clinical trials, or identifying new sites of therapeutic manipulation and targeting them with new drugs. This type of research does not only contribute to advances in science but importantly, is laying the foundation of future clinical trials that will impact on patients. The funding challenges around translational research have been well-documented in the past but the new HRB funding model means that this type of research will not be funded and multistakeholder solutions to this are needed, Prof Watson said.

Prof Liam Gallagher first outlined the vision for the All-Ireland Cancer Research Institute and how this might help to fund translational research as part of CTI. For truly effective cancer research, there must be a fully functioning research ecosystem that allows those involved to move from bench to bedside and back again. The primary challenge has been the fragmented nature of basic and translational cancer research activities, including how these activities are funded. The National Cancer Strategy has even highlighted the lack of an overarching framework for cancer research in Ireland, added Prof Gallagher. "We need to join the dots between basic, translational and clinical cancer research."

Steps have been taken towards a more integrated approach; Prof Gallagher gave the example of BREAST-PREDICT, the first Irish Cancer Society collaborative research centre funded back in 2013, which brought breast cancer researchers from all backgrounds together to integrate not only translational research but also population-based research, also historically underfunded in Ireland.

More recently, he became the director of Precision Oncology Ireland, a consortium of five Irish universities, six Irish Cancer Research Charities, and nine international companies. The next evolution in terms of the integration is the All-Ireland Cancer Research Institute (AICRI), which will also span basic translational and clinical cancer research. Prof Gallagher noted the "groundswell of interest" in the new endeavour. Horizon Europe also presents a potential avenue for funding this type of research. "We need to push forward towards a team-based approach to cancer research."

Dr Jarushka Naidoo followed, explaining the importance of translational research in the newly established Irish Lung Cancer Alliance. Translational research is the "building block of clinical trials", she said. A clinical investigator such as herself can take the insights achieved by researchers such as Prof Gallagher and translate them into a trial that makes an active difference for patients. Having recently returned from Johns Hopkins in the US in the past six months, she noted that all major global research institutes now recognise the value of "team science", with every member a key component.

The Irish Lung Cancer Alliance is attempting to put this into practice. "This is a grassroots movement to try and build translational and clinical lung cancer research in Ireland and I hope we will be able to grow with time." The pandemic has unearthed new challenges but has also presented opportunities and virtual platforms have allowed collaboration to take place in new and more dynamic ways, added Dr Naidoo. Ireland is "small but it is mighty" and there is a wealth of skills and talent in cancer research here that must be maximised, she concluded.

Next was Prof Mark Lawler, who noted that last year he was involved in the publication of a paper that "unequivocally" showed that patients treated in research-active institutions have better outcomes than those who are not. The work carried out by the NCRI over the past 20 years has been "ground breaking", doubling the amount of research carried out in collaborations between scientists and researchers north and south. The recent re-signing of the MoU will ensure that Ireland and Northern Ireland are firmly embedded on the global research map. There is now a huge opportunity that needs to be grasped; the "disastrous" impact of the Covid-19 pandemic on cancer research and cancer services means this is imperative, with up to one million people in Europe currently undiagnosed with cancer, said Prof Lawler. Bringing together the best minds on the island of Ireland makes sense and working together in interdisciplinary teams is essential if we are to defeat the common enemy that is cancer.

Finally, Dr Robert O'Connor described the Irish Cancer Society's commitment to translational research as part of its wider research endeavours. Having seen such a huge increase in survival, we know there is a lot more we can

achieve, he told the panel. To exploit that, we need to gather every piece of information we can, and that is where basic and translational research comes in.

He stressed that cancer is an "upcoming emergency", with numbers set to double in Ireland within a generation. Ireland needs to be competitive in order to gain access to new medicines as they are trialled, and this means adding value to those studies and those trials and that needs a translational research effort, said Dr O'Connor. Irish people tend to be naturally humble but the reality is that we have a lot to contribute. Dr O'Connor acknowledged that translational research is a "longer-term investment"; it generates the ideas that become the trials but he said he sees enormous willingness to invest in that. Dr O'Connor urged people to be more open and vocal about the merits of translational research so there is more awareness and so that people understand its vision.

With most grants in the region of 3-5 years, how do we build a longer-term, more sustainable network so that translational studies can be carried out to their natural conclusion? Dr O'Connor highlighted lessons learned from international experience; success is seen in forward-thinking institutions that are a permanent element of the research infrastructure. Significant investment from charities, industry and state agencies must then come together to ensure the research can continue. Prof Gallagher agreed, and noted that AICRI has this long-term vision. The challenge is that with continual reinvention, some critical elements are lost. Sustainability is key, said Prof Lawler, who noted that UK funding tends to have this "long-haul" vision.

When asked who should be funding medical oncologist time to carry out translational research, Dr Naidoo noted that oncology as a specialty has evolved and oncologists have to be creative about what their positions will look like in the future. This is what diversity means - "collectively we are stronger when we are allowed to bring our own unique skill sets to the table." This means funding needs to take into account the different "pieces of the pie" and the various jobs that make clinical research possible. Most of our funding models should incorporate the part of their roles that is directed towards translational research, she said. "We need to move away from the idea that science and medicine are siloed."

Research "unequivocally" showed that patients treated in research-active institutions have better outcomes than those who are not.

- Prof Mark Lawler, Queens University Belfast

Panel chair, Prof Bill Watson (left) facilitates (clockwise from top left) Professor Liam Gallagher (UCD), Professor Mark Lawler (QUB), Dr Robert O'Connor, Irish Cancer Society, and Dr Jarushka Naidoo (Beaumont).

Improving DSSG performance

SESSION 2

Prof Connolly opened the session by reiterating that the National Cancer Strategy has proposed the "challenge" of having a minimum of 6% new patients with a diagnosis of cancer on trials, to ensure that clinical trials are offered to as many as possible. The HRB restructuring for funding cancer clinical trials has also highlighted this, with changes proposed for how trials are organised. This has led to renewed thinking on how cancer trials can be attracted to Ireland, both via commercial sponsors and collaborative groups, as well as enhancing the portfolio of investigator-led trials and looking at the increasingly important role of patient involvement.

Prof Roisin Connolly, UCC—Chair of Session 2

Prof Ray McDermott presented on the intended purpose and process of DSSGs, both historically and in light of HRB funding changes. "What trials, and types of trials, does Cancer Trials Ireland want to focus on?" Having returned to Ireland in 2004, he recalled the evolution of ICORG from a breast-cancer focused organisation to one dealing with a diverse portfolio of disease subgroups. There are currently 10 different DSSGs, and while breast cancer remains prominent, with strong accrual, this has been matched in other areas such as genitourinary cancer and lung cancer. Haematologists are also keen to become more involved. He echoed earlier presenters by saying one of Ireland's main problems is our relatively low number of clinicians, with just a handful of researchers in Ireland interested in some of the less common disease areas. This makes it difficult to generate discussion about a cohesive strategy going forward, and means the CTI is "very dependent" on the one or two clinicians who are willing to take on a leadership role to try and develop these areas.

One significant challenge that presents itself is how to make the DSSG structure more "relevant" to clinicians, Prof McDermott noted. Work and time pressures make it difficult to begin discussions and drive research efforts forward. The DSSGs need to be more comprehensive and the professor queried whether this meant more regular meetings, or more focused discussions. It is timely to address these issues, and encourage younger clinicians to become involved.

Prof Connolly described the system introduced by the Eastern Cooperative Oncology Group (ECOG) in recent years, whereby there is senior mentorship of junior investigators, with partnerships as younger people are progressing in their career and they are supported in their roles and research by senior colleagues. Such a system could be considered within CTI, she said, and Prof McDermott agreed. More consultants would also transform the landscape, Prof Connolly noted.

She then presented the recent DSSG participant survey results on conducting meetings, engagement, disciplines attending, communication, decision-making. A wide range of specialties responded, she explained, with medical oncologists and haematologists largest in number, but joined by academic researchers, research nurses and radiation and surgical oncologists. Patient advocates also responded to the survey.

- Six out of 10 respondents report attending DSSG meetings more than twice a year.
- Attendance was greatest at breast cancer DSSG meetings but there was also significant representation from genitourinary, gastrointestinal, gynaecological, lung and haematological cancer areas.
- The more niche areas of head and neck, CNS and melanomas are slightly more under-represented so this is an area that requires more attention.

In terms of the information considered important to hear at the DSSG meetings, there was a wide range of responses, with respondents saying they wished to hear about ongoing or pending trials, investigator-led trials in development, and scientific updates, among others. The same spread of answers was seen when respondents were asked which CTI supports are most important to them; sponsorship, networking, collaborative group access and investigator-led trial support were among those most frequently mentioned.

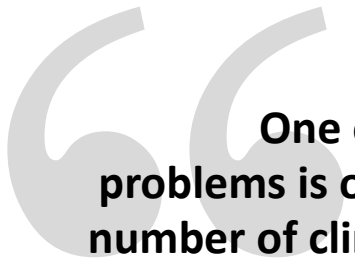
- The majority of respondents felt that one hour duration of DSSG meetings was sufficient, although some suggested that 90 minutes would be better

- Prof Connolly noted that some participants may be involved in several DSSG meetings, which take place in succession.
- Support was also expressed by the majority of respondents for quarterly calls to keep up to date with DSSG activity.
- Strengths of CTI memberships were felt to be the potential for collaboration (across sites, between clinicians and basic/translational scientists), as well as networking, and the value of one central hub.
- Perceived weaknesses should be viewed as opportunities and challenges, Prof Connolly said, and these included communication, study activation timelines, and more support for investigator-led trials activity.

Inclusivity was also highlighted, and Prof Connolly said this is a reminder to ensure that all members of the research team and all disciplines are included. Respondents also highlighted the need for transparency on goals and strategy within CTI DSSGs, clarity on the new feasibility studies and more focus on the role of the patient advocate.

A viewer question followed on from this, noting the focus of CTI on medical oncologists and asking what could be done to foster more engagement among surgery, radiotherapy, nursing, dietetic, and SLT colleagues. Prof McDermott noted that this is partly due to the group's origins and there are inherent issues with funding for some types of studies. He acknowledged CTI does not have a "great track record of involving surgeons" and the new cluster model will hopefully address that. Lisa Tucker confirmed that there are patient advocates in half of the DSSGs, and they would be welcome in the other groups.

CTI's Lisa Tucker then outlined the lead-in to a DSSG from the CTI perspective. She explained the vast amount of preparation involved in organising the meeting, which typically begins two months out. From booking speakers to finalising slides, to arranging NDAs, to liaising with patients, there is a huge amount of administration. The work does not stop when the meeting is over, as the meeting minutes must be drafted and industry feedback communicated. There is an increase in site engagement regarding potential studies, while actions on ongoing studies are also followed up. This adds up to roughly 500 hours per meeting and a total of approximately 1400 hours. A core of 15 staff must pull together information from 100 different sources to have the slides ready for the meeting and Ms Tucker said while this is something they are very passionate about, this time commitment means that it is imperative that the meetings are as productive as possible.



One of Ireland's main problems is our relatively low number of clinicians, with just a handful of researchers in Ireland interested in some of the less common disease areas. ...it means the Cancer Trials Ireland is very dependent on the one or two clinicians who are willing to take on a leadership role to try and develop these areas.

- Prof Ray McDermott, Cancer Trials Ireland

BREAKOUT GROUP: ILTs - Investigator-Led Trials (formerly IITs / 'Academic') - Prof Peter Gorman (RsqVD)

Having been principal investigator on several pharma-sponsored trials, **Prof Peter O'Gorman** noted that he and his colleagues had established credibility and relationships with other investigator peers, and this proven track record led to their involvement in a phase II study looking at subcutaneous bortezomib, lenalidomide and dexamethasone (RsqVD) in the treatment of patients with newly diagnosed multiple myeloma, in collaboration with Dr Paul Richardson from Dana Farber Cancer Institute in the US. He noted that funding was secured and approval granted quite smoothly by the HPRA, and was even faster than the US by six months.

Ultimately, some 42 patients in Ireland at eight sites took part over 15 months. The Irish trial was presented at ASH by poster in 2016 but a joint manuscript on the results from the Irish and US trials has been prepared and is currently being reviewed for publication. Budget on the Irish side was lower than that of the US, coming close to [redacted] and he noted that the drug was provided free of charge by the companies.

The professor explained that building on the collaboration with Dana Farber for the RsqVD trial, they are now in the process of setting up another parallel ILT, which will investigate treatment of newly diagnosed multiple myeloma patients with isatuximab (a CD38 monoclonal antibody) in addition to the RsqVD regimen.

This trial will be funded by Sanofi and will open later this year at six Irish sites and two Danish sites. Prof O'Gorman emphasised that the experience of CTI in establishing this has been "invaluable" and they were a "strong third partner" in the previous collaboration. CTI can effectively take on the clinical sponsor role for ILTs, bringing the necessary experience and professionalism to an international forum, he said. The professor also highlighted the primary challenge he has encountered, which is the time for review and approval of ILT funding and contract finalisation, noting this can take a number of years. His recommendation is that once the initial proposal is accepted for funding that there is engagement with the funder on the proposed timeline for budget review/approval and contract execution; this will assist with overall trial planning, as these timelines can vary significantly between funders.

In response to a question from the chair, Prof O'Gorman noted that the pandemic has eliminated opportunities to "get in a room" with international colleagues at congress etc. Ruth Barrington queried whether Ireland is at the stage that we could consider ILT Phase I trials, and what needs to be in place to ensure their successful execution? Prof O'Gorman agreed that Phase II trials are "the gateway" to Phase I trials, but he noted that not every institution has the appetite to take these on - he has found it a "battle" to break down institutional barriers. Dedicated protected time will be needed for individuals involved in Phase I trials and a dedicated Phase I unit would need to be established.

CTI can effectively take on the clinical sponsor role for ILTs, bringing the necessary experience and professionalism to an international forum

- Prof Peter O'Gorman, Mater Hospital

BREAKOUT GROUP: Collaborative Groups - Dr Paula Calvert

Consultant oncologist at UHW, Dr Paula Calvert outlined the details of the unprecedented CTI Gynae DSSG collaboration with European Network for Gynaecological Oncological Trial groups (ENGOT). Collaboration is how progress will be made across the spectrum of cancer treatments, and this is particularly important in gynaecological cancers, given that they tend to be less common, she noted. "If we were to do gynae cancer trials alone on the island of Ireland, we just wouldn't have sufficient numbers of patients to make any headway therefore it is important for us to collaborate nationally and internationally."

ENGOT was founded in 2007, and CTI (then ICORG) joined as a member in 2008. A network of national and regional cooperative groups, ENGOT coordinates and promotes clinical trials within Europe for patients with gynaecological cancer. The ultimate goal of ENGOT is to bring the best treatment to gynaecological cancer patients through the best science, enabling every patient in every European country to access a clinical trial, and this fits very well with the mission of CTI, Dr Calvert said. A patient-focused organisation, its focus on phase III trials has been broadened to incorporate rare tumours and early disease.

There is also a desire to focus more on unmet medical needs, and patient reported outcomes, and this latter work is something that CTI could be making a bigger contribution to, she noted. CTI has brought its organisational experience of collaboration in other disease sites to ENGOT and they have been able to participate in a range of different clinical trials over the years, including ovarian and endometrial cancer studies, with cervical cancer studies now imminent. This has been a successful collaboration and has brought clinical trials of gynaecological cancers to patients in Ireland but CTI should now seek to enhance its participation in surgical / radiation studies, as well as translational studies. Education and training should also be a key focus going forward, as should CTI-led studies. This collaboration should serve as a model for other DSSG collaborations in the future, concluded Dr Calvert.

Dr Dearbhaile Collins (CUH) noted the existence of a complementary group, the Gynaecological Cancer InterGroup (GCIG), the "big sister" of ENGOT, which is truly international. Ireland has also benefited from that collaboration, despite having to self-fund participation in trials. Following a suggestion from an audience member that Ireland should seek to lead an ENGOT trial, Dr Calvert wholeheartedly agreed but noted funding is always the issue and this has scuppered efforts in the past. "Ireland has the people to put together an appropriate study and ENGOT would be the mechanism to bring that to a wider audience - we could and should be the lead group."

Dr Collins highlighted the "huge value" of being a member of CTI when entering into international collaboration and Dr Calvert agreed saying participation would not be possible without the national network that is CTI. Ms Mulroe noted that the funding necessary to lead a trial can come from industry, and Dr Calvert agreed, saying this may be a means by which CTI could lead a clinical trial. When asked if lobbying industry will be required, both doctors agreed, saying regular contact with pharmaceutical industry partners is necessary as both parties wish to bring new treatments through the trials process and make them available to patients.

ACollaboration is how progress will be made across the spectrum of cancer treatments, and this is particularly important in gynaecological cancers, given that they tend to be less common

- Dr Paula Calvert, University Hospital Waterford

BREAKOUT GROUP: Sponsorship - Roles & Obligations of Academic Sponsors - Lorcan Gregorian, HPRA

Gregorian began by noting the challenges that anyone involved in conducting or participating in clinical trials has faced over the past year. He noted the clear distinction between the role of the investigator and the role of the sponsor. There are various legal obligations when it comes to being a trial sponsor, and this extends to any third parties where the sponsors have governance, as well as the investigator sites. It is a "complex and broad-ranging role" so a robust infrastructure is necessary to ensure compliance with these regulations.

He added that legislation does not differentiate between academic clinical trial sponsors and commercial clinical trial sponsors. Gregorian touched on the road regulatory framework that sponsors must operate within, including national and international guidelines they must be aware of. The role of the sponsor is thus to translate those legal obligations into tangible systems and processes; by assuring compliance with the various regulations, the trial should produce credible data and it should ensure that participants are protected at all times.

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- Lorcan Gregorian, HPRA

The sponsor will plan, conduct, and close out a clinical trial, Gregorian explained; "It is an extensive and complex role - it is not something that should be entered into lightly." The introduction of Clinical Trial Regulation (EU) 536/2014, due to come into force in January 2022, will mean various changes for sponsor role and obligations, he noted. In conclusion, he highlighted the various resources made available by the HPRA for compliance and inspections, as well as authorisations and assessment.

With these new regulations coming into play, there is talk of streamlining processes and Gregorian was asked whether he believed this would be possible, given the differences in approach, even between hospitals. He agreed that significant differences exist between sites and said he believed the new clinical trials regulation will help with this as there will be a single submission; the goal is for member states to work together and align much more closely than they have previously. "The regulation will force countries to come together."

Emma O'Reilly of the HPRA said the regulators also find the concept of a joint assessment challenging, and have been involved in significant preparatory work. Lisa Tucker of CTI also emphasised the "frustrating" challenges in awaiting a country's submission and how this has delayed or even prevented trials from taking place in Ireland. She highlighted her concerns that as things evolve from a regulatory standpoint, the layers of complexity develop even further such as timelines and excessive paperwork, and asked Gregorian if this differed significantly from commercially-led trials. He noted that resources are generally the main differentiator at the end of the day and admitted that HPRA will apply and interpret the rules slightly differently when it comes to academic vs commercial clinical trials; "we wouldn't expect the same systems and processes to be in place as there would be for a commercial trial."

BREAKOUT GROUP: Patient involvement - Judy Needham, Patient Chair, Canadian Clinical Trials Group & wider discussion

Needham delivered an overview of PE by their organisation. Having been asked by CCTG to attend their committee meeting back in 2012, she explained how this invitation, although welcome, did not involve any meaningful participation or engagement. Having communicated her feedback to the Group, a gap analysis in relation to patient participation was carried out and the steps identified needed to bridge those gaps, "to step up the engagement from 'inform' to 'involve'".

The processes, tools and training materials that aligned the Patient Representative role with contributing to achieving CCTG's strategic objectives were then developed. Patient representatives could now participate in meaningful discussions regarding the trials within their disease site committees, at all meetings of these committees throughout the year. Needham also noted that patient reps are "purposefully recruited" to ensure a representative pan-Canadian distribution. Moving to "product-centric" was the most meaningful step for the patient representatives - they are now meaningfully engaged at the appropriate touchpoints throughout the clinical trial life cycle in the development and execution of trials, from ideation to closure.

Needham noted that the views of patient representatives are given the same priority as those of the other members of the committees. The need for patient endpoints was also highlighted with Needham saying that this is where the true value of patient expertise is seen. CCTG trial activity and accrual is now the highest in over a decade, an achievement she says patients contributed directly to.

"In addition to informing practice, patient-centred endpoints inform patients by providing outcomes that are important to them and their quality of life, thereby motivating enrollment and retention." With increasing emphasis on patient engagement from industry, a 50% increase in funding has also been seen.

The ensuing discussion was a lively one as the panel discussed the type of training and preparation required by patients fulfilling these important roles on the PCC and other similar bodies. CTI patient representative Mr Kivlehan said there is no need to involve PCC members in the science but they should be helped to understand the trials process, as well as broad-based training around their specific role, perhaps including media training. There must be a clear understanding and definition of what exactly the patient role is on not only the patient side but the researcher side. This should be done at the earliest stages so that patients are not thrown in the deep end and feel "overwhelmed", Mr Kivlehan added.

Prof O'Reilly agreed that researchers need to be educated on the patient role, as they can find it "intimidating" but the proof and logic is there for how productive the patient representative committee can be. He noted that it was the first meeting he was at where a patient advocate had given such a "powerful" presentation and suggested that the clip should be shown to SpRs in their cancer centres to impress upon the importance of that symbiosis.

Siobhan Gaynor, a former researcher who is now a patient and a member of the PCC, said there has been a lot of cynicism around patient involvement in clinical trials, and presentations such as Ms Needham's help people understand the value of it better. Patients are not "one-size fits all" and different patients will bring different things to the table. "The world is their oyster" as there are very few demonstrations of excellence in this area so this presents an opportunity.

Mr Kivlehan added that there is a "lot of energy" around the PCC programme at the moment, and there are many plans afoot. It was noted during the discussion that the Irish Cancer Society has a longstanding training programme for patients and carers wishing to get involved in research. Ms Gaynor reiterated that it is about establishing what the patient's needs are, and there are many international templates for what the research priorities are for patients; Mr Kivlehan agreed that he believed patient involvement should be kept at the strategic level and not at the operational level.

Prof O'Reilly took this point but noted that patients can help to attract certain trials to Ireland, particularly smaller niche trials in rare cancers. Appropriate training would allow any patient to sit on any DSSG, and it should be about wider involvement, noted Mr Kivlehan. Ms Marron concluded by saying that it is clear there is a real appetite for more information about patient involvement at all stages of the clinical trials process and this will be a major focus going forward.

Streamlining processes: The logistics of cancer trials

SESSION 3

This plenary session was chaired by Prof Ray McDermott and featured Prof Seamus O'Reilly, Lisa Tucker (Head of Clinical Operations, Cancer Trials Ireland) and Jacinta Marron (Head of Biometrics, Cancer Trials Ireland)

When people talk about clinical trials, they think of Kaplan-Meier curves and the end result, but Prof O'Reilly pointed out that the patient journey throughout must also be considered. A recent paper looked at the trajectory of a patient's illness and the various issues they experienced along the way and the attempt was made to look at a trial from the CTI perspective and the various speed bumps they could encounter such as Covid, funding issues, regulatory problems, etc, while outlining how many hours were put into each study. The goal is to identify processes that could be put in place to help avoid or solve these roadblocks.

The life cycle of a sample investigator-led trial was outlined by Jacinta Marron, and she described the intensive timelines and resources required in an operational sense from CTI. This particular trial, a Phase 1b study, involved almost all departments in CTI, from ethics and regulatory coordination to pharmacovigilance, quality, data management and statistical programming. The study had a protocol amendment in a bid to improve accrual, pushing the accrual time out from the expected nine months to 13 months, and the amendment can be quite labour and admin-intensive, noted Marron. A successful study, it did end up publishing some abstracts, posters etc, and while that is positive, it would be helpful to know the publication plan early on in terms of planning and allocating resources, she said.

Approximately 60% of the time spent on the study happened after the final patient had been accrued, something that is perhaps not widely understood, said Ms Marron. The Covid-19 pandemic also had an impact on this particular trial, necessitating a delay in some patients receiving their final treatments and a move to remote monitoring. While this is simply an example, it does offer a realistic timeline of a typical study for CTI and Ms Marron noted that they learned valuable lessons in terms of being agile and adaptable to the changing situation.

Lisa Tucker then outlined some examples of collaborative studies, including one that took place during the pandemic. The CTI role was limited to purely clinical operations and looking after the ethics and regulatory components. What was envisaged was a total of 3,000 hours over the entirety of the trial; this has already been spent, despite accrual still ongoing. Brexit required extra hours and although the pandemic halted accrual for a while, this did not reduce the number of hours spent.

Jacinta Marron, Head of Biometrics, Cancer Trials Ireland

A UK-based sponsor meant that CTI also were forced to fulfil the role of local sponsor. A more typical collaborative trial was also outlined, which CTI spent more than 10,000 hours working on. While these types of studies are less intensive than in-house studies, they are nevertheless strongly impacted by a lack of resources. A lack of CRAs can mean a backlog of work, Ms Tucker noted. Closing out a trial involves a huge spike in work, she added.

Prof O'Reilly then described some of the published efforts to streamline and improve the momentum of clinical trials. He also set out many of the challenges that Covid-19 has brought about, saying many of these will persist; for example, some trials do not allow for remote patient monitoring and necessitate physical visits. Remote monitoring also brings its own challenges. "FISH" plots, assessing different risks and issues, have been used with success, in one case reducing the duration of a trial by 50%.

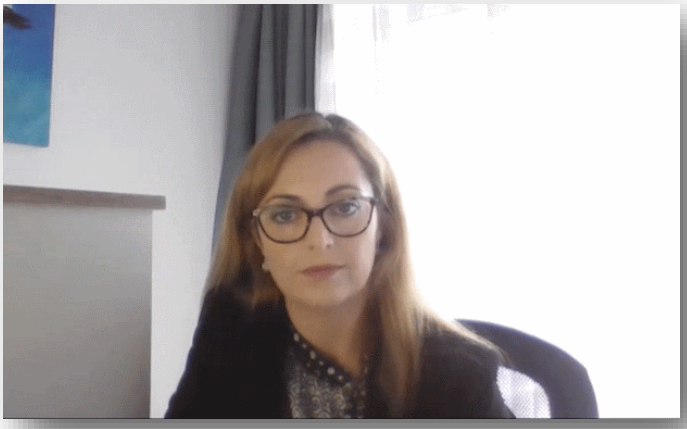
Meanwhile, Canadian research into physician-perceived barriers to clinical trials highlighted the amount of paperwork necessary, although Prof O'Reilly acknowledged that CTI does a large amount of the paperwork that clinicians would otherwise be obliged to do. Trial logistics during the pandemic have also been explored, with decentralised clinical trials and remote monitoring, as well as centralised approval and accelerated ethics, key aspects. Virtual conferences will also remain due to their convenience and inclusivity, although the professor sees a hybrid model evolving.

A discussion ensued on the impact of the pandemic on various research sites. Prof O'Reilly spoke of the shortage of

nurses as they were seconded elsewhere, also the reluctance to place patients on cytotoxic therapies with concern around Covid-19. Lisa Tucker explained that CTI came under pressure as the "uncertainty bled through the trial structure" and she said they received an avalanche of requests and queries.

Internally, the uncertainty was difficult as planning was almost impossible as the restrictions continued to chop and change. CTI worked closely with the HPRA on their guidance to ensure clinical trials could continue but protocol amendments are still ongoing. Remote monitoring remains problematic in practice and the burden on sites is still significant; while it is perceived as timesaving, in reality this is not the case. Jacinta Marron agreed, saying they are working the same hours but doing slightly different work so the day-to-day work builds up in the background. Prof McDermott noted that one of the major challenges during the pandemic was the failure of ethics committees to meet or meeting infrequently, with protocols then being pushed back. He said all cancer researchers will welcome the advent of the NREC for that reason. The NREC process will be good for Ireland as a whole and will sell Ireland as a destination for research, which will benefit CTI, he added.

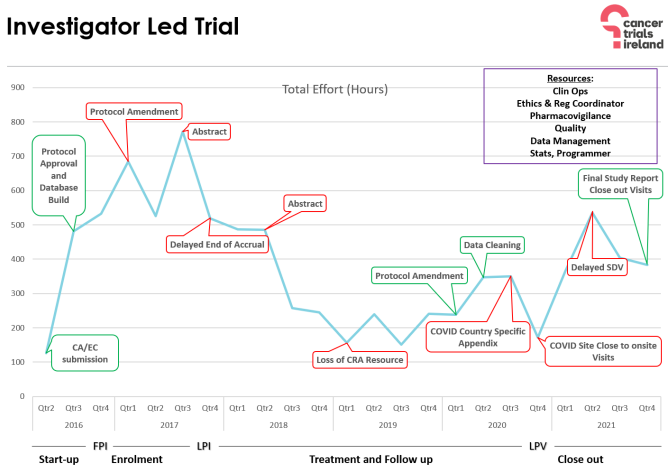
A question from a viewer asked if trials will be more patient-friendly and pragmatic post Covid? Prof McDermott noted that all trials have accommodated vaccinated patients, which is just one example of how trials were adapting. This will be necessary in the medium to long-term, as we learn to live with Covid. Ms Mulroe also raised the prospect of the competitive job market as industry trials are on the rise meaning it is increasingly difficult to recruit and retain staff. All agreed that the clinical trials arena is booming - the hope is that there will be sufficiently qualified people keen to be trained in this area.

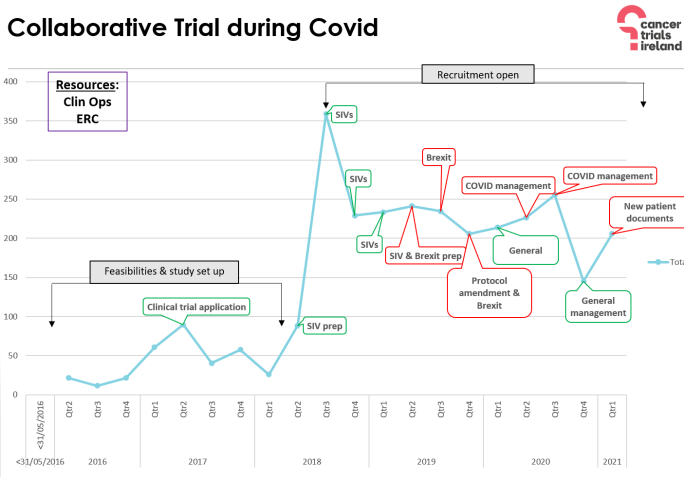


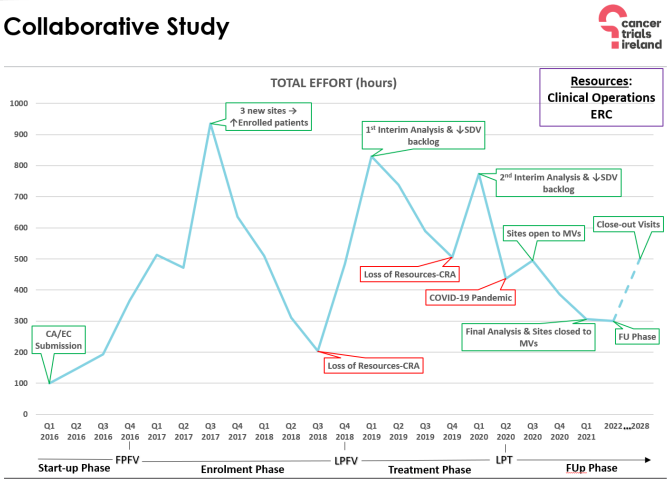
Lisa Tucker Head of Clinical Operations, Cancer Trials Ireland

Approximately 60% of the time spent on this study happened after the final patient had been accrued, something that is perhaps not widely understood

- Jacinta Marron, Cancer Trials Ireland







BREAKOUT GROUP: What defines a trial's complexity and suitability for the community - Dr Jarushka Naidoo & Lisa Tucker

Dr Naidoo, a consultant medical oncologist at Beaumont/RCSI, outlined the work involved in organising the different types of trials. For cooperative group trials there are a number of steps and skills that are required in order to bring them to a network such as Cancer Trials Ireland. These include identifying a relevant patient population by asking what patients do we see commonly, and how a trial can do better. Forming collaborations with cooperative groups is key, said Dr Naidoo; "It is important as a clinical trialist to leverage these networks, or those of others." She also advocated for emailing or even tweeting researchers directly and opening a possible collaboration in that way.

A very different scenario ensues with an investigator-initiated trial. Usually, a trial proposal is developed and then refined with a mentor or research group, with a large amount of work going into conceptualising the study idea, identifying the study population and creating a statistical plan for how many patients will be required. They must seek funding from a source such as pharma, a cooperative group or CTI, and then develop the protocol. The actual work of running the trial, which is often not smooth, she noted.

Dr Naidoo also briefly outlined the CTI trials approval process, explaining that any study proposal is discussed at the relevant DSSG meeting, where its feasibility, its quality and its place in the wider trials portfolio is teased out. The proposal is then sent for international peer review, a process that takes 3-6 weeks, and the goal is to verify whether the proposal is scientifically sound. If approved, budget, feasibility and funding opportunities are then determined before it goes to the CTI Scientific Management Group to see if there is sufficient funding and resources.

More complex studies are more challenging to develop and accrue, but it depends on a balance of these factors as to whether a study will progress or not, Dr Naidoo explained. These include the study population (e.g. rare disease, high clinical needs), study design, type of study (e.g. adaptive designs or basket study, and study logistics. In terms of priorities and challenges, a high priority study is one that serves the population we see, addresses a clinically relevant question, and develops the interest and expertise of investigators. Barriers to success include an evolving funding model, optimal resource availability of CTI staff, and, as echoed throughout the Retreat, a lack of dedicated time for investigators.

Dr Naidoo noted that some institutions utilise an interventional clinical trials "score sheet", by which they prioritise potential studies, scoring studies on whether they will accrue well, garner academic credit, support innovation in the field and "move the needle" in terms of its clinical impact.

Lisa Tucker noted that a complex trial can be defined in multiple ways; for example, even a relatively straightforward trial may be considered complex if the burden on the patient is too onerous in terms of blood samples, biopsies, number of site visits, etc. This can negatively impact recruitment and retention of participants and CTI has had experience of this in the past. The burden on nursing staff and pharmacists can also be detrimental.

Dr Naidoo accepted that complexity may mean different things for different centres, and suggested factors such as staff availability and coordination should also be considered when selecting suitable sites for trials. Ms Tucker agreed, saying the feasibility process must be broader. The goal is to have studies that are rich in correlative science and translational work, because "that's where the gold is - that's where the discovery comes from", whereas simple studies will not necessarily help the cause of cancer research. "It's about achieving the balance between something that is over-burdensome and something that is intense but acceptable."

A patient champion who can build momentum among their peers might help, Ms Tucker said. She also suggested the international model where all patients are moved into a single follow-up protocol after the conclusion of a trial, and can self-report thereafter; CTI will trial this for one of their trials soon. Patient input into what level of complexity or burden would be appropriate is thus necessary, Dr Naidoo said. A comment from an attendee was highlighted, that sites should look into taking bloods that allow for delayed processing, an idea Dr Naidoo was very receptive to.

The question of what is an ideal trial for CTI was also discussed. Ms Tucker explained the trials that work well involve a main sponsor and a collaborative group similar to CTI, with both parties well-funded and resourced. The key issue is access to the drug from Europe instead of the US; Dr Naidoo agreed, saying this is hugely complicated as 99% of oncologists are US-trained and that is where their connections are. She added that she has tried to use her US connections to build new European connections. Irish offices of pharmaceutical companies tend to be quite siloed and while support is forthcoming where possible, often they are unaware that the trial is even taking place or cannot ensure delivery of the necessary drug.

BREAKOUT GROUP: National systems to support Clinical Trials: Clinical Trials Regulation, HRB clusters, National Ethics Review, Shared Investigator Platforms, National Data Entry Systems - Eibhlín Mulroe, Prof Ray McDermott

Eibhlín Mulroe outlined the four main objectives of CTI: to grow a diverse portfolio of cancer trials available to patients in Ireland; provide governance and support for multicentre and HRB cluster-led clinical trials; develop an open and accessible National Cancer Clinical Trials network; and embed public/patient engagement in all National Cancer Clinical Trials Network operations. CTI is an office staffed by 50 highly-experienced people (45 FTEs), 13 of which are covered by a HRB grant.

The remainder is covered by funding they receive from elsewhere, such as industry and other collaborative groups. A new development is the designation of RCSI as their host institution, which means they are now responsible for oversight and governance of the HRB grant. CTI, however, remains responsible for the remainder of their funding. They also work closely with CRCI and the Irish Cancer Society, and are building a relationship with the Trial Methodology Research Network (TMRN). The HRB clusters are also a huge support for CTI, she added.

Ms Mulroe also outlined the new governance structure for CTI, whereby the various committees report into the Board of Directors. The relationship with the HPRA is critical, whether for investigator-led trials, collaborative studies or industry-led trials, in ensuring CTI meets its regulatory obligations as a trial sponsor or as a coordinating centre for a trial sponsored elsewhere, she added. The forthcoming Clinical Trials Regulations means there are changes coming.

The success of the tBRCA study was noted by a viewer; Prof McDermott said this was due to the unmet need in ovarian cancer and its timeliness given the therapeutic implications for patients in the era of PARP inhibitors. A similar study in prostate cancer and even pancreatic cancer would be desirable, and he said CTI could work more closely with the NCCP to roll out a model for genetic testing on a wider basis. “This is something that could be done and will have to be done - there is a problem there and we can help solve it.”

Ms Mulroe noted that the funding of a biobank and biobank activities will not be covered under the HRB grant and in this context the development of the All-Ireland cancer institute (of which she is a member of the steering group will be extremely important. Prof McDermott noted that the mechanisms for funding translational research, which do not alter clinical practice based on the findings, are no longer available under the new HRB structure. Ms Mulroe noted the contribution of private funders, such as Pat Smullen’s fund.

Sandra Bright of HPRA then discussed the forthcoming Clinical Trials Regulation 536/2014. The regulation of clinical trials will undergo “significant change” with the introduction of the CTR, said Bright, who noted that this will be positive; it will serve to simplify and streamline the process for sponsors when making a clinical trial application, particularly so for multinational clinical trials. This means quicker approval times and the rapid accrual of patients into these trials.

The scheduled date for the introduction of the regulation is January 31 2022 but there will first be a three-year transition period. For the first year, new clinical trial applications can be submitted under either legislation but after that it must be under the new regulation, while ongoing trials can continue under the old Directive but will eventually transition by the end of the three-year timeframe. Bright noted the HPRA and the National Office for Research Ethics Committees meet regularly to ensure that both organisations are ready to deliver a single national decision on clinical trials going forward, and they have also worked with CTI on pilot applications as they get ready. “It’s a very exciting time for clinical research.”

Ms Mulroe expressed her delight at CTI’s inclusion in the pilot study applications and how this might mean a smoother transition as the regulation is introduced; she also said that speedier trial approval timelines would help protect Ireland’s reputation internationally. Also discussed was CTI’s significant investment in data management in recent years and the large team now working at CTI that enable trials using the MediData platform.

BREAKOUT GROUP: Challenges in accrual and trial management at sites and streamlining processes. How can CTI help or partner? Prof Seamus O'Reilly

Dr Connolly acknowledged that there are many stages to getting started and running a study and there can be "road blocks" along the way; these can be national at the ethics or HPRA level, or with industry, or with CTI. Clarity on an appropriate activation timeline for a trial should be provided where possible, and that should be reduced wherever possible as often by the time it is ready to open, there may be just three months of accrual time left nationally meaning all that work can result in just a couple of patients being recruited. "We know Ireland can do well with these studies and some of these factors can be beyond our control but showing the community outside Ireland how well we can do things and how quickly, this generates revenue, gives us a high profile and will ultimately attract more studies over time," she said.

The new HRB Cluster mechanism offers everyone an opportunity to look at their own processes and CTI to also explore theirs, so that barriers can be identified and overcome. Verena Murphy noted the major roadblocks in recent years have been identified; these were mainly related to ethics but the introduction of GDPR also caused many difficulties. Educating sites and involving staff will avoid continuity issues, while it is hoped that the National Research Ethics Committees will avoid many of the problems with ethics and delays on that side.

A question from Seamus Cotter asked if the number of hours worked have a direct impact on the accrual rate and how. Jacinta Marron noted that this is hard to correlate but it may be a question of where they best focus their resources and perhaps focusing on a smaller number of sites. Ms Murphy added that there is only so much CTI can do in order to help the process along and speed up the timelines - they and the individual sites must work together to improve this.

Prof O'Reilly noted that one area that could be easily sped up is that of contracts; as each hospital has an individual contract, this could and should become centralised. He also told attendees that an accountant has been appointed to the clinical trial team in CUH to oversee the financial management of the trials and how this could be improved. Ms Murphy commented that it has already been discussed that PIs should be kept better informed of what trials are open where, which might encourage a more active referral system. Integrating trials discussions into the multidisciplinary team meetings is probably the most effective way of doing this, he added, given that this is where decisions on care are made.

A question was asked relating to equity and improving the accrual of patients who might be treated at peripheral sites; equity is probably the most topical issue in cancer care at the money, Prof O'Reilly noted. Digital adaptation will be key, with more remote site access and he added reducing the burden of travel for patients and their families would be hugely significant. The increased adoption of telemedicine during Covid pandemic may well accelerate the adoption of this.

Prof Connolly said that increasing patient awareness is key but also suggested the targeted screening of patients at these sites; although it can be more challenging, it should be an option moving forward. "We need to think outside the box because we need to do much better and ensure that patients at the peripheries do get a chance to access trials if they so wish."

"Showing the community outside Ireland how well we can do things and how quickly, this generates revenue, gives us a high profile and will ultimately attract more studies over time

- Prof Roisin Connolly, UCC

BREAKOUT GROUP: Current communication about Clinical Trials: Feasibilities; coordinating sites (communication), Cancer Trials Ireland, & HRB - and ways to streamline. Prof Joe Eustace, Director, National Clinical Trials Office & Ashley Bazin, Team Leader, TUH

Prof Eustace outlined how one of the historical limitations of the Irish clinical research environment was that there was no single point of contact for external entities who wished to engage in research in Ireland or which could help facilitate interactions internationally, as distinct from those based in local university research groups. The deficit was partly addressed by the HRB in 2015 with the establishment of Clinical Research Coordination Ireland (CRCI); however the establishment of this as part of a private company for independence purposes became quite an expensive endeavour and made it fundamentally unsustainable.

The decision was taken this year by the HRB to establish a new grant as part of an entity called the National Clinical Trials Office, which is now hosted in University College Cork. As a successor to CRCI it has taken over many of the responsibilities of CRCI, one of which is the study feasibility work. The CRCI National Feasibility Service provided a single point of contact for commercial or academic trial feasibility requests and facilitates a rapid national feasibility response (turnaround time of two weeks) with a view to supporting rapid study start-up.

Various types of feasibility requests were processed; from key opinion leader feedback on protocol development, to CROs bidding for business, to investigator identification. Prof Eustace noted that studies had a 15% success rate of progression, a similar rate to what is seen with similar bodies internationally. In 2019 a service level agreement was signed with CTI that saw the CRCI Feasibility Service include oncology trials as part of its brief. Since then it has processed a total of 68 trials and is viewed as having been relatively successful.

Prof Eustace noted the transition from CRCI to the NCTO is still underway, and it will be some weeks before the new public body is fully operational, during which updated CDAs will be agreed with sponsors and CTI. At that point, the goal is to get improved feedback from the sponsors - this can be difficult for various reasons, but the professor pointed out that, as a free service, it is imperative that there is enhanced feedback from the sponsors and CROs. The other goal of the service was to improve trial set-up times - issues such as regulatory, ethics, contractual, and data protection are all being addressed to some extent, he said.

> **...The goal is to get improved feedback from the sponsors - this can be difficult for various reasons, but as a free service, it is imperative that there is enhanced feedback from the sponsors and CROs**
>
> - Prof Joe Eustace, National Clinical Trials Office

During the discussion, the professor confirmed that feedback is sought from DSSGs for all cancer trial feasibility queries. It was also noted that there can be duplication with pharmaceutical companies going directly to CTI as well as using the feasibility service; Prof Eustace agreed it could be useful to track this going forward. When asked if it would be possible for sites to be informed if they are not successful with feasibility, he noted this is a “real bugbear” and said there needs to be more pushback on companies regarding this. A timeline for feedback should also be imposed, he added.

There was also a question on whether CTI can lobby industry on the need for a more even geographic spread of referrals, as currently it is quite Dublin-centric; while the professor said he had not come across this as an issue, he believed that organisations may be choosing the sites based on what suits their demands and he advocated for raising the profile of what is possible at other, regional sites.

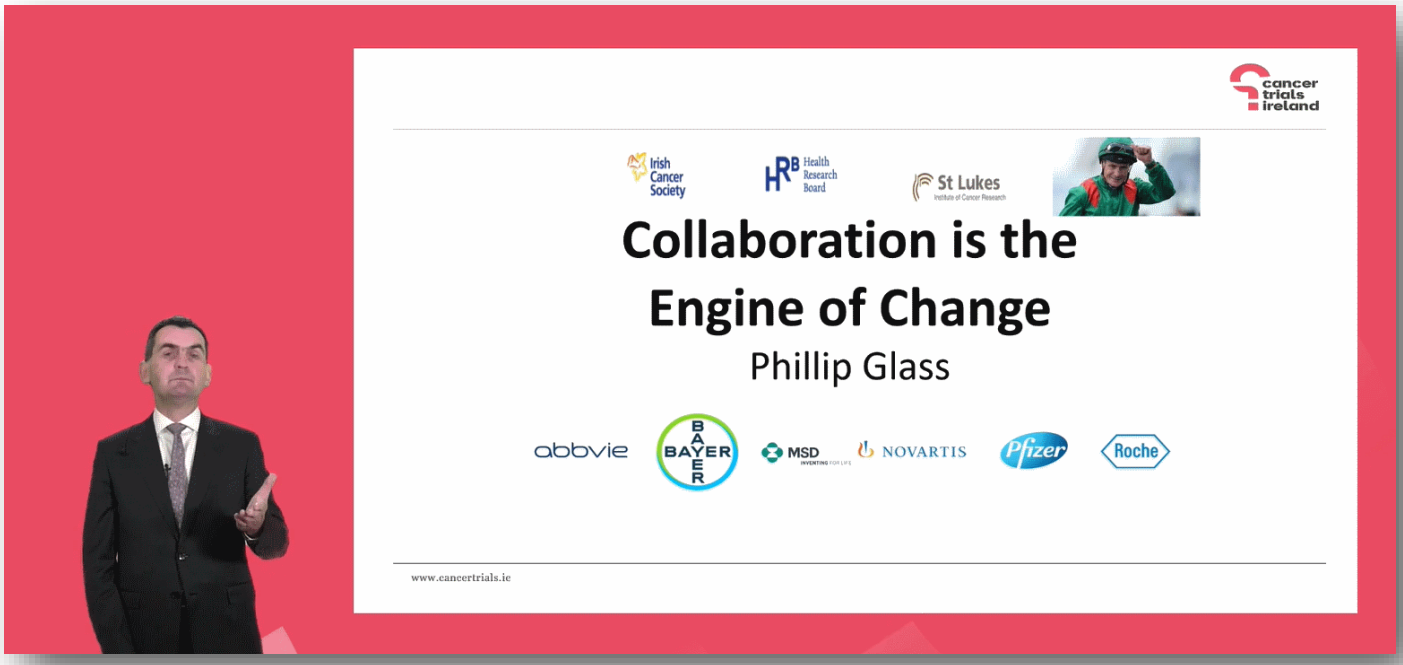
Ashley Bazin suggested that the feasibility decision should be submitted as a word document as it is a working document that must be shared with multiple sites etc., and Prof Eustace agreed that they can lobby for this.

CONCLUSIONS

- Ireland's cancer clinical trials ecosystem enjoys many advantages but there are stumbling blocks as we try to proceed to the next level. With ambitious targets such as the accrual of 6% of all patients into a clinical trial, there are steps that must be taken by all stakeholders working to achieve this goal. The altered HRB "clusters" funding model has focused the mind and forced a re-think of how clinical trials operate in Ireland.
- The perennial issues of time and resources notwithstanding, clinical research must be properly embedded into cancer care and not treated as an afterthought. Clear and defined career pathways and training for clinicians in all disciplines must be considered a priority; while protected research time for clinicians is needed, this is just one part of the puzzle. New developments such as the renewed MoU between North and South and the US National Cancer Institute are hugely positive and will help with the integration of basic, translational, and clinical research.
- A key recurring theme throughout the meeting was that of collaboration - national and international collaboration will help Ireland in attracting more clinical trials to Ireland for the ultimate benefit of patients. Meanwhile, the forthcoming Clinical Trials Regulation and establishment of the National Research Ethics Committees should help to truncate unwieldy timelines and rapidly progress clinical trials.

The target of placing 6% of newly diagnosed cancer patients on a clinical trial is an ambitious one - it is currently at 2% - but HRB core funding support will help make it a reality

- Eibhlin Mulroe, Cancer Trials Ireland



Prof Seamus O'Reilly summing up at the conclusion of the Retreat.

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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The Cancer Retreat was also supported by the Irish Cancer Society.

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